

**Priority Existing Chemical
Assessment Report No. 30**



Australian Government
Department of Health and Ageing
NICNAS

Triclosan

January 2009

© Commonwealth of Australia 2009

ISBN 0-9803124-4-2

This work is copyright. Apart from any use as permitted under the Copyright Act 1968, no part may be reproduced by any process without prior written permission from the Commonwealth. Requests and inquiries concerning reproduction and rights should be addressed to the Commonwealth Copyright Administration, Attorney General's Department, Robert Garran Offices, National Circuit, Canberra ACT 2600 or posted at <http://www.ag.gov.au/cca>

Preface

This assessment was carried out under the National Industrial Chemicals Notification and Assessment Scheme (NICNAS). This Scheme was established by the *Industrial Chemicals (Notification and Assessment) Act 1989* (Cwlth) (the Act), which came into operation on 17 July 1990.

The principal aim of NICNAS is to aid in the protection of people at work, the public and the environment from the harmful effects of industrial chemicals.

NICNAS assessments are carried out in conjunction with the Australian Government Department of the Environment, Water, Heritage and the Arts, which carries out the environmental assessment for NICNAS.

NICNAS has two major assessment programs: the assessment of human health and safety and environmental effects of new industrial chemicals prior to importation or manufacture; and the other focusing on the assessment of chemicals already in use in Australia, in response to specific concerns about their health/or environmental effects.

There is an established mechanism within NICNAS for prioritising and assessing the many thousands of existing chemicals in use in Australia. Chemicals selected for assessment are referred to as Priority Existing Chemicals.

Chemicals that have been assessed as new or existing chemicals may require a reassessment of the risk of the chemical under the secondary notification provisions of the Act.

This priority existing chemical report has been prepared by the Director of NICNAS, in accordance with the Act. Under the Act, manufacturers and importers of priority existing chemicals are required to apply for assessment. Applicants for assessment are given a draft copy of the report and 28 days to advise the Director of any errors. Following the correction of any errors, the Director provides applicants and other interested parties with a copy of the draft assessment report for consideration. This is a period of public comment lasting for 28 days during which requests for variation of the report may be made. Where variations are requested, the Director's decision concerning each request is made available to each respondent and to other interested parties (for a further period of 28 days). Notices in relation to public comment and decisions made, appear in the *Commonwealth Chemical Gazette*.

In accordance with the Act, publication of this report revokes the declaration of this chemical as a Priority Existing Chemical, therefore, manufacturers and importers wishing to introduce this chemical in the future need not apply for assessment. However, manufacturers and importers need to be aware of their duty to provide any new information to NICNAS, as required under section 64 of the Act.

For the purposes of Section 78(1) of the Act, copies of assessment reports for new and existing chemical assessments are freely available from the web. Hardcopies are available from NICNAS from the following address:

NICNAS

GPO Box 58

Sydney, NSW 2001

AUSTRALIA

Tel: +61 (2) 8577 8800

Fax: +61 (2) 8577 8888

Free call: 1800 638 528

Other information about NICNAS (also available on request and on the NICNAS web site) includes:

- NICNAS Service Charter;
- Information sheets on NICNAS Company Registration;
- Information sheets on the Priority Existing Chemicals and New Chemical assessment programs;
- Safety information sheets on chemicals that have been assessed as Priority Existing Chemicals;
- Details for the NICNAS Handbook for Notifiers; and
- Details for the *Commonwealth Chemical Gazette*.

More information on NICNAS can be found at the NICNAS web site:

<http://www.nicnas.gov.au>

Other information on the management of workplace chemicals can be found at the web site of the Australian Safety and Compensation Council

<http://www.ascc.gov.au>

Contents

OVERVIEW	xiv
RECOMMENDATIONS	xix
SECONDARY NOTIFICATION	xxvi
ACRONYMS AND ABBREVIATIONS	xxvii
1. INTRODUCTION	3
1.1 Declaration	3
1.2 Objectives	3
1.3 Sources of information	3
1.4 Peer review	5
1.5 Report structure	5
2. BACKGROUND	6
2.1 International perspective	6
2.2 Australian perspective	7
2.3 Assessments by other national or international bodies	7
3. IDENTITY, PROPERTIES, ANALYSIS, MANUFACTURE AND USE	9
3.1 Chemical identity	9
3.2 Impurities and additives	10
3.3 Physical and chemical properties	10
3.3.1 Physical state	10
3.3.2 Physical properties	11
3.3.3 Chemical properties	11
3.4 Methods of detection and analysis	12
3.5 Manufacture, importation and use	12
3.5.1 Manufacture and importation	12
3.5.2 Uses in Australia	13
3.5.3 Industrial uses	13
3.5.4 Non-industrial uses	17
3.5.5 Overseas uses	18
4. HUMAN EXPOSURE	20
4.1 Occupational exposure	20

4.2	Public exposure	21
4.2.1	Adults	21
4.2.2	Children	22
5.	ENVIRONMENTAL EXPOSURE	24
5.1	Environmental fate	24
5.2	Environmental release	24
5.2.1	Aqueous environment	24
5.2.2	Terrestrial environment	25
6.	HUMAN HEALTH HAZARD ASSESSMENT	27
6.1	Kinetics and metabolism	27
6.1.1	Oral and dermal route	27
6.2	Effects on laboratory animals	29
6.2.1	Acute toxicity	29
6.2.2	Irritation	29
6.2.3	Sensitisation	29
6.2.4	Repeat dose toxicity	29
6.2.5	Genotoxicity – in vitro	30
6.2.6	Genotoxicity – in vivo	30
6.2.7	Carcinogenicity	30
6.2.8	Fertility	31
6.2.9	Developmental toxicity	31
6.2.10	Antimicrobial resistance	31
6.3	Effects on human health	32
6.3.1	Skin irritation	32
6.3.2	Sensitisation	33
6.3.3	Repeat dose toxicity	33
6.4	Regulatory classifications for workplace based hazards	33
6.4.1	Physicochemical hazards	33
6.4.2	Occupational health hazards	33
6.5	Classification and labelling for public health hazards	34
7.	ENVIRONMENTAL HAZARD ASSESSMENT	35
7.1	Wildlife	35
7.2	Terrestrial invertebrates	35
7.3	Terrestrial plants	35
7.4	Aquatic organisms	35
7.5	Micro-organisms	36

8.	HUMAN HEALTH RISK CHARACTERISATION	37
8.1	Health risk characterisation methodology	37
8.2	Occupational risk	37
	8.2.1 Occupational exposures	37
	8.2.2 Critical health effects	38
	8.2.3 Risk estimates	38
	8.2.4 Uncertainties in occupational risk estimates	42
	8.2.5 Areas of concern	42
8.3	Public health risk	42
	8.3.1 Public exposure - Adults	42
	8.3.2 Public health risk estimates - Adults	43
	8.3.3 Public exposure - children	47
	8.3.4 Risk estimates - children	47
	8.3.5 Uncertainties in public risk estimates	49
	8.3.6 Areas of concern	50
8.4	Biological monitoring data	50
9.	ENVIRONMENTAL RISK CHARACTERISATION	51
9.1	Environmental release and degradation	51
	9.1.1 Environmental release of triclosan	51
	9.1.2 Wastewater treatment plant systems	51
9.2	Aquatic risk	53
	9.2.1 Predicted No Effect Concentration (PNEC) for triclosan	53
	9.2.2 Risk to freshwater ecosystems	54
	9.2.3 Risk to marine ecosystems	55
	9.2.4 Risk to sediment dwelling organisms	56
9.3	Terrestrial risk	57
	9.3.1 Risk associated with sludge and biosolids from STPs containing triclosan	58
	9.3.2 Risk associated with triclosan containing effluent from STPs for irrigation	59
	9.3.3 Risks to water-associated wildlife	60
9.4	Risk from degradation products	63
9.5	Data gaps	63
9.6	Conclusions	65
10.	CURRENT HUMAN HEALTH RISK MANAGEMENT	67
10.1	Occupational health and safety	67
	10.1.1 Assessment of current control measures	67
	10.1.2 Hazard communication	69

10.1.3	Education and training	73
10.2	Occupational monitoring and regulatory controls	74
10.2.1	Atmospheric monitoring	74
10.2.2	Occupational exposure standards	74
10.2.3	Health surveillance	74
10.2.4	National transportation regulations	74
10.3	Public health regulations	75
11.	CURRENT ENVIRONMENTAL RISK MANAGEMENT	76
11.1	Environmental regulatory controls	76
11.2	Control of major hazard facilities	76
11.3	Aquatic ecosystems management	76
11.4	Disposal and waste treatment	76
11.5	Emergency procedures	77
12.	DISCUSSION AND CONCLUSIONS	80
12.1	Importation and use	80
12.2	Human health hazards and risks	80
12.2.1	Human health hazards	80
12.2.2	Occupational health and safety risks	81
12.2.3	Public health risks	82
12.3	Environmental hazards and risks	84
12.3.1	Environmental hazards	84
12.3.2	Environmental risks from release to the aquatic environment	85
12.3.3	Environmental risks from release to the terrestrial environment	85
12.4	Data gaps	85
13.	METHODS OF ANALYSIS AND DETECTION	91
13.1	Identification	91
13.2	Methods of analysis	91
13.3	Analysis in water	91
13.4	Atmospheric monitoring	91
13.5	Biological monitoring	91
13.6	Other methods of analysis	94
14.	DATA ON OCCUPATIONAL EXPOSURE	95
14.1	Routes of exposure	95
14.2	Methodology for assessing exposure	95
14.3	Major occupational exposure scenarios	96

14.3.1	Import, transport and storage	96
14.3.2	Repacking	97
14.3.3	Formulation of liquid products for cosmetic and domestic use	98
14.3.4	Treatment of textiles	99
14.3.5	Plastics manufacture	102
14.3.6	Use of triclosan-containing end products in the workplace	104
15.	DATA ON PUBLIC EXPOSURE	106
15.1	Sources of exposure to adults	106
15.2	Routes of exposure to adults	106
15.3	Methodology for assessing exposure	106
15.4	Exposure to cosmetic and personal care products	107
15.4.1	Exposure pattern	107
15.4.2	Measured plasma levels of triclosan	109
15.4.3	Estimated exposure data	109
15.5	Exposure to household cleaning products	113
15.5.1	Exposure pattern	113
15.5.2	Estimated exposure data	113
15.6	Exposure to textile and plastic articles	115
15.6.1	Exposure pattern	115
15.6.2	Estimated exposure data	116
15.7	Painted tile and cabinet/cupboard surfaces	117
15.7.1	Exposure pattern	117
15.7.2	Estimated exposure data	117
15.8	Exposure in children	118
15.8.1	Routes and sources of exposure	118
15.9	Indirect exposure via the environment	122
16.	DATA ON ENVIRONMENTAL EXPOSURE	123
16.1	Fate and transformation processes	123
16.1.1	Water solubility and hydrolysis	123
16.1.2	Chlorination	123
16.1.3	Photolysis	126
16.1.4	Adsorption and mobility	133
16.1.5	Biodegradation and methylation	134
16.1.6	Reaction with metals	149
16.1.7	Products from combustion of triclosan and derivatives	150
16.2	Environmental exposure	152

16.2.1	Import and manufacture	152
16.2.2	Uses, releases and disposal	153
16.3	Occurrence in wastewater and the sewerage system	159
16.3.1	Untreated and treated wastewater	159
16.3.2	Sewage sludge and biosolids	181
16.4	Occurrence in the natural environment	186
16.4.1	Surface waters and sediments	187
16.4.2	Bioaccumulation in aquatic biota	200
16.4.3	Soils	211
16.4.4	Bioaccumulation in soil biota and higher organisms	211
16.4.5	Landfill leachate and groundwater	211
16.4.6	Atmosphere	211
16.4.7	Summary of monitoring studies	211
16.5	Predicted environmental concentrations in Australia	213
16.5.1	Untreated wastewater triclosan	213
16.5.2	Treated effluent triclosan	215
16.5.3	Sludge and biosolids from municipal STPs	218
16.5.4	Effluent and sludge from septic and household systems	220
16.5.5	Aquatic environments	221
16.5.6	Landfill	225
16.5.7	Soils	226
16.5.8	Atmosphere	226
16.5.9	Groundwater	227
16.5.10	Wildlife exposure	227
17.	KINETICS AND METABOLISM	230
17.1	Absorption	230
17.1.1	Animal studies	230
17.1.2	Human studies	239
17.1.3	Other data	246
17.2	Distribution	248
17.2.1	Animal studies	248
17.2.2	Human studies	253
17.2.3	Other data	255
17.3	Metabolism	255
17.3.1	Animal studies	255
17.3.2	Human studies	260
17.4	Elimination and excretion	263
17.4.1	Animal studies	263
17.4.2	Human studies	268

18.	EFFECTS ON LABORATORY ANIMALS AND OTHER TEST SYSTEMS	272
18.1	Acute toxicity	272
	18.1.1 Oral	272
	18.1.2 Dermal	273
	18.1.3 Inhalation	273
	18.1.4 Intravenous	273
18.2	Irritation and corrosivity	274
	18.2.1 Skin	274
	18.2.2 Eye	275
18.3	Sensitisation	276
18.4	Repeat dose toxicity	277
	18.4.1 Inhalation	277
	18.4.2 Oral	277
	18.4.3 Dermal	293
18.5	Genotoxicity	296
	18.5.1 In vitro	296
	18.5.2 Studies in Drosophila	298
	18.5.3 In vivo	298
18.6	Carcinogenicity	300
18.7	Fertility	301
18.8	Developmental toxicity	303
18.9	Other data	308
	18.9.1 Antimicrobial resistance – 2002 EU review	308
	18.9.2 Antimicrobial resistance – studies since the 2002 EU review	309
19.	EFFECTS ON HUMAN HEALTH	317
19.1	Skin irritation	317
19.2	Sensitisation	318
	19.2.1 Skin sensitisation	318
	19.2.2 Photo-sensitisation	320
19.3	Repeat dose toxicity	321
20.	REGULATORY CLASSIFICATION BASED ON HAZARD	323
20.1	Occupational	323
	20.1.1 Physicochemical hazards	323
	20.1.2 Health hazards	323
20.2	Public	330
	20.2.1 Scheduling in SUSDP	330

21.	EFFECTS ON ORGANISMS IN THE ENVIRONMENT	332
21.1	Wildlife	332
	21.1.1 Mammals	332
	21.1.2 Birds	332
21.2	Terrestrial invertebrates	334
21.3	Terrestrial plants	335
21.4	Aquatic organisms	338
	21.4.1 Amphibians	338
	21.4.2 Freshwater fish	342
	21.4.3 Freshwater invertebrates	348
	21.4.4 Freshwater algae and cyanobacteria	352
	21.4.5 Methyl-triclosan	362
	21.4.6 Marine organisms	362
	21.4.7 Aquatic ecotoxicity of treated sewage effluent	363
	21.4.8 Sediment dwelling organisms	364
21.5	Micro-organisms	366
	21.5.1 Laboratory cultures	366
	21.5.2 Freshwater microbial populations	367
	21.5.3 Marine micro-organisms	368
	21.5.4 Sewage sludge organisms	368
	21.5.5 Soil micro-organisms	370
	APPENDIX A – Australian Sewerage System	373
	APPENDIX B – Wildlife Exposure Model	379
	APPENDIX C – Occupational Exposure Calculations	390
	APPENDIX D – Consumer Exposure Calculations	398
	APPENDIX E – Determination of Triclosan in the Australian Population by Analysis of Human Breast Milk	409
	APPENDIX E.1 – Ethics Approval Letter	416
	APPENDIX E.2 – Levels of Triclosan in Australian Breast Milk Samples	419
	APPENDIX F – Classification under the Globally Harmonized System of Classification and Labelling of Chemicals and the Stockholm Convention on Persistent Organic Pollutants –	420
	APPENDIX G – Wildlife Risk Quotients	425
	APPENDIX H – BurrliOZ Modelling	428

APPENDIX I – Sample Material Safety Data Sheet for Triclosan	431
APPENDIX J – Material Safety Data Sheet Assessment Summary	438
APPENDIX K – Applicants	439
REFERENCES	445
GLOSSARY	479
INDEX	

Overview

Background

Phenol, 5-chloro-2-(2,4-dichlorophenoxy)-, commonly known as triclosan (CAS No. 3380-34-5), was declared a Priority Existing Chemical for full assessment under the *Industrial Chemicals (Notification and Assessment) Act, 1989* (the Act) by notice in the *Chemical Gazette* of 6 May 2003. Triclosan was declared a Priority Existing Chemical because of environmental concerns. The widespread use of triclosan provides a number of pathways for the chemical to enter the environment, and laboratory tests have shown it to be toxic to aquatic species, with algae being the most sensitive species. The chemical properties of triclosan indicate that it may also bioaccumulate and persist in the environment. In addition, there are reports that suggest incineration of textile products containing triclosan may result in the formation of dioxin-like substances.

Scope

A full risk assessment was conducted on public health, occupational health and safety, and environmental effects of industrial uses of triclosan. Quantities of triclosan in pesticides and veterinary medicines and therapeutic products were collected for this assessment, but no further assessment of these products were conducted as they are not within the scope of the ICNA Act. This assessment considered the quantities of triclosan included in locally manufactured articles and leaching from all articles (locally manufactured or imported), but no information was provided to NICNAS on the amounts of triclosan in imported articles and leaching from articles.

Uses

Triclosan is not manufactured in Australia but is imported into Australia as the raw chemical (>99% (w/w) powder); as a liquid solution (10 - < 20% (w/v)); as plastic pellets; and as an ingredient in various products. Triclosan is included in many consumer products because of its antimicrobial activity. The main use of triclosan in Australia is in the formulation of personal care and cosmetic products, therapeutic products and cleaning agents. Other uses of triclosan are in the treatment of textiles and in plastics manufacture. It is also used in the formulation of some oil-based paints. Additionally, triclosan is imported into Australia as an ingredient in a large number of end products intended for consumer use, including cosmetic and personal care products, therapeutic products, veterinary products, pesticides, household cleaning products, and grouting material. Triclosan is reported to be used in a similar range of products overseas.

This assessment did not take into account the health or environmental effects of triclosan imported as part of finished plastic and textile articles, as no information was provided on the amounts of triclosan in imported articles.

Health effects

In humans, triclosan is rapidly and completely absorbed from the gastrointestinal tract while a lower rate of absorption occurs dermally. It is also rapidly removed from the blood, and extensive first pass metabolism occurs following oral administration. The major metabolic pathways in humans and animals involve glucuronide and sulphate conjugation, and metabolism to these conjugates has also been observed in the skin. In

humans excretion is relatively rapid; the major route of excretion being the urine, while the faeces is of secondary importance. Triclosan has also been observed in human breast milk samples. The human oral and dermal data provide no evidence of a bioaccumulation potential. Additionally, enterohepatic circulation has been demonstrated in rats, while limited evidence is available in mice and hamsters.

Triclosan has low acute oral and dermal toxicity in animals, although there is some evidence of higher acute toxicity via inhalation. A repeat dose inhalation toxicity study indicates triclosan is a respiratory irritant in rats. Both animal and human data indicate it is a skin irritant, and a study in rabbits indicates it is an eye irritant. Data from both humans and animals indicate that triclosan has at most a very weak skin sensitisation potential. No data on respiratory sensitisation are available.

Systemic toxicity was observed following repeated exposure to triclosan in oral and dermal animal studies. No reliable human data are available. Animal data indicate that the liver is the target organ following ingestion of triclosan, with hepatocyte hypertrophy and hepatocyte vacuolisation in cells observed. While the mouse is the most sensitive species, there is evidence that (unlike the rat and hamster) it is sensitive to peroxisome proliferator-type effects in the liver that are not considered relevant to humans. Similar effects on the liver are seen in dermal studies.

A number of in vitro and in vivo genotoxicity studies are available, and, although some positive results were obtained, overall, there is no evidence of an in vivo genotoxic potential. Oral carcinogenicity studies in the rat and hamster provide no evidence of a carcinogenic potential. No effects on fertility were seen in a 2-generation study in the rat, and there was no evidence of teratogenicity in developmental toxicity studies conducted in rats and rabbits.

Triclosan is listed in the Australian Safety & Compensation Council's (ASCC) *List of Designated Hazardous Substances*, contained in the Hazardous Substances Information System (HSIS). Prior to July 2008, triclosan was classified as a hazardous substance in the HSIS with the risk phrase, 'Toxic by inhalation (R23)'. ASCC updated the HSIS in July 2008 to adopt the changes in Europe's 29th Adaptation to Technical Progress (ATP) to Directive 67/548/EEC dated April 2004. With this update in July 2008, triclosan is now listed on the HSIS with the risk phrase, 'Irritating to eyes and skin (R36/38)'. Based on the current NICNAS assessment and according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004), triclosan is classified as 'Toxic by inhalation (R23)' and 'Irritating to eyes, respiratory system and skin (R36/37/38)' (see recommendation 1).

Triclosan is not specifically listed in the Australian Dangerous Goods (ADG) Code. Due to its moderate inhalation toxicity, triclosan raw material (100% powder) would fall under Class 6.1 (Toxic substances), packaging class III (Substances presenting low danger) and UN number 2811 (toxic, solid, organic) (see recommendation 2a).

Occupational exposure and health risks

Workers may be potentially exposed to triclosan by skin and eye contact and inhalation. Oral exposure is not expected in occupational settings. The low vapour pressure of triclosan means inhalation exposure will be low, although there is still potential for inhalation of triclosan powder. The main route of exposure is likely to be dermal route.

No occupational monitoring data for triclosan are available in Australia or reported in the literature. Therefore, the Estimation and Assessment of Substance Exposure (EASE)

model developed by the United Kingdom Health and Safety Executive was used to estimate inhalation and dermal exposure.

It was determined that under normal occupational conditions the risk of workers being exposed to concentrations that would lead to adverse health effects such as skin and eye irritation and chronic effects is low. However, in cases of accidental spills or leaks of triclosan, the risk of skin and eye irritation would increase, especially where personal protective equipment is not used. The risk of inhalation toxicity and respiratory irritation would increase in formulation workers when using triclosan powder without local exhaust ventilation (LEV).

Public exposure and health risks

Public exposure to triclosan can occur through the use of cosmetic and personal care products, household cleaning products, paint, and textile articles containing triclosan. Given the types of triclosan-containing products available to the public, the main route of exposure is likely to be dermal. However, oral exposure may occur through accidental or incidental ingestion of lip balm, toothpaste or mouthwash formulations. Also inhalation exposure may occur through breathing aerosols generated from the use of cosmetic and personal care products or cleaning products.

Exposure data from direct measurement is limited and available only for the use of cosmetic and personal care products. Consequently, various exposure models have been used to estimate consumer exposure to triclosan-containing consumer products. No data are available on the leaching of triclosan from plastic products and therefore the potential dermal and oral exposure of babies or young children as a result of sucking or mouthing these products cannot be determined.

The risk to the public of inhalation toxicity, skin, eye or respiratory irritation is low because of the low concentrations of triclosan in cosmetic and personal care products, and in textiles and plastic products. Under normal conditions of consumer use, the risk of adults and children being exposed to levels of triclosan that would lead to chronic health effects is low. Furthermore, although there is a potential for breast-feeding babies to be exposed to triclosan via breast milk, this assessment indicates it is likely to be the lowest source of exposure to babies, and therefore the risk of an adverse health effect during lactation is very low.

Potentially, the greatest source of exposure to consumers (adults, young children and babies), and thus the risk of an adverse health effect, is from the use of cosmetic and personal care products containing triclosan. Although the chronic health risk from such products is generally considered to be low, there are exposure data from volunteer studies that suggest that repeated use of a range of triclosan-containing products could increase the exposure levels, and therefore the potential health risk (see Recommendation 4).

The available data in humans and animals provide no evidence that triclosan has the potential to cause harm to breastfed babies.

On the basis of available data, there is also no evidence that the use of triclosan is leading to an increase in triclosan-resistant bacterial populations or that there is any increased risk to humans regarding antibiotic resistance.

Environmental effects

For terrestrial organisms, triclosan is slightly toxic to birds by the oral route of exposure, based on acute data available for two standard test species. Triclosan is toxic to plants

when grown in sandy soil, though toxicity is less for plants grown in sandy loam, probably due to the higher organic matter content of the sandy loam soil binding the triclosan (see Recommendation 8a with regard to biosolids applied as soil conditioners). The only terrestrial invertebrate data available are for earthworms, for which triclosan was found to be very slightly toxic. Triclosan does not affect soil respiration or nitrification. Only limited data were available to examine the effects of triclosan on activated sewage sludge microorganisms. These data indicate that triclosan can initially reduce the ability of the sludge microorganisms to remove ammonia as well as reduce their nitrification capacity, although the effects decrease with acclimation.

In the aquatic compartment, triclosan is highly to very highly toxic to a number of freshwater aquatic organisms such as fish, plants and invertebrates. From the limited data available, freshwater algae are the most sensitive species. Algae form an important food source for numerous other organisms. In both acute and chronic tests with freshwater invertebrates, triclosan is much more toxic to freshwater invertebrates in neutral or acidic waters than in alkaline waters. Consequently, because the tests on algae were performed under alkaline pH conditions, the toxicity values for algae may under-estimate algal toxicity through the full environmental pH range. Recent research has indicated that effects on hormonally-induced metamorphosis of tadpoles can occur at concentrations around the predicted no-effect concentration (PNEC). However, the biological significance of these effects is currently unclear.

Both triclosan and a minor metabolite (methyl triclosan) have a high potential to bioaccumulate in aquatic organisms. Bioaccumulation potential is also evident from laboratory-scale bioconcentration factor (BCF) studies and field monitoring studies. The bioconcentration of triclosan is dependent on water pH (greater accumulation at lower pH) and exposure concentration.

In summary, various microbial species and algae are highly sensitive to triclosan, consistent with its antimicrobial properties. Triclosan is highly toxic to fish and daphnids, and slightly toxic to birds and earthworms. Triclosan is also very highly toxic to sediment dwelling organisms when exposed through the water column. Limited data are available for the toxicity of triclosan to marine organisms. The available data indicates that triclosan is highly toxic to grass shrimp with larvae being the most sensitive life stage. Triclosan is also very highly toxic to the marine bacterium *Vibio fischeri*. There is a lack of data for the effects of triclosan to soil organisms, with the limited data indicating that it does not affect soil respiration or nitrification.

Environmental exposure and risks

The exposure of the environment to triclosan from accidental spills and leaks during transport should be limited by engineering controls (e.g. container specifications) and emergency clean-up procedures. Triclosan is predominantly released to the sewerage system in various cosmetic and personal care products during washing and bathing, or from the disposal of cleaning products. Triclosan can also be discharged from formulating facilities. The use of triclosan in oil-based paints is not expected to result in significant release to the aquatic compartment as the vast majority of the triclosan is expected to be contained within the cross-linked inert paint matrix and will share its fate. This is likely to be disposed of to landfill (either as paint dust resulting from sanding back the painted surface or bound to the surface) at the end of its useful lifetime. As the triclosan will be bound within the inert paint matrix, leaching from landfill is not expected, and it will slowly degrade through a mixture of biotic and abiotic processes. The use of the tile paint in shower cubicles raises the potential for release of triclosan to the environment through

leaching from the paint. However, the rate of leaching is expected to be extremely low and hence, the release from this source is expected to be insignificant.

Environmental exposure can occur through beneficial re-use of treated effluent and biosolids (sewage sludge) that may also contain triclosan. Throughout Australia, treated effluent is increasingly being utilised in a range of agriculture (irrigation), agroforestry and industrial applications, which provides a pathway for release of triclosan and its derivatives to soils. Similarly, application of biosolids to soils as a soil conditioner also provides another pathway for transfer of triclosan from the sewerage system to soils.

Consequently, triclosan largely enters the environment in Australia through discharges from Sewage Treatment Plants (STPs). Constant emission to sewer occurs, leading to ongoing environmental exposure in waters and sediments downstream of sewage outfalls.

The risk of toxicity to birds and most mammals that are not solely dependent on the freshwater aquatic environment for food is considered to be low and at an acceptable level. There is potential for indirect effects on birds and mammals to occur near STP outlets as a result of adverse effects of triclosan on their food supply. There is also potential for direct toxicity arising through triclosan residues in food resulting from the presence of triclosan in surface waters. The risk to platypus living in the vicinity of a sewage outfall is considered to be low and at an acceptable level at the triclosan concentrations reported in Queensland. However, the triclosan concentrations in the vicinity of sewage outfalls in other parts of Australia, and the subsequent risk to platypus, is unknown.

The use of triclosan and subsequent release to the Australian sewage system, at current levels of use, may likely to result in concentrations of the chemical within natural waterways which may pose risks to algae, aquatic plants and fish at all levels of wastewater treatment. If the limited data available from Queensland are representative of data for the rest of Australia, the risks of adverse impacts on fish and aquatic plants are at worst marginal. However, for algae, these limited data confirm that triclosan is present at levels that could result in adverse effects. In the absence of data on the concentrations downstream of representative STPs in Australia, it is not possible to exclude the possibility of adverse effects to certain species of algae within inland waterways (see Recommendation 7). As dilution is high in ocean outfalls, risks to marine species are considered to be low and at an acceptable level.

Studies indicate that triclosan is present in biosolids at levels which, when applied to soil, may result in adverse effects on plants. Some data are also available which point to the persistence of triclosan in treated soils. Although recent studies indicate that triclosan will degrade relatively rapidly in aerobic soils, which would mitigate potential risks, triclosan will persist if the soil is anaerobic. The continual application of triclosan to soil through use of biosolids (as soil conditioners) or effluent (for irrigation) from STPs also has the potential to disrupt microbial soil populations, but it does not appear to affect soil respiration or nitrification. Consequently, an understanding of the toxicity of triclosan to soil dwelling organisms is also important to fully determine the effects in the field of triclosan release to the soil environment and to establish the level of risk (See Recommendation 8b).

Recommendations

This section provides recommendations arising from the priority existing chemical assessment of triclosan. Recommendations are directed principally at regulatory bodies and importers and formulators of triclosan and triclosan products. Implicit in these recommendations is that best practice is implemented to minimise occupational and public exposure, and environmental impact.

Occupational Health and Safety

Recommendation 1. Revised occupational hazard classification (ASCC)

Based on the hazard assessment of the available data and in accordance with the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004), triclosan is determined to be hazardous and should be classified as:

- R23 Toxic by inhalation
- R36 Irritating to eyes
- R37 Irritating to respiratory system
- R38 Irritating to skin

It is recommended that this revised classification for triclosan be included in the Hazardous Substances Information System (HSIS) as soon as possible.

The appropriate risk phrases for mixtures containing triclosan are as follows:

<u>Risk Phrase</u>	<u>Concentration Cut-off</u>
R23, R36/37/38	≥25%
R20 ¹ , R36/37/38	25% > conc ≥20%
R20	20% > conc ≥3%

The following safety phrases are also recommended for triclosan:

- S22 Do not breathe dust
- S26 In case of contact with eyes, rinse immediately with plenty of water and seek medical advice
- S37 Wear suitable gloves
- S38: In case of insufficient ventilation, wear suitable respiratory equipment
- S39 Wear eye/face protection
- S45: In case of accident or if you feel unwell seek medical advice immediately (show the label where possible)
- S60: This material and its container must be disposed of as hazardous waste

¹ R20 Harmful by inhalation.

Recommendations 2a and 2b. Hazard communication (Industry)

The industry should take note of the revised hazard classification (i.e. toxic by inhalation, irritating to eyes, skin and respiratory system) and UN numbers (according to the Australian Code for the Transport of Dangerous Goods by Road & Rail, 2007) for triclosan.

Recommendation 2a. Australian Code for the Transport of Dangerous Goods by Road & Rail

It is recommended that the industry should take note of the UN numbers applicable for triclosan according to the Australian Code for the Transport of Dangerous Goods by Road & Rail (ADG Code, 2007).

According to the ADG Code, due to its moderate inhalation toxicity, triclosan powder (100%) falls under Class 6.1 (Toxic substances), packaging class III (Substances presenting low danger) and UN number 2811 (toxic, solid, organic) for road and rail transport.

The other forms of triclosan imported to Australia (liquids and pellets) should have the appropriate UN number (solid or liquid) depending on the concentration of triclosan. Class 6.1 applies only if the estimated LC50 value (1 hour) falls within the ADG Code (2007) classification range for inhalation toxicity (1 hour $LC50 \leq 4.0$ mg/L).

Triclosan is highly toxic (acute and chronic) to some aquatic species. If the LC50 value (1 hour) of triclosan liquids or solids falls outside the Class 6.1 classification range for inhalation toxicity (1 hour $LC50 > 4$ mg/L), Class 9 (Miscellaneous dangerous substances and articles) and UN number 3077 (environmentally hazardous substance, liquid, not otherwise specified) or 3082 (environmentally hazardous substance, solid, not otherwise specified) is applicable to triclosan (ADG Code, 2007).

Recommendation 2b. MSDS and label amendments

It is recommended that suppliers and employers take note of the revised hazard classification (i.e. toxic by inhalation, irritating to eyes, skin and respiratory system) and UN numbers and, amend Material Safety Data Sheets (MSDS), labels and training material accordingly.

MSDS (see Sample MSDS, Appendix I):

Under the *National Model Regulations for the Control of Workplace Hazardous Substances* (NOHSC, 1994c) and the Commonwealth State and Territory regulations introduced in accordance with these National Model Regulations, employees shall have ready access to MSDS for hazardous substances at their workplace.

In accordance with the *National Code of Practice for the Preparation of Material Safety Data Sheets 2nd Edition* (NOHSC, 2003), it is recommended that all manufacturers, suppliers and employers review their hazard communication, paying particular attention to the following points:

- (i) correct identification of health hazards and risk phrases as contained in Recommendation 1;
- (ii) correct information on the concentration cut-offs for mixtures containing triclosan as provided in Recommendation 1;

- (iii) inclusion of safety phrases as noted in Recommendation 1; and
- (iv) inclusion of ADG Code Class and UN number for transport by Road & Rail as provided in Recommendation 2a.

Labels:

In accordance with the *National Code of Practice for the Labelling of Workplace Substances* (NOHSC, 1994a), it is recommended that importers and suppliers review their hazard communication paying particular attention to the following points:

- (i) correct signal word; and
- (ii) correct risk and safety phrases as contained in Recommendation 1.

Recommendation 3. Compliance with state and territory legislation (Government)

It is recommended that the State and Territory Occupational Health and Safety authorities review compliance in the workplace with the revised MSDS and labels which take into consideration the above information.

Public Health and Safety

Recommendation 4. Poison scheduling (Government)

Given the acute toxicity profile (inhalation toxicity and irritation effects) of triclosan and the potential for human exposure, it is recommended that the National Drugs and Poisons Schedule Committee (NDPSC) consider scheduling triclosan in the *Standard for the Uniform Scheduling of Drugs and Poisons* (SUSDP).

The levels of triclosan and its metabolites in some volunteer studies following repeated use of a cosmetic or personal care product containing triclosan raise a concern. The plasma levels may have increased in some individuals through combined use of many products containing triclosan, and/or using products containing relatively high concentrations of triclosan.

The major source of exposure of the public to triclosan comes from cosmetics and personal care products with about 15 tonnes per year being used in these products. Consequently it is also recommended that NDPSC consider establishing a maximum level for triclosan as a preservative in cosmetic and personal care products.

The EU maximum concentration level for triclosan in cosmetic and personal care products is provided below as being protective to public health and promotes international harmonisation:

*Triclosan (as a preservative) for cosmetic use:
0.3% or less in all cosmetic preparations*

The public can also be exposed to triclosan used in cleaning products. Currently the level of exposure from this source is relatively low with less than 1 tonne/year being used in industrial cleaning products that may also be available to the general public through retail outlets. NICNAS will monitor the use of triclosan in cleaning products and consider the need for a maximum level in these products based on the potential public health risk. Further recommendations may be made to the NDPSC.

The final report will be forwarded to the NDPSC for their consideration.

Recommendation 5. Utilisation of the health hazard assessment (Government)

It is recommended that other government organisations, such as Australian Pesticides and Veterinary Medicines Authority (APVMA) and Therapeutic Goods Administration (TGA), take the findings of the human health hazard assessment into consideration in future work on triclosan or products containing triclosan, noting use of triclosan in therapeutic and agricultural and veterinary products.

It is recommended that the APVMA should also take note of Recommendation 4 of this report regarding the poison scheduling of triclosan, which may have impact on currently registered Agricultural and Veterinary products containing triclosan.

It is also recommended that the National Health and Medical Research Council (NHMRC) take the findings of the hazard assessment of antimicrobial resistance discussed in this report into consideration in any future advice being provided on triclosan. Noting that this report recognizes that there is presently limited information available on the following:

- The prevalence of triclosan resistant organisms in clinical environments;
- The exact mechanisms of antibacterial action of triclosan;
- The kinetics of triclosan antibacterial resistance mechanisms and their possible transferability; and
- The fate of triclosan in the environment, the rate and extent of degradation of triclosan and the anti-microbial activity of degradates or low concentrations in the environment.

Recommendations 6a and 6b. Impurities in triclosan (Government and Industry)

Australia ratified the Stockholm Convention on Persistent Organic Pollutants (POPs), whose aim is to protect human health and the environment from the effects of POPs, on 20 May 2004. Dioxins and dibenzofurans, which are found in varying low-level amounts as synthesis impurities in triclosan, were included in the first 12 POPs identified by the Stockholm Convention. Annex C of the Stockholm Convention on POPs dealing with unintentional production of POPs provides general prevention measures relating to both best available techniques and best environmental practices, that includes “minimisation of these chemicals [i.e. dioxins and dibenzofurans] as contaminants in products” (UNEP, 2002).

For Australia to meet its obligations under the Stockholm Convention for POPs, the levels of dioxins and dibenzofurans in triclosan imported into Australia should be kept as low as possible.

Recommendation 6a. Impurities in triclosan (TGA)

It is recommended that the Therapeutic Goods Administration particularly note that the U.S. Pharmacopoeia² have set limits for dioxins and dibenzofurans as impurities in triclosan used in therapeutics.

² The U.S limits are set by the U.S. Pharmacopoeia (USP) and these recommendations form the basis of enforcement actions by the U.S. Food and Drug Agency. In the US, impurities in triclosan were first regulated in 2000 when the chemical was included in USP Volume XXIV.

This assessment of triclosan notes the following:

1. It is possible that several polychlorodibenzo-p-dioxins (dioxins) and polychlorodibenzofurans (dibenzofurans) can be found in varying low-level amounts as synthesis impurities in triclosan. Their presence or absence is dependent upon the type and purity of the starting materials used to synthesize triclosan as well as reaction conditions such as temperature and pressure. If present, their relative concentrations as impurities can vary from batch to batch.
2. As guidance, the limits of dioxins and dibenzofurans as impurities in the U.S. Pharmacopoeia (USP) are as below:
 - less than 10 µg/g for monochlorophenols;
 - less than 10 µg/g for 2,4-dichlorophenol;
 - less than 0.25 µg/g for 1,3,7-trichlorodibenzo-p-dioxin;
 - less than 0.5 µg/g for 2,8-dichlorodibenzo-p-dioxin;
 - less than 0.25 µg/g for 2,8-dichlorodibenzofuran;
 - less than 0.5 µg/g for 2,4,8-trichlorodibenzofuran;
 - less than 1 pg/g for 2,3,7,8-tetrachlorodibenzo-p-dioxin; and
 - less than 1 pg/g for 2,3,7,8-tetra chlorodibenzofuran
3. Evidence is available in the literature that some grades of triclosan may not meet USP specifications. This assessment could not conclusively determine from the data submitted that all the triclosan imported into Australia met the specifications of the current edition of the USP.
4. Limiting the amount of dioxin and dibenzofuran impurities in triclosan is consistent with the Australian Government National Action Plan for addressing dioxins in Australia under the National Dioxins Program³. The National Action Plan sets out a range of actions that will be taken by Australian governments to minimise, and where feasible, eliminate sources of dioxin release.
5. The basis for the US (or the Canadian) limits cannot be determined. Though NICNAS has been informed by the USP that such documents may not be available or may be confidential, it is assumed that these limits have a health basis. It is known that industry overseas has met the US regulations indicating that it is practically feasible to achieve these limits.

Recommendation 6b. Impurities in triclosan (Industry)

It is recommended that importers of triclosan, as a voluntary measure, ensure that triclosan imported into Australia meets the concentration limits specified in Recommendation 6a for dioxins and dibenzofurans as impurities. These limits are based on those in the U.S. Pharmacopoeia (USP) and are technically achievable.

³ The recent Australian National Dioxins Program concluded that the Australian Tolerable Monthly Intake (TMI) “should be adequately protective of the general population with respect to effects of dioxin-like compounds” (National Dioxins Program Technical Report No. 12, 2005). The Australian TMI value for dioxins and furans combined is 70 pg TEQ/kg bw/month as recommended by the NHMRC and the Office of Chemical Safety in 2002, and is equivalent to that set by the Joint Expert Committee on Food Additives, a committee of the United Nations Food and Agriculture Organization and the World Health Organization (Environment Protection and Heritage Council, 2005).

Environmental Safety

Recommendation 7. Releases from sewage treatment plants (Federal, State and Territory agencies through Environment Protection and Heritage Council (EPHC) Chemicals Working Group)

The major route by which triclosan is released to the environment is through the sewer. Constant discharge occurs, leading to ongoing environmental exposure. The rate of removal of triclosan by wastewater treatment varies substantially, depending on whether anaerobic or aerobic processes are used, acclimation of the sludge microbes and the concentrations in the influent. The measured levels are at the lower end of internationally observed values for sewage effluent, biosolids and surface water, however, the limited available data do not cover the full range of urban plants in Australia.

Based on the uncertainty in the available data, there is sufficient cause to recommend the conduct of targeted short term sampling of the levels of triclosan in sewage effluent and receiving freshwater in order to determine the extent of release to, and levels in the environment, together with impacts on biota. Freshwater environments with larger quantities of receiving waters will lead to dilution of the effluent, indicating that any monitoring should be focused on areas with limited flow in receiving waters, such as in smaller rivers and creeks.

It is recommended that:

- A targeted sampling study of the levels of triclosan in sewage effluent and receiving freshwaters, focused on areas of highest potential risk of adverse effects, should be conducted in order to clarify risks in the field associated with representative conditions. Federal, state and territory agencies, through the EPHC Chemicals Working Group, should consider how to design and implement the study, including the associated funding sources.
- The targeted sampling study should also focus on plants that have large urban catchments to ensure that there is good coverage of the possible upper range triclosan levels. Areas where only primary treatment occurs should also be monitored for a limited period, and the data provided to DEWHA.
- Triclosan levels above the predicted-no-effect concentration (PNEC) detected in effluent as a result of sampling will require toxicity tests of the effluent to most sensitive algal species to be conducted. Federal, state and territory agencies, through the EPHC working group, should develop mechanisms to facilitate any such testing according to OECD or equivalent guidelines and consider the associated funding sources.

Recommendations 8a, 8b and 8c. Biosolids applied as soil conditioners (Federal, State and Territory agencies, through the EPHC Chemicals Working Group)

Re-use of biosolids for soil improvement, and as a fertiliser substitute has a number of benefits, and reduces the need to dispose of biosolids at landfill sites. Several states have biosolids guidelines that detail acceptable uses of biosolids. Triclosan has been measured in samples of biosolids from 19 waste water treatment plants around Australia (19 out of about 900, excluding New South Wales and Northern Territory). The measured levels were similar to those recorded overseas and similar to those predicted by modelling.

It is recommended that the maximum concentrations of triclosan present in the biosolids and/or maximum application rate of biosolids should be measured in a targeted and short-term sampling strategy. The toxicity of triclosan to soil dwelling organisms is also important to fully determine the effects in the field of triclosan release to the environment in Australia.

Recommendation 8a. Targeted study of triclosan in biosolids (Federal, State and Territory agencies, through the EPHC Chemicals Working Group)

It is recommended that a targeted study of the level of triclosan in biosolids used as a soil conditioner should be conducted in order to clarify risks in the field associated with common use practices. Federal, state and territory agencies, through the EPHC Chemicals Working Group, should consider possible mechanisms to design, develop and implement the study, including the associated funding sources and any relevant industry input or support that may be required.

Recommendation 8b. Toxicity tests for soil dwelling organisms (Federal, State and Territory agencies, through the EPHC Chemicals Working Group)

In addition to the above study, it is further recommended that toxicity tests for soil dwelling organisms, potentially in conjunction with the sampling strategy outlined above, should also be conducted. Federal, state and territory agencies, through the EPHC Chemicals Working Group, should also consider how to design and implement this testing, including the associated funding sources.

Recommendation 8c. Proactive management actions to reduce risks (Federal, State and Territory agencies, through the EPHC Chemicals Working Group)

Given the uncertainty regarding the persistence and effects of triclosan in soils, it is recommended that proactive management actions to reduce risks should be developed. Such actions to ameliorate risks include further ageing of biosolids prior to incorporation into soil, or incorporation in smaller proportions. Federal, state and territory agencies, through the EPHC chemicals working group, should collaborate on the development and implementation of such actions, including the associated funding sources.

Secondary Notification

Under section 64 of the *Industrial Chemicals (Notification and Assessment) Act 1989*, the secondary notification of a chemical that has been assessed under the Act may be required where an applicant or other introducer (importer) of a chemical becomes aware of any circumstances which may warrant a reassessment of its hazards and risks. In the case of triclosan, specific circumstances include:

- The function or use of triclosan has increased, or is likely to change, significantly;
- The amount of triclosan introduced by each importer into Australia has increased significantly compared to their usual importation volume, or likely to increase significantly;
- Manufacture of triclosan in Australia is proposed;
- Significant new information has become available to the applicant/notifier as to adverse environmental effects of triclosan such as those identified in this assessment (e.g. methyl-triclosan and 2,8-dichlorodibenzo-p-dioxine);
- Additional data has become available to the applicant/notifier to confirm and clarify the biological significance of the observed effects of triclosan on the development of tadpoles of the North American bullfrog, *Rana catesbeiana*.
- Additional information has become available to the applicant/notifier as to the adverse health effects of triclosan, including development of antimicrobial resistance to triclosan in clinical or natural settings; or
- Additional information has become available on the amount of triclosan that may be leached from textile and plastic articles under normal conditions of use, or from the sucking or mouthing of such (i.e. extraction into saliva).

The Director (Chemicals Notification and Assessment) must be notified within 28 days of the introducer becoming aware of any of the above or other circumstances prescribed under section 64(2) of the Act.

The information from the environmental monitoring, recommended in the report, will be forwarded to NICNAS. If environmental monitoring detects the presence of triclosan in the Australian aquatic environment above levels of concern (i.e. 0.05 µg/L), a secondary notification may be required under section 65(2) of the Act to determine further risk mitigation measures.

Acronyms and Abbreviations

ACT	Australian Capital Territory
ADG Code	Australian Code for the Transport of Dangerous Goods by Road and Rail
AE	atomic emission
AICS	Australian Inventory of Chemical Substances
APVMA	Australian Pesticides and Veterinary Medicines Authority
ARTG	Australian Register of Therapeutic Goods
AS	activated sludge
ASCC	Australian Safety and Compensation Council
AUC	area under the curve
BCF	bio-concentration factor
BOD	biological oxygen demand
BTEB	basic transcription element binding protein
CAS	Chemical Abstracts Service, OR continuous activated sludge
cfu	colony-forming units
cm ²	square centimeter
cm ³	cubic centimetre
CO ₂	carbon dioxide
COD	chemical oxygen demand
d	day
dh°	Deutsche Härte (German degree of hardness)
DEWHA	Australian Government Department of the Environment, Water, Heritage and the Arts
DMSO	dimethylsulfoxide
DNA	deoxyribonucleic acid
DOM	dissolved organic matter

DPV	differential pulse voltametry
EAR	enoyl-ACP reductase
EASE	Estimation and Assessment of Substance Exposure
EbC0	concentration at which the biomass of 50% of the test population is impacted (<i>OR median effective concentration in terms of reduction of biomass</i>)
EC	European Commission
EC50	median effective concentration
EHD	estimated or measured human dose or exposure
EPA	environmental protection agency
EPHC	Environment Protection and Heritage Council
ErC50	concentration at which the rate of growth of 50 percent of the test population is impacted (<i>OR median effective concentration in terms of reduction of growth rate</i>)
EU	European Union
g	gram
GC	gas chromatography
GC/AE	gas chromatography with atomic emission detection
GC/EC	gas chromatography with electron capture
GC/MS	gas chromatography/mass spectrometry
GHS	Globally Harmonized System of Classification and Labelling of Chemicals
GLC	gas liquid chromatography
GLC/EC	gas liquid chromatography with electron capture
h	hour
HPLC	high performance liquid chromatography
HPLC/MS	high performance liquid chromatography/mass spectrometry
HPLC/VD	high performance liquid chromatography/voltametric detection
HSIS	Hazardous Substances Information System
IC50	median inhibition concentration

ip	intraperitoneal
iv	intravenous
kg	kilogram
L	litre
LC	liquid chromatography
LC/MS	liquid chromatography/mass spectrometry (LC/MS).
LC50	median lethal concentration
LD50	median lethal dose
L(E)C50	LC50 or EC50
LEV	local exhaust ventilation
LOAEL	lowest-observed-adverse-effect level
LOEC	lowest-observed-effect concentration
LSC	liquid scintillation counting
M	Molar
MATC	maximum acceptable toxicant concentration
MBC	minimal bacterial concentration
MIC	minimum inhibitory concentration
µg	micrograms
mg	milligram
mg/cm ² /day	milligrams per square centimetre per day
mg/kg bw	milligrams per kilogram body weight
mg/kg bw/day	milligrams per kilogram bodyweight per day
mg/m ³	milligrams per cubic meter
MIC	minimum inhibitory concentration
min	minute
mL	millilitre
MOE	margin of exposure
MRSA	multi (methicillin) resistant <i>Staphylococcus aureus</i>

MRSE	multi (methicillin) resistant <i>Staphylococcus epidermidis</i>
MS	mass spectrometry
MSDS	Material Safety Data Sheet
MSSA	multi (methicillin) sensitive <i>Staphylococcus aureus</i>
MTCS	methyl-triclosan
NDPSC	National Drugs and Poisons Schedule Committee
ng	nanogram
NHMRC	National Health and Medical Research Council
NICNAS	National Industrial Chemicals Notification and Assessment Scheme
NMR	Nuclear magnetic resonance
NOAEC	no-observed-adverse-effect-concentration
NOAEL	no-observed-adverse-effect-level
NOEC	no-observed-effect concentration
NOHSC	National Occupational Health and Safety Commission
NSW	New South Wales
NT	Northern Territory
OECD	Organisation for Economic Cooperation and Development
PCNA	proliferating nuclear cell antigen
PEC	predicted environmental concentration
pg	picogram
PNEC	predicted-no-effect concentration
POPs	persistent organic pollutants
ppb	parts per billion
PPE	personal protective equipment
ppm	part per million
QLD	Queensland
RF	retention factor

RQ	risk quotient
S	spectrophotometer
+S9	with rat liver microsome preparations
-S9	without rat liver microsome preparations
SIDS	Screening Information Data Set
SPE	solid phase extraction
SSC	Scientific Steering Committee (European Commission)
STP	sewage treatment plant
SUSDP	Standard for Uniform Scheduling of Drugs and Poisons
TCS	triclosan
TGA	Therapeutic Goods Administration
TLC	thin layer chromatography
TF	trickling filter
TR	thyroid hormone receptor
TRV	toxicity reference value
TWA	time-weighted average
UDS	unscheduled DNA synthesis
UN	United Nations
US EPA	United States Environmental Protection Agency
USP	United States Pharmacopoeia
V	volume
VD	voltametric detection
WHO	World Health Organization
w/o	wash-off
wt	weight
WWTP	wastewater treatment plants

PART 1 - Scientific Assessment

1. Introduction

1.1 Declaration

Triclosan (phenol, 5-chloro-2-(2,4-dichlorophenoxy)-), CAS No 3380-34-5, was declared a Priority Existing Chemical for a full risk assessment under the *Industrial Chemicals (Notification and Assessment) Act 1989* (Cwlth) (the Act) by notice in the *Commonwealth Chemical Gazette* of 6 May 2003. The basis for the declaration was that triclosan has been shown, in laboratory studies, to be toxic to aquatic species, particularly to algae, which is the most sensitive species. The widespread use of triclosan in consumer products provides a number of pathways for the chemical to enter the environment. In addition, the chemical properties of triclosan indicate that it may be bioaccumulative and persistent in the environment. There are also reports that suggest incineration of textile products containing triclosan may result in the formation of dioxin-like substances.

1.2 Objectives

The objectives of this assessment are to:

- identify the extent of use of triclosan;
- characterise the human health hazards and environmental effects of triclosan;
- determine the potential occupational, public and environmental exposure to triclosan;
- determine the risk of adverse effects to the environment, workers and the general public resulting from exposure to triclosan; and
- make recommendations for minimizing environmental, occupational and public health risks, and for appropriate hazard communication measures, where applicable.

1.3 Sources of information

Consistent with these objectives, the report presents an extensive and critical evaluation of relevant information relating to the potential human health effects and environmental effects from exposure to triclosan.

Importers of triclosan and triclosan-containing products and some formulators provided relevant scientific data, including information on quantities imported into Australia, uses, physicochemical properties, human and environmental exposure, transport, handling, storage, manufacture and disposal, and toxicity (published and unpublished data). Information was also obtained from published papers identified in a comprehensive literature search of several online databases up to December 2006, and retrieved from other sources such as the 2002 review of triclosan antimicrobial resistance undertaken by the European Union (EU) Scientific Steering Committee (European Commission Health & Consumer Protection Directorate General, 2002b). With the exception of the studies contained in this

overseas report on antimicrobial activity, all primary sources of data were evaluated.

Data provided by applicants indicated no manufacture of triclosan occurs in Australia.

Quantities of triclosan in pesticides and veterinary medicines and therapeutic products were collected for this assessment, but no further assessment of these products were conducted as they are not within the scope of the ICNA Act. The Australian Pesticides and Veterinary Medicines Authority (APVMA) provided the information on pesticides and veterinary medicines containing triclosan imported into Australia and triclosan imported into Australia as raw material to be used in pesticide and veterinary medicine manufacture. Quantities of triclosan used for therapeutic purposes were identified in a survey undertaken by NICNAS in 2004 of registrants listed on the Australian Register of Therapeutic Goods (ARTG) as sponsors of products containing triclosan. Of the 30 registrants contacted 27 responded to the initial survey for import data for the calendar years 2001, 2002 and 2003. In contrast, 11 registrants responded to an updated survey for the calendar years 2004 and 2005 that was conducted in 2006.

Additionally, a telephone survey of companies using triclosan for industrial purposes in the textile and plastics industry was conducted in 2004. Four companies using triclosan to treat plastics and 11 companies using triclosan in textile treatments provided information.

The information obtained on industrial uses of triclosan together with that obtained on therapeutic, pesticide and veterinary uses resulted in a more accurate estimation of the total environmental load of triclosan in Australia and, thus, environmental risk assessment. The characterisation of health risks in Australia was based upon information on toxicology data, product specifications made by the applicants, and overseas use patterns and occupational exposure models.

Information to assist in this assessment was also obtained through site visits to workplaces involved in formulating triclosan into personal care and therapeutic products, and a workplace using triclosan for textile treatment. This assessment did not take into account any triclosan imported as part of finished plastic and textile articles, as no information was provided on the triclosan quantities in imported articles.

Additionally, NICNAS commissioned two projects for this assessment:

1. Determination of triclosan levels in national breast milk samples, which was undertaken by the National Centre for Environmental Toxicology, at the University of Queensland.
2. Evaluation, by a national expert on antimicrobial resistance, of studies on this issue published in scientific journals from 2002 to December 2005. These studies have been published since the 2002 EU review of antimicrobial resistance (European Commission Health & Consumer Protection Directorate General, 2002b).

1.4 Peer review

During all stages of preparation, the report has been subject to internal peer review by NICNAS and the Australian Government Department of the Environment, Water, Heritage and the Arts (DEWHA). In addition, the Advisory Group on Chemical Safety peer reviewed the sections of the report describing the kinetics and metabolism of triclosan along with the models used to estimate occupational and public exposure, the methodology used for the human health risk characterisation, the NICNAS commissioned study to determine triclosan levels in national breast milk samples, and the potential for triclosan in breast milk to cause harm to breast-fed babies. The environmental sections of the report were peer reviewed overseas by Dr Helen Wilkinson of the United Kingdom Environmental Agency.

1.5 Report structure

Part 1 of this report is the scientific assessment of the available data on triclosan. It examines the manufacture, importation and use of triclosan, the potential human and environmental exposure, and the potential human and environmental hazards associated with triclosan. It also characterizes the human and environmental risks associated with the use of triclosan and provides information on the current risk management practices.

Part 2 of the report contains detailed data which support the scientific assessment of Part 1.

2. Background

2.1 International perspective

The first US patent for triclosan was in 1964 (Merck, 1983) and triclosan has been marketed for over 30 years. The chemical is listed on the Organisation for Economic Cooperation and Development's (OECD) High Production Volume Chemicals list (OECD, 2004) and is being sponsored through the OECD SIDS program by Australia.

Triclosan is not listed under the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade (Rotterdam Convention, Annex III, 2006). The Convention enables listed hazardous chemicals to be monitored and their trade controlled on a global scale. Triclosan is not listed under the Stockholm Convention on Persistent Organic Pollutants (UNEP, 2005). The Convention is an international treaty that Australia has ratified, and is aimed at restricting and ultimately eliminating the production, use, release and storage of persistent organic pollutants (POPs). Additionally, the World Health Organisation (WHO) has not set guidance values for triclosan levels in drinking water (WHO, 2006).

In the European Union the Cosmetics Directive (76/768/EEC) has set a maximum allowable concentration of 0.3% triclosan in cosmetic products (European Commission, 1999). In Japan, triclosan is included in the Standards for Cosmetics (as established by the Pharmaceutical Affairs Law, 1960), which sets a maximum allowable concentration of 0.1% triclosan in cosmetic products (Ministry of Health and Welfare Notification No. 331, 2000).

In Canada the use of chemicals in cosmetics is regulated via section 16 (Cosmetic Regulations) of the *Food and Drugs Act 1985*. Maximum allowable concentrations of 0.03% triclosan in mouthwash and 0.3% triclosan in other cosmetic products are allowed. In addition for all triclosan containing products, the concentration of the impurities 2,3,7,8-tetra-chlorodibenzo-p-dioxin and 2,3,7,8-tetra chloro dibenzofuran must not exceed 0.1 ng/g, the total concentration of all other chlorinated dibenzodioxin and dibenzofuran impurities must not be greater than 10 µg/g, and no other individual impurity should be greater than 5 µg/g (Health Canada, 2005).

Similarly, due to the potential for the formation of dioxins and dibenzofurans as unwanted low level trace by-products in triclosan (ECB, 2002), the United States Pharmacopoeia (USP) recommends concentration limits for the following impurities in triclosan: less than 10 µg/g for monochlorophenols; less than 10 µg/g for 2,4-dichlorophenol; less than 0.25 µg/g for 1,3,7-trichlorodibenzo-p-dioxin; less than 0.5 µg/g for 2,8-dichlorodibenzo-p-dioxin; less than 0.25 µg/g for 2,8-dichlorodibenzofuran; less than 0.5 µg/g for 2,4,8-trichlorodibenzofuran; less than 1 pg/g for 2,3,7,8-tetrachlorodibenzo-p-dioxin; and less than 1 pg/g for 2,3,7,8-tetra chlorodibenzofuran (USP, 2004). USP recommendations form the basis of enforcement actions by the U.S. Food and Drug Administration.

However the basis for the derived European, Japanese and Canadian maximum allowable concentration of triclosan in cosmetics, and American and Canadian impurities concentration limits, could not be determined.

2.2 Australian perspective

Triclosan is not manufactured in Australia. Imported triclosan has been reported for use as an antibacterial ingredient in personal care products; manufacture of carpet underlay, PVC swimming pool liners, chopping boards and textile fabric. In 1999, a total of 22 tonnes was notified to NICNAS as having been imported. The chemical is not reported on the Australian High Volume Industrial Chemicals list.

Triclosan is listed in the Australian Safety and Compensation Council's (ASCC) *List of Designated Hazardous Substances*, contained in the Hazardous Substances Information System (HSIS). Prior to the July 2008 HSIS update triclosan was classified as a hazardous substance with the risk phrase, 'Toxic by inhalation (R23)'. The source for this listing was a registration report by the Australian Pesticides and Veterinary Medicine Authority (ASCC, 2005). In July 2008, the triclosan hazard classification in the HSIS was updated to adopt the changes in Europe's 29th Adaptation to Technical Progress (ATP) to Directive 67/548/EEC (April, 2004). Due to this update triclosan is classified in the HSIS as 'Irritating to eyes and skin (R36/38)'.

An atmospheric occupational exposure standard has not been assigned for triclosan in the ASCC *Exposure Standards for Atmospheric Contaminants in the Occupational Environment* as provided by HSIS (ASCC, 2005). Triclosan is not specifically regulated for transport under the National Road Transport Commission's Dangerous Goods Code (ADG Code) (FORS, 1998).

Triclosan is not currently regulated for either public health or environmental purposes. The *Australian Drinking Water Guidelines* (National Health & Medical Research Council, 2004) do not stipulate a limit for triclosan in drinking water. Triclosan is not listed in the *Standard for Uniform Scheduling of Drugs and Poisons* (SUSDP No: 23, June 2008).

2.3 Assessments by other national or international bodies

The health and environmental effects of triclosan have recently been evaluated and its classification and labelling determined under EC Directive 67/548/EEC (Annex 1 of Directive 67548 EEC, 2005). Triclosan is classified in the European Union as a skin and eye irritant (with risk phrases R38 and R36 respectively) and dangerous to the environment (risk phrases R50 and R53).

The European Commission's Scientific Steering Committee (SSC) specifically reviewed antimicrobial resistance to triclosan in 2002 and concluded that "there is no convincing evidence that triclosan poses a risk to humans or to the environment by inducing or transmitting antibacterial resistance under current conditions of use" (European Commission Health & Consumer Protection Directorate-General, 2002a).

No international assessment of the health and/or environmental risk for triclosan has presently been carried out in the EU. However, in the European Union triclosan has been 'notified' under the Biocidal Products Directive (98/8/EC) in the following product types (PTs): human hygiene biocidal products (PT1); private and

public disinfectants (PT2); veterinary hygiene biocidal products (PT3); film preservatives (PT7); fibre, leather, rubber and polymerized materials preservatives (PT9). Under the Directive industry will be required to submit a data-package for triclosan to support its use in each of these product types. This will include an assessment of potential risks to human health and the environment. These data packages were due to be submitted to Denmark (the Rapporteur Member State) between 1 February and 31 July 2007 for PTs 1, 2 and 3 and between 1 May and 31 October 2008 for PTs 7 and 9 (Commission Regulation [EC] No 2032/2003, 2003).

Currently there are no restrictions in relation to the use of triclosan as a biocide in the European Union other than those placed on chemicals in relation to their classification and labelling under EC Directive 67/548/EEC.

A Preliminary Risk Assessment of the pesticide uses of triclosan was released by the US EPA in April 2008 for public comment. In addition, an aggregated risk assessment was conducted by the US EPA as part of the Reregistration Eligibility Decision (RED) Document using biological monitoring data for non-EPA regulated uses such as toothpaste, hand soaps and deodorants (US EPA, 2008).

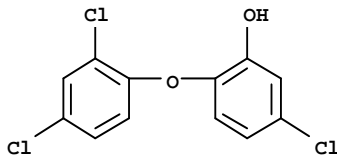
3. Identity, Properties, Analysis, Manufacture and Use

3.1 Chemical identity

Triclosan is listed on the Australian Inventory of Chemical Substances (AICS) as:

Phenol, 5-chloro-2-(2,4-dichlorophenoxy)-. Synonyms, trade name and formula are shown in Table 3.1.

Table 3.1 - Chemical identity

Property	Value, name or structure
CAS No.:	3380-34-5
EINECS No.:	222-182-2
Synonyms:	Triclosan; 2,4,4' – trichloro-2'-hydroxydiphenyl ether; Ether, 2'-hydroxy-2,4,4'-trichlorodiphenyl; Phenyl ether, 2'-hydroxy-2,4,4'-trichloro-; 2',4',4'-Trichloro-2-hydroxydiphenyl ether; 2',4,4'-Trichloro-2-hydroxydiphenyl ether; 2'-Hydroxy-2,4,4'-trichlorodiphenyl ether; 2,2'-Oxybis(1',5'-dichlorophenyl-5-chlorophenol); 2-Hydroxy-2',4,4'-trichlorodiphenyl ether; 3-Chloro-6-(2,4-dichlorophenoxy)phenol; 4-Chloro-2-hydroxyphenyl 2,4-dichlorophenyl ether.
Trade Names:	CH 3565; Bacti-Stat soap; DP 300; Irgacare MP; Irgacide LP 10; Irgaguard B 1000; Irgasan; Irgasan CH 3565; Irgasan DP 30; Irgasan DP 300; Irgasan DP 3000; Irgasan PE 30; Irgasan PG 60; Microban Additive B; Microban B; NM 100; TCCP; THDP; Tinosan AM 100; Tinosan AM 110; Tinosan NW 500; Tinosan CEL Liquid; Ultrafresh NM 100; Vinyzene DP 7000; Yujiexin; Zilesan UW
Molecular Formula:	C ₁₂ H ₇ Cl ₃ O ₂
Structural Formula:	
Molecular Weight:	289.54

3.2 Impurities and additives

Commercial grades of triclosan are typically over 99% pure. Impurities that may be present in trace amounts are:

- 2,4 Dichlorophenol
- 3-Chlorophenol
- 4-Chlorophenol
- 2,3,7,8 Tetrachlorodibenzo-p-dioxin
- 2,3,7,8 Tetrachlorodibenzo-furan
- 2,8-Dichlorbenzo-furan
- 2,8-Dichlorbenzo-p-dioxin
- 1,3,7 Trichlorodibenzo-p-dioxin
- 2,4,8 Trichlorodibenzo-furan

There are no permitted levels of impurities specified for triclosan in the British Pharmacopoeia (BP). Information on impurities of triclosan imported into Australia were compared to the maximum permitted levels of impurities in the US and Canada. The United States Pharmacopoeia (USP) sets a concentration limit for the following impurities in triclosan: less than 10 µg/g for monochlorophenols; less than 10 µg/g for 2,4-dichlorophenol; less than 0.25 µg/g for 1,3,7-trichlorodibenzo-p-dioxin; less than 0.5 µg/g for 2,8-dichlorodibenzo-p-dioxin; less than 0.25 µg/g for 2,8-dichlorodibenzofuran; less than 0.5 µg/g for 2,4,8-trichlorodibenzofuran; less than 1pg/g for 2,3,7,8-tetrachlorodibenzo-p-dioxin; and less than 1pg/g for 2,3,7,8-tetra chlorodibenzofuran (USP, 2004). Canada also regulates the dioxins and dibenzofurans in triclosan (see section 2.1).

From the data submitted, the imported grade of triclosan from the major local importer meets the specifications of the current edition of the USP. For the remaining local importers of triclosan, it could not be conclusively determined for three importers from the data submitted whether the imported grade of triclosan met the specifications of the current edition of the USP.

Evidence is available that some grades of triclosan traded commercially may not meet USP specifications. Analysis of triclosan manufactured by five different producers in India and a producer in China for the presence of 2,3,7,8-tetrachloro-dibenzo-p-dioxin and 2,3,7,8-tetrachloro-dibenzofuran indicated the samples did not meet USP specifications (Menoutis and Parisi, 2002). Levels of 2,3,7,8-tetrachloro-dibenzo-p-dioxin and 2,3,7,8-tetrachloro-dibenzofuran were observed to range from 17.2 to 1720 pg/g and 0.43 to 207.3 pg/g respectively.

3.3 Physical and chemical properties

3.3.1 Physical state

Triclosan appears as a white to off-white crystalline powder with a faint aromatic odour (Merck Index, 1983). The chemical is commercially available in solid form. The purity for triclosan for commercial use is 99% minimum (Ciba Specialty Chemicals, 2001a).

3.3.2 Physical properties

Few published data on the physical properties of triclosan could be located. Values derived from data provided by the applicants and where possible, published sources are summarised in Table 3.2.

Table 3.2 - Physical properties of triclosan

Property	Value	Reference
Melting point	54 ⁰ C to 57.3 ⁰ C	Merck Index (1983)
Decomposition temperature	280 ⁰ C to 290 ⁰ C	Fiege et al. (2000)
Density	1.55 g/cm ³ at 22 ⁰ C	Ciba-Geigy Limited (1990a)
Specific gravity	1.58 ± 0.03	Ciba Specialty Chemicals (2001a)
Solubility		
Water	0.001g/100g (1x10 ⁻⁵ g /mL) at 20 ⁰ C	Ciba Specialty Chemicals (2001a)
<i>n</i> -hexane	8.5 g/100g (0.085 g/mL) at 25 ⁰ C	
ammonium hydroxide	0.30 g/100g (0.003 g/mL) at 25 ⁰ C	
acetone	> 100 g/100g (> 1.0 g/mL) at 25 ⁰ C	
PKa (acid dissociation constant)	7.9	Merck Index (1983)
Vapour pressure	4 x 10 ⁻⁶ mm Hg (4 x 10 ⁻⁴ Pa) at 20 ⁰ C	Merck Index, (1983)
	2.6 x 10 ⁻² mm Hg (2.6 Pa) at 100 ⁰ C	Fiege et al. (2000)
Partition coefficient (<i>Log P_{ow}</i>)	4.8	Ciba-Geigy Limited (1990b)
Henry's Law Constant	0.000000005 (estimated) atm/m ³ mole at 25 ⁰ C	PBT Profiler (2004)
Autoignition temperature	> 350 ⁰ C	Ciba Specialty Chemicals (2001a)

3.3.3 Chemical properties

Triclosan is produced by treatment of 2,4,4'-trichloro-2'-methoxydiphenyl ether with aluminium chloride in benzene under reflux. Under extreme conditions such as high alkalinity and heat, conversion to chlorinated dibenzo-*p*-dioxins can occur (Fiege et al., 2000). The type and purity of the starting materials in the synthesis of triclosan will influence the extent of contamination by the impurities dioxins and dibenzofurans.

Triclosan is sparingly soluble in water, moderately soluble in dilute alkaline solutions, and readily soluble in most organic solvents. While triclosan in powder form is highly stable to intense radiation, solutions may show instabilities when exposed to intense UV-light radiation. Additionally, solutions are not stable to chlorine and have only moderate stability in the presence of oxidising compounds (Ciba Specialty Chemicals, 2001a).

Triclosan has some volatility in steam. When a suspension of 1000 mg triclosan in 800 ml water is distilled, 180 – 200 mg triclosan are found in the first 500 mL of the distillate (Ciba Specialty Chemicals, 2001a).

3.4 Methods of detection and analysis

Various methods are described in the literature to analyse triclosan and more generally, organic halogen compounds and chlorophenols in a variety of media. Some of the main methods include High Performance Liquid Chromatography (HPLC) and Gas Chromatography/Mass Spectrometry (GC/MS). The methods of detection and analysis of triclosan are provided in **Part 2, Section 13**.

3.5 Manufacture, importation and use

3.5.1 Manufacture and importation

Data provided by applicants indicated no manufacture of triclosan occurs in Australia. The APVMA provided the information on triclosan imported into Australia in pesticides and veterinary medicines or as a raw material to formulate them. Quantities of triclosan used for therapeutic purposes were identified in surveys undertaken by NICNAS in 2004 and 2006.

In addition, telephone and written surveys of a number of users of triclosan in the textile and plastics industries were conducted in 2004. Information in this chapter is based on data from these sources.

Triclosan is imported into Australia both as the raw chemical (>99% powder), as a liquid solution (10% to <20%), and as an ingredient in various products. Types of imported products containing triclosan include non-therapeutic personal care and cosmetic products, therapeutic goods, textile additives, plastics additives, and grout. In addition, it is probable that finished plastic and textile articles that have been manufactured with triclosan additives are imported into Australia.

Table 3.3 below shows the total amount of triclosan imported into Australia for the years 2001-2005. The figures do not take into account any triclosan imported as part of finished plastic and textile articles, as no information was provided on the triclosan quantities in imported articles. Articles such as these fall outside the scope of this assessment.

Raw triclosan is imported into Australia as a powder (purity >99%) under the brand names Irgasan DP 300, Irgacare MP, Irgaguard B1000, Cansan TCH, and Triclosan USP25 in 20, 25 and 30 kg antistatic polyethylene lined fibreboard containers. Triclosan is also imported as 10%-<20% aqueous solutions, under the brand name Irgacide LP 10, in 30 kg blue plastic drums. The containers and drums are imported by sea freight and transported typically by road and rail within Australia directly to customers without being opened or re-packed by importers. Triclosan is occasionally stored in warehouses prior to delivery to customers.

Table 3.3 - Importation of triclosan into Australia annually from 2001 to 2005 (approximate)

Year	Raw triclosan (>99% purity) (tonnes)	Triclosan contained in imported products (tonnes)	Total (tonnes)
2001	27	3	30
2002	27	4	31
2003	26	2	28
2004	22	1	23
2005	20	1	21

Imported textile and plastic additives containing triclosan are stored by importers in licensed warehouses and mostly transported to customers unopened, although one importer formulates a plastic additive product using raw imported triclosan. Information from one importer indicates that personal care and cosmetic products are transferred from ships to trucks by cranes and forklifts, transported by road to the importer's warehouse, and thence to customers.

3.5.2 Uses in Australia

Triclosan is imported into Australia both as the raw chemical and as an ingredient in various products. In Australia, triclosan is an ingredient in non-therapeutic cosmetic and personal care products, therapeutic products, veterinary products, pesticides, household and industrial cleaning products, grouting material, tile paint, and laminate paint. It is also incorporated in the manufacture of some plastics and textile products, and is probably present in some imported finished plastic and textile articles. Triclosan is used for its broad-spectrum anti-microbial activity against bacteria, as well as moulds and yeast.

3.5.3 Industrial uses

Cosmetic and personal care products

Approximately 200 cosmetic and personal care end products containing triclosan were imported into Australia from 2001 - 2005. The concentration of triclosan in these formulations ranges from 0.00125% to 0.87% and equates to approximately 2 tonnes of triclosan imported annually. Cosmetic and personal care products ranging in size from 5 mL to 500 mL are imported in the form of soaps, creams, gels, sticks, liquids, and powders, in pre-packaged tubes, jars, and bottles.

It is estimated that about 45% – 59% of the total amount of triclosan imported annually into Australia (as 100% powder or 10% aqueous solution) is used in the formulation of personal care and cosmetic products. Therefore, the total amount of triclosan present in personal care and cosmetic products in Australia, from both imported finished products, and from products formulated within Australia, is estimated to be approximately 11 – 18 tonnes per annum (see Table 3.4).

Table 3.4 – Estimated amount of triclosan in cosmetic and personal care products (non-therapeutic) annually from 2001 to 2005.

Year	Tonnes (approximate)		
	Present in imported finished end products	Formulated into products in Australia	TOTAL
2001	2.1	15.9	18.0
2002	1.8	14.3	16.1
2003	1.1	15.0	16.1
2004	0.9	9.9	10.8
2005	0.9	11.6	12.5

The following is a list of cosmetic and personal care product types containing triclosan marketed in Australia, compiled from data provided to NICNAS by industry for this assessment:

- Body sprays
- Underarm deodorants (spray, stick, roll-on)
- Feminine deodorants
- Colognes
- Foot and shoe deodorant sprays and talc
- Soaps, including liquid hand wash, shower and bath gels
- Face and skin cleansers, moisturisers, toners, exfoliants
- Facial masks
- Eye make-up
- Pre-wax skin wipes
- Baby wipes
- Skin purifying patches
- Anti-acne formulations
- Cuticle and nail conditioners
- Toothpaste
- Mouthwash
- Cotton buds
- Sunscreens
- Insect repellents

Use in household and industrial cleaning products

Triclosan is present in a number of household and industrial-grade cleaning products formulated in Australia, at concentrations ranging from 0.04% – 0.30%. No household or industrial-grade cleaning products containing triclosan were imported into Australia. The total amount of triclosan used in Australia for the formulation of these products for the years 2001 – 2003 is estimated to be at least 0.5 tonnes annually. Limited data was provided for 2004 and 2005, and so no estimates are made for these years. Products notified to NICNAS by industry for this assessment included:

- Dishwashing detergents
- A wool wash laundry detergent

- Bathroom surface cleaning products
- A commercial kitchen surface cleanser
- A hospital grade disinfectant/cleaner
- Floor mop cartridges

Household cleaning products are packed in 500 mL, 600 mL, 750 mL and 1 L containers, while the industrial-grade products are packed variously in a 750 mL trigger container, 500 mL, 1 L, 5 L, 15 L and 25 L containers.

Use in textile manufacture

Textile additives containing triclosan are imported as liquids in 20 L, 25 kg, and 30 kg plastic containers and 200 L drums, and as a powder in 25 kg containers.

Triclosan is used in textiles to impart odour-protection properties to wool, synthetics, blends, and non-wovens by inhibiting the growth of bacteria and fungi on these surfaces, and to eliminate house dust mites from material.

Several products containing triclosan for use in textile manufacture have been imported into Australia from 2001 to 2005. These products contain triclosan at concentrations ranging from >1% to <20%. It is estimated less than 1 tonne of triclosan was used annually between 2001 and 2005 in these products. One formulator of a product for use in textile manufacture has been identified in Australia. This company uses an imported textile additive solution containing 1.25% triclosan as an ingredient in a chemical product used for coating fabric subsequently used in the manufacture of vertical blinds. No other formulators of textile additive products were identified.

The following is a list of textile end-use products manufactured in Australia that use a triclosan additive in their manufacture:

- Wool bedding
- Quilts (wool filling)
- Pillows (wool filling)
- Doona filling (polyester blend)
- Under-blankets
- Furniture upholstery
- Woollen goods and general textiles
- Towels
- Curtains, blinds
- Fashion, swimwear and sports apparel
- Hosiery
- Socks
- Shoe insoles
- Zippers
- Insulation bats

Application of triclosan to textile products is generally by inclusion in a dye bath, other treatment baths, or by padding. One manufacturer of polyester blend wadding sprays a triclosan solution on to batches of textile. The chemical coating treatment for vertical blind fabric is reported to be applied by a knife coating technique.

Generally the products are completely applied and no waste is expected to be generated.

It is not known how much triclosan is imported into Australia in finished textiles, such as bedding and clothing. Such products are classed as 'articles' under the *Industrial Chemicals (Notification and Assessment) Act 1989* and as such are outside the scope of this report. A market and internet web page survey by the Danish Environmental Protection Agency for textile articles (Danish Environmental Protection Agency, 2003a) containing biocides, including triclosan, indicates that the following types of imported textile articles may contain triclosan: clothing for hospital workers, hospital bedding, sports clothing, socks, and tights. Triclosan is either built-in to the textile fibres during manufacture or applied as a coating by various techniques (Danish Environmental Protection Agency, 2003a). A NICNAS search of web pages marketing antibacterial products undertaken in 2004 indicated that the following types of products may also contain triclosan: mattress pads, pillows, sports clothing, shoes, underwear, socks, tights, gloves, hats, scarves, sleeping bags, pet beds, non-woven wipes, filters, and surgical type masks (Sterling Fibres, 2005; Safety and Security Centre, 2003; Manufacturabrasil, 2004).

Use in plastic manufacture

Plastic additives containing triclosan are imported as liquid in 25 kg and 100 kg plastic drums, as granules in 20 kg plastic bags, and as pellets in 20 kg, 25 kg or 30 kg polyethylene lined fibreboard drums and 200 kg plastic lined drums with seal system.

Triclosan is used in plastics manufacture as an antimicrobial additive, to protect the articles from deterioration and from odours and discoloration.

Several products intended for this use have been imported between 2001 - 2005, containing triclosan at concentrations ranging from $>1\%$ - $\leq 10\%$. In addition, some plastic additive products, containing $\leq 5\%$ triclosan, are formulated in Australia from imported raw triclosan. The total annual amount of triclosan used in plastics additives annually is estimated to be approximately 0.5 tonne.

Plastic end products manufactured in Australia using triclosan additives include various household moulded plastic products including:

- Food storage containers
- Wheelie bins
- Toilet seats
- Toilet tidy sets
- PVC carpet backing
- Swimming pool liners
- Toothbrushes, and
- Pet accessories such as litter trays, food bowls, and Frisbees.

Triclosan is also used in the manufacture of a cling wrap for export, which contains triclosan at 0.6 % concentration.

It is not known how much triclosan is imported into Australia already incorporated into finished plastic products. Some of the types of imported plastic products that could incorporate triclosan include: domestic and commercial kitchenware such as

food storage bins, knives, cutting boards, sponges, appliances, gloves, kitchen and bathroom fixtures, medical devices, toys and high chairs, and flooring materials (Ciba Specialty Chemicals, 2001a).

Other industrial uses

A product containing triclosan is being developed in Australia for use as an antimicrobial treatment agent for air conditioning heat exchange coils. The product, a spray-on aerosol containing 0.6% triclosan to be used by air conditioning service contractors, has not yet been released for sale. To date < 1 kg has been used annually in development.

There is very limited use of triclosan in grout, with one such product containing the chemical imported into Australia.

Triclosan is added to some oil-based paint formulated in Australia for interior use on tiles and laminates, as an antimicrobial agent, at a concentration of 1g/L. The amount of triclosan used annually for this purpose is <0.1 tonne.

3.5.4 Non-industrial uses

Therapeutic uses

In 2003, triclosan was an ingredient in 84 therapeutic goods registered on the Australian Register of Therapeutic Goods (ARTG). For 56 of these products, triclosan is the 'active' ingredient, meaning that therapeutic claims are being made with respect to the triclosan as used in that product. For the remainder of the products (28), triclosan is listed on the ARTG as an 'excipient' ingredient, meaning that triclosan is not the ingredient in the product responsible for the making of therapeutic claims. Generally the triclosan in these latter products is considered as a preservative rather than a bacteriocide. The concentration of triclosan in therapeutic goods ranges from 0.5 mg/g to 20 mg/g.

As stated in Section 1.3, NICNAS conducted two surveys of the registrants of therapeutic goods containing triclosan listed on the ARTG in 2004 and 2006. Survey responses indicated that most therapeutic products are formulated in Australia from locally sourced triclosan. A small number (10) are imported as finished products. Twenty-eight of the 84 registered products were not being marketed at the time of the 2004 survey. From the survey responses, it is estimated that about 39% – 47% of the total amount of triclosan imported either as 100% raw powder or 10% aqueous solution per annum was utilised in the formulation of therapeutic products annually in the period 2001 – 2005. Less than one tonne per annum is imported as an ingredient in finished therapeutic products. Therefore, a total of approximately 10 - 13 tonnes of triclosan was formulated into therapeutic products or imported in finished therapeutic goods, per annum, for the period 2001 – 2005. This data is presented in Table 3.5.

Table 3.5 - Estimated quantities of triclosan present in therapeutic products annually from 2001 to 2005.

Year	Tonnes (approximate)		
	Imported in finished products	Formulated in Australia	TOTAL
2001	0.4	10.5	10.9
2002	0.7	12.3	13.0
2003	0.6	10.7	11.3
2004	0.3	9.2	9.5
2005	0.3	9.3	9.6

The following range of product types are represented:

- Medicated soaps
- Pimple creams
- Burn gels
- Toothpastes
- Insect repellents
- Antiseptic hand washes and barrier lotions
- Bath oil emollient
- Face washes,
- A pre-operative surgical liquid hand wash
- Lip balm
- Sunscreens
- Surface disinfectant

Veterinary uses

Triclosan is an ingredient in 22 products used for veterinary purposes: six pet shampoos, fifteen insect repellents, and a cattle teat ointment. The approximate total annual amount of triclosan used in these products is less than 66 kg per year.

3.5.5 Overseas uses

Overseas, triclosan is reported to be used in a similar range of products as reported in Australia, including cosmetic and personal care products, dermatological and topical care preparations for the skin, dentifrices and oral rinses, dishwashing and laundry detergents, fabric softeners, surface cleansers, and in textiles and plastics (Bhargava and Leonard, 1996; European Commission Health & Consumer Protection Directorate-General, 2002b; Ciba Specialty Chemicals, 2001b; US NPIRS, 2005).

Overseas uses reported in the literature but not reported in Australia include as an ingredient in toilet cleaners and as a biocide in cutting oils (Grattan et al., 1989).

Information from a technical brochure for a product marketed in Australia primarily for use as a textile additive states it can be: used as a laundry additive to be used with softener in the final rinse stage; added to pigment presscakes, dispersion and inks; used for carpet cleaning; and applied to synthetic and cellulosic sponges. These uses were not reported as occurring in Australia, and it is not known whether these are uses that occur overseas.

Summary of uses

A summary of the uses of triclosan (industrial and non-industrial) is presented in Table 3.6.

Table 3.6 - Estimated average annual distribution of triclosan in Australia by use category based on information provided for the assessment

Use	Approximate average (tonnes)
Industrial	
Cosmetic/personal care products (non-therapeutic)	15
Household and industrial cleaning products*	<1
Textile additives	<1
Plastic additives	0.5
Therapeutic goods	11
Veterinary use	<0.1

* Based on 2001 to 2003 data. The others are the average of 2001 to 2005 data.

Among the industrial sectors, the cosmetic/personal care sector is the major user of triclosan (Table 3.6), and the use appears to be declining over time (Table 3.4).

The range of uses of triclosan in Australia is very similar to the uses of triclosan overseas.

4. Human Exposure

4.1 Occupational exposure

Occupational exposure to triclosan may occur during transport, storage, repacking, formulation of personal care/cosmetic products, therapeutic products, cleaning agents and paints, treatment of textiles, plastic manufacture and/or during use of end products containing triclosan.

During occupational use of triclosan powder, solutions and triclosan-containing end-use products, the main exposure routes are dermal and inhalation, though ocular exposure may also occur.

In the absence of worker exposure data, exposure to triclosan (except for use of end products) was estimated using the Estimation and Assessment of Substance Exposure (EASE) model (version 2.0 for Windows) developed by the United Kingdom Health and Safety Executive (UK HSE). Occupational exposure during use of end products containing triclosan was estimated according to the European Commission's Technical Guidance Document on Risk Assessment (EC, 2003a). The estimated internal doses resulting from occupational inhalation and dermal exposure to triclosan and the integrated internal doses are summarised in Table 4.1.

Table 4.1 - Internal dose levels for processes using triclosan

Occupational Scenario	Triclosan	Inhalation ($\mu\text{g}/\text{kg bw}/\text{d}$)	Dermal ($\mu\text{g}/\text{kg}/\text{d}$)	Integrated internal dose* ($\mu\text{g}/\text{kg bw}/\text{d}$)
Repacking	100% powder	0.25-0.64 (with LEV)	5.5-55	5.8-55.6 (with LEV)
		0.64-6.36 (without LEV)		6.1-61.4 (without LEV)
Formulation of end products	100% powder	15.9-39.7 (with LEV)	85.5-855	101-895 (with LEV)
		39.7-397 (without LEV)		125-1252 (without LEV)
Textile	13.5% powder	2.14-5.36 (with LEV)	11.5-115	13.6-120 (with LEV)
		5.36-53.6 (without LEV)		16.9-169 (without LEV)
	20% liquid	- **	17-170	17-170
Plastic manufacture	100% powder	15.9-39.7 (with LEV)	85.5-855	101-895 (with LEV)
		39.7-397 (without LEV)		125-1252 (without LEV)
	10% liquid	- **	8.6-86	8.6-86
End use	0.3% maximum	- **	16.7	16.7

*Integrated internal dose is the total dose following inhalation and dermal exposure for the activity undertaken.

**Inhalation dose not calculated as considered negligible.

Although work processes with triclosan in the textile and plastic industry can involve high temperature heating which could result in vapour formation and an increased potential for inhalation exposure, most of the equipment used at high temperatures are closed systems. In addition, inhalation exposure is reduced where local exhaust ventilation (LEV) is present (Table 4.1). Furthermore, workers are

not required to perform any tasks around these 'heat' zones during these operations, and thus the potential for exposure to triclosan vapour is considered minimal.

The EASE model predicts that occupational tasks using 100% powdered triclosan result in the greatest exposure, and for each major occupational task (i.e. repackaging, formulation, and plastic manufacture) the EASE scenario that best describes the process resulted in total internal doses ranging from 5.8 - 895 µg/kg bw/day with LEV (Table 4.1). For textile treatment using 13.5% triclosan powder, the integrated internal dose is much lower, 13.6 - 120 µg/kg bw/day with LEV. Workers handling 10%-20%⁴ liquid forms of triclosan in the textile and plastic industries and handling end-use products containing triclosan are predicted to have lower occupational exposure ranging from 8.6 - 170 µg/kg bw/day (Table 4.1).

In the industrial setting, the real exposure level and subsequent internal dose that workers receive are likely to be lower as the estimations by EASE does not take into account Personal Protective Equipment (PPE) which were reported to be worn at all the sites surveyed by NICNAS. Consequently the use of PPE together with the use of mechanised, closed or partially enclosed work processes mean that the actual exposures are likely to be lower than that predicted by the EASE model.

A detailed analysis of occupational exposure to triclosan is provided in **Part 2, Section 14**. The occupational exposure calculations are detailed in **Appendix C**.

4.2 Public exposure

4.2.1 Adults

Exposure estimations indicate that of the industrial uses of triclosan, for adults in the general public the major source of exposure is likely to be from topical application of cosmetic and personal care products, though inhalation exposure following the use of household surface sprays can also contribute significantly to the overall body burden. However, it should be noted that for cosmetic and personal care products the predicted dermal exposure is based on the combined use of 17 products. The total maximum internal dose is estimated to be 578.1 µg/kg bw/day (Table 4.2). This is considered the worst-case scenario and is obtained from combined exposure through all potential routes of exposure. However, as individual use and hence exposure to these products will vary widely the actual exposure is likely to be significantly less in some sub-populations of the public who do not use these products on a regular daily basis.

In addition to the modelled data, limited measured exposure data are also available arising from the use of personal care products. Generally exposure to single and multiple personal care products containing triclosan resulted in steady state plasma levels of total triclosan less than 40 ng/mL, though higher levels up to 229 ng/mL were also occasionally seen.

The estimated internal doses in adults in the general public for various exposure scenarios following the use of products containing triclosan are presented in Table 4.2.

⁴ Liquid products used in the manufacture of textiles contain >1 % to < 20 % triclosan. For determining a worst-case exposure scenario for textile manufacture it is assumed that the product contains 20 % triclosan.

Table 4.2 - Summary of internal dose levels in adults using exposure models

Public exposure scenario	Inhalation (µg/kgbw/day)	Dermal (µg/kgbw/day)	Oral (µg/kgbw/day)	Total exposure (µg/kg bw/day)
Cosmetic & personal care products ¹	18.0 - 53.9	145.5	24.4	187.9-223.8
Household cleaning products ¹	1.7 – 349.5	0.34	ND	2.04-349.84
Article surfaces	3.8	ND	ND	3.8
Painted surfaces	ND ²	0.56	ND	0.56
Total internal dose	23.5 – 407.2	146.5	24.4	194.4-578.1

¹ Determined for the maximum concentration of triclosan reported for each product type in Australia

² Included under article surfaces

ND=No data

4.2.2 Children

Babies and young children are likely to be exposed to triclosan through use of cosmetic, personal care and household products. Furthermore, breast milk consumption may provide an additional source of exposure. When determining exposures in this assessment a baby is defined as a child less than one year old and exposures are determined in young children up to five years old.

No measured exposure data for babies and young children following use of consumer products containing triclosan was identified in the literature. Consequently, the same exposure models used to predict adult exposure to triclosan from consumer products have been used to predict exposure to babies and young children (see Appendix D). The use data available for these consumer products is for adults with no use data available in literature for babies and young children. Therefore, as a rough approximation of exposure and when considered 'reasonable', the adult use data has been used to predict exposure to babies and/or young children though it is recognised that the predicted values will be over-estimates and should be regarded as such.

With regards to breast milk consumption mean intake values and body weight are taken from the interim draft report of the US Environmental Protection Agency Child-Specific Exposure Factors Handbook (US EPA, 2002).

From the available data it is predicted that in young children the major source of exposure is likely to be from personal care products and accidental/intentional ingestion of toothpaste. For a worst-case scenario, where the exposure from all routes are combined, a maximum total internal dose of 105.3 and 71 µg/kg bw/day in a two and five year old respectively was estimated. For babies it was observed that for an exclusively breast-fed baby exposed to the highest concentration of triclosan detected in an Australian breast milk sample (19 ng/g of milk), the

internal dose of triclosan received was less (3.04 µg/kg bw/day – see Appendix D) than predicted from other sources of exposure in both babies and young children.

A summary of the predicted internal dose level in babies and young children is shown in Table 4.3.

Table 4.3 - Summary of internal dose levels in babies and young children

Public exposure scenario ¹	Inhalation (µg/kg bw/day)	Dermal (µg/kg bw/day)	Oral (µg/kg bw/day)	Total (µg/kg bw/day)
Baby				
<1 year	6.1	90.9	3.0 ²	100.0
Young children				
2 years	5.3	84.5	15.5	105.3
5 years	4.3	56.4	10.3	71.0

¹ Determined for the maximum concentration of triclosan reported for each product type, and observed in a breast milk sample, in Australia

² This is the highest value determined in a 1-month old baby

Maternal and cord blood serum samples received from the Academic Hospital of Groningen, Netherlands were analysed for selected man-made chemicals including triclosan (Peters, 2005). Triclosan was detected in approximately half of the samples analysed (16 out of 39 maternal blood and 8 out of 17 cord blood samples). In maternal blood the concentration of triclosan ranged from 0.1 to 1.3 ng/g serum and in cord blood from 0.5 to 5.0 ng/g serum (limit of detection <0.1 ng/g serum). The levels of triclosan in cord blood were higher than in maternal blood.

Three quarters of the urine samples (2517) collected from the US general population (age 6 years and older from 2003 – 2004) contained free and/or conjugated triclosan (95th percentile = 459.0 µg/L). Concentrations differed by age and socio-economic status but not by race/ethnicity and sex. The concentrations of triclosan appeared to be highest during the third decade of life and among people with the highest household income (Clafat et al., 2007).

A detailed analysis of the exposure of the general public to triclosan is provided in **Part 2, Section 15**.

5. Environmental Exposure

Triclosan is widely used in Australia, particularly in consumer applications (personal care products) and therapeutic products that entail discharge to sewer, and to natural surface waters after treatment.

5.1 Environmental fate

The water solubility of triclosan is low (10 mg/L) but environmentally significant as the solubility allows triclosan to be transported in solution. Triclosan is stable to hydrolysis, but can be regarded as inherently biodegradable in aerobic aquatic environments because of its susceptibility to microbial metabolism. Degradation of triclosan in soil incubated under aerobic conditions proceeds primarily via the formation of methyl triclosan and significant amounts of bound residues. Some mineralization of the residues is observed. In aerobic aquatic systems, triclosan dissipates rapidly from the water phase by degradation and adsorption to the sediment. In both compartments, it degrades to numerous minor metabolites, bound residues and carbon dioxide. Photolysis also contributes to the loss of triclosan from sunlit surface waters. In contrast to its degradation in aerobic environments, triclosan degrades very slowly and is persistent under anaerobic conditions, for example in soil and sediment.

A minor metabolite, methyl triclosan, forms during aerobic treatment of sewage and is discharged in sewage effluent together with residues of triclosan. This metabolite occurs at much lower concentrations than triclosan, but is more persistent and bioaccumulative.

Consistent with its low water solubility, triclosan can sorb strongly to soils and sediment.

5.2 Environmental release

The release of triclosan to the sewage system as a result of its use in personal care products will result in its partitioning to both the aqueous effluent, which is subsequently discharged to receiving waters, and to sludge (nutrient rich organic matter, also known as biosolids).

5.2.1 Aqueous environment

A recent Australian screening study determined the concentrations of triclosan in the effluent from nineteen sewage treatment plants (8 from South Australia (SA), 5 from Queensland, 2 from the Australian Capital Territory (ACT), 1 from Western Australia (WA) and 3 from Victoria) which ranged from 23 ng/L to 434 ng/L with mean and median concentration of 142 and 108 ng/L, respectively. A follow up study on five of these sewage treatment plants in SA and WA indicated substantial removal (72-93%), with influent concentrations of 573-845 ng/L reducing to 60-159 ng/L in effluents discharged to surface waters. There is uncertainty as to whether these data are reflective of larger sewage treatment plants serving major urban populations, for example in Melbourne and Sydney, but these Australian data are comparable to or slightly below overseas measurements.

Recent Australian monitoring in five rivers/estuaries receiving effluents from sewage treatment plants in Queensland has found triclosan at concentrations up to 75 ng/L near the sewage outfall (Ying and Kookana, 2007). The range of concentrations detected was 21-75 ng/L in 2004 and 14-60 ng/L in 2005. Respective effluent concentrations were 51-222 ng/L and 45-187 ng/L. Concentrations were reduced at upstream and downstream sampling locations, both about 200 m from the outfall, particularly during 2005 when sampling occurred under summer conditions conducive to rapid degradation of triclosan. The authors of this study caution that riverine concentrations could exceed 75 ng/L during drought conditions as there would be limited dilution of the discharged effluent. Overseas measurements are comparable to or slightly higher than the Australian data.

Concentrations of triclosan entering and leaving Australian sewage treatment plants have been estimated, based on the assumptions that 96% (Ciba Specialty Chemicals, 1998a) of the import volume is discharged to sewer, and 28-39% (estimated using the SimpleTreat 3.0 model assuming that triclosan is inherently biodegradable or not biodegradable, respectively) of this amount discharged in treated effluent (Table 5.1) for the various levels of sewage treatment possible in Australia. The estimates obtained are about ten to twenty times higher than the measured values listed above. This adds to the uncertainty as to whether the limited available Australian data are truly representative, and indicates a need for further monitoring.

Table 5.1 - Predicted surface water triclosan concentrations using SimpleTreat, reported triclosan removal rates, various levels of wastewater treatment and the estimated Australian triclosan introduction quantity

Level of Treatment	Removal rate (%)*	PEC Freshwater (triclosan, ng/L)	PEC Marine (triclosan, ng/L)
Untreated wastewater	---	14500-17400	1450 - 1740
Primary Treatment	2-96	581-17000	58 - 1700
Secondary Treatment			
Trickling Filter	58-96	581-7300	581 - 730
Activated Sludge	55-99	145-7820	14.5 - 782
Activated sludge (SimpleTreat)	61-72	4070-6780	407 - 678
Tertiary treatment	87-≥99	≤145-2260	≤14.5 - 226

* Removal rate obtained from literature sources. Freshwater and marine PEC values obtained by dividing the estimated effluent concentration by receiving environment dilution factors of 1 and 10, respectively.

5.2.2 Terrestrial environment

Triclosan can be substantially removed by adsorption to biosolids during sewage treatment. The rate of removal is highly variable and dependant on the type and level of treatment of the effluent. These triclosan containing biosolids may be added to soil as an ameliorant. The terrestrial environment may also be exposed to triclosan through irrigation using triclosan containing effluent. The predicted concentrations from these uses are summarized below in Table 5.2.

Recent Australian data from sewage treatment plants in South Australia and Western Australia indicate that biosolids may contain 0.090-16.790 mg/kg triclosan on a dry weight basis. Again, there is some uncertainty as to whether these data are reflective of other parts of Australia, but they are comparable to overseas measurements. The predicted concentration in soil amended with biosolids approaches but does not exceed 1 mg/kg, while limited data indicate that actual levels will be much lower than predicted.

A detailed analysis of the environmental exposure is provided in **Part 2, Section 16**.

Table 5.2 - Soil PECs resulting from use of biosolids and a soil conditioner and treated effluent for irrigation

Parameter	Environment Australia (2003) STP model		ASTE (2004) and Dillon (2000) model	
Estimated quantity of triclosan to sewer (kg/y)	26000		26000	
Estimated quantity of triclosan to sewer (mg/y)	2.60×10^{10}		2.60×10^{10}	
Estimated fraction in sludge based on SimpleTreat model (%)	55% ^a	61% ^b	55% ^a	61% ^b
Estimated sludge triclosan conc. (mg/kg dry wt)	95.6	106	79.9	88.6
Soil Application Rate (tonnes/ha/year)			10	
PEC _{Soil} biosolid application (mg/kg dry wt)	0.735	0.815	0.614	0.681
Influent Concentration (µg/L)	17400	17400	14500	14500
Overall Removal Rate (%)	61% ^a	72% ^b	61% ^a	72% ^b
Concentration in effluent (µg/L)	6.78	4.86	5.66	4.07
Waste water application rate to land (m/ha/year)			1.0	
PEC _{Soil} irrigation (mg/kg dry wt)	0.0521	0.0374	0.0436	0.0313

Notes: The SimpleTreat model output refers only to an activated sludge treatment process. a: Assumes no biodegradation; b: Assumes inherently biodegradable.

6. Human Health Hazard Assessment

6.1 Kinetics and metabolism

Numerous human and animal studies are available on the toxicokinetics of triclosan following both oral and dermal exposure and these are summarized below.

6.1.1 Oral and dermal route

Absorption

Following oral administration of triclosan, absorption from the gastrointestinal tract is rapid and extensive in both humans and animals. Data in one study in humans indicates absorption to be at least 97% while comparative oral and intravenous studies in rodents indicate absorption to be from 70% to ‘virtually complete’. Consequently, for the purposes of this risk assessment, absorption is considered to be 100% following oral administration in humans. Following dermal application of triclosan-containing products, absorption in humans was generally at least 3% to 7%, though at least 14% was observed in one volunteer for a 12 h exposure. Animal data indicates that the extent of triclosan absorption is dependent on the formulation applied. A number of studies in the rat indicate absorption to be 21% to 28% following application in ethanol-based, soap suspension and cream formulations, while skin biopsy and in vitro evidence suggest that the rate of dermal absorption is less in humans than animals. Thus, it is considered that dermal absorption in humans is 14%, as this may be observed in some individuals. In vitro dermal absorption studies using human skin preparations and various formulations containing triclosan showed dermal absorption values for triclosan ranging from 11-20% in these formulations (US EPA, 2008). Additionally, limited buccal absorption was also seen in humans. Following normal toothpaste use absorption was up to 14% of the amount that would be absorbed if an equivalent dosage of triclosan were ingested.

The US EPA evaluated dermal absorption studies on triclosan or its formulations and estimated a dermal absorption value of around 20% for rat skin and possibly a lower value for human skin. The US EPA report stated that additional verification is needed for determination of dermal absorption of triclosan (US EPA, 2008).

Distribution

Triclosan was rapidly removed from the blood, and metabolism data indicate extensive first pass metabolism following absorption from the gastrointestinal tract. The half-life of elimination for orally administered triclosan ranged from approximately 13 to 29 h in humans compared to 10 to 15 h in rats, 8 to 12 h in mice and 25 to 32 h in hamsters. In rodents, radioactivity was widely distributed to organs and tissues following oral or dermal exposure to ¹⁴C- or ³H-triclosan. Well-perfused and excretory organs such as liver, lung, kidney, gastrointestinal tract and gall bladder showed highest levels following oral and dermal absorption in rodents. Additionally, evidence is available in the mouse that suggests that the liver is a specific target organ. Triclosan has also been detected in human breast milk

samples at levels ranging from below the limit of quantification to 19 ng/g milk. However, due to pronounced first pass metabolism the bioavailability of unconjugated triclosan is likely to be very limited following oral exposure. Enterohepatic circulation has been demonstrated in rats, while limited evidence is available for such in mice and hamsters.

Metabolism

The major metabolic pathways in humans and animals involve glucuronide and sulphate conjugation. Data in rodents indicates that the liver has a high conjugating capacity for triclosan, while human and animal data demonstrate triclosan is metabolised to the glucuronide and sulphate conjugate in the skin. The relative proportion of these metabolites varies depending on plasma steady state of triclosan and these conjugates combined, with higher concentrations resulting in a shift from predominantly glucuronide- to predominantly sulphate- conjugates in rodents and humans. No difference in metabolic patterns was seen between different human racial groups. In humans and rodents triclosan glucuronide and triclosan are predominantly found in the urine and faeces respectively.

Excretion

The major route of excretion is via the urine with the faeces being of secondary importance in humans, hamsters, rabbits and primates following oral exposure, whilst the reverse was seen in rats, mice and dogs. The available dermal data, in rats and rabbits, indicates the same predominant routes of excretion. In humans up to 87% of the administered dose was excreted in the urine and elimination was relatively rapid; the majority of the dose was excreted by 72 h post dose. Though a significant difference was observed in the rate of elimination between some Negroid (black) volunteers compared to Caucasians (white), there are no data available to explain why this difference was observed. However, the human oral and dermal data provide no evidence of a bioaccumulation potential. Likewise, the tissue distribution data in rats and hamsters following single and repeated dosing provides no evidence of bioaccumulation in these species, though there is limited evidence in mice that retention of triclosan and/or its metabolites may occur in the liver.

The observance of triclosan and/or its metabolites in human breast milk indicates potential excretion in breast milk. However, the data do not allow a reliable quantitative determination to be made on the potential dose excreted by this route following exposure to triclosan. The first pass metabolism and relatively rapid elimination of triclosan, though, suggest that the potential for transfer to the foetus and bioaccumulation may be limited.

Inhalation route

There are no data on the toxicokinetics of triclosan following inhalation exposure. However, the observation of clinical signs of toxicity such as muscle spasms seen in a repeat inhalation study in the rat indicates that absorption via the inhalation route can occur, but the data do not allow a quantitative estimation of absorption to be made. Furthermore, because first pass metabolism would not take place following exposure by this route, bioavailability of triclosan is likely to be substantially greater than is associated with the oral route, or the dermal route where metabolism of triclosan to its conjugates has been demonstrated in the skin.

A detailed analysis of the kinetics and metabolism is provided in **Part 2, Section 17**.

6.2 Effects on laboratory animals

6.2.1 Acute toxicity

The most recent and well-conducted LD50 study indicates that triclosan has low acute toxicity by the oral route (LD50 >5000 mg/kg bw), though there is evidence from older and less well reported studies that it is moderately toxic and produces nephrotoxicity. No clinical signs of toxicity were observed following a 4 h exposure to an aerosol of 0.15 mg triclosan/L, which was the highest technically achievable rat respirable concentration used in this study. The LC50 was greater than 0.15 mg/L. Due to this very low dose tested in this study it is not possible to derive a conclusion about the acute inhalation toxicity of triclosan. However, in a repeat dose inhalation toxicity study in rats, more than 50% rats died after a single 2-h exposure to 1300 mg triclosan/m³ air. Therefore, LC50 for triclosan is considered as <1300 mg/m³ or <1.3 mg/L. Limited evidence is available that triclosan is of low acute toxicity by the dermal route (LD50 >9300 mg/kg bw for a slurry with propylene glycol) and that its acute toxicity is increased if administered intravenously.

6.2.2 Irritation

The available data shows that triclosan produces both skin and eye irritation in studies in rabbits but is not phototoxic in a study in guinea-pigs. Respiratory tract irritation was observed in rats exposed to triclosan in the repeat dose inhalation toxicity study and therefore, triclosan is considered a respiratory irritant.

6.2.3 Sensitisation

The available data indicate that at most triclosan possesses a very weak skin sensitisation potential in studies conducted in guinea-pigs.

6.2.4 Repeat dose toxicity

Inhalation

In the only available 21-day inhalation study conducted in rats (2 h/day nose only exposure), clinical signs of toxicity and death in the high dose animals at 1300 mg triclosan/m³ air (in 10% ethanol) indicate systemic toxicity. More than 50% rats in the highest dose group died (11 out of 18) on the first two days of the experiment, after a single 2 h exposure, compared to no deaths in other treatment groups or the control group exposed to 10% ethanol. All other observed treatment related effects are due to local irritation for which a NOAEC of 0.05 mg/L was identified.

Oral

Studies are available in the mouse, rat, hamster, rabbit, dog and baboon.

A NOAEL could not be identified in the 13-week mouse study, although a LOAEL of 25 mg/kg bw/day was identified based on effects on haematology parameters, relative liver weight and total cholesterol in both sexes. However, while the mouse is the most sensitive species, there is evidence that (unlike the rat and hamster) it is

sensitive to peroxisome proliferator type effects that are not considered relevant to a human health risk assessment. Consequently, a NOAEL of 40 mg/kg bw/day (m) and 56 mg/kg bw/day (f) was identified from a two-year carcinogenicity study in the rat based on clinical chemistry changes, together with histopathological changes in the liver in males and a trend for reduced body weight gain in females.

Dermal

Local irritant effects have been clearly seen in animal studies. A NOAEL of 7.5 and 3.5 mg/kg bw/day was identified in 14-day studies in male and female rats, respectively. No systemic toxicity was seen in the rat studies and the only available robust dog study. However, histological changes to the liver were seen in two 14-day studies in the mouse, with a NOAEL of 20 and 24 mg/kg bw/day identified in males and females respectively.

In a 90-day rat study, no treatment related effects were seen on mortality, clinical signs of toxicity, body weight gain, food or water consumption, haematology, clinical chemistry or organ weight. Coagulative necrosis of the liver, focal cortical tubular degeneration of the kidney and microscopic changes to the bladder were seen at necropsy in a small number of animals. In the absence of a dose response effect these observations were not considered treatment related. Occult blood was seen in the urine of 3 to 4 males per group at 40 mg/kg bw/day and above, including the recovery group, and 2 females in the 40 mg/kg bw/day and recovery group. However, as the significance of this finding is unknown, it is not considered to provide reliable evidence of systemic toxicity based on the weight of evidence, and a NOAEL of 80 mg/kg bw/day is identified. For local irritant effects a NOAEL could not be identified, and thus the LOAEL was 10 mg/kg bw/day.

6.2.5 Genotoxicity – in vitro

Negative results have been seen in numerous studies in bacteria, with only a single weakly positive result seen in a briefly reported study at a very high dose level. Similarly, no robust evidence of an in vitro mutagenic activity was seen in studies in fungi or mammalian cells. Both a positive and negative chromosome aberration study is available, while only negative results were seen in Unscheduled DNA Synthesis (UDS) assays. Thus, the weight of evidence (a single robust positive chromosome aberration assay from numerous in vitro studies) does not indicate a significant genotoxic potential.

6.2.6 Genotoxicity – in vivo

In vivo, negative results have been seen in a number of bone marrow chromosome aberration and micronucleus studies. Both a negative and positive result has been seen in the mouse spot test though there are limitations in the methodology employed in both studies. Similarly, there are limitations in methodology in the available studies in germ cells that were all negative. Therefore, there is no robust evidence of a genotoxic potential in vivo.

6.2.7 Carcinogenicity

Neither of the carcinogenicity bioassay conducted in the rat or hamster provided evidence of a carcinogenic potential.

6.2.8 Fertility

No evidence of an effect on fertility was seen in a two-generation dietary study in the rat. Furthermore, data from numerous repeat dose studies of 90-day or longer duration that examined the reproductive organs support the finding of the only available fertility study.

6.2.9 Developmental toxicity

No evidence of a developmental effect was seen with triclosan in robust studies in the rat at doses that produced marked maternal toxicity. Additionally, no evidence of a postnatal developmental effect was seen in this species. Similarly, no evidence of a developmental effect was seen at a level that produced marked maternal toxicity in the only available study in the rabbit. In the mouse, the only treatment related finding of delayed ossification of forelimb phalanges is considered to be a secondary non-specific consequence of maternal toxicity. Therefore, the available data in animals provide no evidence that triclosan has a direct effect on development. The NOAEL for both developmental and maternal toxicity is 50 mg/kg bw/day.

6.2.10 Antimicrobial resistance

Recent laboratory studies

Data from recent laboratory studies of resistance mechanisms, sometimes in clinical isolates, more usually with laboratory generated variants, have demonstrated the following four resistance mechanisms, which have been manipulated both genetically and biochemically in the laboratory:

- mutational change in gene(s) encoding the target enzyme EAR such that binding of triclosan and thus inhibition of EAR and fatty acid synthesis does not occur⁵;
- mutational changes leading to overproduction of EAR within the cell such that some molecules of EAR escape the inhibitor and thus remain active⁵;
- impermeability of the bacterial cell envelope such that triclosan does not readily penetrate beyond this outer layer of the cell⁶; and
- effects on efflux pumps that pump triclosan (usually along with other xenochemicals such as antibiotics and other biocides) from the cell such that the triclosan concentration does not rise to a damaging level within the cell⁵.

Though there is sometimes disagreement as to which mechanism(s) is primarily responsible for triclosan resistance, and whether more than one may be functioning, resistance mechanisms involving multidrug efflux pumps and outer envelope impermeability are likely to give rise to cross resistance towards other biocides and antibiotics.

⁵ A form of selected resistance.

⁶ A form of intrinsic resistance.

Studies from clinical or natural settings

Overall these recent environmental studies, and analyses of clinical isolates from collections taken over the course of time, point to the conclusion that the use of biocides (including triclosan) in homes and hospitals has not lead to any notable selection of antibiotic resistance in bacteria, nor where it has been examined, to cross resistance.

Physiological fitness of bacteria resistant to biocides and antibiotics

By varied measures of physiological fitness, mutants of both *Pseudomonas aeruginosa* and *Stenotrophomonas maltophilia* that overproduce multi-drug efflux pumps were found to be significantly less fit than their parental wild types in a number of important regards. The mechanism by which this occurs remains for the moment a matter for speculation.

Overall conclusions regarding antibiotic resistance

The studies up to 2002 reviewed both by the European Union Scientific Steering Committee (see EC Health & Consumer Protection Directorate-General, 2002a) and those studies published between 2002 and 2005 reviewed here, published since 2002, show that triclosan resistance is readily generated in a range of bacterial species (both gram positive and negative) by selection under laboratory conditions in partially inhibitory concentrations of triclosan. In contrast, triclosan resistant mutants are present at low frequency in natural (including clinical) isolates of gram-positive and gram-negative bacteria. Furthermore, investigations to determine if the frequency of triclosan resistance has risen as a result of exposure of natural populations of bacteria to this biocide have shown minor or no change. Therefore, the data suggest that conditions exist in laboratory experiments that differ in some important way(s) (unidentifiable from the experiments reported) from conditions which natural populations experience.

Hence, overall, the new studies available since the EU review provide no evidence that triclosan poses a risk to humans or to the environment by inducing or transmitting antibacterial resistance under current conditions of use. Though the recent limited number of studies do not resolve specific technical/use issues identified by the SSC (see EC Health & Consumer Protection Directorate-General, 2002a), and therefore the relationship between the use of biocides and the development of clinically relevant antimicrobial resistance should be kept under regular review.

A detailed analysis of the effects on laboratory animals and other test systems is provided in **Part 2, Section 18**.

6.3 Effects on human health

6.3.1 Skin irritation

There is evidence available that triclosan produces skin irritation in studies conducted with human volunteers, however, there was no evidence of phototoxicity.

6.3.2 Sensitisation

Although there is potential widespread consumer exposure to triclosan only a small number of case studies have been reported where humans who are not atopic have demonstrated positive reactions to triclosan. The available data indicate that at most triclosan possesses a very weak skin sensitisation potential.

There is also only very limited evidence for photo-sensitisation by triclosan in healthy volunteers or those with dermatological conditions.

6.3.3 Repeat dose toxicity

There was no evidence of a treatment related effect in a human tolerance study with oral doses of triclosan up to 30 mg/day for 15 days and 30 mg/day for 52 days. There has also been no evidence of adverse effects in human studies examining the use of personal care products containing triclosan.

A detailed analysis of the effects on human health is provided in **Part 2, Section 19**.

6.4 Regulatory classifications for workplace based hazards

The classification of the health effects of triclosan has been conducted according to the *Approved Criteria for Classifying Hazardous Substances* (the Approved Criteria) (NOHSC, 2004) or, in the case of physicochemical hazards, the *Australian Code for the Transport of Dangerous Goods by Road and Rail* (ADG Code) (FORS, 1998).

The Approved Criteria are cited in the *National Model Regulations for the Control of Workplace Hazardous Substances* (NOHSC, 1994c) and provide the mandatory criteria for determining whether or not a workplace chemical is hazardous.

6.4.1 Physicochemical hazards

Triclosan does not meet the ADG Code (FORS 1998) for classification as a dangerous good on the basis of physicochemical hazards.

6.4.2 Occupational health hazards

Acute toxicity

Based on the available animal data triclosan does not meet the Approved Criteria (NOHSC, 2004) for classification for acute oral and dermal toxicity.

The acute inhalation toxicity data in rats is limited. The dose used in the acute inhalation study was low with no deaths reported (LC50 >0.15 mg/L). However, based on effects seen after a single exposure in a repeat dose inhalation toxicity study, triclosan meets the Approved Criteria (NOHSC, 2004) for classification as 'Toxic by inhalation (R23)'.

Irritation and corrosive effects

Based on the human and/or animal data triclosan meets the Approved Criteria (NOHSC, 2004) for classification as irritating to eyes (R36), respiratory system (R37) and to skin (R38).

Sensitising effects

Based on the available human and animal data triclosan does not meet the Approved Criteria (NOHSC, 2004) for classification as a skin sensitiser.

Effects from repeated or prolonged exposure

Based on the available animal data triclosan does not meet the Approved Criteria (NOHSC, 2004) for classification as causing serious damage to health by prolonged exposure through inhalation, ingestion or dermal contact.

Genotoxicity

Based on the available in vitro and animal data triclosan does not meet the Approved Criteria (NOHSC, 2004) for classification as a mutagen.

Carcinogenicity

Based on the available animal data triclosan does not meet the Approved Criteria (NOHSC, 2004) for classification as a carcinogen.

Reproductive effects

Based on the available animal data triclosan does not meet the Approved Criteria (NOHSC, 2004) for classification as a reprotoxicant, as a developmental toxicant, or for lactational effects.

6.5 Classification and labelling for public health hazards

Scheduling in the SUSDP

The acute oral toxicity of triclosan is greater than 5000 mg/kg bw in rats, and acute dermal toxicity is ≥ 9300 mg/kg bw in rabbits. Triclosan has a LC50 of less than 1300 mg/m³ in rats with 2 h nose-only exposure (expected to be ≤ 650 mg/m³ with 4 h exposure). It is a skin and eye irritant in rabbits. The eye irritation effects were not completely reversible by day 7 (mean score for cornea opacity = 1 on day 7).

Overall based on the toxicity profile, triclosan meets the Interim Guidelines of the NDPSC for scheduling (TGA, 2008).

Triclosan is used widely in a number of consumer products. Based on its inhalation toxicity and irritation effects, inclusion of triclosan in the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP) is considered appropriate with cut-offs and/or exemptions for consumer products.

Details of the hazard classification based on the above are provided in **Part 2, Section 20**.

7. Environmental Hazard Assessment

Ecotoxicity data for several trophic levels (animals and plants) from aquatic and terrestrial environments were available; however, the data were limited in quantity in all categories.

7.1 Wildlife

Based on the data available for two standard test species, triclosan is slightly toxic to birds by the oral route of exposure, with the lowest toxicity data for the bobwhite quail of LD50 862 mg/kg bw (single oral dose).

7.2 Terrestrial invertebrates

Triclosan exhibited very slight toxicity to earthworms, with a recorded no-observed-effect concentration (NOEC) of 1026 mg/kg dry wt. Triclosan did not effect the soil microbial processes of respiration and nitrification at concentration up to 2 mg/kg of dry soil.

7.3 Terrestrial plants

In soils, triclosan is toxic to plants when grown in sandy soil (time-weighted average (TWA) NOEC for cucumber 65 µg/kg); however, toxicity was less (TWA NOEC for cucumber 446 µg/kg) when grown in sandy loam. The attenuation of phytotoxicity is potentially due to the higher organic matter content of the sandy loam soil binding to the triclosan.

7.4 Aquatic organisms

Triclosan is very toxic to freshwater aquatic organisms with LC50 or EC50 values <1 mg/L (Mensink et al., 1995). From the limited data available, freshwater algae are the most sensitive species (lowest NOEC 0.5-0.69 µg/L and 72-96 h EC50 0.7-1.4 µg/L). Morphological analysis generally indicated enlarged cell sizes when algae were exposed to concentrations ≥ 2.2 µg/L. Data from two algae studies involving the assessment of recovery post-exposure indicates that algae growth resumed, hence, triclosan is algistatic rather than algicidal at concentrations up to 13 µg/L.

Data for freshwater algae indicates that ecotoxicity decreases slightly in the presence of dissolved organic matter (*S. subspicatus* EC50 3.5 µg/L), perhaps with adsorption to organic matter reducing bioavailability.

In both acute and chronic tests with freshwater invertebrates, EC50 values increase as pH increases, and triclosan is much more toxic to freshwater animals in neutral or acidic waters than in alkaline waters. For example, in a 7 d test with *C. dubia*, the maximum acceptable toxicant concentration (MATC) at pH 7 was ~30 times less than at pH 8.5. The above mentioned data for freshwater algae were obtained from toxicity tests performed under alkaline pH conditions (pH ≥ 7.5) and given the higher toxicity of triclosan to other aquatic animals under neutral to acidic

conditions, the toxicity values for algae may under-estimate algal toxicity through the full environmental pH range.

Triclosan was highly toxic to sediment dwelling organisms (the midge *Chironomus tentans* and the freshwater amphipod *Hyalella azteca*) when exposed through the water column. In contrast, exposure of the the midge *Chironomus riparius* to triclosan through spiked sediment showed no effect at concentrations up to 100 mg/kg dry sediment.

Limited data are available for the toxicity of triclosan to marine organisms. The available data indicates that triclosan is highly toxic to grass shrimp with larvae being the most sensitive life stage. Triclosan is also very highly toxic to the marine bacterium *Vibio fischeri*.

None of the aquatic toxicity tests undertaken investigated or discussed the actual mode of toxic action of triclosan in the aquatic organisms affected.

Preliminary data indicate that triclosan (or metabolite) is not potently estrogenic to freshwater fish but it may be weakly estrogenic, anti-estrogenic or androgenic.

7.5 Micro-organisms

Triclosan is an antimicrobial compound to many bacteria, fungi, moulds and yeasts. Some species are resistant to triclosan and others are able to use it as a sole carbon source. Effects occur in sensitive micro-organisms at concentrations of ≥ 0.01 ppm.

The limited data available indicate that effect levels of triclosan on activated sewage sludge micro-organisms vary depending on the level of acclimation. A concentration of 2 mg/L inhibited activated sludge micro-organisms that had not been acclimated to triclosan; however, the same concentration had no effect on acclimated organisms. Laboratory-derived IC50 values range from 20-239 mg triclosan/L based on carbon dioxide (CO₂) evolution and glucose utilisation. Triclosan (≥ 2 mg/L) had a slight effect on chemical oxygen demand (COD) removal under laboratory conditions, but had a major inhibitory effect on the nitrification process. Anaerobic sludge digestion was significantly inhibited at a concentration of 10 mg/L. A NOEC for sewage microbes was not available.

A detailed analysis of the effects on organisms in the environment is provided in **Part 2, Section 21**.

8. Human Health Risk Characterisation

8.1 Health risk characterisation methodology

A margin of exposure methodology is used frequently in international assessments to characterise risks to human health (EC, 2003a). The risk characterisation is conducted by comparing quantitative information on exposure to the NOAEL/NOAEC and deriving a Margin of Exposure (MOE) as follows:

1. Identification of critical effect(s).
2. Identification of the most appropriate/reliable NOAEL (if available) for the critical effect(s).
3. Where appropriate, comparison of the estimated or measured human dose or exposure (EHD) to provide a Margin of Exposure (MOE):

$$\text{MOE} = \text{NOAEL}/\text{EHD}$$

4. Characterisation of risk, by evaluating whether the MOE indicates a concern for the human population under consideration.

The MOE methodology was used for characterising occupational and public health risk following exposure to triclosan.

The MOE provides a measure of the likelihood that a particular adverse health effect will occur under the conditions of exposure. As the MOE increases, the risk of potential adverse effects decreases. In deciding whether the MOE is of sufficient magnitude, expert judgment is required. Such judgments are usually made on a case-by-case basis, and should take into account uncertainties arising in the risk assessment process such as the completeness and quality of the database, the nature and severity of effect(s) and intra/inter species variability.

The MOE methodology was used for characterising occupational and public health risk following exposure to triclosan.

8.2 Occupational risk

8.2.1 Occupational exposures

All triclosan used in Australia is imported either as powder or liquid solution. Triclosan is also present in imported end-use products. Exposure to triclosan may occur during:

- Repacking;
- Formulation of personal care/cosmetic products, cleaning agents, and paints;
- Treatment of textiles;
- Plastics manufacture; and

- Use of triclosan-containing end-use products.

Potential routes of exposure to triclosan in the occupational setting are via inhalation and dermal contact. The likelihood of exposure by ingestion in occupational settings is expected to be low.

Exposure monitoring data were not available for levels of triclosan in the air for the different occupational exposure scenarios. Consequently, the UK EASE model (version II) was used to determine both inhalation and dermal exposure.

8.2.2 Critical health effects

Triclosan is of low acute toxicity via the oral and dermal routes. The limited acute inhalation toxicity data indicate a LC50 of less than 1300 mg/m³ (equivalent to 1.3 mg/L) in rats for a 2 h exposure period. The critical health effects from acute exposure to triclosan are skin, eye and respiratory irritation. Skin irritation was observed in both humans and animals following dermal application. Only data in experimental animals are available for eye irritation, which was observed following instillation of triclosan into the eyes of rabbits.

For repeat dose toxicity, the available human data provide no reliable information to identify a robust NOAEL or profile the systemic toxicity of triclosan. Animal data are available for the oral, dermal and inhalation routes of exposure. Overall, the data from rodent studies indicates that the principal effect following ingestion and topical application of triclosan are hepatic effects, with local irritation often seen at the site of contact.

While the mouse is the most sensitive species, there is evidence that (unlike the rat and hamster) it is sensitive to peroxisome proliferator type effects in the liver that are not considered a risk to human health. Consequently, for ingestion a NOAEL of 40 mg/kg bw/day was identified in the rat for mild clinical chemistry and/or haematology changes, with hepatocyte hypertrophy and hepatocyte vacuolisation in cells from males only. In this species no reliable evidence of systemic toxicity was seen in a dermal study up to the top dose of 80 mg/kg bw/day. Irritation of the nasal tract and changes in clinical chemistry parameters were seen in rats in the only repeat dose inhalation study following exposure to an aerosol of triclosan in 10% ethanol at doses more than 50 mg/m³ air.

Triclosan did not cause in vivo genotoxicity, carcinogenicity, reproductive or developmental toxicity in rodents.

8.2.3 Risk estimates

Physicochemical hazards

Triclosan is a non-flammable powder that does not undergo autoignition and has no evidence of an explosive property. It has a melting point of 54 °C to 57.3 °C and decomposition occurs at 280 °C to 290 °C.

Triclosan is stable under normal storage conditions, although solutions are not stable to chlorine and have only moderate stability in the presence of oxidising compounds. Triclosan itself has no oxidising properties. Triclosan powder, like other dusts, may be explosive if ignited when present at a critical concentration in air.

Based on the properties of triclosan the risk from physicochemical hazards during storage and handling of triclosan is considered to be low.

Acute risks due to occupational exposure

The toxicological profile of triclosan indicates that contact with the raw material or concentrated solutions may result in skin and eye irritation. Inhalation of triclosan powder may cause toxicity and irritation to the respiratory tract.

Workplace activities related to triclosan are repacking, formulation, use in textile treatment, plastics manufacture and use of end use products.

Formulation of products containing triclosan is essentially an enclosed, automated process with closed mixing tanks employed.

Similarly at most workplaces textile treatment is essentially an enclosed, automated process. Solutions used contain triclosan at less than 20% concentration, with the exception of one workplace that used a powder containing 13.5% triclosan. At a wool processing plant site with daily exposure, a solution containing 3% or less triclosan is used. Similarly, cleaning of baths through which fabrics or articles are passed in the treatment of textiles is of little concern as the triclosan is very dilute at this point and the baths are first emptied of solution.

Manufacture of polyolefin masterbatches using raw triclosan occurs on a periodic basis. Other plastic manufacturing processes use solutions or plastic pellets containing triclosan. There is little potential for exposure where triclosan is used encapsulated in a plastic matrix, while when solutions are used the maximum concentration of triclosan is up to 10%.

The risk of acute effects such as inhalation toxicity, skin, eye and respiratory irritation during the processes described above is expected to be low due to periodic rather than daily exposure and use of engineering controls such as local exhaust ventilation (LEV) at some workplaces. In addition the reported use of PPE, such as safety goggles and gloves, at some sites would minimise exposure. Nevertheless, there is the possibility of accidental spills as manual handling procedures are employed during repacking, at some stages of formulation such as transfer of raw material to another container or mixing vessel, and during textile treatment such as transfer of triclosan solutions to another container, mixing vessel or dye machine. The manual handling stages are of short duration and potential exposure would normally be minimal. Therefore, overall, the potential for exposure to triclosan is low. Consequently, the risk to workers from handling triclosan is considered to be low.

End-use products

Workers may be exposed to triclosan through the use of commercial personal care and cleaning products containing the chemical. In addition to normal usage, acute exposure of end users to triclosan may occur following accidental spillage. Exposure would not be significant as the maximum concentration of triclosan identified in an occupational end-use product was only 0.3%. Consequently, the risk of acute effects such as inhalation toxicity, skin, eye and respiratory irritation is assessed as low.

Secondary transfer

Manual handling of triclosan and triclosan products occurred during the majority of the identified uses. In addition to the risk of inhalation toxicity, skin, eye and respiratory irritation from acute exposure to triclosan and/or products containing triclosan following direct skin contact and contact with air borne particles, secondary transfer from hands or gloves may also occur. The risk of secondary transfer is expected to be higher in the following situations:

- use of raw material or products containing high percentages of triclosan; and
- where PPE is not used.

PPE was reported to be used at all sites surveyed, and the risk of acute effects from secondary transfer is expected to be low.

Chronic risks

There are no Australian or overseas worker health effects monitoring data available during repacking, formulation, treatment of textiles, and plastic manufacture or for use of end products. Consequently, the UK EASE model has been used to predict exposure, and a NOAEL of 40 mg/kg bw/day was selected for effects on the liver in rats (as described in Section 8.2.2) to calculate MOE for risk assessment. Table 8.1 provides MOEs calculated using the EASE model and the appropriate formulae are detailed in Appendix C.

In deciding whether the MOE is of sufficient magnitude for these occupational scenarios expert judgment is required taking into account the risk assessment process, the nature and severity of effect(s) on which the NOAEL is based, and intra/inter species variability.

With regards to the nature and severity of effects on which the NOAEL is based, not only are the critical effects seen in the two-year rat carcinogenicity study considered minimal but the minor histopathological changes seen in hepatic cells in males only were not consistently seen at the identified NOAEL (40 mg/kg bw/day) in interim sacrifice groups throughout the study. Furthermore, no increase in the severity of these histopathological changes was seen with dose (Part 2, Section 18.4). However, while the effects seen are minimal and the mechanism by which changes arise and their significance for human health is not clear, they cannot be dismissed as being of no significance. With regard to inter species variability there are no data to suggest that humans are more sensitive than animals.

A MOE of 100 or greater is usually not considered a flag for concern as it represents the conservative default uncertainty factors of 10 each for both intra- and inter- species variability used for risk characterisation.

The MOEs for repacking, treatment of textiles, and plastics manufacture using 10% triclosan solution, with and without the use of LEV, were all >100 indicating that the risk of chronic effects to workers from repeated handling of triclosan in these scenarios is low. The MOE for the use of end-use products was also >100. Inhalation exposure was not estimated for the use of end-use products. Inhalation exposure may occur if commercial spray cleaning products are used. However, the triclosan concentration reported in cleaning products ranged from 0.04 % - 0.30%.

Table 8.1 – Calculated margins of exposure (MOE) for effects on the liver for each occupational exposure scenarios

Process		Estimated body burden from		Combined body burden (µg/kg bw/day)	MOE (based on NOAEL of 40 mg/kg bw/day)
		Inhalation exposure (µg/kg bw/day)	Dermal exposure (µg/kg bw/day)		
Repacking (100% powder)	With LEV	0.25 - 0.64	5.6 - 55	5.8 – 55.6	6897 - 719
	Without LEV	0.64 – 6.36		6.1 – 61.4	6557 - 651
Formulation of end-use products (100% powder)	With LEV	15.9 – 39.7	85.5 - 855	101 - 895	396 - 44.7
	Without LEV	39.7 - 397		125 - 1252	320 - 31.9
Treatment of textiles (13.5% powder)	With LEV	2.14 – 5.36	11.5 - 115	13.6 – 120	2941 - 333
	Without LEV	5.36 – 53.6		16.9 – 169	2367 - 237
Treatment of textiles (assumed to be a 20% liquid) ¹	With LEV	-	17 - 170	17 - 170	2353 - 235
	Without LEV	-			
Plastic manufacture (100% powder)	With LEV	15.9 – 39.7	85.5 - 855	101 - 895	396 - 44.7
	Without LEV	39.7 - 397		125 - 1252	320 - 31.9
Plastic manufacture (10% liquid)	With LEV	-	8.6 - 86	8.6 - 86	4651 - 465
	Without LEV	-			
Use of end-use products (0.3%)	With LEV	-	16.7	16.7	2395
	Without LEV	-			

¹ Liquid products used in the manufacture of textiles contain >1% to < 20% triclosan. For determining a worst-case exposure scenario/MOE for textile manufacture it is assumed that the product contains 20% triclosan.

MOEs < 100 were identified for two scenarios. The MOE for formulation ranged from 44.7 – 396 with LEV and 31.9 – 320 without LEV, as did that for plastic manufacture when using raw triclosan powder.

The lower levels of the MOE in these ranges are considered likely to be overestimates. However, as the predictive dermal model is less developed than the inhalation model and its outputs should be regarded as no more than approximations. Furthermore, the semi-automated processes for formulation and plastic manufacture mean that dermal exposure is only likely during manual handling procedures such as transfer of raw material to another container or mixing vessel in the case of the formulation process and as these procedures are of short duration exposure would be minimal. Additionally, EASE does not quantify the actual protection provided by PPE, such as gloves. Risk of chronic effects will therefore be less at workplaces where PPE are used. Consequently, it is considered that the MOEs will be at the higher levels of the predicted range (i.e. >100) and the risk of chronic effects to workers in the formulation and plastics manufacture industry from repeated exposure to triclosan is low.

8.2.4 Uncertainties in occupational risk estimates

Uncertainties in any risk characterisation process arise from inadequate information, assumptions made during the process and variability in experimental conditions. The uncertainties inherent in the characterisation of risk for triclosan arise mainly from inadequate data and include:

- absence of representative atmospheric monitoring;
- absence of dermal exposure data;
- lack of data on the health effects of triclosan in humans following repeated exposures; and
- use of a default oral NOAEL for determination of MOE estimates as no reliable evidence of systemic toxicity was seen in dermal studies in a suitable animal model.

In addition, the assumptions used in EASE modelling add uncertainties to the risk characterisation.

8.2.5 Areas of concern

Risk characterisation has indicated that under occupational conditions the risk to workers of adverse health effects such as inhalation toxicity, skin, eye and respiratory irritation and chronic effects is low. However, the risk of skin, eye and respiratory irritation are likely to increase during accidental spills or leaks of triclosan and/or products containing high concentrations of triclosan, especially where PPE is not used.

8.3 Public health risk

8.3.1 Public exposure - Adults

Exposure may occur through the use of consumer products containing triclosan. The major exposure scenarios are:

- Use of cosmetic and personal care products containing triclosan;
- Use of household products containing triclosan; and
- Use of articles containing triclosan.

Potential routes of exposure are via inhalation and dermal contact. The likelihood of exposure by ingestion is expected to be low in adults.

Measured exposure data are limited for consumer exposure scenarios. Some data are available for repeated use of cosmetic and personal care products. Consequently, exposure models have been used to predict consumer exposure to triclosan during use of various categories of products (see Part 2, Section 15.3) and, as conducted for occupational risk, a MOE methodology has been used by comparing quantitative information on exposure to the NOAEL/NOAEC and deriving a MOE (see Section 8.1 for further details).

The limited measured data available has been used to undertake risk characterisation by an alternative method, namely, comparing it with levels of total

triclosan (i.e. triclosan and its metabolites) in the plasma at the identified NOAEL/NOAEC.

MOE = plasma levels at NOAEL/plasma level following use of consumer product.

As stated previously in sub-section 8.1:

- as the MOE increases the risk of potential adverse effects decreases;
- in deciding whether the MOE is of sufficient magnitude, expert judgment is required; and
- the critical health effects from acute exposure to triclosan are inhalation toxicity, skin, eye and respiratory irritation, and hepatic effects from repeated exposure.

8.3.2 Public health risk estimates - Adults

Acute risks

The potential for acute inhalation toxicity, skin, eye and respiratory irritation could arise as a result of consumer use of:

- cosmetic and personal care products containing triclosan; and
- household products containing triclosan.

The concentration of triclosan in cosmetics and personal care products ranges from < 0.01 - 0.5% and in household goods ranges from 0.04 – 0.3%. At these low concentrations the risk of the irritant effects and inhalation toxicity of triclosan is not expected.

Additionally, textile and plastic articles containing triclosan do not present a risk for inhalation toxicity or skin, eye and respiratory irritation.

Risks from repeated exposure

Potential concerns for repeat dose toxicity arise from those consumer exposure scenarios that involve repeated exposure to triclosan. The use of cosmetic, personal care and household products and articles containing triclosan can all occur on a daily basis and so are relevant.

The calculations of consumer exposure for cosmetic and personal products, and household cleaning products using estimated data (see Part 2, Section 15.3 and 15.4 respectively) are based on the maximum levels of triclosan in each type of product in Australia. Furthermore a worst-case exposure scenario has been determined, that assumed a person was exposed to all possible types of product (e.g. deodorant, body lotion, facial mask etc) containing triclosan. Consequently, it is recognised that the determined body burdens and subsequent MOE range presented are unlikely to be applicable to all consumers (i.e. MOE's would be greater).

Measured plasma levels - cosmetic and personal care products

There is potential for minor hepatic effects to arise as a result of repeated use of cosmetic and personal care products (see Section 8.2.3 chronic effects). Limited studies are available measuring plasma levels of total triclosan in volunteers following repeated use of triclosan-containing cosmetic and personal care products.

Such studies are considered the most appropriate as repeated use allows steady state plasma levels to be reached. A NOAEL of 41 µg/mL (level in animal plasma) for hepatic effects was used to estimate MOE for repeated use of cosmetic and personal care products. A summary of appropriate studies with estimated MOEs derived from measured data are presented in Table 8.2.

Table 8.2 – Calculated margins of exposure (MOE) in adults for effects on the liver from measured exposure to cosmetic and personal care products

Product	Plasma level of total triclosan in humans (ng/mL)	MOE based on plasma levels¹
<i>Single product use</i>		
Hand wash (1%)	229 ²	179
	158 ³	259
Unspecified bath product (0.75%)	Approx 20 - 30	2050 - 1367
Dentifrice (0.2%)	26.7	1536
Dentifrice (0.28%)	22.7 ⁴	1806
	25.7 ⁵	1595
	20.5 ⁶	2000
Toothpaste (0.3%)	132 ²	311
	159 ³	258
<i>Multiple product use</i>		
Soap bar (0.75%) Deodorant (0.39%)	36.7 ⁴	1117
Dentifrice (0.28%)	34.3 ⁵	1195

¹ Calculation based on animal plasma level of total triclosan at the NOAEL: plasma level of 41 µg/mL which is the combined average of male and female values observed at 3, 6, 12, 18 and 24 months.

² Maximum level observed in male volunteers

³ Maximum level observed in female volunteers

⁴ Maximum level observed in Caucasian (white) volunteers

⁵ Maximum level observed in Negroid (black) volunteers

⁶ Maximum level observed in Mongoloid (oriental) volunteers

The lowest MOE was 179 in male volunteers following use of a soap containing 1% triclosan. However, a MOE of 1367 – 2050 was obtained following use of an unspecified bath product containing a comparable amount of triclosan (0.75%). Similarly, while MOEs of 258 and 311 were seen in female and male volunteers following use of a toothpaste containing 0.3% triclosan, MOEs of 1595 – 2000 were seen following use of a dentifrice containing 0.28% triclosan.

Thus, considerable variation has been seen in plasma steady state levels of total triclosan in volunteers following single use of similar products containing similar concentrations of triclosan. Though the majority of the studies, including a multiple product use study with triclosan concentrations ranging from 0.28% – 0.75%, indicate MOEs >1000 which are considered satisfactory, there is evidence of MOEs of approximately 180 – 310 in some studies. Considering the nature of the health effect used to derive the NOAEL (minor histopathological changes in hepatic cells in male rats that were not consistently seen in interim sacrifice groups throughout a carcinogenicity study), all the derived MOEs are considered to

indicate a low risk of chronic effects following repeated use of consumer products containing triclosan.

However, the above data does raise a potential concern, namely, that MOEs lower than those observed may be possible in some individuals through combined use of many products containing triclosan, and/or products containing relatively high concentrations of triclosan.

Risks from repeated exposure to cosmetic and personal care products using estimated exposure data

Information on triclosan concentrations in cosmetic and personal care products was available, however, there was no information on Australian use patterns. Consequently, use patterns and exposure models were adopted from the EU technical guidance document on risk assessment (EC, 2003a) and guidance note for the testing of cosmetic ingredients and their safety evaluation (SCCNFP, 2003). The estimated MOEs are presented in Table 8.3.

Table 8.3 – Calculated margins of exposure (MOE) in adults for effects on the liver from estimated exposure to cosmetic and personal care products

Inhalation (µg/kg bw/day)	Dermal (µg/kg bw/day)	Oral (µg/kg bw/day)	Combined body burden (µg/kg bw/day)	MOE (based on NOAEL of 40 mg/kg bw/day)
18.0 - 53.9	145.5	24.4	187.9 - 223.8	212.9 - 178.7

The body burden level used to estimate MOE is derived from a worst-case scenario, where exposure is assumed to all products containing triclosan by all exposure routes. The estimated MOE range is therefore, a worst-case range. It is expected that for the majority of the population the MOE will generally be at the higher end of the predicted range. However, there may be a subgroup of consumers who repeatedly use multiple products containing triclosan. In this subgroup the MOE may be at the lower end of the predicted range. The estimated MOE range is considered to indicate a low risk by chronic effects following repeated use of consumer products containing triclosan in the majority of the population.

Estimated risk from repeated exposure - household cleaning products

Information was only available on triclosan levels in Australian household cleaning products, and the use patterns and exposure models were adopted from the EU technical guidance document on risk assessment (EC, 2003a). These estimated MOEs are presented in Table 8.4.

Table 8.4 – Calculated margins of exposure (MOE) in adults for effects on the liver from estimated exposure to household cleaning products

Inhalation (µg/kg bw/day)	Dermal (µg/kg bw/day)	Oral (µg/kg bw/day)	Combined body burden (µg/kg bw/day)	MOE (based on NOAEL of 40 mg/kg bw/day)
1.7 - 349.5	0.34	ND	2.04 - 349.84	19608 - 114.3

The estimated MOE range is a worst-case scenario based on exposure to a number of household cleaning products and is unlikely to be reflective of normal use. Exposure to all the cleaning products is also unlikely to occur on a daily basis. It is therefore considered that the realistic MOE is likely to be at the higher end of the predicted range. Consequently, the risk of chronic effects from the use of household products containing triclosan is low.

Estimated risks from repeated exposure – articles

Minimal data on triclosan levels in articles in use in Australia is available. Furthermore, potential dermal and oral exposure from articles containing triclosan could not be determined as no data on the migration of triclosan from such are available. Dermal exposure is based only on contact with painted surfaces. Inhalation exposure was calculated using the OECD Environmental Directorate model (OECD, 1993) and is likely to be an overestimate. However, the derived MOE (see Table 8.5) still indicates that the risk of chronic effects from the use of articles containing triclosan is low.

Table 8.5 – Calculated margins of exposure (MOE) in adults for effects on the liver from estimated exposure to articles

Inhalation (µg/kg bw/day)	Dermal (µg/kg bw/day)	Oral (µg/kg bw/day)	Combined body burden (µg/kg bw/day)	MOE (based on NOAEL of 40 mg/kg bw/day)
3.8	0.56	No Data	4.4	9090

Summary of estimated risks from repeated exposure in adults

Table 8.6 below provides a summary of the data including an overall body burden and MOE when major exposure scenarios are combined. In determining an overall total body burden and MOE for cosmetic and personal care products estimated exposure data has been used, as values are reported in µg/kg bw/day as for other scenarios. Additionally for cosmetic and personal care products, though the MOEs derived from measured data were generally >1000 some studies had values similar to the estimated range.

Table 8.6 – MOEs in adults for exposure scenarios to triclosan

Public exposure scenario	Combined body burden (µg/kg bw/day)	MOE (based on NOAEL of 40 mg/kg bw/day)
Cosmetic & personal care products	187.9 - 223.8	212.9 - 178.7
Household cleaning products	2.04 - 349.84	19608 - 114.3
Article surfaces	4.4	9090
All exposure scenarios combined	194.34 – 578.04	205.8 – 69.2

Individual public exposure scenarios showed MOE ranges greater than 100, indicating low risk (Table 8.6). The higher value in the predicted MOE range for all exposure scenarios combined is similar to that for cosmetic and personal care products, indicating that the greatest contributor to the overall body burden are

from the use of such products. The lower MOE value less than 100 in the predicted MOE range for combined scenario (MOE = 69.3) indicates that there could be risks when using cosmetic and personal care products, and household cleaning products together with exposure to article surfaces by the same person.

8.3.3 Public exposure - children

This section focuses on babies and young children up to five years old. Exposure to this sub-group may occur from direct contact with consumer products containing triclosan. The major exposure scenarios are:

- Use of personal care products containing triclosan; and
- Use of articles containing triclosan.

In addition, exposure to triclosan may also occur via breast milk in breast-fed babies.

Potential routes of exposure are via inhalation and dermal contact, and the oral route from the sucking or mouthing of textile articles and/or breast-feeding.

As for consumer exposure to adults, measured exposure data is limited and exposure models have been used to predict exposure to various categories of products. Additionally, a MOE methodology was undertaken.

8.3.4 Risk estimates - children

Acute risks

As for adults (see Section 8.3.1) the risk of inhalation toxicity, skin, eye and respiratory irritation as a result of exposure to personal care products is low. Articles containing triclosan present a low risk.

Risks from repeated exposure

Limited data are available on the concentration of triclosan and patterns of use for triclosan containing products that may be used on children. In determining exposure to these products assumptions have been made regarding application volume to children (see Section 4.2.2 for more details). Consequently, it is likely that the predicted exposure levels may be over-estimates.

Estimated risks from repeated exposure - personal care products

Dermal exposure was estimated for use of a body lotion on babies and children up to five years old. Additionally, oral exposure was estimated from use of toothpaste in children between one and five years. The data is presented in Table 8.7.

The estimated MOEs are for a worst-case scenario, as the maximum concentration of triclosan in Australian consumer goods likely to be used by children have been taken to determine body burdens. The estimated MOEs for all the age groups are >100 and are based on the minor health effects observed in animals at the selected NOAEL of 40 mg/kg bw/d. Thus, these MOEs for children are considered to indicate a low risk of chronic effects following repeated use of multiple consumer products containing triclosan.

Table 8.7 - Calculated margin of exposure (MOE) in children for effects on the liver from estimated exposure to cosmetic and personal care products

Age (years)	Dermal (µg/kg bw/day)	Oral (µg/kg bw/day)	Combined body burden (µg/kg bw/day)	MOE (based on NOAEL of 40 mg/kg bw/day)
<1	85	N/A	85	471
2	84	15.5	99.5	402
5	56	10.3	66.3	603

Estimated risks from repeated exposure – articles

The OECD Environmental Directorate model (OECD, 1993) was used to determine exposure from a textile or plastic article based on the chemical's vapour pressure. However, no data is available on the leaching of triclosan from articles that would allow potential oral or dermal exposure to be predicted. It is considered that oral and dermal exposure to triclosan through use of articles containing triclosan will be low and, thus, the contribution to the total body burden is likely to be negligible. Dermal exposure to triclosan through contact with painted surfaces has been estimated based on 100% availability from the thin films. The data is presented in Table 8.8 and the derived MOEs indicate that the risk of chronic effects from exposure to articles containing triclosan is low.

Table 8.8 - Calculated margin of exposure (MOE) in children for effects on the liver from estimated exposure to articles

Age (years)	Body burden - inhalation (µg/kg bw/day)	Body burden - inhalation (µg/kg bw/day)	Body burden - total (µg/kg bw/day)	MOE (based on NOAEL of 40 mg/kg bw/day)
Infant				
<1	7.40	5.90	13.30	3007
Children				
2	5.27	0.46	5.73	6981
5	4.28	0.42	4.70	8511

Estimated risks from repeated exposure – breast milk

Exposure was determined in exclusively breast-fed babies based on the maximum level of total triclosan observed in an Australian breast milk study (see Appendix E). The data is presented in Table 8.9 and the derived MOEs indicate that the risks of chronic effects from exposure through breast milk containing triclosan is low.

Table 8.9 - Margin of exposure (MOE) in children for effects on the liver from the maximum level of total triclosan measured in Australian breast milk

Age (month)	Body burden - oral - (µg/kg bw/day)	MOE (based on NOAEL of 40 mg/kg bw/day)
1	3.04	13 158
2	2.46	16 260
3	2.22	18 018
4	2.10	19 048

Summary of estimated risks from repeated exposure in children

Table 8.10 below provides a summary of the data including an overall body burden and MOE when major exposure scenarios are combined. As stated previously the derived MOEs are likely to be overestimates. As for adults, it can be seen that the predicted MOE for all exposure scenarios combined is similar to that for cosmetic and personal care products, indicating that the greatest risk by far comes from the use of cosmetic and personal care products. Furthermore, Table 8.10 also indicates that the lowest risk for children is from exposure through breast-milk containing triclosan.

Table 8.10 – MOEs in children for exposure scenarios to triclosan

Source of exposure	Age (years)	Combined body burden (µg/kg bw/day)	MOE (based on NOAEL of 40 mg/kg bw/day)
Cosmetic & personal care products	<1	85	471
	2	99.5	402
	5	66.3	603
Breast milk	<1	9.82	4073
Article surfaces	<1	13.30	3007
	2	5.73	6981
	5	4.70	8511
All sources of exposure combined	<1	108.12	370
	2	105.23	382
	5	71.0	563

8.3.5 Uncertainties in public risk estimates

Uncertainties involved in the public health risk characterisation for both adults and children result from database limitations. There is a lack of Australian data on the use patterns of consumer products containing triclosan to allow a realistic exposure assessment. Additionally there is very limited measured data, meaning that generally exposure models have been used to determine the sources of exposure

that represent the greatest risk to consumers. Such models are not as reliable as measured data as they mostly use conservative assumptions.

8.3.6 Areas of concern

The available information indicates that public use of triclosan products and hence potential exposure is widespread. The risk characterisation has indicated that under normal conditions of consumer use the risk of adults and children being exposed to levels of triclosan that would lead to adverse health effects such as inhalation toxicity, skin, eye and respiratory irritation and chronic effects is low. Of all the sources of exposure the risk estimation indicated that the lowest MOEs, using modelled data, were from combined use of triclosan containing products (cosmetic and personal care products, cleaning products and exposure to article surfaces). However, the use patterns of triclosan-containing products vary greatly among individuals.

Some studies in humans show a high level of exposure following use of a single cosmetic or personal care product. This raises concerns that chronic health effects may potentially occur in some individuals through the combined use of a range of cosmetic and personal care products containing triclosan, or use of certain products containing relatively high concentrations of triclosan. However, these limited incidences are not reflective of general consumer exposure.

8.4 Biological monitoring data

The population-based biological monitoring data are believed to be a more accurate predictor of aggregate exposure because not only are the data triclosan specific, they are also based on actual consumer use of the various triclosan products as they naturally co-occur (US EPA, 2008). However, there are uncertainties in the biological monitoring data.

In the US EPA aggregated risk assessment, the population-based biological monitoring data based on spot urine concentrations were obtained from the National Health and Nutrition Survey. Based on the results at the mean and 99th percentile, the aggregated risk to triclosan from all uses did not trigger a risk of concern (using an oral NOAEL of 30 mg/kg bw/d in baboons MOEs were >100 even for the most conservative dose and conversion method) (US EPA, 2008).

9. Environmental Risk Characterisation

9.1 Environmental release and degradation

This section provides a characterisation of risks to the Australian environment from use of triclosan as an anti-microbial agent. A risk quotient (RQ) approach has been used to predict the risk to aquatic organisms, terrestrial (soil-dwelling) organisms, and wildlife associated with aquatic and terrestrial environments. To predict an acceptable environmental risk using the RQ approach, the quotient of the predicted environmental concentration (PEC) divided by the predicted no effect concentration (PNEC) needs to be 1 or less (i.e. $RQ \leq 1$).

9.1.1 Environmental release of triclosan

Environmental release of triclosan is unlikely during importation, storage and transportation. Containers of triclosan will be transported directly from port facilities to several industrial facilities throughout Australia for use in the manufacture of various products. In addition, triclosan in finished products will be imported (in ready-to-use products and articles) and distributed throughout Australia for consumer use. Accidental spills, leaks and catastrophic mechanical failure during a transport accident are the most likely reasons for environmental release. Engineering controls (e.g. container specifications) and emergency clean-up procedures (i.e. spill response instructions on Material Safety Data Sheet and label) will limit the impact on the environment of such incidents.

Triclosan is incorporated into cosmetics and personal care products that after application may wash off directly into natural surface waters, such as during bathing and primary aquatic recreational activities. Due to the uncertainty in estimating environmental release by this pathway, no predicted environmental concentration (PEC) in surface waters has been derived. Greater risks to the aquatic environment would be more likely in populated areas during peak usage times, and in surface waters with limited flow or longer hydraulic residence time (e.g. ponds, lakes).

9.1.2 Wastewater treatment plant systems

The majority of triclosan used in Australia will eventually be washed off or otherwise enter the Australian sewerage system where it will mix with a wide range of chemical and biological constituents typically found in wastewater. Most wastewater treatment plants (WWTPs) and sewage treatment plants (STPs) rely on microbial processes to enable treatment and degradation of wastewater constituents. In general, wastewater with inhibitory levels of contaminants may reduce or cease the treatment plant's ability to degrade wastewater constituents, potentially resulting in the release of poorly treated wastewater into the environment in effluent and sludge with potential adverse impacts.

Although triclosan has anti-microbial properties, the international literature indicates that microbial biodegradation processes (e.g. secondary treatment) enable significantly greater treatment and degradation of triclosan relative to primary treatment processes. This indicates that the communities of sewage microorganisms within the STPs tested were capable of treating some if not most

of the triclosan during operational conditions. In addition, variable rates of biodegradation of triclosan, particularly through mineralisation to CO₂, have been demonstrated over time in laboratory tests involving sewage sludge microorganisms exposed to triclosan at concentrations in the range of 10-5000 µg/L, and in one long-term study with a triclosan concentration of 500 000 µg/L (Table 16.3). Furthermore, specific microorganisms have been identified in sewage sludge that are capable of partially mineralising triclosan through a series of co-metabolic steps.

However, biodegradation studies indicate that the rate of biodegradation of triclosan is generally proportional to exposure time and inversely proportional to triclosan concentration, and the degradation rate probably also depends on the microbial community and whether it has been acclimatised to triclosan as well as the environmental conditions (e.g. aerobic versus anaerobic; Table 16.3). At elevated concentrations, triclosan may potentially inhibit sewage microbes, species or communities. At concentrations of up to 20000 µg/L, triclosan was not readily or inherently biodegradable under aerobic conditions and the inability to degrade triclosan is attributed to inhibition of microbial growth as a 3-hour IC₅₀ of 20000 µg/L has been reported. Inhibition of growth, CO₂ evolution and nitrification have been reported under aerobic conditions at concentrations ≥600 µg/L; however, some studies show that inhibition at an exposure concentration of 2000 µg/L may be relatively minor if microbes have been pre-exposed to low concentrations of triclosan. A lag phase before degradation has also been demonstrated in some microbial degradation studies.

For triclosan, anaerobic microbial degradation, a process used in many STPs, is slow relative to aerobic biodegradation. In one study, ~91% of the extractable residues remained as ¹⁴C-triclosan after 147 days of incubation with anaerobic inoculum and anaerobic conditions (Springborn Laboratories Inc., 1994a). Microbial analysis of the sludge during the study indicated that the sludge microbes remained viable.

Based on the estimated use and disposal pattern for triclosan in Australia, a mean annual wastewater concentration for triclosan in the Australian sewerage system of 14500-17400 ng/L (see Section 16.5) has been estimated. Recently, triclosan levels have been measured in the influent of five Australian STPs in concentrations ranging from 573 to 845 ng/L, and triclosan concentrations in secondary and tertiary treated effluents have been observed in the range 23-434 ng/L (with a median measured concentration of 108 ng/L and a mean of 142 ng/L) from 19 STPs (Ying and Kookana, 2007). This compares with a range of <100-740 ng/L in effluent from three primary treated STPs measured in the mid 90s. As a comparison, the available monitoring data from international sources indicate triclosan concentrations in untreated wastewater in the range of <100-562000 ng/L and secondary and tertiary treated effluents of 10-2700 ng/L (see Table 16.54). Hence, estimated concentrations of triclosan in Australian sewage systems are at the lower end of the range of concentrations measured internationally. However the study by Ying and Kookana (2007) did not cover many urban STPs (none in the largest urban areas in Australia) and as a result the full range of triclosan concentrations in influent and effluent across Australia is not yet clear.

STP monitoring studies indicate that a relatively high rate of removal of triclosan (95%) can be achieved after secondary (activated sludge and trickling filter) treatment processes even when the influent triclosan concentration was 7500-

21900 ng/L (Sabaliunas et al., 2003). However, in another STP, removal efficiency of only 35%-42% was achieved after secondary treatment (aerobic digestion) of influent containing triclosan in the range of 30100-37800 ng/L, though at the same STP, a lower influent triclosan concentration of 1300-2600 ng/L resulted in a higher treatment efficiency (69%). At relatively low influent concentrations, the available data from STP monitoring do not indicate a particular trend of decreasing treatment efficiency with increasing triclosan concentration; however, at higher influent concentrations, treatment efficiency apparently declines. Although this apparent trend may potentially be related to inhibition of the microbial processes by triclosan (as discussed above), it is not possible to extrapolate between STPs due to the different treatment processes and environmental conditions and other factors may have also resulted in the lower treatment efficiency of triclosan when at relatively high influent concentrations. The available data has been collected from a range of treatment processes across a number of countries. The measured removal rate for five STPs (3 tertiary and 2 secondary) ranged between 72-93%. However, given that this is a small sample of the nearly 900 STPs across Australia it is uncertain how representative this would be of the wider Australian sewage treatment system. Consequently, the following assessment has been conducted based on the ranges removed that have been observed in international data.

9.2 Aquatic risk

9.2.1 Predicted No Effect Concentration (PNEC) for triclosan

Although triclosan has been used in Australia and internationally for many years, and has been discharged into aquatic receiving environments (freshwater, estuarine, marine) in treated wastewaters and other products, no published freshwater or marine water or sediment quality guidelines were available from the Australian or international literature for triclosan for the protection of aquatic ecosystems. Consequently, predicted no effect concentrations (PNECs) have been derived in this assessment from the ecotoxicity data available using recognised Australian methodology for deriving guidelines (ANZECC and ARMCANZ, 2000).

While no published guidelines are available, several other authors/agencies have also derived PNECs or equivalent values for triclosan for the protection of freshwater organisms:

- The Danish Environmental Protection Agency (Danish EPA, 2003b), using the European Union principles for derivation of Predicted No Effect Concentrations (PNECs), derived a $PNEC_{\text{aquatic}}$ of 0.05 $\mu\text{g/L}$ for triclosan by dividing the lowest available NOEC, for a freshwater alga (0.5 $\mu\text{g/L}$; RCC, 1995), by a safety factor of 10.
- The quality and reliability of the algae toxicity data available for triclosan have been reviewed elsewhere by Hanstveit and Hamwijk (2003) and the NOEC of 0.69 $\mu\text{g/L}$ (*S. subspicatus*; ABC Laboratories, 1997a) was considered the most reliable value in their view, stating that the lower NOEC of 0.5 $\mu\text{g/L}$ (RCC, 1995) was from a test which had discrepancies between the control and acetone control that cast doubt on the incubation conditions used. A PNEC of 0.069 $\mu\text{g/L}$ was derived by dividing this NOEC by an assessment factor of 10.

- The abovementioned PNEC_{freshwater} of 0.069 µg/L (~0.07 µg/L) is also referred to in a Briefing Note prepared by the Environment Agency (2004) and a report of the fate of triclosan in wastewater treatment (Thompson et al. 2005).
- In an environmental risk assessment for Europe (Environ 2006), a surface water PNEC 5th percentile of 1.7 µg/L has been determined using a species sensitivity approach, utilising the NOECs, EC5s, EC10s or EC20s of 16 species. These authors (Environ 2008) have also derived a surface water 5th percentile of 3.5 µg/L using acute EC50 or IC50 data for 17 species as part of an aquatic risk assessment for the United States.

Recent work by Veldhoen et al. (2006) on the effects of triclosan on the development of tadpoles of the North American bullfrog, *Rana catesbeiana* demonstrated alterations in gene expression at concentrations of 0.03 µg/L triclosan. Precocious hormonally-induced metamorphosis was recorded after exposure to concentrations of 0.15 ± 0.03 µg/L triclosan. In isolation, this work is not considered sufficient demonstration that exposure to such concentrations during development in the wild would result in lasting adverse effects such as reduced survivorship. Nevertheless, these early results do indicate the potential for interference with thyroid hormones at extremely low concentrations.

While this study in isolation is considered insufficient to determine the regulatory endpoint, these data contribute to the weight of evidence that adverse effects are likely to occur at concentrations below those measured in the field.

9.2.2 Risk to freshwater ecosystems

Aquatic toxicity data are available for four freshwater taxa with 13 species (acute studies) and three taxa with 10 species (chronic studies).

The aquatic toxicity data available indicate that the green algae (*Scenedesmus subspicatus*) and the cyanobacterium (*Anabaena flos-aquae*) are relatively sensitive to the adverse effects of triclosan (refer Table 21.5). A PNEC_{freshwater} of 0.05 µg/L (50 ng/L) is adopted for this assessment based on dividing the NOEC, for the freshwater alga *Scenedesmus subspicatus* (0.5 µg/L; RCC, 1995), by a safety factor of 10, in line with the Danish Environmental Protection Agency (Danish EPA, 2003b). This is in agreement with the PNEC of 58 ng/L determined using the protective concentration of 0.29 µg/L to protect 95% of species derived using BurrliOZ modelling and applying an assessment factor of 5 in line with the EC Technical Guidance Document (Appendix H). It is also a compromise with the PNEC of 20 ng/L which would be derived from the lowest reported NOEC for green alga (0.2 µg/L for the green alga *Pseudokirchneriella subcapitata*) and applying the same assessment factor of 10.

The derived risk quotients in Table 9.1 based on the predicted environmental concentrations near STP outlets indicate that the current use rate of triclosan presents an unacceptable risk to freshwater organisms. A risk to aquatic organisms is indicated for each type of wastewater treatment considered, from primary to tertiary; moreover, in each case this is so even at the lowest predicted concentration. It should be noted that higher levels of wastewater treatment are applied where the receiving water is freshwater. Unacceptable risk quotients are also predicted based on the limited Australian measured triclosan levels for untreated wastewater, treated effluent and surface waters. The risk quotients for the

measured Australian data are much lower than those for the predicted concentrations.

Table 9.1 - Risk Quotients ($PEC_{\text{Freshwater}}/PNEC_{\text{Freshwater}}$) for freshwater ecosystems based on removal rates for sewage treatment levels

Level of Treatment	Removal rate (%) ^a	$PEC_{\text{Freshwater}}$ (triclosan, $\mu\text{g/L}$)	$PNEC_{\text{Freshwater}}$ (triclosan, $\mu\text{g/L}$)	$\frac{PEC_{\text{Freshwater}}}{PNEC_{\text{Freshwater}}}$
Untreated wastewater	---	14.5-17.4	0.050	290-347
Primary Treatment	2-96	0.581-17	0.050	12-341
Secondary Treatment				
Trickling Filter	58-96	0.581-7.3	0.050	12-146
Activated Sludge	55-99	0.145-7.82	0.050	3-156
Activated sludge (SimpleTreat)	61-72	4.07-6.78	0.050	81-136
Tertiary treatment	87- \geq 99	\leq 0.145-2.26	0.050	3-45
Measured Australian Data				
		$PEC_{\text{Freshwater}}$ (triclosan $\mu\text{g/L}$)	$PNEC_{\text{Freshwater}}$ (triclosan, $\mu\text{g/L}$)	$\frac{PEC_{\text{Freshwater}}}{PNEC_{\text{Freshwater}}}$
Untreated Effluent		0.573-0.845	0.050	11-17
Treated Effluent		0.023-0.740	0.050	0.46-14.8
Surface Waters		0.014-0.070	0.050	0.28-1.4
International surface waters		\leq 2.300 ^b	0.050	\leq 46

a Removal rate obtained from literature sources (see Section 16.5). Freshwater PEC values obtained by dividing the estimated effluent concentration by receiving environment dilution factors of 1. Data are from Table 16.6.

b excludes levels near manufacturing facility

9.2.3 Risk to marine ecosystems

Many large sewerage systems discharge into marine environments, but there is a paucity of aquatic toxicity data for triclosan to marine organisms. In the absence of adequate marine toxicity data, the $PNEC_{\text{freshwater}}$ of 0.05 $\mu\text{g/L}$ is adopted as a PNEC for marine waters for this assessment. This approach is supported by a preliminary review of comparative freshwater and marine ecotoxicity data by ECETOC (2003).

The derived risk quotients in Table 9.2 based on the predicted environmental concentrations indicate that the current use rate of triclosan also presents an unacceptable risk to marine organisms, though the risk quotients are significantly lower than the corresponding freshwater situation. Risk is only marginal from treated effluent based on the available although quite limited Australian figures. While significant quantities of Sydney's wastewater (~75%) are discharged to the marine environment after receiving only high flow primary treatment, Table 9.2

includes data from three of the major plants, including Malabar STP which is responsible for the highest value. However, the risk is acceptable to the Australian marine environment once a minimum level of dilution has taken place.

Table 9.2 - Risk Quotients ($PEC_{\text{Marine}}/PNEC_{\text{Marine}}$) for marine ecosystems based on removal rates for sewage treatment levels

Level of Treatment	Removal rate (%)*	PEC_{Marine} (triclosan, $\mu\text{g/L}$)	$PNEC_{\text{Marine}}$ (triclosan, $\mu\text{g/L}$)	$\frac{PEC_{\text{Marine}}}{PNEC_{\text{Marine}}}$
Untreated wastewater	---	1.5-1.7	0.050	29-34.7
Primary Treatment	2-96	0.058-1.7	0.050	1.2-34.1
Secondary Treatment				
Trickling Filter	58-96	0.058-0.73	0.050	1.2-14.6
Activated Sludge	55-99	0.015-0.78	0.050	0.3-15.6
Activated sludge (SimpleTreat)	61-72	0.41-0.68	0.050	8.1-13.6
Tertiary treatment	87- \geq 99	\leq 0.015-0.23	0.050	0.3-4.5
Measured Australian Data				
		PEC_{Marine} (triclosan $\mu\text{g/L}$)	$PNEC_{\text{Marine}}$ (triclosan, $\mu\text{g/L}$)	$\frac{PEC_{\text{Marine}}}{PNEC_{\text{Marine}}}$
Untreated Effluent		0.0573-0.0847	0.050	1.1-1.7
Treated Effluent		0.0023-0.0740	0.050	0.046-1.48
Surface Waters		0.0014-0.0070	0.050	0.028-0.14

* Removal rate obtained from literature sources (see Section 16.5.2). Marine PEC values obtained by dividing the estimated effluent concentration by receiving environment dilution factors of 10.

9.2.4 Risk to sediment dwelling organisms

Toxicity data are available for two freshwater taxa with 2 species. The most sensitive organism is the amphipod *Hyaella azteca* which has a reported LC50 of 200 $\mu\text{g/L}$ (Dussault et al. 2008). Based on this endpoint and applying an assessment factor of 1000 (based on the lack of data) the $PNEC_{\text{sediment}}$ for sediment dwelling organisms has been determined to be 0.2 $\mu\text{g/L}$. It is inappropriate to use the result of 100 mg/kg for exposure to spiked sediment as aquatic organisms will be exposed through the water column and also the triclosan used in this study was strongly bound to the sediment. The derived risk quotients in Table 9.3 based on the predicted environmental concentrations near STP outlets indicate that the current use rate of triclosan presents an unacceptable risk to sediment dwelling organisms. A risk to sediment dwelling organisms is indicated for each type of wastewater treatment considered, from primary to tertiary; moreover, in each case this is so even at the lowest predicted concentration. Once again, it should be noted that higher levels of wastewater treatment are applied where the receiving water is freshwater. Unacceptable risk quotients are also predicted based on the limited

Australian measured triclosan levels for untreated wastewater and treated effluent. However, the risks based on the measured levels in Australian surface waters are acceptable.

Table 9.3 - Risk Quotients ($PEC_{SDO}/PNEC_{SDO}$) for Sediment Dwelling Organisms (SDO) based on removal rates for sewage treatment levels

Level of Treatment	Removal rate (%) ^a	PEC_{SDO} (triclosan, $\mu\text{g/L}$)	$PNEC_{SDO}$ (triclosan, $\mu\text{g/L}$)	$\frac{PEC_{SDO}}{PNEC_{SDO}}$
Untreated wastewater	---	14.5-17.4	0.2	72-87
Primary Treatment	2-96	0.581-17	0.2	2.9-85
Secondary Treatment			0.2	
Trickling Filter	58-96	0.581-7.3	0.2	2.9-36
Activated Sludge	55-99	0.145-7.82	0.2	0.72-39
Activated sludge (SimpleTreat)	61-72	4.07-6.78	0.2	20-34
Tertiary treatment	87- \geq 99	\leq 0.145-2.26	0.2	0.72-11.3
Measured Australian Data				
		PEC_{SDO} (triclosan $\mu\text{g/L}$)	$PNEC_{SDO}$ (triclosan, $\mu\text{g/L}$)	$\frac{PEC_{SDO}}{PNEC_{SDO}}$
Untreated Effluent		0.573-0.845	0.2	2.86-4.22
Treated Effluent		0.023-0.740	0.2	0.115-3.7
Surface Waters		0.014-0.070	0.2	0.07-0.35
International surface waters		\leq 2.300 ^b	0.2	2.86-4.22

a Removal rate obtained from literature sources (see Section 16.5). Sediment Dwelling Organisms PEC values obtained by dividing the estimated effluent concentration by receiving environment dilution factors of 1. Data are from Table 16.6.

b excludes levels near manufacturing facility

Sediment dwelling organisms also include microbial populations that have been shown to play an important role in the recycling of essential elements such as carbon, nitrogen and phosphorus (Alongi 1994 and Costanzo et al. 2005). The continual discharge of triclosan has the potential to disrupt these microbial populations possibly affecting the recycling of these nutrients.

In addition, there are data to suggest that triclosan accumulates in sediments that are distant from catchment sources (Singer et al., 2002), as well as the persistence of triclosan in sediments.

9.3 Terrestrial risk

Most of the triclosan used each year will, after use, be sent to sewer where treatment in STPs is expected to account for degradation of much of the triclosan

present. However, a fraction entering the sewerage system is expected to partition in the sludge phase with a proportion remaining in the treated water. This is supported by international monitoring data from a range of unit processes. Hence, terrestrial organisms may be exposed to triclosan through contact with STP sludge or treated water containing triclosan. The following sections look at the risk associated with exposure to these sources of triclosan in the environment.

9.3.1 Risk associated with sludge and biosolids from STPs containing triclosan

Traditionally, sewage sludge was disposed of to landfill or incinerated and these practices continue in parts of Australia (e.g. incinerated in the Australian Capital Territory). However, an increasing proportion is being reclaimed as biosolids and re-used for soil conditioning (see Appendix A). For example, in Sydney in 2002-3, Sydney Water Corporation captured solids to the equivalent of ~51000 dry tonnes of biosolids of which 100% was used for soil conditioning applications in agriculture (60%), forestry (20%-35%), land rehabilitation, landscaping and horticulture (5%-20%). The use of biosolids as a soil conditioning agent results in the exposure of soil dwelling organisms such as earthworms as well as crops through their roots and seeds, to triclosan.

Limited data is available for soil dwelling organisms; NOEC values are available for six plant species (Table 21.2) and earthworms (1026 mg/kg dry wt; Section 21.2). Based on this data, an assessment factor of 50 has been adopted for this assessment. The lowest available NOEC is for cucumber of 96 µg/kg (dry wt) (see Table 21.2) resulting in a PNEC of 1.92 µg/kg dry wt. This endpoint is less conservative than the PNEC_{soil} of 0.096 µg/kg (dry wt) derived by the Danish Environmental Protection Agency (2003b), based on dividing the lowest available NOEC by a safety factor of 1000. This PNEC was considered preliminary due to the lack of soil ecotoxicity data available.

The predicted soil (PEC_{soil}) concentrations outlined in Section 16.5.7 (Table 16.63) derived for use of STP biosolids as a soil conditioner have been used to estimate the risk to soil dwelling organisms resulting from this practice (Table 9.4).

The calculated PEC_{soil}/PNEC_{soil} ratios presented in Table 9.4 for the predicted biosolids concentrations indicate potential risks to soil dwelling organisms through the use of sewage sludge contaminated with triclosan as a soil conditioner when used at a rate of 10 tonnes of biosolids per hectare per annum. The PEC_{soil}/PNEC_{soil} ratios derived from the Australian measured data range from an acceptable risk at the lowest measured concentration (0.07 µg/kg dry weight) to an unacceptable risk at the highest measured concentration (129 µg/kg dry weight), with the large range reflecting that of the measured concentrations. Ying and Kookana (2007) reached a similar conclusion based on their data, but with an assessment factor of 1000 (RQ ≤1360).

Consequently, the calculated risk quotients for both the predicted and some of the measured levels of triclosan in biosolids indicate an unacceptable risk when biosolids from STPs are used as soil ameliorants. Given the small amount of the Australian data available it is unclear how representative this is of the levels in biosolids produced across Australia.

Table 9.4 - Risk Quotients ($PEC_{Soil}/PNEC_{Soil}$) for soil dwelling organisms based on the use of sewage sludge as a soil conditioner.

Parameter	Environment Australia (2003) STP model		ASTE (2004) and Dillon (2000) model ^a		Measured Australian Data ^d	
Estimated fraction in sludge based on SimpleTreat model (%)	55% ^b	61% ^c	55% ^b	61% ^c	-	-
PEC_{Soil} (biosolid application) ($\mu\text{g}/\text{kg}$ dry wt)	735	815	614	681	0.07	129
Lowest NOEC ($\mu\text{g}/\text{kg}$ dry wt)	96	96	96	96	96	96
Assessment Factor	50	50	50	50	50	50
$PNEC_{soil}$ ($\mu\text{g}/\text{kg}$ dry wt)	1.92	1.92	1.92	1.92	1.92	1.92
$PEC_{soil}/PNEC_{soil}$	383	424	320	355	0.36	67

Notes: The SimpleTreat model output refers only to an activated sludge treatment process. a. Based on a sludge generation rate of 100 kg/ML of wastewater. b. Assumes inherently biodegradable. c. Assumes no biodegradation. d. Ying and Kookana (2007).

9.3.2 Risk associated with triclosan containing effluent from STPs for irrigation

The irrigation of crops with sewage effluent containing triclosan will also result in exposure to soil dwelling organisms. The risk to soil dwelling organisms as a result of this practice has been determined based on the PEC_{soil} for irrigation presented in Table 16.63 and the $PNEC_{soil}$ determined above. These are summarised below in Table 9.5.

Table 9.5 - Risk Quotients ($PEC_{Soil}/PNEC_{Soil}$) for soil dwelling organisms based on the use of treated effluent for irrigation.

Parameter	Environment Australia (2003) STP model		ASTE (2004) and Dillon (2000) model ^d		Measured Australian Data	
PEC_{Soil} (irrigation) ($\mu\text{g}/\text{kg}$ dry wt)	52.1 ^a	37.4 ^a	43.6 ^a	31.3 ^a	0.18 ^b	5.7 ^b
$PNEC_{Soil}$ ($\mu\text{g}/\text{kg}$ dry wt)	1.92	1.92	1.92	1.92	1.92	1.92
$PEC_{soil}/PNEC_{soil}$	27.1	19.5	22.7	16.3	0.09	2.97

^a. See Table 16.63 ^b. Determined in an analogous manner to the values derived in Table 16.63 with the range of measured triclosan effluent concentrations of 0.023-0.740 $\mu\text{g}/\text{L}$ from Ying and Kookana (2007).

Once again the generated $PEC_{soil}/PNEC_{soil}$ of Table 9.5 indicate that there is a potential risk to soil dwelling organisms at a total application rate of 1 m depth irrigation water per hectare per annum, including the higher end of the range of measured Australian data. The peak soil concentration is likely to be significantly reduced by degradation between irrigation events and deeper movement into the soil. While a potential risk is still indicated (risk quotients approximately 2-3) if it is assumed the triclosan from a single irrigation event delivering 10 cm is adsorbed

in the surface 10 cm of soil, based on PECs estimated from modelling, the risk would be acceptable based on PECs estimated from measured Australian biosolid levels. Recent studies indicate that triclosan will degrade relatively rapidly in aerobic soils which would mitigate potential risks. However, triclosan will persist if the soil is anaerobic.

9.3.3 Risks to water-associated wildlife

Derivation of the toxicity reference values (TRVs) for birds and mammals

Effects on algae and other aquatic organisms indicated above (Table 9.1) may be sufficient to indirectly impact higher organisms through reduction in their food supply. The potential for direct toxicity from exposure to triclosan to arise in wildlife should also be considered. This may arise from dietary exposure (exacerbated by bioaccumulation in the food chain), from drinking surface water, or from incidentally or accidentally ingesting sediment.

Due to data limitations, avian and mammalian oral toxicity reference values (TRVs) have been derived using an assessment (safety) factor (AF) approach rather than more sophisticated and accurate statistical approaches that are data intensive. The Approximation Approach of United States Army Center for Health Promotion and Preventive Medicine (USACHPPM, 2000) has been adopted for this assessment to derive TRVs as this method is applicable to small sets of toxicity data. The methodology is scientifically based, and is an important internationally published guide that describes the rationale and methods for deriving wildlife TRVs.

Studies are available for the mouse, rat, hamster rabbit, dog and baboon. The data indicate that the mouse is the most sensitive species to the systemic toxicity of triclosan. A LOAEL of 25 mg/kg bw/day was identified from a 13-week study in mice for effects on haematology parameters, relative liver weight and total cholesterol in both sexes.

An avian repeat dose oral toxicity data of adequate quality is available for triclosan and has been used to derive the avian TRV. The five day repeat dose in diet oral NOAEL of 179 mg TCS/kg bw/day for Bobwhite quail, based on the study by Bio-Life Associates (1993c), has been selected to derive the avian TRV for triclosan as this was the highest dose tested that resulted in no adverse effects (mortality).

Oral TRVs derived for the assessment of risks from exposure to triclosan by mammals and birds and the aquatic TRV have been presented in Table 9.6. A high level of confidence of wildlife health protection is afforded by the derived TRVs for triclosan.

Wildlife TRVs are expressed as an acceptable dose of chemical by a specific exposure route (e.g. oral, inhalation, or dermal) or as an acceptable environmental media concentration (e.g. mg/kg of soil). The derived TRVs have been used in an analogous manner to PNEC values in the risk quotient approach to predict the risks to mammalian and avian wildlife.

Table 9.6 - Derived mammalian and avian oral TRVs for triclosan (TCS)

Taxa and Toxicity Data	Reference	AF	Derived TRV (mg TCS/kg bw/day)
<u>Mammals</u>			
Sub-Chronic LOAEL: 25 mg TCS/kg bw/day	Chapter 18	20	1.25
<u>Birds</u>			
Acute NOAEL (Bobwhite mortality): 179 mg TCS/kg bw/day	Bio-Life Associates (1993c)	30	6.0

AF = Assessment Factor

Wildlife exposure

In general, wildlife may potentially be exposed to one or more environmental media (e.g. surface waters, sediments, soils, air), each of which may potentially contain triclosan, and multi-media exposure may occur concurrently (e.g. oral, dermal and/or inhalation). Triclosan has a high affinity to lipids and a high propensity for bioaccumulation, as indicated by biological tissue residue monitoring conducted in other parts of the world, and wildlife may be exposed to triclosan through consumption of foods (food chain or secondary exposure).

Total exposure to environmental media by wildlife may be estimated using the following model equation:

$$\text{Exposure}_{\text{total}} = \text{Exposure}_{\text{oral}} + \text{Exposure}_{\text{dermal}} + \text{Exposure}_{\text{inhalation}} \quad (\text{Eq. 1})$$

In the above equation, oral exposure routes are considered more likely to occur or be relatively more significant for triclosan. Although all potential pathways for exposure to triclosan have been considered in this assessment, oral exposure routes are of greatest importance (e.g. food consumption, drinking water, incidental sediment ingestion). Triclosan is not volatile and inhalation exposure is unlikely to be a significant exposure pathway for wildlife. Although dermal absorption of triclosan can potentially occur, there is considerable uncertainty in estimation of dermal uptake rates by wildlife from exposure to solutions containing triclosan. In general, features such as oily fur and feathers and toughened skin, are likely to reduce the potential for skin contact with environmental media and absorption (Sample et al., 1997).

For this assessment, it is assumed that wildlife obtain all of their food and water within the area of contamination based on the calculated PEC values (Appendix B Tables B-2 to B-5). The derived PECs for food intake are based on the consumption of biota allowing for a BCF of 5000 based on data for fish (see Section 16.4.2), which may be different for the organisms in the wildlife diet. Further, wildlife that have home ranges of size greater than the area of contamination will likely have less exposure than animals with smaller home ranges. Exposure may be seasonal or intermittent for migratory species of wildlife relative to sedentary species. In addition, their prey may move in and out of contaminated areas, thereby the potential for bioaccumulation of triclosan in prey may be less than for sedentary prey.

Avian and mammalian risk

The risk to birds and mammals for the ingestion of triclosan through the intake of water, food and sediment has been estimated by comparing the PECs for the various routes of exposure (See Appendix B Tables B-3, B-4, B-5 and B-6) with the TRVs of 6.0 and 1.25 triclosan/kg bw/day derived for birds and mammals respectively.

As a worst case, wildlife triclosan intake rates by birds and mammals during drinking have been estimated using the upper value PEC surface water values ($\leq 17.4 \mu\text{g/L}$) and the wildlife exposure model equations for surface water ingestion (see Appendix B). Using this method, the maximum bird and mammal intake rates of triclosan by the drinking water exposure route are $\leq 0.005 \text{ mg/kg bw/day}$.

Wildlife triclosan intake rates by birds and mammals from incidental or intentional sediment ingestion have been estimated using PEC sediment and the wildlife exposure model equations for sediment ingestion (see Appendix B). Using this method, the maximum bird and mammal intake rates of triclosan by the sediment exposure route are $\leq 3.6 \text{ mg/kg bw/day}$.

Triclosan in the aquatic environment has the potential to bioaccumulate in aquatic organisms and food chain exposure by wildlife may occur. Estimated wildlife dietary intake of triclosan has been presented in Tables B-2, B-3, B-4 and B-5 (Appendix B) based on a BCF of 5000 (derived from fish data). This is considered to be highly protective. Dietary exposure for birds to triclosan is estimated in the range of 3.3-126 mg/kg bw/day (freshwater) and 0.3-12.6 mg/kg bw/day (marine) depending on taxa, weight and the discharge source. The food chain potentially provides a significantly greater level of exposure than other routes of exposure evaluated. A similar scenario may be expected for mammals.

The calculated risk quotients (PEC/TRV) for the total oral intake (sum of the water, food and sediment exposure routes) are presented below (Table 9.7). The risk quotients for the various modes of intake are presented in Appendix G. The risk quotients for drinking water of various levels of water treatment are all below 0.01 and the maximum risk quotient for sediment intake was 0.6, indicating that these modes of intake are not expected to present a risk to wildlife.

The risk quotients in Table 9.7 indicate that at worst-case predicted concentrations for each type of sewerage treatment, there is a potential risk for birds and mammals ingesting biota from downstream of STP outfalls at all levels of treatment except for those exposed to tertiary treated wastewater discharging to the marine environment. Calculations based on the maximum measured concentration in Australian surface waters indicate there is not a potential risk for birds that are solely dependent on the aquatic compartment for their food and water intake. Similar calculations for mammals indicate a potential risk for mammals that are solely dependent on the freshwater aquatic environment for their food and water intake. However, most Australian mammals are not solely dependent on the freshwater aquatic compartment for both their food and water intake and are therefore unlikely to reach the above levels of exposure. The exception to this may be the platypus.

The potential risk to platypuses has been evaluated using the mammalian TRV and the potential exposure as determined in Section 16.5.10. The risk quotients for total exposure (water, sediment and biota) are in the range 4.6-7.6 for the predicted

secondary treatment effluent scenarios, the minimum level of treatment expected for discharges to inland rivers suggesting potential risk to platypuses. However, calculations based on the maximum measured concentration in surface waters of 0.070 mg/L (Ying and Kookana 2007) yields risk quotients of 0.5-0.7 indicating no potential risk to platypus. It should be noted that the PECs derived for food exposure are based on extrapolating a BCF of 5000 from fish data to the freshwater invertebrates that make up the bulk of the platypus diet.

Table 9.7 - Estimated Risk Quotients (PEC/TRV) for birds and mammals (0.01-1.0 kg bw) potentially exposed to freshwater and marine ecosystems containing triclosan released in STP effluent, based on removal rates for sewage treatment levels

Effluent Source	Body weight (kg live wt)	Birds Total Oral PEC/TRV		Mammals Total Oral PEC/TRV	
		Freshwater	Marine	Freshwater	Marine
Untreated wastewater	0.01 kg	21.6	2.2	54.8	5.5
	0.1 kg	9.7	1.0	43.5	4.3
	1.0 kg	4.3	0.4	34.5	3.5
Primary Treatment	0.01 kg	21.2	2.1	53.7	5.4
	0.1 kg	9.5	0.9	42.6	4.3
	1.0 kg	4.2	0.4	33.9	3.4
Trickling Filter	0.01 kg	9.1	0.9	23.0	2.3
	0.1 kg	4.1	0.4	18.3	1.8
	1.0 kg	1.8	0.2	14.5	1.5
Activated Sludge	0.01 kg	9.7	1.0	24.6	2.5
	0.1 kg	4.4	0.4	19.6	2.0
	1.0 kg	2.0	0.2	15.5	1.6
Activated sludge (SimpleTreat)	0.01 kg	8.4	0.8	21.4	2.1
	0.1 kg	3.8	0.4	17.0	1.7
	1.0 kg	1.7	0.2	13.5	1.3
Tertiary treatment	0.01 kg	2.8	0.3	7.1	0.7
	0.1 kg	1.3	0.1	5.7	0.6
	1.0 kg	0.6	0.06	4.5	0.4
Measured Australian Data	0.01 kg	0.9	0.09	2.3	0.2
	0.1 kg	0.4	0.04	1.9	0.2
	1.0 kg	0.2	0.02	1.5	0.1

9.4 Risk from degradation products

Little or no toxicity data is available for the triclosan degradation products. Hence, it is not possible to quantify the risks associated with these compounds. However, these compounds are only formed in small quantities from triclosan and any steps put in place to mitigate the potential risks posed by triclosan will mitigate any potential risks associated with the degradation products.

9.5 Data gaps

The following significant data gaps were identified when undertaking the risk characterisation.

Monitoring data

Triclosan has been used in Australia for many years with most eventually being disposed to sewer. There is some local monitoring data (Ying and Kookana, 2007) which indicates that it is found in sewage influent (five samples; 573 to 845 ng/L), effluent (19 samples; 23 to 434 ng/L) and in surface waters near STP outfalls (five rivers, 14 to 75 ng/L) at levels exceeding the freshwater PNEC of 50 ng/L. Earlier data indicate levels of <100-740 ng/L in primary treated effluents from three major Sydney STPs. However, apart from these the identities as well as details of sewage treatment and receiving waters are not known. There is also limited Australian STP monitoring data, and environmental monitoring data, for the methylated or chlorinated derivatives of triclosan. A survey during this assessment found that none of the major Australian wastewater utilities routinely monitor wastewaters, effluent or receiving environments/ecological receptors (e.g. shellfish, fish) for triclosan.

Triclosan has a high affinity to sediments, where it may be stable in anaerobic conditions in the long term based on international sediment core dating research, and biota; however, no sediment or tissue monitoring studies have been undertaken for triclosan or methyl-triclosan in Australia.

Triclosan has a high affinity to STP sludge; however, limited monitoring data are available on the concentration of triclosan in these sludges, or in biosolids, used as a soil fertility conditioner in Australia.

Triclosan is known to photolyse to various chlorinated derivatives including 2,7/2,8-dichlorodibenzo-p-dioxin (DCDD). No STP or field monitoring data were available on the occurrence of these dioxins in effluent or surface waters in the aquatic environment. Very limited toxicity data are available for these compounds as well.

Microbial effects

Triclosan is widely used due to its known anti-microbial properties. However, there is a paucity of microbial toxicity data or field monitoring data on the ecological effects of triclosan.

Toxicity data

While there are toxicity data for triclosan for a few species of mammals and birds (none for reptiles or amphibians), there is a paucity of data for native Australian wildlife for triclosan, and no toxicity data for the methylated product of triclosan. Ethical constraints on vertebrate testing will mean this gap is unlikely to be filled. International studies indicate that the methylated product of triclosan, has a higher affinity to bioaccumulate and is present in biota at comparatively higher concentrations. Further, comparisons between Australian native species and standard test species have shown that where data is available the variation is within a factor of 10. Therefore, this would be accounted for within the interspecies variation allowed for in the assessment factors applied in determining the PNECs.

There is also a lack of data available for the toxicity of triclosan and methyl-triclosan to sediment dwelling organisms. There have been triclosan related effects observed on the development of tadpoles of the North American bullfrog, *Rana catesbeiana* although the biological significance of these results is unknown.

9.6 Conclusions

The annual import volume and use pattern of triclosan has been used to estimate potential levels of triclosan entering Australian STPs. The estimated potential levels between 14.5-17.4 µg/L are 17-20 times higher than the highest observed influent concentration (0.845 µg/L), but these data are quite limited. The estimated concentrations are at the lower end of those observed overseas (<0.10-562 µg/L). These influent levels have been used to derive PECs for Australian freshwater and marine environments based on varying levels of wastewater treatment. For freshwater, the predicted levels range between ≤0.1-15.2 µg/L, are consistent with the observed levels overseas of 0.01-269 µg/L, but higher than the limited Australian effluent data (0.023-0.74 µg/L) that are available. Measurements of triclosan in Australian surface waters have found triclosan levels between 0.014 and 0.075 µg/L.

Based on the predicted concentrations and the use of triclosan and subsequent release to the Australian sewage system at current levels of use, is likely to result in concentrations of the chemical within natural waterways which indicate potential risk to aquatic ecosystems at all levels of wastewater treatment. Algae and aquatic plants are the most susceptible organisms. However, if the levels obtained close to the outfall from five Australian rivers are representative of all Australian conditions then the risk is only marginal. Given the significant difference between the predicted and limited measured levels it is important to determine how reflective the measured data is of the wider Australian environment. However, based on the limited measured Australian data it is likely that the growth of sensitive algal species downstream of some sewage outfalls is inhibited by exposure to triclosan residues in the discharged effluent. As the distance from the outfall increases, the level of triclosan is expected to be reduced through a combination of photolysis and absorption (see Section 16.5.5), and at least with ocean outfalls through further dilution of the effluent plume. The distance downstream of the point of release triclosan before levels fall below harmful levels has not been estimated in this assessment, but it is noted that in Europe triclosan has been detected at levels >50 ng/L approximately 20 km downstream (see Figure 16.13).

There is potential for indirect effects on birds and mammals to occur near STP outlets resulting from effects of triclosan on their food supply, and also direct toxicity arising primarily through food consumption based on the predicted levels of triclosan in surface waters. However, the endpoint on which the mammalian wildlife TRV value is based is a sub-chronic endpoint and therefore highly protective, and the avian value is also considered conservative. Furthermore, direct toxicity has been assessed assuming bioaccumulation occurs in the entire diet to a similar extent to that found in laboratory studies with fish, and that triclosan concentration in water is at the upper end of predicted concentration ranges for various types of sewage treatment, which results in a very conservative assessment. When the highest measured concentration in Australian surface waters is used the potential effects are predicted for mammals and not for birds. However, as noted above, the predictions are based on the mammals being solely dependent on the freshwater aquatic environment for food. This is unlikely to be the case for most Australian mammals with the exception of the platypus. Calculations based on platypus specific data and the maximum measured Australian surface water

concentration indicate that there is an acceptable level of risk to platypuses living in the vicinity of a sewage outfall.

A potentially unacceptable risk toward soil dwelling organisms as a result of the use of biosolids (as soil conditioners) or effluent (for irrigation) from STP has also been indicated based on the levels of triclosan potentially present in the sludge and effluent.

10. Current Human Health Risk Management

10.1 Occupational health and safety

10.1.1 Assessment of current control measures

According to the *National Model Regulations for the Control of Workplace Hazardous Substances* (NOHSC, 1994c), exposure to hazardous substances should be prevented or, where this is not practicable, adequately controlled so as to minimise risks to health and safety. The *National Code of Practice for the Control of Workplace Hazardous Substances* (NOHSC, 1994) provides further guidance in the form of a hierarchy of control strategies, namely:

- Elimination;
- Substitution;
- Isolation;
- Engineering controls;
- Safe work practices; and
- Personal protective equipment (PPE).

These measures are not mutually exclusive and effective control usually requires a combination of these strategies.

Elimination and substitution

Elimination is the removal of a chemical from a process and should be the first option considered in minimising risks to health. In situations where it is not feasible or practical to eliminate the use of a chemical, substitution should be considered. Substitution includes replacing with a less hazardous substance or the same substance in a less hazardous form.

Triclosan is not manufactured in Australia but is imported both as the raw chemical and as an ingredient in products. Of all the applicants providing data, only one was actively seeking to replace triclosan in their product with a less hazardous chemical. Therefore, elimination and substitution do not appear to be being locally pursued. Substitution and elimination of triclosan may not have been considered as it is less hazardous than a number of other antimicrobial agents.

Isolation

Isolation as a control measure involves separation of the process from employees by distance or the use of barriers or enclosure to prevent exposure. In this regard, the following controls were identified for triclosan and products containing triclosan:

- Stored in original containers in a cool dry ventilated chemical storage area, not segregated and no special storage precautions taken;

- Polymer pellets are stored above ground, with restricted access to employees; and
- All raw materials, triclosan included, are stored in a banded dangerous goods area segregated from the rest of the site.

Engineering controls

Engineering controls are plant or processes which minimise the generation and release of hazardous substances. They include enclosure or partial enclosure, local exhaust ventilation and automation of processes.

The engineering controls in place to prevent exposure to triclosan vary and include:

- Triclosan is delivered to site in 25 kg fibre drums and dispensed from a laminar flow dispensing booth into plastic bags, which are then dispensed as needed to be mixed with other ingredients to make bulk product;
- Weighing of triclosan in a ventilated and extracted dispensing area. At the manufacturing area material are added to the mixer under local extraction and the batch is filled into containers through a sealed system;
- Mechanical air extraction at point of weighing and point of addition of triclosan to product;
- During weighing and dispensing activities, a stand-alone dust extraction system is used to collect air-borne particles; and
- Automated mixing systems.

Safe work practices

Safe work practices have an important role in reducing exposure to triclosan. Work practices vary and include:

- Restricted access to triclosan, reducing the number of employees exposed;
- The mixture is left to stand for 24 h before transport by road to contract filler. Safety and emergency procedures are detailed in the relevant Material Safety Data Sheet (MSDS) located within the dispensary;
- Triclosan is weighed out in a ventilated room;
- For weighing out and dispensing, a plastic bag is placed into another plastic bag and the chemical is dispensed into this double plastic bag arrangement to minimise the risk of puncturing and hence exposure; and
- Workers follow written standard operating procedures, which cover receipt and storage, dispensing, cleaning equipment and waste disposal. The chemical's MSDS is required to have been read and understood by those handling triclosan. Following weighing and/or dispensing, overalls and gloves are immediately disposed of as hazardous waste.

Personal protective equipment (PPE)

PPE is used to minimise exposure to or contact with chemicals. PPE should be used in conjunction with other controls and not as a replacement. Where other control measures are not practicable or adequate to control exposure, then PPE

should be used. From the information submitted some companies used PPE alone whilst others used PPE in combination with engineering controls. Furthermore, submitted details on PPE varied with some companies simply advising wearing of “appropriate” PPE whilst other detailed the type of equipment to be used.

For workers handling triclosan the PPE used are mainly to protect the hands, face and eyes. In addition, inhalation of dusts is also minimised by appropriate PPE. Instructions given for PPE were:

- Waterside transport and warehouse workers wear coats, overalls and heavy duty gloves;
- During weighing, operators wear overalls, safety glasses, gloves and appropriate respiratory protections (e.g. a face mask or dust mask fitted with particulate dust cartridge);
- Workers wear overalls, protective eyewear, footwear, face masks etc in accordance with Workcover requirements;
- Workers wear PPE including overalls, PVC gloves, safety glasses and appropriate respiratory protection. Handled as per supplier’s MSDS;
- Workers follow written standard operating procedures and wear P3 Powered Air Purifying Respiratory protection which includes a hood, disposable overalls, and impervious gloves; and
- Prior to formulation of the product, workers wear gloves, eyeglasses, protective clothing, boots and organic respirator. After formulation, workers wear all these PPE except for the respirator.

10.1.2 Hazard communication

Labels

The *National Code of Practice for the Labelling of Workplace Substances* (NOHSC, 1994a) is applicable to labels for workplace substances. Labels of consumer products are required to comply with the *Standard for the Uniform Scheduling of Drugs and Poisons* (SUSDP) (NDPSC, 2003). Triclosan is currently not listed in the SUSDP. Triclosan is classified as a hazardous substance in the Australian Safety and Compensation Council (ASCC) Hazardous Substances Information System (HSIS).

Labels submitted for assessment were assessed for requirements under the *National Code of Practice for the Labelling of Workplace Substances* (NOHSC, 1994a). The assessment took the form of a qualitative appraisal, which included the following categories of information:

- Substance identification;
- Hazard category/signal word;
- ADG Code classification/packaging group;
- Details of manufacturer or supplier;
- Risk information (or phrase);
- Safety information (or phrase);

- Information on spills/leaks or fires; and
- Reference to MSDS.

Triclosan is classified as a hazardous substance in HSIS, and depending on the concentration, labels for products containing triclosan should contain the following hazard classification, risk and safety phrases based on the HSIS classification prior to July 2008:

Classification of mixtures containing triclosan as presented in HSIS prior to July 2008:

Triclosan Concentration	Risk Phrases	Classification of Mixtures
≥ 25%	R23	Toxic
3% ≤ conc < 25%	R20	Harmful

The most appropriate safety phrases are:

- S38: In case of insufficient ventilation, wear suitable respiratory equipment
- S45: In case of accident or if you feel unwell seek medical advice immediately (show the label where possible)
- S60: This material and its container must be disposed of as a hazardous waste

This assessment supports the additional classification for triclosan.

Additional risk and safety phrases may be applicable in products depending on the presence of other hazardous ingredients.

The labels provided by applicants were assessed against the classification appearing in the HSIS prior to July 2008. No safety phrases were given under the HSIS for triclosan prior to July 2008.

A total of four labels for triclosan raw material were provided (two for different grades from the same company). One label gave the concentration though all identified the substance. Three labels included the UN number of 3077 and of those, two gave a packaging class of 9. The EU risk phrases (for skin and eye irritation) were given in three and no label gave the risk phrase as provided in HSIS prior to July 2008 (toxic by inhalation). Therefore, the ADG Class for toxicity (6.1) or the relevant UN number was not provided on any label. Although no safety phrases are mandated all labels presented adequate safety precautions/instructions. Information on spills was provided on three labels.

MSDS

Under NOHSC *National Model Regulations for the Control of Workplace Substances* (NOHSC 1994c) and the corresponding State and Territory legislation, suppliers are required to provide MSDS to their customers for all hazardous substances. Employers must ensure that a MSDS, prepared in accordance with the NOHSC *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC 1994b), is readily accessible to employees with potential exposure to triclosan used in the workplace. A sample MSDS for triclosan prepared in accordance with this Code is provided in Appendix I. This sample MSDS is for

guidance only. Under the NOHSC MSDS Code, manufacturers and importers have the responsibility of compiling their own MSDS and to ensure information is up-to-date and accurate.

In April 2003, NOHSC declared under the NOHSC Act, the *National Code of Practice for the Preparation of Material Safety Data Sheets 2nd Edition* (NOHSC, 2003) (MSDS Code). The MSDS Code forms part of the Hazardous Substances Framework and the revision addressed various technical elements and facilitates Australia remaining consistent with international approaches to hazard communication. The major focus of the revised MSDS Code however is to incorporate the information provisions of the *National Standard for the Storage and Handling of Workplace Dangerous Goods* (NOHSC, 2001). Notification of the declaration appeared in the *Commonwealth Government Notices Gazette* of 23rd July 2003 and the *Commonwealth Chemical Gazette* of 5th August 2003.

In declaring the MSDS Code, NOHSC decided that it should not come into effect under Commonwealth, State and Territory regulations until 24 April 2006 to minimise the impact on industry and allow time for the Commonwealth, States and Territories to amend their regulations. The 2nd Edition of the MSDS Code is available on the ASCC web site at:

http://www.ascc.gov.au/ohslegalobligations/nationalstandards/COP_MSDS.htm

A number of MSDS for triclosan and triclosan-containing products were provided for assessment. MSDSs provided for assessment fall into four main categories:

- 1) Triclosan raw chemical
- 2) Triclosan containing industrial products
- 3) Triclosan containing consumer products; and
- 4) Triclosan containing articles.

The content and format of MSDSs for raw chemical were assessed according to NOHSC *National Code of Practice for the Preparation of Material Safety Data Sheets 2nd Edition* (NOHSC, 2003). This assessment focused on the adequacy of the information provided in relation to the 'core' elements; product identification, health hazard information; precautions for use and safe handling information. The quality/adequacy of information presented in MSDS for triclosan is summarised in Appendix J.

Numerous types of products containing triclosan at varying concentrations are available. Due to the large number of product MSDS and the inability to identify a product reflective of standard use containing a 'typical' concentration of triclosan, no assessment was undertaken on MSDSs for triclosan containing products.

MSDS for products containing other hazardous substances in addition to triclosan should address the hazards of all ingredients/residues, taking into account combined/additive effects of chemicals where relevant.

Assessment of MSDS for triclosan raw material

A total of seven MSDS from five suppliers were provided for assessment. Appendix J provides a summary of this assessment against 'core' elements as described above. In general all but one MSDS attempted to cover the majority of

core elements but there was inconsistency in the information provided between the MSDSs. One supplier produced two MSDSs for the raw material under different product names. In these MSDSs differences between the two documents were found in the following sections: materials to avoid, ingredients, health effects, first aid, precautions for use, personal protection, storage and transport, spills and disposal, fire/explosion hazard. In most cases the differences were that one MSDS provided more detailed information than the other, however in the first aid section, one document stated that vomiting should not be induced whilst the other document provided no statement on vomiting.

Another importer had simply copied the MSDS produced by their overseas supplier and that MSDS was totally inadequate (see MSDS number 6 at Appendix J). In terms of the core elements, only product identification and formulation were adequately addressed in this MSDS.

With regard to the hazardous nature triclosan was classified in Australia in the ASCC HSIS prior to July 2008 as:

R23 – Toxic by inhalation.

The source for this listing was an assessment by the Australian Pesticides and Veterinary Medicine Authority (APVMA).

All MSDS addressed health effects, however, they were inadequate in that none indicated the then Australian classification as in the HSIS prior to July 2008. Instead, the EU classification ‘Irritating to eyes and skin (R36/38)’ was provided. ASCC updated the HSIS in July 2008 to adopt the EU classification of R36/38 for triclosan.

The following is a discussion of the key findings of this assessment.

Product identification

This was adequately covered in all but two MSDSs, one of which provided only the product name.

Triclosan is not specifically listed in the ADG Code. Due to its moderate inhalation toxicity (HSIS classification prior to July 2008 and NICNAS classification in this report), triclosan powder (100%) falls under Class 6.1 (Toxic substances), packaging class III (Substances presenting low danger) and UN number 2811 (toxic, solid, organic) (see recommendation 2a).

The other forms of triclosan imported to Australia (liquids and pellets) should have the appropriate UN number (solid or liquid) depending on the concentration of triclosan. Class 6.1 applies only if the estimated LC50 value (1 hour) falls within the ADG Code (2007) classification range for inhalation toxicity (≤ 4.0 mg/L).

Triclosan is highly toxic (acute and chronic) to some aquatic species. If the LC50 value (1 hour) of triclosan liquids or solids falls outside the Class 6.1 classification range for inhalation toxicity (> 4 mg/L), Class 9 (Miscellaneous dangerous substances and articles) and UN number 3077 (environmentally hazardous substance, liquid, not otherwise specified) or 3082 (environmentally hazardous substance, solid, not otherwise specified) is applicable to triclosan (ADG Code, 2007).

Health hazard information

This information was poorly covered in that the ASCC classification (prior to July 2008) (R23)) was not given in any MSDS. One MSDS gave no risk phrases whilst the remaining MSDSs listed the EU classification, with one MSDS including the additional risk phrase R37: 'Irritating to respiratory system'.

Precautions for use

Overall the information on personal protective equipment was considered satisfactory but again one MSDS gave no information under this element.

Safe handling information

Adequate information was provided on storage and transport. Handling of spills and disposal and fire/explosion hazards was adequately covered in five of the seven MSDS.

10.1.3 Education and training

Guidelines for the induction and training of workers exposed to hazardous substances are provided in the National Commission's *National Model Regulations for the Control of Workplace Hazardous Substances* (NOHSC 1994c) (the Model Regulations). Under these regulations, employers are obliged to provide training and education to workers handling hazardous substances.

The Model Regulations stipulate that training and induction should be appropriate for the workers concerned. It is important that each workplace implement a program that is suitably designed to accommodate the needs of different workers.

It is important that training be given to the workers at induction and repeated at regular intervals to reinforce the information. Review of training and education needs for workers on a regular basis is useful.

Information obtained for assessment indicates that very few importers and/or formulators of triclosan or triclosan containing products have written instructions or formal training for workers, as only six companies have a training program in place. Furthermore, while ongoing training reinforces what was taught at initial induction it appears from the data submitted that training was not ongoing.

Information provided stated:

- Staff are trained generally in good manufacturing practice under the supervision of the Quality Assurance Manager;
- Staff using triclosan are instructed to wear protective clothing and follow good hygiene practices;
- Storemen, samplers and operators are trained in chemical and manual handling and records of training kept;
- Workers receive training in accessing information from MSDSs and on safe handling of chemicals;
- Workers are trained in safe handling of hazardous substances; and

- Written standard operating procedures mandate training that is supervised by the Training Team Leader but no further details are provided.

10.2 Occupational monitoring and regulatory controls

10.2.1 Atmospheric monitoring

Under the NOHSC Model Regulations (NOHSC, 1994c), employers are required to carry out an assessment of the workplace for all hazardous substances, the methodology of which is provided in the NOHSC *Guidance Note for the Assessment of Health Risks Arising from the Use of Hazardous Substances in the Workplace* (NOHSC, 1994d). When assessment indicates that the risk of exposure via inhalation is significant, atmospheric monitoring should be conducted to measure levels of the hazardous substances in the workplace as a precursor to the implementation of suitable control measures to reduce exposure. Subsequent monitoring is also required to ensure that such measures are effective. No atmospheric monitoring programs for triclosan in the workplace have been identified. Triclosan was classified as Toxic by inhalation (i.e. R23) in the ASCC HSIS prior to July 2008.

10.2.2 Occupational exposure standards

Triclosan is not listed in the NOHSC *Exposure Standards for Atmospheric Contaminants in the Occupational Environment* (NOHSC, 1995) nor do any overseas exposure standards exist.

10.2.3 Health surveillance

In accordance with NOHSC Model Regulations (NOHSC, 1994c), employers have a responsibility to provide health surveillance in those workplaces where the workplace assessment indicates that exposure to a hazardous substance may lead to an identifiable substance-related disease or adverse health effect. Triclosan is not listed in Schedule 3 (list of substances requiring health surveillance) and as such there are no formal requirements for health surveillance programs for exposed workers.

10.2.4 National transportation regulations

The Australian Dangerous Goods Code (ADG Code) (FORS, 1998) sets out various requirements relating to the transport of dangerous goods by road or rail. Triclosan is not specifically listed in the ADG Code. According to the MSDSs from three suppliers, the solid form of the chemical fits into the ADG Code category of “environmentally hazardous substance, solid, n.o.s.” and has the UN Number 3077 associated with it.

However, due to its inhalation toxicity (HSIS classification prior to July 2008 and NICNAS classification in this report), triclosan powder (1-h LC50 of 2.6 mg/L estimated from 4-h LC50 of 0.65 mg/L) falls under ADG Code Class 6.1 and UN number 2811 – toxic, solid, organic.

The other forms of triclosan imported to Australia (liquids and pellets) should have the appropriate UN number (solid or liquid) depending on the concentration of triclosan. Class 6.1 applies only if the estimated LC50 value (1 hour) falls within the ADG Code (2007) classification range for inhalation toxicity (≤ 4.0 mg/L).

Triclosan is highly toxic (acute and chronic) to some aquatic species. If the LC50 value (1 hour) of triclosan liquids or solids falls outside the Class 6.1 classification range for inhalation toxicity (> 4 mg/L), Class 9 (Miscellaneous dangerous substances and articles) and UN number 3077 (environmentally hazardous substance, liquid, not otherwise specified) or 3082 (environmentally hazardous substance, solid, not otherwise specified) is applicable to triclosan (ADG Code, 2007).

Considering that liquid triclosan formulations imported to Australia contains only $<20\%$ triclosan, those would fall under UN number 3082 (Class 9) based on the acute and chronic toxicity to aquatic life.

10.3 Public health regulations

Australian Drinking Water Guidelines and SUSDP

Triclosan is not listed in the *Australian Drinking Water Guidelines* (NHMRC, 2004) or in the *Standard for the Uniform Scheduling of Drugs and Poisons* (SUSDP) (NDPSC, 2003). However, given the acute toxicity profile of triclosan and the potential for consumer exposure to products containing triclosan, some public health regulatory controls may be warranted.

Cosmetics

The majority of cosmetic products used in Australia contain 0.3% or less of triclosan. However, some products, such as shower/bath gels, body washes, face washes and face masks, can contain up to 0.5% triclosan. There is no Australian standard limiting the amount of triclosan allowed in cosmetic products. In contrast the EU, Canada and Japan have all set maximum allowable concentrations for triclosan in cosmetic products (see sub-section 2.1).

Labels for consumer products

Forty-five companies submitted data on consumer products containing triclosan, which fell into three broad categories and amounted to 383 products. The categories were:

1. Cosmetics, including toothpastes, deodorants/antiperspirants, perfumes, body washes and moisturisers;
2. Disinfectants and surface cleaners, including bathroom cleaners and anti-mould products; and
3. Articles, including cling wrap and cotton buds

The number of cosmetic products by far exceeded the numbers of other products.

Labels for consumer products were provided by 19 companies and covered 114 cosmetics and 4 surface cleaners. Of these 118 labels provided, 77 listed triclosan as an ingredient. As triclosan is not listed in the SUSDP there are no specific labelling requirements for consumer goods that contain the chemical (as opposed to industrial products containing triclosan which must be labelled according to the classification in the HSIS).

11. Current Environmental Risk Management

11.1 Environmental regulatory controls

This section provides information with reference to international initiatives on the environmental regulatory controls in Australia applicable to triclosan.

In summary, the management of environmental pollution and waste in Australia is regulated through individual State and Territory regulatory systems rather than at a national level and each State and Territory has legislative frameworks and strategies for managing emissions and environmental pollution to air, land and waters.

11.2 Control of major hazard facilities

According to the *National Standard for the Control of Major Hazard Facilities* (NOHSC, 2002), triclosan is not one of the specifically identified chemicals that must be considered when determining whether a site is a major hazard facility.

11.3 Aquatic ecosystems management

The Australian water quality guidelines (ANZECC/ARMCANZ, 2000), established under the National Water Quality Management Strategy, provide water and sediment quality guidelines (trigger levels) for freshwater and marine ecosystems throughout Australia. The guidelines provide a decision-tree framework for the assessment and management of risks from chemicals to water and sediment quality.

Although no Australian trigger values are available for triclosan or its methylated or chlorinated products, aquatic toxicity data are available for triclosan and have been utilised in this assessment to develop water quality benchmark level (predicted no effect concentrations, PNECs). Each State and Territory has legislative frameworks and strategies for managing water and sediment pollution.

11.4 Disposal and waste treatment

Each Australian State and Territory provides statutory controls on waste generation and management. Triclosan-containing materials classified as wastes should be sent to licensed waste disposal contractors in accordance with State and Territory requirements. No specific waste disposal guidelines, standards or management issues were identified for triclosan wastes. Due to the ecotoxicity of triclosan product, care should be exercised in disposing of contaminated wastes to avoid pollution of the environment.

In some States/Territories, waste disposal licences are required to be held by waste contractors managing triclosan wastes. In NSW, transporters conveying triclosan waste in quantities greater than 200 kg per load or waste facilities treating triclosan wastes require a licence under the *Protection of the Environment Operations Act 1997* issued by the NSW Environment Protection Authority.

Although no specific waste disposal guidelines, standards or management issues were identified for triclosan, 11 companies provided detailed disposal information. Most companies indicated that there was no routine disposal of waste chemical, as batch sizes are determined so as to use full containers of triclosan. If disposal was needed the following were given as the methods used:

- Cardboard packaging is recycled and inner empty triclosan plastic bag disposed of at approved landfill. If product waste occurred it is disposed of as condemned stock, that is collected by a waste collection agency and taken to an EPA licensed waste facility;
- Mixing vessels and filling machines are routinely washed. The washings are processed in a waste treatment plant, the treated water pumped to the sewer and sludge disposed of by a licensed waste operator;
- Waste is released to sewers (estimated total annual release 20 kg);
- Spills swept up and then flushed to an onsite liquid waste treatment plant and;
- Workers follow written standard operating procedures. Spills are treated as hazardous waste. The chemical is swept and placed in a plastic bag that is sealed and then encased in a fibre container. A label identifying the hazardous waste is affixed to the outside of the fibre container and an outside contractor is called to collect and dispose of the waste by high temperature incineration. The waste is tracked by giving the contractor a hazardous waste handover certificate and after destruction the contractor must supply a Certificate of Destruction that is filed on site. The empty cardboard drums in which triclosan was shipped are recycled and the plastic liner is disposed of at approved landfill.

11.5 Emergency procedures

Handling and storage incidents

Recommendations for dealing with spills involving solids and aqueous solutions are provided in MSDSs and are similar for both forms and state:

- Shovel into approved disposal container;
- Vacuum contaminated area;
- Avoid creating dusty conditions;
- Spills to be promptly removed;
- Prevent material from entering sewers, waterways or low areas; and
- Report large spills to local environmental authorities.

However, one importer of triclosan raw material provided specific procedures for spills on site:

- Isolate spill or leak area immediately;
- Warn other personnel;
- Wear appropriate PPE before touching damaged containers;

- If safe to do so, for liquids, contain with suitable absorbent material and prevent spilled material from spreading to drain, watercourse or soil. Use sand or earth to make a dam to contain spill;
- If safe to do so, for powders, dampen down first, scoop up, then absorb/vacuum up all remaining residue using small quantities of water and detergent if necessary;
- Place collected spilled material into a sealable container and label “Waste Environmentally Hazardous Solid, UN No3077”;
- Do not wash down residue to drains. Dampen down area and repeat clean-up and containerization of spilled material until all residue is collected; and
- Dispose as chemical waste according to State/Territory waste disposal regulations.

Recommendations for fighting fires involving solids and aqueous solutions are provided in MSDSs and are the same for both forms and state:

- Use self contained breathing apparatus; and
- Extinguish using carbon dioxide, dry chemical, foam, or water.

Road transport incidents

Procedures provided by an importer of the raw chemical for spills during road transport include the following:

- Stop vehicle engine and turn off electrical equipment;
- No smoking, no naked lights, or sources of ignition in immediate area;
- Warn other traffic;
- Send message to fire brigade and police. Tell location, material, UN No., quantity, condition of vehicle and emergency contact;
- Inform emergency services (e.g. Fire Brigade, Police, Environment Protection Agency) of incident location, substance, UN Number, quantity, container type, condition of vehicle and emergency contact;
- Stop leak if safe to do so, wear chemical resistant gloves, boots and protective clothing;
- Prevent spilled material from spreading to drain, watercourse or soil. Use sand or earth to make a dam to contain spill. Absorb liquid to suitable absorbent material (e.g. dry sand or earth). Collect spilled substance in a sealable container and label waste with the UN number;
- Do not wash down residues to drains. Dampen down area and repeat clean-up and containerization of spilled material until all residues are collected; and
- Dispose of waste according to instructions from EPA

Procedures provided by an importer of the raw chemical for fires during transport are:

- Carry out actions described for full emergencies;
- If a minor fire extinguish using dry powder or foam extinguisher; and
- Major fire handled by emergency services - wear chemical resistant gloves, boots and protective clothing. Use dry powder, foam or water fog. Use sand or earth to make a dam. Prevent contaminated fire fighting water from spreading to drain, watercourse or soil.

Maritime incidents

For managing spills and leaks of triclosan during maritime transportation, the procedures followed will depend on the type, extent and location of the spill incident and whether the spill is contained within the ship or released to the marine environment. Recommendations include the following:

- Initiate ship chemical emergency procedures;
- Identify the source of the spill or leak and isolate the area immediately;
- Stop the leak if safe to do so, (e.g. reposition the container). Wear chemical-resistant gloves, boots and protective clothing. Clean-up spill as per above recommendations (*Handling and storage incidents*);
- Prevent spilled material from spreading. Use sand or earth to make a dam to contain spill. Absorb liquid to suitable absorbent material (e.g. dry sand or earth). Collect spilled substance in a sealable container and label waste with the UN number. Do not wash down residues;
- If product has been released off-ship, identify the location of the spill or leak (e.g. GPS co-ordinates), quantity, container type, weather conditions and current. Warn other shipping traffic in the area;
- Inform emergency services (e.g. Dockyard chemical safety officer, Fire Brigade, Police, Australian Maritime Safety Authority, Environment Protection Agency) of incident location, substance, UN Number, quantity, container type, condition of ship and emergency contact; and
- Dispose of any containerised waste in accordance with state/territory waste disposal regulations by incineration.

12. Discussion and Conclusions

12.1 Importation and use

Triclosan is not manufactured in Australia. It is imported into Australia in various forms, such as the raw chemical (>99% powder), a liquid solution (10% to <20%), plastic pellets and as an ingredient in various products (see below). The total amount of triclosan imported annually into Australia has decreased each year from 30 tonnes in 2001 to 21 tonnes in 2005.

The main occupational use of triclosan in Australia is in the formulation of personal care and cosmetic products, therapeutic products and cleaning agents. Other major uses of triclosan are in the treatment of textiles and plastics manufacture. A minor use is in the formulation of some oil-based paints for interior use on tiles and laminates. Triclosan is included in many consumer products because of its antimicrobial activity. Consumer uses of triclosan in Australia include cosmetic and personal care products, therapeutic products, veterinary products, pesticides, household and cleaning products.

It is possible that several polychlorodibenzo-p-dioxins and polychlorodibenzofurans may be found as low-level trace by-products in triclosan. The trace levels are dependent on the starting materials and reaction conditions. This led to the United States Food and Drug Administration (via the United States Pharmacopoeia) and Health Canada to set concentrations limits for these impurities in triclosan.

The European Union, Canada and Japan have set maximum allowable concentration limits for triclosan in cosmetic products.

A summary of the health and environmental hazards, and the potential risk to workers and the public are discussed in the following sections.

12.2 Human health hazards and risks

12.2.1 Human health hazards

In humans, triclosan is rapidly and completely absorbed from the gastrointestinal tract while a lower rate is seen for dermal absorption. It is also rapidly removed from the blood, and extensive first pass metabolism occurs following oral administration. The major metabolic pathways in humans and animals involve glucuronide and sulphate conjugation, and metabolism to these conjugates has also been observed in the skin. In humans, excretion is relatively rapid. Though a significant difference was observed in the rate of elimination between some Negroid (black) volunteers compared to Caucasians (white), there are no data available to explain this difference. The major route of excretion being the urine, while the faeces is of secondary importance. The human oral and dermal data provide no evidence of a bioaccumulation potential. Additionally, enterohepatic circulation has been demonstrated in rats, while limited evidence is available in mice and hamsters.

Triclosan has low acute oral and dermal toxicity in animals. The limited inhalation toxicity data in rats indicate moderate toxicity. Both animal and human data indicate it is a skin irritant, and a study in rabbits indicates it is an eye irritant. The repeat dose inhalation toxicity study in rats showed irritation effects to the respiratory tract. Data from both humans and animals indicate that triclosan has at most a very weak skin sensitisation potential. No data on respiratory sensitization are available.

Systemic toxicity was observed following repeated exposure to triclosan in oral and dermal animal studies. No reliable human data are available. Animal data indicates that the liver is the target organ following ingestion of triclosan, with hepatocyte hypertrophy and hepatocyte vacuolization in cells observed. While the mouse is the most sensitive species there is evidence that (unlike the rat and hamster) it is sensitive to peroxisome proliferator type effects in the liver that are not considered a risk to human health. Similar effects on the liver were seen in dermal studies.

A number of in vitro and in vivo genotoxicity studies are available, and, although some positive results were obtained, overall, there is no evidence of an in vivo genotoxic potential. Oral carcinogenicity studies in the rat and hamster provide no evidence of a carcinogenic potential. No effects on fertility were seen in a 2-generation study in the rat, and there was no evidence of teratogenicity in developmental toxicity studies conducted in rats and rabbits.

Triclosan is listed in the Office of the Australian Safety & Compensation Council's (ASCC) *List of Designated Hazardous Substances*, contained in the Hazardous Substances Information System (HSIS). Prior to July 2008, triclosan was classified as a hazardous substance in the HSIS with the risk phrase, 'Toxic by inhalation (R23)'. ASCC updated the HSIS in July 2008 to adopt the Europe's 29th Adaptation to Technical Progress (ATP) to Directive 67/548/EEC (April, 2004). With this update in July 2008, triclosan is now on the HSIS with the risk phrase, 'Irritating to eyes and skin (R36/38)'. Based on the current assessment and according to the *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 2004), triclosan is classified as 'Toxic by inhalation (R23)' and 'Irritating to eyes, respiratory system and skin (R36/37/38)'.

Triclosan is not listed in the *Standard for Uniform Scheduling of Drugs and Poisons* (SUSDP). However, the acute toxicity profile of triclosan suggests that it could be considered for listing in the SUSDP.

12.2.2 Occupational health and safety risks

Workers may be potentially exposed to triclosan by skin and eye contact and inhalation. The likelihood of exposure by ingestion in occupational settings is expected to be low. Similarly, the low vapour pressure of triclosan means that the main route of exposure is likely to be via the dermal route. However, there is potential for inhalation exposure when using triclosan powder.

Exposure during importation and storage is unlikely except in the case of accidental breakage of containers and spillage of triclosan powder or liquid. The potential for exposure following accidental spillage of plastic pellets containing triclosan is low, as the triclosan itself is encapsulated in the plastic matrix. The major occupational exposure scenarios are formulation of personal care, cosmetic and cleaning products, treatment of textiles and plastics manufacture. In these

scenarios, enclosed automated processes are reported to be used. Exposure is expected to be low as generally the process is periodic, engineering controls such as local exhaust ventilation are reported to be in place at most work sites and personal protective equipment (PPE), such as safety goggles and gloves, are reported to be worn at some sites. Consequently, the risk of acute effects such as inhalation toxicity, skin, eye and respiratory irritation is low, though the risk would increase for accidental spills or leaks of triclosan and/or products containing high concentrations of triclosan, especially where personal protective equipment is not used in the clean up of spills. Exposure would not be significant during use of commercial cleaning products containing triclosan, as the maximum concentration of triclosan identified in an occupational end-use product was 0.3%.

However, no occupational monitoring data for triclosan are available in Australia or reported in the literature. Therefore, the Estimation and Assessment of Substance Exposure (EASE) model was used to predict inhalation and dermal exposure. For chronic effects, a Margin of Exposure (MOE) approach was undertaken for risk characterisation using a NOAEL of 40 mg/kg bw/day identified in a 2-year study for effects on the liver in the rat. The lowest MOE ranges determined were 32–320 for formulation/plastic manufacture with 100% triclosan. However, it is considered that the MOEs for these scenarios will be at the higher end of the predicted range (i.e. > 100 for formulation/plastic manufacture) and the risk of chronic effects to workers from repeated exposure to triclosan is low. The determination of a low risk is based on the nature and severity of effects seen in repeated dose studies in animals. The histopathological changes observed in hepatic cells were minor and seen only in male rats. In addition, these changes were not seen consistently throughout the carcinogenicity study and, there are no data to suggest that humans are more sensitive than animals. Additionally, EASE does not take into account the use of PPE and it is considered that the use of closed or partially enclosed automated work processes and other engineering controls and PPE mean that the actual exposures are likely to be lower than that predicted by the EASE model.

MSDS and labels for imported raw triclosan were assessed qualitatively against the NOHSC MSDS and Labelling Codes. In general, labels were lacking information on the concentration (i.e. purity) of triclosan. No label gave the risk phrase for inhalation toxicity as provided in the HSIS, but all except one label gave the risk phrases for eye and skin irritation. All labels provided adequate safety precautions/instructions. There was inconsistency in the information provided between the MSDS, generally relating to the level of detailed information provided. However, overall, information on product identification, precautions for use, and safe handling were adequate. The risk phrases for eye and skin irritation were provided in all but one MSDS, though one included the additional risk phrase R37: 'irritating to respiratory system'. A sample MSDS for triclosan is included in Appendix I.

Due to the large number of product MSDS and the inability to identify a product reflective of standard use containing a 'typical' concentration of triclosan, no assessment was undertaken on MSDS for triclosan containing products.

12.2.3 Public health risks

Public exposure can occur through the use of consumer products containing triclosan. The major exposure scenarios are from the use of consumer products

containing triclosan such as cosmetic and personal care products, household cleaning products and from textile articles containing triclosan. Given the types of triclosan containing products available to the public the main route of exposure is likely to be dermal, though oral exposure may occur through accidental or incidental ingestion of lip balm, toothpaste or mouthwash formulations, and inhalation exposure may occur through breathing aerosols generated from the use of cosmetic, personal care or cleaning products. Additionally, oral exposure may potentially occur in young children and babies through the sucking or mouthing of textile/plastic articles. The detection of triclosan and/or its metabolites in human breast milk samples indicates a further potential source of exposure in breast-feeding babies.

For acute health effects such as inhalation toxicity, skin, eye and respiratory irritation the risk is considered to be low due to the low concentration of triclosan in consumer products. Additionally, accidental ocular exposure is expected to occur only infrequently. Textile and plastic articles do not present a risk for irritation.

Measured exposure data are limited for the consumer exposure scenarios. Some data are available for repeated use of cosmetic and personal care products. Consequently, various exposure models have been used to predict consumer exposure to various categories of products. The absence of data on the leaching of triclosan from articles prevents the potential dermal and oral exposure to be determined from such. As for occupational risk characterisation, an MOE approach was undertaken for chronic effects. A worst-case exposure scenario was determined with the exposure models and MOEs were determined using the maximum level of triclosan detected for each type of product in Australia and with exposure to all possible types of products for that exposure scenario.

All MOE ranges derived from exposure models indicated that the risk of chronic effects from repeated exposure to consumer products containing triclosan is low, as in addition to being worst-case scenarios and thus likely to be overestimates, the nature and severity of the effects seen in animals are minor and there are no data to suggest that humans are more sensitive than animals. The lowest MOE ranges in both adults and young children/babies using modelled data, and hence greatest potential risk of an adverse effect, was for exposure to cosmetic and personal care products: 179-213 in adults; 471 in babies less than 1 year old; 402 in 2 year old children; and 603 in 5 year old children. In adults, similar MOE ranges were seen in some volunteer studies (i.e. measured data) using a single cosmetic or personal care product containing triclosan: 179–311⁷. This measured data raise a concern that cannot be completely dismissed, that is, the risk of chronic effects may potentially increase to levels that cause concern in some individuals through combined use of many cosmetic and personal care products containing triclosan, and/or use of such products containing relatively high concentrations of triclosan.

This assessment indicates that the lowest potential source of exposure to babies, and hence the lowest risk of an adverse effect, is from triclosan in breast milk.

⁷ For the measured data, the majority of MOEs following use of a single cosmetic or personal care product were greater than 1000.

12.3 Environmental hazards and risks

12.3.1 Environmental hazards

Limited ecotoxicity data were available for several trophic levels (animals and plants) from aquatic and terrestrial environments.

In the aquatic environment, triclosan is very toxic to freshwater aquatic organisms such as *Daphnia* and fish. From the limited data available, freshwater algae are the most sensitive species (NOEC = 0.2-0.69 µg/L and 72-96 h EC₅₀ = 0.53-1.44 µg/L). Recent research has indicated that effects on hormonally-induced metamorphosis of tadpoles can occur at concentrations around the predicted no effect concentration (PNEC). However, the biological significance of these effects is currently unclear, particularly as higher concentrations showed no effect.

In both acute and chronic tests with freshwater invertebrates, EC₅₀ values increase as pH increases, and triclosan is much more toxic to freshwater animals in neutral or acidic waters than in alkaline waters. There was a paucity of data for marine organisms, which precludes conclusions on toxicity for this compartment.

Both triclosan and its methylated derivative methyl-triclosan have a high potential to bioaccumulate in aquatic organisms (Log Pow values of 4.8 and 5.2, respectively, indicating partitioning to lipids). Bioaccumulation potential is also evident from laboratory-scale bioconcentration factor (BCF) studies and field monitoring studies. However, no data were available that correlate tissue concentrations with effect levels.

In the terrestrial environment, data for two standard test species indicates that triclosan is slightly toxic to birds by the oral route of exposure, with a LD₅₀ of 862 mg/kg bw in bobwhite quail. In soils, triclosan is toxic to plants when grown in sandy soil (time-weighted average (TWA) NOEC for cucumber 65 µg/kg); however, toxicity was less (TWA NOEC for cucumber 446 µg/kg) when grown in sandy loam. The attenuation of phytotoxicity is potentially due to the higher organic matter content of the sandy loam soil binding to triclosan.

Triclosan is also slightly toxic to earthworms. No other terrestrial invertebrate toxicity data were available, and no data were available on the effects of triclosan on soil microbial process (e.g. respiration, nitrification).

The limited data available indicate that effect levels of triclosan on activated sewage sludge micro-organisms can vary depending on the level of acclimation, but can significantly reduce their ability to remove ammonia as well as their nitrification capacity for several days at least.

For assessing potential risks to the environment, the annual import volume and use pattern of triclosan was used to estimate potential levels of triclosan entering Australian STPs. The estimated amount is between 14.5-17.4 µg/L. The estimated concentrations are consistent with those observed overseas (<0.10-562 µg/L). These influent levels were used to derive predicted environment concentrations for Australian freshwater and marine environments based on varying levels of wastewater treatment. For freshwater, the predicted levels range between ≤ 0.1-15.2 µg/L, which are consistent with the observed levels overseas of 0.01-269 µg/L. However, limited measured Australian data for the levels of triclosan in some sewage effluent and biosolids indicate that measured levels are at the lower end of internationally observed values. Notably, the measured data do not include

the larger STPs or any NSW STPs. Consequently, it is difficult to extrapolate these data to all freshwater ecosystems in Australia.

12.3.2 Environmental risks from release to the aquatic environment

There is potential for indirect effects on birds and mammals to occur near STP outlets as a consequence of the effects of triclosan on their food supply, and also direct toxicity arising primarily through food consumption based on the predicted levels of triclosan in surface waters. Based on exposure and toxicity data, the risks to birds and most Australian mammals (with the possible exception of the platypus) are considered to be acceptable. Modelled data indicate potentially unacceptable risks to mammals such as the platypus that subsist exclusively on water-based organisms such as fish (from bioaccumulation in food). To refine the risk estimate, platypus specific data was compared to the maximum measured Australian surface water concentration taken from five rivers in Queensland, and indicated that there is an acceptable level of risk to platypuses. However, these surface water measurements were only conducted in Queensland and do not cover the full range of urban STPs in Australia, particularly the larger STPs.

Modelled data indicate a potentially unacceptable risk to freshwater organisms for each type of wastewater treatment. Available data for concentrations of triclosan in surface waters near STPs in five rivers in Queensland indicate that concentrations are likely to be lower than those predicted through modelling, but confirms that triclosan is still present at levels which could potentially result in adverse effects on algae. These surface water measurements are unlikely to be representative of broader environmental concentrations, which could potentially be much higher around other, larger STPs. Because no data were submitted for sediment-dwelling organisms, it is not possible to determine potential effects in this particular compartment. As dilution is high in ocean outfalls, risks to marine species are considered acceptable.

12.3.3 Environmental risks from release to the terrestrial environment

Both modelled and measured data indicate that triclosan is present in biosolids at levels which, when applied to soil, may result in adverse effects on plants. While some evidence is also available which points to its persistence in treated soils, a standard laboratory study indicates that triclosan degrades rapidly in aerobic soils. Although modelled data indicate potential risks to soil dwelling organisms from irrigation by effluent water, limited measured data indicate that risks to plants from irrigation are acceptable.

Overall, in the absence of additional data indicating concentrations downstream of representative STPs in Australia, it is not possible currently to exclude the possibility of unacceptable risks to certain species such as algae. Algae form an important food source for numerous other organisms. Potentially unacceptable risks to soil dwelling organisms from the use of biosolids (as soil conditioners) or effluent (for irrigation) from STPs also currently cannot be excluded.

12.4 Data gaps

For the purposes of human health and environmental risk assessment, this report identified a number of data gaps.

The environmental assessment identified the following monitoring data gaps:

- lack of comprehensive Australian data on the concentration of triclosan in representative STP effluents and surface waters;
- lack of Australian data on the concentration of methylated or chlorinated derivatives of triclosan in representative STP effluents and surface waters;
- lack of measured data on the concentration of triclosan and its methylated or chlorinated derivatives in aquatic sediments;
- lack of comprehensive data on the concentration of triclosan and its methylated or chlorinated derivatives in STP sludge, or in biosolids, used as soil conditioners in Australia; and
- lack of field monitoring and microbial toxicity data on the ecological effects of triclosan.

The environmental assessment identified the following data gaps for toxicity:

- lack of toxicity data for triclosan for native Australian wildlife, and no toxicity data for the methylated products of triclosan;
- limited data on the toxicity of triclosan and no data for methyl-triclosan to sediment dwelling organisms;
- lack of data on the effects of methyl-triclosan on soil micro-organisms and nutrient recycling; and
- limited data regarding effects of triclosan on marine organisms and no data for methyl-triclosan.

The human health assessment identified the following monitoring and toxicity data gaps:

- absence of representative atmospheric monitoring in formulation plants;
- absence of dermal exposure data;
- absence of data on the leaching of triclosan from textile and plastic articles;
- lack of data on the health effects of triclosan in humans following repeated exposure; and
- use of a default oral NOAEL for determination of MOE estimates as no reliable evidence of systemic toxicity was seen in dermal studies in a suitable animal model.

The assumptions used in EASE modelling also add uncertainties to the human risk characterisation.

Furthermore, while it is concluded that there is no risk to humans or the environment with regard to antimicrobial resistance to triclosan, it is recognized that there is limited information on:

- The prevalence of triclosan resistant organisms in clinical environments;
- The exact mechanisms of antibacterial action of triclosan;
- The kinetics of triclosan antibacterial resistance mechanisms and their possible transferability; and

- The fate of triclosan in the environment, the rate and extent of degradation of triclosan and the anti-microbial activity of degradates or low concentrations in the environment.

PART 2 - Supporting Data

13. Methods of Analysis and Detection

13.1 Identification

Triclosan can be identified by infra-red absorption spectrum between 400 cm^{-1} and 4000 cm^{-1} , and by ultra-violet absorption between 249 nm and 350 nm with a peak at 281 nm (Ciba Specialty Chemicals Pty Ltd, personnel communication).

13.2 Methods of analysis

Various methods are described in the literature to analyse triclosan and more generally, organic halogen compounds and chlorophenols in a variety of media. Methods cover Variable wavelength spectrophotometer (S); High Performance Liquid Chromatography (HPLC); High Performance Liquid Chromatography/Voltametric Detection (HPLC/VD); High Performance Liquid Chromatography/Mass Spectrometry (HPLC/MS); Gas Chromatography/Mass Spectrometry (GC/MS); Gas Chromatography (GC); Gas Liquid Chromatography with Electron Capture (GLC/EC); Gas Chromatography with Electron Capture (GC/EC); Gas Chromatography with Atomic Emission detection (GC/AE); Differential Pulse voltammetry (DPV); Liquid Chromatography (LC); and Liquid Chromatography/Mass Spectrometry (LC/MS). Not all papers found in the literature are discussed below. Where similar techniques have been used in more recent articles, earlier papers are not cited.

13.3 Analysis in water

Measurement of triclosan in water has been accomplished by HPLC, LC/MS, GC/MS and GC/EC. Limits of detection ranged from 0.2 ng/L to 350 ng/L. The media covered is mainly wastewater however some studies have assayed triclosan in water used to rinse the mouth following oral exposure to the chemical. These samples contained saliva and involved precipitation of salivary proteins as a first step. Other samples involved an extraction phase as a first step prior to assay.

Table 13.1 summarises methods that are reported to be useful for analysing triclosan in water.

13.4 Atmospheric monitoring

No methods for atmospheric detection of triclosan were found in the literature.

13.5 Biological monitoring

Measurement of triclosan in biological fluids has been accomplished by HPLC, GLC/EC, GC/EC, GC/MS, GC/AE and S. Limits of detection ranged from 1 – 3 ng/mL in human plasma, 2 – 3 ng/mL in human urine, 0.02 - 0.6 ng/g in human milk, while a detection limit of 500 ng/g in human dental plaque, 1 ng/mL in rabbit serum and urine, and 0.89 – 2.5 ng/g in a fish sample have been reported (Table 13.2).

Triclosan is an interfering contaminant in screening urine samples that closely elutes with clenbuterol during GC analysis while screening for abuse of drugs in sports (data provided by Australian Government Analytical Laboratories, personnel communication).

Table 13.1 - Methods for determination of triclosan in water

Media	Method	Detection Limit	Reference
Water ¹	HPLC	Not reported	Gilbert et al. (1987)
Urban wastewater & lake water	GC/MS	1 ng/L	Muller et al. (2000)
Urban wastewater & surface waters from rivers & lakes	GC/MS	< 1-2 ng/L for wastewater < 0.4 ng/L for surface waters	Lindstrom et al. (2002)
Urban wastewater & surface water from a lake	GC/MS	Wastewater 5 ng/L Lake water 1 ng/L	Singer et al. (2002)
Urban sewage effluent, surface water from a river & lake, & water from various stages of a water treatment plant	GC/MS	0.2 ng/L	Boyd et al. (2003)
Urban sewage influent & effluent	GC/MS	10 ng/L	Lee et al. (2003)
Urban sewage influent & effluent	GC/MS LC/MS	20 ng/L 350 ng/L	Aguera et al. (2003)
Urban sewage influent & effluent	GC/MS	100 ng/L	McAvoy et al. (2002)
Urban sewage influent & effluent, & river water	GC/MS	4 ng/L	Canosa et al. (2005a)
Stream water	GC/MS	50 ng/L ²	Kolpin et al. (2002)
River & sea water	GC/MS	30 – 59 ng/L	Okumura and Nishikawa (1996)
Slaughterhouse wastewater	GC/EC	0.2 ng/L	Graovac et al. (1995)

¹ Water rinsed around the mouth, after an aqueous slurry of toothpaste containing triclosan was rinsed around the mouth and expelled.

² Determined by either an evaluation of instrument response, calculation of limit of detection, or from a previously published procedure.

Table 13.2 summarises methods that are reported to be useful for analysing triclosan in biological samples.

Table 13.2 - Methods for determination of triclosan in biological samples

Media	Method	Detection Limit	Reference
Human plasma	GLC/EC	1 ng/mL	Birkel et al. (1993)
Human plasma	GLC/EC	2 ng/mL	Sioufi et al. (1977)
Human plasma	GC/EC	3 ng/mL	Thompson et al. (1975a)
Human plasma	GC/EC	Not reported	Hovander et al. (2002)
	GC/MS	Not reported	
Human urine	GLC/EC	2 ng/mL	Sioufi et al. (1977)
Human urine	GC/EC	3 ng/mL	Thompson et al. (1975a)
Human urine	HPLC/MS	2 ng/mL	Ye et al. (2005)
Human milk	GC/MS	0.02 ng/g	See Appendix E
Human milk	GC/MS	0.6 ng/g	See Appendix E
Human milk	GC/MS	Not reported	Adolfsson-Erici et al. (2002)
Human saliva	HPLC	Not reported	Gilbert et al. (1987)
Human oral plaque	HPLC	Not reported	Gilbert et al. (1987)
Human dental plaque	GC/AE	500 ng/g	Rasmussen et al. (1996)
Human keratin (callus)	S	Not reported	Hagedorn-Leweke and Lippold (1998)
Bovine keratin (hoof & horn)	S	Not reported	Hagedorn-Leweke and Lippold (1998)
Rabbit serum	HPLC/VD	1 ng/mL	Wang and Chu (2004)
Rabbit urine	HPLC/VD	1 ng/mL	Wang and Chu (2004)
Fish sample	GC/MS	0.89-2.5 ng/g	Okumura and Nishikawa (1996)
Fish bile fluid	GC/MS	Not reported	Adolfsson-Erici et al. (2002)

13.6 Other methods of analysis

Measurement of triclosan in a range of other media has been reported, largely for consumer products but also for marine and wastewater treatment sludges. Methods employed are HPLC, LC, LC/MS, GC/MS and DPV.

Table 13.3 summarises methods that are reported to be useful for analysing triclosan in a variety of non-aqueous and non-biological media.

Table 13.3 - Methods for determination of triclosan in various media

Media	Method	Detection Limit	Reference
Cosmetics	HPLC	Unknown ¹	Quercia et al. (1979)
Cosmetics	GC/MS	0.5 ng/mL	Facino et al. (1990)
Soaps & deodorant sticks	HPLC	Not reported	Achari and Chin (1981)
Commercial toothpaste & mouth rinse	DPV	1.2 µM	Pemberton and Hart (1999)
Toothpaste	LC	Not reported	Jordan et al. (1996)
Commercial cleaners/disinfectants	HPLC	Not reported	Data provided by 3M Australia Pty Ltd, personnel communication
Commercial phenolic disinfectants	LC	0.67 µg/mL	Thompson (2001)
Consumer goods ²	GC/MS	Not reported	Adolfsson-Erici et al. (2002)
Textiles	HPLC	Unknown	Amemiya et al. (1984) ¹
Foodstuffs ³	HPLC	25 ng/mL	Sanches-Silva et al. (2005)
Effluent sludge	GC/MS	40 ng/g	McAvoy et al. (2002)
Sludge & sediment	GC/MS	5 ng/g	Muller et al. (2000)
Sludge & lake sediment	GC/MS	5 ng/g	Singer et al. (2002)
Marine sediment	GC/MS LC/MS	0.09 ng/g 3.50 ng/g	Aguera et al. (2003)
Sediment	GC/MS	1.7 - 4.6 ng/g	Okumura and Nishikawa (1996)

¹Only the abstract is available in English.

² Bicycle shorts, socks, cutting boards, shoe insoles, kitchen sponges and WC-cleaners with antibacterial treatment.

³ Triclosan levels in oranges, chicken breast and Gouda cheese which had migrated from packaging materials

14. Data on Occupational Exposure

14.1 Routes of exposure

Occupational exposure to triclosan may occur during transport, storage or use of the chemical. Triclosan is not manufactured in Australia. It is imported mostly in powdered form (>99% purity). Triclosan is also imported as a liquid solution (10%, and at >1% to <20% in a product for use in textile manufacture) and plastic pellets.

Workers may be potentially exposed to triclosan by skin and eye contact and inhalation. Ingestion is unlikely to be a route of exposure in the occupational environment.

The physico-chemical properties of triclosan indicate that vapour/gas is unlikely to be a main source of inhalation exposure. Exposure through inhalation of airborne particles of triclosan powder is possible, although no information was available on the percentage of particles in the respirable range. Triclosan in plastic pellets used by plastics manufacturers is not expected to be a source of inhalation exposure due to the encapsulation of the triclosan in the plastic matrix.

In addition to potential dermal exposure to triclosan powder or solutions, exposure may also occur through the use of finished end products containing triclosan in the workplace e.g. antibacterial liquid soaps, surface disinfectants, dishwashing detergents and laundry detergents. Triclosan in end-use plastic articles is not expected to be a source of dermal exposure since triclosan is incorporated into the plastic matrix.

14.2 Methodology for assessing exposure

Applicants to the assessment submitted information on typical work scenarios and duration of exposure to triclosan by workers. Telephone and written surveys were also conducted of users of triclosan in the plastics and textile industries, to supplement information provided by applicants.

Exposure assessment is ideally based on workplace monitoring data, however no occupational monitoring data for triclosan were made available by industry or reported in the literature. There is no Australian occupational exposure standard for triclosan. The recommended Australian exposure standard for dusts not otherwise classified is 10 mg/m³.

Due to lack of monitoring data, the Estimation and Assessment of Substance Exposure (EASE) model (version 2.0 for Windows) developed by the United Kingdom Health and Safety Executive (UK HSE) was used to predict exposure. EASE is a general-purpose predictive model for workplace exposure assessments. It is an electronic, knowledge-based, expert system in widespread use across the European Union for occupational exposure assessment when exposure data are limited or not available. All models are based upon assumptions, and EASE is essentially a series of decision trees that can estimate exposure when the patterns of use and control, and physical properties of the substance under investigation are known. EASE can be used to estimate inhalation and dermal exposure.

The output ranges generated by EASE for inhalation exposure are in the form of a conventional 8-h time-weighted average (TWA) that assumes steady-state conditions and exposure is to the pure form of the substance (i.e. 100%). The concentration ranges of inhalation exposure predicted by the EASE model is then combined with information on bodyweight, respiration rate and duration and frequency of exposure in typical work scenarios, to estimate the internal dose to workers expressed as mg/kg bw/day. The mathematical formulae and reference values used are shown in Appendix C. It should be noted that in these calculations absorption has been considered to be 100%.

The EASE dermal model is less developed than the inhalation model, and its outputs should be regarded as no more than first approximation estimates. The model assumes dermal exposure to be uniform and that there is manual contact. The EASE output of mg/cm²/day is converted to mg/kg bw/day (i.e. internal dose) by factoring in the concentration of triclosan, bodyweight and the exposed skin area, which is assessed as the potential exposure to both hands or a hand and a forearm (a total skin area of approximately 1000 cm² for each). The mathematical formula and reference values used are shown in Appendix C. It should be noted that in these calculations absorption is taken as 14%, as determined in Section 6.

It should be noted that the EASE model has estimated occupational exposure to triclosan without taking into account any personal protective equipment (PPE) that might be in use. This permits the effects of controls other than PPE to be assessed and avoids the problem of trying to quantify the actual protection provided by PPE.

Occupational exposure during use of end products containing triclosan is estimated according to the European Commission's Technical Guidance Document on Risk Assessment (EC, 2003a). Again, exposure is estimated without taking into account any PPE that might be in use. The mathematical formula and reference values used are shown in Appendix C.

Occupational exposure to triclosan is discussed below for each major exposure scenario, namely:

- Importation, transport and storage;
- Repacking;
- Formulation of personal care/cosmetic products, therapeutic products, cleaning agents and paints;
- Treatment of textiles;
- Plastics manufacture; and
- Use of triclosan-containing end-use products.

14.3 Major occupational exposure scenarios

14.3.1 Import, transport and storage

Most of the triclosan imported into Australia is in the form of powder (>99.5% purity) in fibreboard containers lined with polyethylene, in quantities ranging from 20 to 30 kg, by sea freight. Liquid solutions are imported in plastic drums in quantities of 20 L and 25 to 200 kg. Triclosan is also imported as plastic pellets in 20 kg plastic bags and in plastic drums in quantities ranging from 25 to 200 kg.

These containers are transported by road and rail within Australia to distributors, chemical formulators and end-users without being opened.

Exposure during importation and storage is unlikely except in the case of accidental breakage of containers and spillage. In the case of accidental spillage of plastic pellets containing triclosan, there is little potential for exposure as the triclosan itself is encapsulated in the plastic matrix.

Additionally, cosmetics and personal care products containing triclosan are imported into Australia in pre-packaged tubes, jars, and bottles. Information from one importer indicates that products are imported by sea freight then transported by road to the importer's warehouse, and thence to customers. There is little potential for exposure to triclosan except in the case of accidental breaking of containers and spillage of contents.

Since occupational exposure during importation, transport or storage is unlikely except in an accident, the exposure has not been predicted using the EASE model.

14.3.2 Repacking

Exposure during repacking

Information supplied indicates at least one company repacks imported raw triclosan powder from 25 kg containers into smaller sealed packs weighing 1 – 10 kg for sale to industry. One worker wearing PPE, including gloves and safety goggles or face mask, performs this task for approximately 15 min a day, 10 days a year. Stainless steel scoops are used to transfer the material, and repacking takes place in a designated room with HEPA filter and local exhaust ventilation (LEV). The information provided allowed modelling of inhalation and dermal exposure.

Exposure estimation - inhalation exposure

The EASE scenario that best fits this activity is dry manipulation of respirable/inhalable dust that does not aggregate readily. The estimated exposure to triclosan with use of local exhaust ventilation (LEV) is 2-5 mg/m³. Exposure at workplaces without LEV was estimated to be 5-50 mg/m³ (see Appendix C).

The estimated internal dose with LEV is 0.25-0.64 µg/kg bw/day and without LEV is 0.64-6.36 µg/kg bw/day. Details of calculations and assumptions are shown in Appendix C.

Exposure estimation – dermal exposure

The EASE scenario that best describes re-packing processes is use of the chemical in non-dispersive ways, with intermittent direct handling. This means that triclosan is handled directly 2-10 times per day. The predicted exposure to triclosan ranges from 0.1-1 mg/cm²/day.

The estimated internal dose is 5.5-55 µg/kg bw/day. Details of the assumptions made and calculations can be found in Appendix C.

14.3.3 Formulation of liquid products for cosmetic and domestic use

Exposure during formulation

Most of the raw triclosan imported into Australia each year is used in the formulation of a range of personal care/cosmetic products, household and industrial cleaning products and oil-based paints. Triclosan is mainly in powder form (purity >99%) although a very small amount is imported as a 10% - <20% aqueous solution.

Twenty companies that formulate these products provided information on work processes for this assessment. Additional information was also obtained from site visits to 3 of these workplaces. However it is estimated that there may be at least 80 worksites where the chemical is used in the formulation of such products.

Nine companies provided information on the number of workers handling triclosan, and the duration and frequency of work activities. In addition to those workers directly handling triclosan, truck drivers, forklift truck operators, storemen, filling/packing staff and cleaners may also be potentially exposed to triclosan, albeit at much lower concentrations.

The formulation processes for the range of products are similar, and workers generally wear safety glasses, gloves, and either dust masks or cartridge style respirators. However, some work sites did not report the use of any respiratory PPE. Additionally, most workplaces had LEV at weighing out stations, while three had dispensing rooms with positive air pressure ventilation.

Formulation is a batch process where measured amounts of triclosan and other ingredients are added to mixing vessels, blended, transferred to containers and then dispatched to customers. Each batch can take about 6 h. Batch sizes vary from site to site as does the frequency of batch process. Generally formulation occurs only a few days in the year, although a few companies process batches containing triclosan on a more regular week-to-week basis. Furthermore, the amounts of triclosan used annually at these 20 work sites ranged from 1 kg to 5000 kg, with 12 sites using less than 100 kg triclosan per annum (p.a.), 3 sites 100-1000 kg p.a. and 5 sites used greater than 1000 kg p.a.

From the information provided by formulators, the majority of formulation processes involved manual pre-weighing of triclosan into plastic bags (usually double-lined) or buckets, and manual addition of triclosan to mixing tanks. At one worksite, the triclosan is pre-mixed in a drum with fragrance chemicals, stirred with a ladle, and the drum contents are then emptied into the mixing tank using a drum lift. In paint manufacture, triclosan is pre-mixed with ethanol. Mixing is usually done in a closed vessel, although one workplace reported using open-topped vessels for milling of soap ingredients. The final products are usually packaged into plastic or metal bottles, cans or tubes on filling lines that are generally automated. For some non-aerosol products, filling staff place caps on bottles.

Additionally at some workplaces, samples are taken of the raw triclosan for analysis for quality control purposes. Sampling and analysis of the formulated end mixture was also undertaken at some work sites for quality control purposes.

The information provided was detailed enough to allow modelling of inhalation and dermal exposure.

Exposure estimation - inhalation exposure

For workers using triclosan powder the EASE scenario that best describes the formulation process (including quality control activities) is dry manipulation of respirable/inhalable dust that does not aggregate readily. The EASE model estimates the airborne concentration for this scenario as 2-5 mg/m³ at workplaces with LEV. Exposure at workplaces without LEV is estimated to be 5-50 mg/m³.

Weighing and addition of the chemical to mixing vessels is an intermittent activity. Estimates provided by formulators indicate that the duration of this activity ranges from 10 min to 1 h a day, and is undertaken from 3 days a year to 3 days a week. Assuming an exposure duration of 1 h a day and 3 days per week, the internal dose is estimated as 15.9-39.7 µg triclosan/kg bw/day with LEV and 39.7-397 µg/kg bw/day without LEV. Details of the assumptions and calculations are shown in Appendix C.

For workers using liquid solutions containing triclosan, inhalation exposure is expected to be negligible.

Exposure estimation - dermal exposure

The EASE scenario that best describes the formulation processes (including quality control activities) to estimate dermal exposure is use of the chemical in non-dispersive ways with intermittent direct handling (2 – 10 times per day). The predicted exposure to triclosan for this scenario was 0.1-1 mg/cm²/day.

The internal dose was estimated to be 85.5-855 µg/kg bw/day. Details of the assumptions and calculation can be found in Appendix C.

14.3.4 Treatment of textiles

Exposure in the textile industry

Products marketed in Australia for use in the textile industry are antimicrobial additives containing triclosan at concentrations ranging from >1% to <20%. Most of these products are liquids, although one is a powder containing 13.5% triclosan. These products are used in the finishing treatment of woven or knitted fabric articles, such as hosiery and sportswear, most commonly through the addition of the triclosan additive product to a bath through which the fabric or articles to be treated are passed. Triclosan can be exhausted (i.e. picked up by fibres from the dye bath) at a very high exhaustion rate on to polyester and polyamide fibres when added to the dye bath (Ramachandran et al., 2004). Additives containing triclosan are usually applied at rates ranging from 1%-10% by weight on fabric. Processes range from being fairly open to enclosed, automated processes. Heating of the treatment solution sometimes occurs.

In the wool processing industry, liquid products containing triclosan are sometimes used to treat wool 'top'. Top is an intermediate stage in the processing of wool into worsted yarn. Triclosan-treated top is used in the manufacture of products such as quilts, mattresses and other bedding articles, and fleeced clothing. Triclosan is applied as part of a washing treatment using baths.

Triclosan additives are also used to treat wadded polyester fibre blends that are used in the manufacture of doona fill and mattress quilting, using a spray-on

technique, while in the non-woven textiles industry they are used in the manufacture of skin wipes.

It is estimated that there may be at least 25 worksites where the chemical is used. Information on the use of triclosan in the textile industry was provided by 7 companies in response to a NICNAS survey. Information provided by these companies indicates that the number of workers handling triclosan ranges from 1-12, with most worksites having 1-3 workers. Work scenarios obtained from some textile processing companies using triclosan products are characterised below. The information provided was detailed enough to allow modelling of inhalation and dermal exposure.

Manufacture of top in wool processing

At one top making wool processing plant in Australia, an antimicrobial solution containing $\leq 3\%$ triclosan is incorporated into a wool washing process. The product is mechanically pumped from 200 L drums through closed pipework to an open bowl surrounded by exhaust ventilation. The bowl holds about 500 L of water at 45°C and the product is added so that a 1% concentration of the anti-microbial solution is obtained. The wool is passed through the bowl then into a closed drying chamber at about 60°C . Bowls are cleaned out about every 12-15 h, at which time the solution is emptied and goes into sewer. About 3 workers wearing protective clothing including splash aprons who do not come into direct contact with the antimicrobial solution are involved in the addition of the product and monitoring of the bath. If workers are required to pull loose wool from the bowl, nitrile gloves are worn, and eye wash station and showers are available. The factory operates 8 h a day, 5 days a week and the antimicrobial solution applied most days of the week to 50% of produced batches.

Manufacture of blended polyester wadding for bedding material

A triclosan-containing textile additive is used in the production of blended polyester wadding that is used for mattress quilting, doona fill and furniture upholstery. Twelve workers wearing gloves and masks perform this task for about half a day, 100 days a year. The product is manually pumped out of 205 L drums into a 20 L bucket, and manually poured from the bucket into a tank, where water is added and the mixture automatically stirred. The mixture is then automatically pumped from the tank to an automated semi-enclosed spray booth and sprayed on to batches of fibre that then proceed into a drying oven.

Manufacture of non-woven 'wet wipes'

At a non-woven textile manufacturing plant a triclosan additive is added to a cylinder and mixed into a foam application containing acrylic binders, which is pumped into a machine and on to non-woven polyester/viscose fibers. The fibre is then contact dried over heated cylinders. Residue in the cylinder is washed out after use. One worker wearing protective glasses and rubber gloves is involved in the addition of triclosan to the pump once per month. There is no direct handling of the foam formulation once in the machine.

Manufacture of fabric and hosiery

A variety of methods for treating fabric and finished hosiery were reported by industry.

At one hosiery manufacturing plant, a 100 mL container of triclosan product containing <2% triclosan is manually emptied into an open dye bath holding approximately 900 L of water warmed to about 45 °C. Approximately 1 L is used each year, with the process being performed about 3 days of the year, by one worker who wears safety glasses and gloves. Another manufacturer applies triclosan additive in an exhaust dyeing application. The product is measured into a plastic jug and poured into a bucket, then diluted with water and added to a dye machine. At this site 11 workers handle triclosan additive daily for less than 10 min each. At a third manufacturer two workers handle the triclosan additive 2-3 times per week. It is measured into a pail and poured through the feed shoot into a dye machine. At another hosiery manufacturer, an experimental process for treating finished socks involves the manual addition of a product containing 3% triclosan to a water mixture at a final triclosan concentration of 0.3%, which is then pumped through enclosed pipework into an enclosed tumble wetting machine. Socks are tumble-dried in the same machine after the treatment and then packed into bags.

At one fabric manufacturing plant where operators wear gloves and goggles, a triclosan additive containing approximately 10% triclosan is used on average about 3 times a year, for a period of about 3 days each time, in the dyeing of knitted synthetics (mainly polyester) for use in garment manufacture. The triclosan is transferred by means of a dipper from 30 kg drums into a bucket, in a storeroom with extraction fans, and manually added to an open tank on the side of an enclosed, pressurised jet dyeing machine. The solution in the side tank is then pumped into the dye machine. An average dye cycle takes about 6 h, and up to 20 kg of triclosan additive solution can be applied, with the solution being applied at 8%-10% by weight on fabric. A rinse cycle follows the dye cycle, and on leaving the machine, the fabric is hydroextracted to remove excess moisture in a rotating drum and dried in a stenter oven at about 150 °C. Exhaust fumes are removed to atmosphere via exhaust fans/ducting.

At another fabric processing plant with exhaust ventilation, a worker wearing gloves and a face shield or goggles pours the solution into a bucket and manually tips it into an open tank. The water in the tank feeds into an enclosed bath. This task is undertaken once or twice a year.

Formulation of textile coatings for use in vertical blind manufacture

At least one textile additive is used in the further formulation of two chemical products used for the coating of fabrics in the manufacture of vertical blinds. One worker wearing PPE including impervious gloves and safety glasses performs this task for 5 min a day, 50 days a year. A product containing <2% triclosan is manually weighed into a bucket from a keg and poured into an open-topped mixing vessel. After mixing end products containing <0.0026% – 0.027% triclosan are pumped into 200 L drums. The end product is knife-coated onto fabric that is dried in a stenter oven at 150 °C, although the final temperature of the coating itself is unlikely to reach more than 130 °C.

Coating of carpet tiles

At one workplace, a textile additive containing triclosan is pre-mixed into a PVC mixture by weighing the solution out into a bucket and emptying it into a vat that mixes the ingredients under vacuum pressure. The mixture is then automatically pumped into a machine that coats carpet tiles. It is screeded onto a belt, which then

goes through a drying oven. The workers do not come into contact with the belt, but they wear gloves. The plant is vented to atmosphere and the process is done only a few days each year.

Exposure estimation - inhalation exposure

The EASE scenario that best describes the use of triclosan powder in textile additive applications is dry manipulation of respirable/inhalable dust that does not aggregate readily. The EASE model estimates the airborne concentration in this scenario as 2-5 mg/m³ at workplaces with LEV. Exposure at workplaces without LEV is estimated to be 5-50 mg/m³.

The EASE estimation assumes exposure to a 100% concentration of a substance, and the exposure levels have therefore been adjusted to account for exposure to a dust containing 13.5% triclosan such as is found in textile additives. Using this assumption together with a duration of 1 h and 3 days per week, the internal dose is calculated to be 2.14-5.36 µg/kg bw/day with LEV and 5.36-53.6 µg/kg bw/day without LEV. Details of assumptions and calculation are in Appendix C.

For workers using liquid solutions of triclosan, inhalation exposure is expected to be negligible.

Exposure estimation - dermal exposure

For workers using triclosan powder, the EASE scenario that best describes use in textile additive applications is use of the chemical in non-dispersive ways with intermittent direct handling (2 – 10 times per day). The EASE model predicts an exposure to triclosan of 0.1-1 mg/cm²/day.

The EASE model assumes exposure to 100% concentration of a substance. As the textile additive contains only 13.5% triclosan, the exposure estimate is further adjusted. Using assumptions as listed in Appendix C the estimated internal doses from dermal exposure to triclosan for the textile industry workers ranges from 11.5-115 µg/kg bw/day.

For workers using liquid solutions containing triclosan the EASE scenario that best describes the textile treatment processes described above is for a substance being included onto a matrix with intermittent direct handling (2-10 times per day). The estimated dermal exposure to triclosan is 0.1-1 mg/cm²/day. A worst-case scenario would comprise a worker handling a 20% solution of triclosan. Using assumptions in Appendix C, the estimated worst-case internal doses from dermal exposure to triclosan range from 17-170 µg/kg bw/day.

14.3.5 Plastics manufacture

Occupational exposure in plastics industry

Triclosan is used as an additive in polymer matrices such as polyolefin and polyethylene. In Australia, raw triclosan is used in the compounding of polymeric pellets. The solid pellets or the masterbatch with encapsulated triclosan are used in injection moulding and blow moulding to produce plastic articles. In addition, some reformulation of imported plastic additives also occurs.

Triclosan is also present as liquid solutions that are used at least at two workplaces in Australia as an additive to PVC compounds. The PVC compound is used to make calendered film, and cast PVC plastisol for soft PVC.

It is estimated that there are at least 16 workplaces in the plastics industry in Australia using triclosan-containing additives in their work processes. The number of workers handling triclosan at four worksites that responded to the NICNAS survey ranged from 1-6 workers. Duration and frequency of handling liquid additives ranged from 8 h a day, 200 days a year, to infrequent handling only one or two days a year. Similarly use of masterbatch pellet triclosan additives ranged from only a few days a year to quite regular weekly use.

The following are details of some work processes provided by applicants and notifiers to this assessment. The information provided was detailed enough to allow modelling of inhalation and dermal exposure.

Compounding of polyolefin masterbatches

Pure triclosan is used in Australia at one work site in the manufacture of polyolefin masterbatches containing 1%-10% triclosan. Up to 12 operators wearing PPE (including safety glasses, gloves, dust mask, and particle respirator) may work on this process for a total of approximately 30 h a year. The production process involves weighing triclosan powder into a weighing vessel and then manually pouring the contents into a mixing vessel that is then sealed. The dry mixture is transferred through an outlet into a feed hopper above an extrusion machine, which feeds the material onto a feed conveyer belt that takes it into the extruder machines. The output of the extrusion machine is a granular masterbatch product with triclosan encapsulated in the polyolefin, that are taken under vacuum to a hopper for manual-assisted packing into 25 kg plastic bags. The only potential for skin contact or inhalation of dust in this process is during the weighing out and transfer of triclosan powder which is done under LEV and accounts for about 3 production hours a year.

Injection and blow moulding

Plastic pellets containing triclosan at concentrations from 1% to 10% are used in the workplace for injection moulding and blow moulding of plastic articles. These moulding processes operate at Australian worksites from only a few days a year to every second week. In the process, no dust is generated during weighing out and addition of the pellets to the mould due to the encapsulation of the triclosan in the plastic pellet. The closed nature of injection and blow moulding operations prevent workers' exposure to the molten plastics.

Cast moulding of PVC films

Solutions containing triclosan concentrations at 1% -10% are used as an additive to PVC compounds in the cast moulding manufacture of soft PVC and in the manufacture of PVC calendered film. About 6 workers wearing gloves and a mask are involved 8 h a day for about 200 days a year in these processes. In the cast moulding process, the solution is added to a mixing tank. The production line is approx 90% closed and a ventilation system connects to a 700°C burner which burns out any escaping gases. In the calendering process, the solution is pumped out of a 100 kg drum into a bucket, which is poured into a soft PVC dye bag that is thrown into a kneading machine.

Exposure estimation - inhalation exposure

The estimated exposure for workers using triclosan powder in the compounding process is expected to be similar to those at the formulation sites and the same EASE scenario and assumptions were applied. Consequently, the estimated internal dose is 15.9-39.7 µg/kg bw/day and 39.7-397 µg/kg bw/day with and without LEV respectively.

Inhalation exposure to both triclosan pellet masterbatch and liquid PVC formulations is considered to be negligible.

Exposure estimation - dermal exposure

The estimated exposure for workers using triclosan powder in the compounding process is expected to be similar to that at formulation sites, and the same EASE scenarios and assumptions were applied. Consequently, the estimated internal dermal dose is 85.5-855 µg/kg bw/day.

Dermal exposure to liquid PVC additives containing triclosan could occur through splashes onto skin when weighing out and transferring the additive. The EASE scenario that best describes this process is intermittent direct handling (2-10 times per day) in non-dispersive use. This results in an estimated dermal exposure of 0.1-1 mg/cm²/day. A worst-case scenario would comprise a worker handling a 10% solution of triclosan. Adjusting for the concentration and use assumptions described in Appendix C, the estimated internal doses range from 8.6-86 µg/kg bw/day.

Dermal exposure to triclosan pellet masterbatch is considered to be negligible.

14.3.6 Use of triclosan-containing end products in the workplace

Workers may be exposed to triclosan through the use of commercial antibacterial hand soaps, surface cleaners, dishwashing detergents, and laundry detergents containing the chemical. Customer lists provided by applicants to this assessment indicate that the following groups are the most likely to be exposed:

- Staff of hospitals and similar institutions (e.g. nursing homes, medical clinics, veterinary clinics);
- Dentists and dental technicians;
- Contract cleaners;
- Food industry workers;
- Hospitality industry workers;
- Commercial linen services workers; and
- Other users of end products containing triclosan.

Dermal contact is the main route of exposure in end users. Inhalation exposure is considered to be negligible. Exposure levels to triclosan in these industries vary widely, due to differences in types of products used, frequency and duration of use of triclosan products, methods of application and precautions taken during use.

Exposure estimation - dermal exposure

Neither measured data for end users nor information on the frequency of use and the quantities handled were obtained from Australian workplaces. A worst-case scenario would involve a worker using a surface cleaner or dishwashing detergent containing 0.3%⁸ triclosan for 8 h per day and 5 days per week.

Estimation of dermal exposure for end users is based on the European Commission's Technical Guidance for Risk Assessment (EC, 2003a). The mathematical formula from EU guideline is modified to incorporate a duration factor for the estimation. The following assumptions are used in the calculation.

- Exposed skin area for both hands or a hand and a forearm is 1000 cm².
- Thickness of the liquid layer on skin is 0.01 cm.
- Duration of exposure is 8 h per day.
- The dermal absorption rate for triclosan is 14%.
- The average bodyweight of workers is 70 kg.

Using these assumptions, the estimated internal dose from dermal exposure to triclosan for the worst-case scenario is 16.7 µg/kg bw/day. Details of the calculation are presented in Appendix C.

The internal dose for other scenarios (e.g. hand washing) is expected to be much lower than the worst-case scenario above.

⁸ 0.3 % is the maximum concentration of triclosan in an industrial-grade cleaning product reported as being in use in Australia.

15. Data on Public Exposure

15.1 Sources of exposure to adults

Triclosan is included in many consumer products because of its antimicrobial activity, particularly cosmetic, personal care and cleaning products. The range of cleaning products includes dishwashing detergent, laundry detergent, bathroom surface cleaning products and kitchen surface cleaners/ disinfectants. Though these cleaning products are primarily marketed for industrial use (e.g. health care industry) they may also be available to the public through retail outlets. Personal care products include bar soaps, liquid hand soaps, liquid body soaps, antiperspirants/deodorants and toothpaste/mouthwashes.

A possible source of consumer exposure to triclosan that is also considered in this assessment is from its use in articles, including textiles (bedding, clothing and wipes), plastics (e.g. food storage containers, toilet seats, PVC carpet backing and swimming pool liners), and painted surfaces, as the potential may exist for its migration from the article surface.

The potential for exposure of the public to triclosan during its importation, transport and storage is expected to be negligible and, hence, will not be characterised further.

15.2 Routes of exposure to adults

The main route of public exposure is likely to be through dermal contact given the types of triclosan-containing products available to the public (cosmetic, personal care and cleaning products).

Oral exposure may occur through accidental or incidental ingestion of lip balm, toothpaste or mouthwash formulations containing triclosan. Inhalation exposure may occur through breathing aerosols generated from the use of cosmetic, personal care or cleaning products containing triclosan, or dusts generated from the use of talcs containing triclosan.

Accidental ocular exposure is likely to occur only infrequently and will involve very small amounts of triclosan. Therefore, as the potential for public exposure via this route is expected to be negligible it will not be characterised further.

15.3 Methodology for assessing exposure

Potential consumer exposure to a product containing triclosan has been determined by evaluating the various use patterns. To carry out a quantitative exposure assessment to a product containing triclosan information on a number of parameters is required, such as the amount of product used, the frequency of use and the exposure duration.

Exposure data on the use of consumer products containing triclosan in Australia is limited. Consequently exposure models from the following documents have been used to predict consumer exposure to various categories of products:

- Occupational and consumer exposure assessments from OECD Environment Directorate (1993)
- Technical Guidance Document on Risk Assessment from the European Chemicals Bureau (EC, 2003a)
- Guidance note for the testing of cosmetic ingredients and their Safety evaluation (5th revision) from the Scientific Committee on Cosmetic Products and Non-Food Products Intended for Consumers (SCCNFP) (2003)

The mathematical formula and reference values used in these models for each exposure scenario are shown in Appendix D. It should be noted that in these calculations absorption following inhalation and dermal exposure are considered to be 100% and 14%, respectively as determined in Section 6.1 (Kinetics and Metabolism). Oral exposure to products containing triclosan (e.g. toothpastes) is likely to be low as only small amounts of triclosan are likely to be ingested during use. Consequently, calculations for oral exposure in this section have used the absorption value of 14% (termed ‘buccal’ absorption’) as determined in section 6.1 from studies in volunteers. Additionally, for adults, in all calculations of exposure, the average human body weight of females of 60 kg is used as compared to 70 kg in males. Consequently, the internal doses presented in this assessment will be slightly greater than those that would be calculated for adult males.

Public exposure to triclosan is assessed for each major exposure scenario, namely:

- Exposure to cosmetic and personal care products containing triclosan;
- Exposure to household cleaning products containing triclosan; and
- Exposure to triclosan from articles and painted surfaces.

15.4 Exposure to cosmetic and personal care products

Cosmetic and personal care products containing triclosan are available in the form of liquids, foaming liquids, creams, gels, powders, aerosol sprays, masks, bars/sticks and wipes. From the information provided by industry, the product categories marketed in Australia along with the range of triclosan concentrations in these products is provided in Table 15.1. Skin care products are divided into rinse-off and leave-on.

Table 15.1 shows that the concentration of triclosan in most cosmetic and personal care products is less than 0.3%. The highest concentration observed was 0.5% in rinse-off products. Rinse-off products have short exposure durations and/or the concentration of triclosan is likely to be diluted during use.

15.4.1 Exposure pattern

Dermal exposure to triclosan from cosmetic and personal care products is expected to be the significant source of public exposure. Dermal contact may be limited to specific areas of the body such as the eye region, face, hands, nails, or feet, or may be more extensive, with the product in contact with large areas of the trunk as well as the face. The duration of exposure for rinse-off products may be only a few minutes, though residual triclosan may exist after use, in contrast, exposure to leave-on products can be several hours. Similarly, buccal absorption from the use of oral care products would only be for a short duration, though some degree of ingestion may occur from the use of these products (and lipstick/lip balm). There is

also potential for inhalation exposure through the use of aerosol products and talcs containing triclosan.

Table 15.1 - Categorisation of cosmetic and personal care products and triclosan concentrations

Product Category	Triclosan Concentrations (%)
Aerosol products	
Deodorants and body sprays	0.05 – 0.3
Foot sprays	0.05 – 0.2
Shoe sprays	0.3
Rinse-off Products	
Face and skin cleansers, moisturisers, toners, exfoliants	0.075 – 0.3
Face masks	0.5
Liquid hand soaps	0.1- 0.3
Shower and bath gels, body washes, face washes	0.01 – 0.5
Leave-on products	
Anti-pimple/blemish formulations	0.15 – 0.3
Body lotions	0.05 – 0.3
Colognes	0.024 – 0.1
Cuticle and nail conditioners	0.1 - 0.2
Deodorants (stick, roll-on)	0.01 – 0.31
Eye make-up	<0.1
Face creams	0.05 – 0.3
Feminine wash	0.05 – 0.12
Foot talcs	0.05 – 0.2
Insect repellents	<0.2
Lip treatments	0.1 - 0.25
Pre-wax skin wipes	0.15
Shoe talcs	0.25-0.3
Skin purifying patches	0.3
Sunscreens	0.05 – 0.1
Oral care products	
Mouthwash	0.3
Toothpaste	0.2-0.3
Other products	
Baby wipes	Not reported
Cotton buds	<0.01

It is expected that cosmetic and personal care products containing triclosan are likely to be used by many people. However, the use pattern is variable between people and depends on a number of factors. No data on Australian use patterns such as typical amount used per application, frequency of use and exposure

duration are available for these products. However, collected data on typical use patterns of some classes of these products in Europe are provided in the Technical Guidance Document on Risk Assessment of the European Chemicals Bureau (EC, 2003a) and the Guidance Notes for the Testing of Cosmetic Ingredients and their Safety Evaluation of the (EU) Scientific Committee on Cosmetic Products and Non-Food Products Intended for Consumers (SCCNFP, 2003). It is considered that Australian use will be similar to that in Europe and consequently, this data has been used in determining exposure.

15.4.2 Measured plasma levels of triclosan

Limited measured exposure data are available in the form of total triclosan levels, consisting of triclosan and its metabolites in plasma following use of consumer products containing triclosan (Section 17.1). Total triclosan levels in the plasma are also available in the key animal study identifying a no-observed-adverse-effect-level (NOAEL) for health effects following repeated exposure. A summary of the most robust and relevant measured exposure data is provided in Table 15.2.

In these studies, human volunteers were given one or more products containing triclosan and instructed to use them under simulated conditions of use (i.e. the amount of product used per event, use frequency and duration). The combined level of triclosan and its metabolites ('total' triclosan) in the plasma provides an estimate of absorption under real life conditions. It is considered that the most appropriate studies to determine absorption following exposure would be repeated use studies of significant duration and exposure in which steady state plasma levels were reached. It is recognised that data from these studies are unlikely to be applicable to all consumers, as individual use patterns will vary. A summary of the most appropriate data is presented below.

Studies using a surgical scrub containing 0.5% or 0.75% triclosan (Ciba-Geigy Corporation, 1972a; Thompson, 1975) are not included in Table 15.2 as it is considered that this product is unlikely to be used by consumers. Furthermore, in a single study using a soap bar containing 1% triclosan (Wagner and Le Sher, 1997) a steady state plasma level of 2580 ng/mL was seen in one individual. Such a high plasma level was not seen in any other individual in numerous other studies. Consequently, the data from this study is not considered reflective of general consumer exposure and is not presented in Table 15.2.

Table 15.2 includes oral exposure data from studies in which dental products containing triclosan were correctly used with the dental slurry being expelled. Data from studies either with limited details (Lin, 1988, 2000) or inappropriate use of a product (deliberate ingestion of dental slurry) are not provided in Table 15.2 (Colgate-Palmolive, 1997b).

15.4.3 Estimated exposure data

Exposure to cosmetic and personal care products is estimated according to models described in the Technical Guidance Document on Risk Assessment of the European Chemicals Bureau (EC, 2003a) and the EU Guidance Notes for the Testing of Cosmetic Ingredients and their Safety Evaluation (SCCNFP, 2003). As individual use and hence exposure to these products will vary widely the highest concentrations of triclosan marketed in these products in Australia has been used to represent reasonable worst-case exposure scenarios.

Table 15.2 – Plasma levels of triclosan following use of personal care products

Product and triclosan concentration (%)	No of volunteers	Mean product dose (g/event)	Frequency (events/day)	Plasma conc. of total triclosan (ng/mL)	Reference
Single product use					
Hand wash (1%)	7 males 6 females	3.5	6	229 ¹ 158 ²	Ciba Specialty Chemicals Corp. (2002)
Unspecified bath product (0.75%)	2	10	1	Approx 20 and 30	Ciba-Geigy Corp. (1972a)
Dentifrice (0.2%)	9 males	Not reported	2	26.7 ³	Colgate-Palmolive Company (1989)
Dentifrice (0.28%)	35 Caucasian 26 Negroid 22 Mongoloid	Not reported	At least 2	22.7 ³ 25.7 ³ 20.5 ³	Beiswanger & Tuohy (1990)
Toothpaste (0.3%)	3 males 3 females	Not reported	4	132 ³ 159 ³	BIBRA Internat. (1997)
Multiple product use					
Soap bar (0.75%)	33 Caucasian 28 Negroid	Not reported	At least 2 for dentifrice and 1 for other products	36.7 ³ 34.3 ³	Beiswanger & Tuohy (1990) ⁴
Deodorant (0.39%)					
Dentifrice (0.28%)					

¹ Maximum level of total triclosan observed in males; ² Maximum level of total triclosan observed in females; ³ Mean maximum concentration of total triclosan; ⁴ Data for Oriental volunteers is not presented due to concerns of non-compliance with regards to use of the soap and deodorant

Inhalation exposure

Data on amounts used and frequency of use are available for anti-perspirant/deodorant sprays but not foot or shoe spray products and is presented in Table 15.3. In order to estimate the internal dose following use of anti-perspirant/deodorant sprays a volume of 2 m³ is taken to represent the volume of air immediately surrounding the user (EC, 2003a). The following assumptions are also used in the calculation.

- A respiratory volume of 23 m³/day
- The bioavailability of triclosan via inhalation is 100%

The internal doses of triclosan following inhalation exposure during use of anti-perspirant or deodorant spray is provided in Table 15.3. Under these assumptions the internal doses ranges from 18 - 53.9 µg/kg bw/day.

Table 15.3 - Typical use pattern and inhalation exposure of anti-perspirant/deodorant spray product

Product	Amount per event (g)	Use frequency (events/day)	Duration (min/event)	Triclosan in product (%) ¹	Internal dose (µg/kg bw/day)
Anti-perspirant/deodorant spray	3.0	1-3	15	0.3	18.0-53.9

¹ Maximum concentration of triclosan reported in these products in Australia

Dermal exposure

Use data are available for a number of cosmetic and personal care products, excluding shoe talcs, anti-acne formulations, feminine wash and insect repellents and is presented in Table 15.4. In addition to use data the model incorporates a retention factor for rinse-off products, which is the amount of residual chemical considered retained on the skin. Experimental data in a kinetics and metabolism study indicates that approximately 14% triclosan is absorbed through the skin.

In the model it is assumed that sunscreens are used up to three times a day for two weeks in a year in the EU. In Australia, exposure to this product may be greater in some sub-populations of the general public who use sunscreens on a more regular daily/yearly basis.

It is predicted that the major body burden will be from the use of leave-on products with sunscreens providing the largest internal dose. For a worst-case scenario estimation, assuming that a person was exposed to all the products listed in Table 15.4, the combined internal dose would be approximately 145.5 µg/kg bw/day.

Buccal exposure

Use data are available for lipstick, toothpaste and mouthwash and is presented in Table 15.5. In addition to use data the model incorporates a retention factor, which is the amount of residual chemical considered retained on the lips/in the buccal cavity. Buccal absorption of 14% obtained from experimental data is also used in the calculations.

For a worst-case scenario estimation under these assumptions, if a person was exposed to all these products the internal dose would be 24.4 µg/kg bw/day.

Table 15.4 - Typical use pattern and dermal exposure of selected cosmetics and personal care products

Product Type	Amount per event (g)	Use frequency (events/day)	Triclosan in product (%) ¹	Retention factor ²	Internal dose (µg/kg/day)
Leave-on products					
Deodorant	0.5	1	0.31	1	3.62
Body lotion	8	0.71	0.3	1	39.76
Colognes	5	0.29	0.1	1	3.38
Eye make-up ³	0.11	1-2	0.1	1	0.28
Face cream	0.8	2	0.3	1	11.20
Foot spray	3	2	0.2	1	28.00
Nail polish/remover	0.25	0.28	0.2	1	0.33
Sunscreen	8	3	0.1	1	56.00
Rinse-off products					
Bath products	17	0.29	0.5	0.001	0.06
Eye removal lotion	0.5	1	0.1	0.1	0.12
Facial masks	3.7	0.1	0.5	0.1	0.43
Make-up remover	2.5	1	0.3	0.1	1.75
Shower gel	5	1.07	0.5	0.01	0.62

¹ Maximum concentration of triclosan reported in these products in Australia

² A retention factor of 1, 0.1, 0.01 and 0.001 represents 100%, 10%, 1% and 0.1% retention of the chemical respectively

³ Is the sum of five different products: eye shadow; mascara; eyeliner; eyebrow pencil; and concealer

Table 15.5 - Typical use pattern and oral membrane exposure of some cosmetic and personal care products

Product	Amount per event (mg product/event)	Use frequency (events/day)	Triclosan in product (%) ¹	Retention factor ²	Internal exposure (µg/kg/bw/day)
Lipstick	10	4	0.1	1.0	0.09
Toothpaste	1400	2	0.3	0.17	3.33
Mouthwash	10000	3	0.3	0.1	21

¹ Maximum concentration of triclosan reported in these products in Australia

² A retention factor of 1, 0.17 and 0.1 represents 100%, 17% and 10% retention of the chemical respectively

15.5 Exposure to household cleaning products

Household cleaning products containing triclosan include dishwashing detergent, laundry detergent, bathroom surface cleaning products, kitchen surface cleaners, and disinfectant/cleaner. All these products are primarily marketed for industrial uses within Australia, though some may be available to the public through retail outlets. A summary of the triclosan concentration in these products is presented in Table 15.6.

Table 15.6 - Cleaning products containing triclosan

Product	Triclosan Concentration (%)
Surface disinfectants/cleaners	
Liquid/gel	0.04
Liquid	0.2
Liquid spray	0.25
Dishwashing detergents	0.1 - 0.2
Laundry detergent	0.3

Some surface disinfectants and surface cleaners are formulated as sprays and used without dilution. However, as most of these products are diluted prior to use the final triclosan concentration is expected to be lower than those listed in Table 15.6.

15.5.1 Exposure pattern

The main route of exposure to household cleaning products will be through dermal contact, which is expected to be limited to the hands and possibly forearms. Ingestion of cleaning products is unlikely. Inhalation exposure may occur through the use of disinfectant/cleaner sprays.

The duration of exposure while adding laundry detergents is expected to be only a few seconds. Exposure to dish washing detergents will be longer, though the products are diluted prior to use.

Household cleaning products are used in Australia, on a regular basis, mainly by adults. No data on Australian use patterns such as typical amount used per application, frequency of use and exposure duration are available for these products. However, such information is available in the Technical Guidance Document on Risk Assessment of the European Chemicals Bureau (EC, 2003a). It is considered that Australian use will be similar to use in Europe and consequently, this data has been used in determining exposure.

15.5.2 Estimated exposure data

Exposure to cleaning products is estimated according to the model described in the Technical Guidance Document on Risk Assessment of the European Chemicals Bureau (EC, 2003a). As individual use and hence exposure to these products will vary widely, the highest concentration of triclosan marketed in these products in Australia have been used to represent reasonable worst-case exposure scenarios.

Inhalation exposure

Use data is available for surface disinfectants/cleaners and is presented in Table 15.7. In order to estimate the internal dose it is assumed that a surface disinfectant/cleaner spray is used in the bathroom with a room volume of 4 m³ (EC, 2003a). The same assumptions as used in section 15.4.3 are used in calculating the internal dose.

Table 15.7 - Typical use pattern and inhalation exposure from household cleaning products

Product	Amount per event (g)	Use frequency (events/day)	Duration (min/event)	Triclosan in product (%) ¹	Internal dose (µg/kg bw/day)
Surface disinfectants/cleaners	5-30	1-7	2-10	0.25	1.7 – 349.5

¹ Maximum concentration of triclosan reported in these products in Australia

The internal dose is determined to range from 1.7-349.5 µg/kg bw/day.

The use of dishwashing/laundry detergents containing triclosan is expected to result in negligible inhalation exposure.

Dermal exposure

Use data is available for dishwashing and hand laundry detergents, and surface cleaners, and is presented in Table 15.8. The same assumptions as used in section 15.4.3 are used with the following additional assumptions:

- a duration factor in calculating the internal dose.
- the area of skin in contact with the product is 1000 cm² (i.e. the area of both hands or a hand and forearm) for all products except surface cleaners where it is assumed to be 500 cm² (i.e. the area of one hand).
- the thickness of the liquid layer on the skin is 0.01cm.
- a dilution factor for hand dishwashing and laundry detergents. All other products are used neat and therefore have no dilution factor.

It is predicted that the major body burden will arise from the use of (undiluted) surface cleaners rather than hand washing activities.

- Thus, a worst-case scenario estimation under these assumptions would be a person exposed to regular liquid dishwashing detergent, a hand laundry detergent and a liquid surface cleaner. The maximum combined internal dose is estimated to be approximately 0.34 µg/kg bw/day.

Table 15.8 - Typical use levels and dermal exposure from household cleaning products

	Amount used (g/event)	Frequency (event/week)	Duration (min)	Triclosan in product (%) ¹	Internal dose (µg/kg bw/day)
Hand dishwashing					
Liquid regular ²	3-10	3-21	10-45	0.2	Negligible ⁵ – 0.0088
Liquid concentrate ²	2-5	3-21	10-45	0.1	Negligible ⁵ – 0.0022
Hand laundry detergent					
Liquid ³	78-230	1-18	10	0.3	Negligible ⁵ – 0.013
Surface cleaners					
Liquid ⁴	30-110	1-7	10-20	0.2	0.023–0.32
Gel ⁴	20-40	1-7	10-20	0.04	0.0046–0.065
Spray ⁴	5-30	1-7	2-10	0.25	0.0058–0.20

¹ Maximum concentration of triclosan reported in these products in Australia

² The amount used is given per 5L of wash water volume

³ Diluted so as to give a 0.1% - 1% wash solution during the duration of hand washing laundry

⁴ Used neat, no dilution

⁵ Values less than 0.0001 µg/kg bw/day are shown as negligible.

15.6 Exposure to textile and plastic articles

Textile articles containing triclosan include bedding (doona and pillow fill, mattress quilting), clothing (sportswear, socks, fashion, swimwear, shoe insoles), and wipes. Although information was supplied on the use of triclosan in the manufacture of these textiles no information is available on the fixation rate and the amount of triclosan present in the final product. Similarly, while plastic articles such as food storage containers, toilet seats, PVC carpet backing, swimming pool liners and toothbrushes may contain triclosan the concentration present in these products is unknown.

15.6.1 Exposure pattern

The main potential route of exposure to these textile and plastic articles will be through dermal contact. These articles may be a source of potential exposure if migration of triclosan to the outer surface occurs. Migration is a slow diffusion process that is dependent on the properties of the chemical (volatility, solubility and stability) and the matrix into which it is bound. Inhalation exposure from textile and plastic articles is expected to be low due to the low vapour pressure of triclosan. The oral route may be a potential route of exposure from the use of plastic cups, plates and food storage containers containing triclosan and through the sucking or mouthing of textile articles containing triclosan. The latter behaviour is likely to occur in infants and children.

There is potentially widespread exposure to textile and plastic articles containing triclosan in Australia, though the only data available on the amount of triclosan present in an article in Australia is for cling wrap. Limited information on triclosan

levels in clothing articles in Denmark is also available (Danish Environmental Protection Agency, 2003a). These data have been used in determining exposure.

15.6.2 Estimated exposure data

Exposure to textile and plastic articles is estimated according to models described in the Occupational and Consumer Exposure Assessments from the OECD Environmental Directorate (OECD, 1993) and the Technical Guidance Document on Risk Assessment of the European Chemicals Bureau (EC, 2003a). As potential exposure to these articles will vary widely the highest concentrations of triclosan in textile and plastic articles have been used to represent reasonable worst-case exposure scenarios.

Inhalation exposure

No leaching rate of triclosan from the surface of textile or plastic products into air has been reported. The OECD Environmental Directorate model (OECD, 1993) determines exposure from a textile or plastic article based on the chemical's vapour pressure. Based on a vapour pressure of 5×10^{-4} Pa at 20°C the concentration of triclosan in the air from an article is 0.01 mg/m³. Triclosan is reported to be used in low concentrations in textile and plastic articles and the estimated concentration in air is likely to be an over estimate.

Under these assumptions the internal dose received from a textile or plastic article is determined to be 3.8 µg/kg bw/day.

Dermal exposure

The concentration of triclosan in 17 clothing articles from Danish retail outlets was analysed. Triclosan was detected in 5 articles⁹: ski underwear (7 ppm), cycle shorts (at 9 and 22 ppm) and ladies underwear (16 ppm) and the soles of sandals (195 ppm). The limit of detection was 5 ppm (Danish Environmental Protection Agency, 2003a). However, no data on the migration of triclosan from clothing over time are available and hence exposure cannot be predicted from this source. Considering that only low levels of triclosan were detected in a few consumer articles, contribution to the overall body burden from dermal exposure to textile articles is likely to be negligible.

The amount of triclosan in cling wrap articles in Australia is 0.6%. However, no data on the migration of triclosan from cling wrap over time are available and exposure from this source cannot be predicted. It is considered that only low levels of triclosan would migrate from cling wrap and therefore contribution to the total body burden from dermal exposure is likely to be negligible.

Oral exposure

Oral exposure is potentially possible from the leaching of triclosan from plastic cups, cutlery, plates, and food storage containers into food or drink. However, no experimental data on the rate of leaching is available and, hence, exposure cannot be determined. It is considered, however, that leaching from articles will be very

⁹ No triclosan was detected in the following textile articles analysed: cycle shorts (2 articles), mans pullover, ladies bathing costume, ladies cycle shorts, sports sole, mans jogging shoes, socks, ankle protector, bra-insert for breast feeding (2 articles) and ladies underwear.

low and the contribution to the total body burden from oral exposure to plastic articles is likely to be negligible.

15.7 Painted tile and cabinet/cupboard surfaces

Some tile and laminate paints have a triclosan concentration of 1g/L. A litre of paint covers 12 m². No data regarding the diffusion or migration rate of triclosan in dry paint is available. However since the paint manufacturer claims that the chemical is added to the paint for surface anti-microbial protection, it may be assumed that triclosan is available for absorption or inhalation.

15.7.1 Exposure pattern

The main route of exposure will be through dermal contact via the skin of the soles of the feet when walking barefooted on bathroom and kitchen tiles; dermal exposure from rubbing onto laminated cabinets and cupboards may be deemed negligible. Inhalation exposure from painted surfaces is expected to be low due to the low vapour pressure of triclosan. Oral exposure may occur when unpackaged foods such as fruit are left on laminated benches. However this is expected to be negligible.

15.7.2 Estimated exposure data

The models described in the Occupational and Consumer Exposure Assessments from the OECD Environmental Directorate (OECD, 1993) and the Technical Guidance Document on Risk Assessment of the European Chemicals Bureau (EC, 2003a) are used in the estimation of exposure from tile and laminate paints containing triclosan.

Inhalation exposure

The OECD Environmental Directorate model (OECD, 1993) used for estimation of inhalation exposure from the surface of textile or plastic products accounts for release of triclosan from all article surfaces, and no separate determination of release from painted surfaces is required.

Dermal exposure

A surface area of 12 m² contains 1g of triclosan. Despite the absence of migration rate data for triclosan on dry painted surfaces, a worst-case estimate of 1g/12 m² concentration can be assumed; this same assumption can be carried through even for recoated surfaces. Triclosan concentration on painted surfaces is 8.3 x 10⁻⁵ kg/m².

The average surface area of male and female adult feet is 1061 cm² (EC, 2003a). Estimating the sole area that comes in contact with the floor surface to be a third of the surface area of adult feet, 3.5 x 10⁻² m² of skin is exposed to triclosan assuming a worst-case situation of not wearing footwear when spending time in tiled areas of the home. The time spent in the bathroom and kitchen per day is 2 hours (enHealth, 2003).

The estimated internal dose using the above assumptions is 0.56 µg/kg bw/day.

Oral exposure

The oral exposure that may occur when unpackaged foods such as fruit are left on laminated benches is expected to be negligible. Foodstuffs such as fruit may be washed or peeled before consumption or food processing. If this is not the case, only a small proportion of the surface area is in contact with the painted surface, as in spherical- or elliptical-shaped fruit.

15.8 Exposure in children

In general, this group refers to a sub-population that is less than 18 years old. This section focuses on babies and young children up to 5 years old, and assumes that exposure to triclosan over 15 years is similar to adults.

Currently, there is no harmonised international approach for grouping children by age when assessing exposure to chemicals. The age groups depend on the availability of data and are based on professional judgment. In this section, the age groups are based on the *Child-Specific Exposure Factors Handbook* of the US EPA (2002), with values for body weight taken as the mean for males and females combined.

15.8.1 Routes and sources of exposure

The routes of exposure to triclosan in babies and young children include inhalation, dermal and oral, as in adults.

The sources of exposure in babies and young children could be divided into direct exposure and indirect exposure. Direct exposure refers to the potential for children to come into contact with one or more of the consumer products containing triclosan. The common triclosan-containing products used in children include soap, shower gel, baby wipes, toothpaste, body lotion, sunscreen, talc and other products.

Textile articles that are a potential source of exposure to triclosan include bedding, clothing and wipes. Plastic articles that are a potential source of exposure include cups, plates, food storage containers and toothbrushes. These articles may be a source of exposure if migration/leaching of triclosan occurs in the article.

A significant indirect source of exposure to triclosan in babies is their intake of breast milk that contains triclosan. Indirect exposure to triclosan via breast milk in babies is assessed in the section of oral exposure.

Inhalation exposure

The leaching rate of triclosan from the surface of textile or plastic products into air is not known. Using the OECD Environmental Directorate model (OECD, 1993) inhalation exposure from textiles, plastic articles and painted surfaces was determined to provide a concentration in the air of 0.01 mg/m³ (see section 15.6.2). This air concentration of triclosan is used for the estimation in children. The respiratory volumes in children are adopted from the *Child-Specific Exposure Factors Handbook* (US EPA, 2002), and the bioavailability of triclosan via inhalation is 100% in the calculation. The results are presented in Table 15.9.

Table 15.9 - Internal dose of triclosan in children via inhalation

Population (years)	Respiration volume (m ³ /day)	Bodyweight (kg)	Internal dose (µg/kg bw/day)
Infant			
<1	4.5	7.4 ¹	6.08
Children			
2	6.8	12.9	5.27
5	8.3	19.4	4.28

¹Body weight is the mean for male and female 2 – 6 month old infants combined.

The calculated internal doses decrease with increase in age. The highest internal dose is seen in infants (6.1 µg/kg bw/day). This internal dose is 1.6 times greater than that estimated in adults (3.8 µg/kg bw/day).

Dermal exposure

Personal care products such as baby wipes, bath products, and sunscreens, are considered likely to be used on babies. The information on dermal exposure to triclosan is limited in babies and young children.

Baby wipes, which have been identified as containing triclosan, are designed to be used on young babies. Although the exact concentration of triclosan in baby wipes is unknown, it is expected to be at low concentrations (less than 0.05% triclosan), based on the concentrations of triclosan in other similar products. Baby wipes are likely to be used only on small areas of the body and on an infrequent basis. Therefore dermal exposure from use of baby wipes is expected to be low.

Products that may be used on children for which both the concentration of triclosan and use data are known are bath products and sunscreens. However, the use data available, such as the typical amount used per event and number of events per day, are for adults and consequently a reliable estimation of exposure in children cannot be undertaken.

Body lotion is a leave-on product that may be used on babies and young children. The dermal exposure from the use of body lotion in children is estimated based on an assumption that the application volume per surface area is the same to both adults and children. The amount applied onto adults is known to be 8 g body lotion per event and the amount applied onto children have been calculated based on the ratio of surface areas between adults and children. Information on body surface areas in children was obtained from the *Child-Specific Exposure Factors Handbook* (US EPA, 2002).

Concentration of triclosan in body lotion is 0.3% and the lotion and use is assumed to be once a day in children. The bioavailability of triclosan via dermal application is 14%. The internal doses following use of body lotion containing triclosan at various ages are shown in Table 15.10. Under these assumptions, the internal dose of triclosan in babies is twice that in adults.

Considering the small concentrations of triclosan in textile (<0.02%) and plastic (0.6% in cling wrap) products and use pattern, their contribution to dermal exposure and the overall body burden in young children is likely to be negligible.

Table 15.10 - Internal dose of triclosan in children via dermal applications of body lotion

Age (year)	Body surface area (m ²)	Amount applied (g)	Frequency (event/day)	Bodyweight (kg)	Internal triclosan dose (µg/kg bw/day)
<1	0.487	1.4	1	7.4 ¹	85
2	0.833	2.6	1	12.9	84
5	0.761	2.6	1	19.4	56
Adults	2.538	8	0.71	60	40

¹Body weight is the mean for male and female 2 – 6 month old infants combined.

Dermal exposure from floor surfaces painted with tile and laminate paints containing 1g/L triclosan may occur in infants during the crawling stage. An infant with a skin surface area of 0.35 m² (enHealth, 2003) may expose half of his arms (13.7% of total skin surface area; US EPA, 2002) and half of his legs (20.6% of total skin surface area; US EPA, 2002) during crawling. Assuming only half of the legs and arms are in contact with floor surfaces, 0.06 m² of an infant's skin is directly exposed to triclosan. Children are estimated to spend an hour everyday in the kitchen and bathroom areas (compared to adults' 2 hours/day). Assuming that infants spend more time in these areas when in the company of adult carers compared to older children, but less the time adults do, an estimate of 1.5 hours can be used in the dermal exposure approximation for infants in the crawling stage. The internal dose of triclosan for infants is 5.9 µg/kg bw/day.

Dermal exposure for 2 year old and 5 year old children may occur through walking barefooted on bathroom and kitchen tiles. The following assumptions are made:

- 1 hour/day spent in the bathroom and kitchen
- Total skin surface area of 2 year old is 0.59 m² (enHealth, 2003); feet comprise 6.27% of surface area (US EPA, 2002)
- Total skin surface area of 5 year old is 0.69 m² (enHealth, 2003); feet comprise 7.25% of surface area (US EPA, 2002)
- Bioavailability of triclosan through dermal exposure is 14%.

Assuming a third of the feet are in contact with floor surfaces, the skin surface expose to triclosan is 0.012 m² and 0.017 m² for 2 year old and 5 year old children, respectively. The internal dose of triclosan for 2 year old children is 0.46 µg/kg bw/day and for 5 year old, 0.42 µg/kg bw/day.

Oral exposure - breast milk

For the purposes of this calculation, breast milk consumption has been determined for a baby that is exclusively breast-fed. Additionally, it is assumed that breast-feeding is not extended beyond 12 months, and hence has not been determined for young children.

Data is available on levels of triclosan in human breast milk samples from 3 countries: Sweden (Adolfsson-Erici et al., 2002; Allmyr et al., 2006), USA (Plautz, 2005) and Australia (see Appendix E). The maximum levels detected were

approximately 10, 55 and 19 µg/kg milk respectively. The value of 19 µg/kg milk is taken forward in determining ingestion of triclosan in breast milk. It is the maximum level observed nationally and is therefore reflective of Australian use of triclosan containing products.

The weighted average intake of breast milk ranges from 723-751 g/day in 1-4 month babies (Butte at al., 1984, as reported in US EPA, 2002). The intake decreases from 9 to 12 months as breast milk is gradually replaced by other foods. The mean breast milk intake among exclusively breast-fed infants during the first 4 months of life is provided in Table 15.11. These intakes are used to estimate potential exposure in Australian infants. Oral absorption of triclosan in breast milk is assumed to be 100%.

Table 15.11 - Internal dose of triclosan via breast milk in babies

Age (month)	Mean milk intake (g/day)	Body weight (kg)	Internal triclosan dose (µg/kg bw/day)
1	751	4.7	3.04
2	725	5.6	2.46
3	723	6.2	2.22
4	740	6.7	2.10

The highest internal triclosan dose is seen in one-month old babies due to the higher milk intake and low bodyweight at this age. The internal dose in one-month old babies is selected as a worst-case scenario.

Buccal exposure - toothpaste

Use data are available in adults for use of toothpaste. As young children's toothbrushes are smaller than adults it has been assumed that approximately half the amount of toothpaste used by an adult would be used by/on a young child in calculating exposure. Use frequency is assumed to be comparable to that of adults. In order to determine the internal dose the following assumptions are used in the calculations.

- Buccal absorption of triclosan is 14%
- The average 2 and 5 year old body weight is 12.9 and 19.4 kg respectively

Under these assumptions the internal dose is determined to be 15.5 and 10.3 µg/kg bw/day for a 2 and 5 year old, respectively.

Oral exposure - Textile and plastic articles

There is potential for oral exposure to babies and young children through mouthing or sucking of textile and plastic articles. Additionally for young children, exposure may occur from the leaching of triclosan from plastic cups, cutlery, plates, and food storage containers into food or drink. However, no experimental data on the rate of leaching of triclosan from a textile or plastic article into saliva, food or drink are available and hence exposure from these potential sources cannot be determined. However, it is considered likely that leaching from articles will be very low and as a source of exposure ingestion of triclosan from textile and plastic

articles is likely to be negligible to the overall body burden in babies and young children.

15.9 Indirect exposure via the environment

Exposure via air

As there is no Australian data on atmospheric concentrations of triclosan, no estimate of inhalation exposure can be made that is directly relevant to Australian conditions. However, given the very low volatility of triclosan the concentration in the air, and hence exposure, is likely to be very low. This is supported by data from Sweden where triclosan was detected in 8 of 13 urban air samples at concentrations ranging from $<0.003 - 0.17 \text{ ng/m}^3$ (Remberger et al., 2002).

Exposure via drinking water, food and soil

No data are available on the concentrations of triclosan in Australian drinking waters, and so no estimates of exposure can be made. Similarly, information on triclosan concentrations in food in Australia is not available, but exposure is only likely to occur to food products that have been exposed to contaminated water or soil during growth. Furthermore, no monitoring data are available on concentrations of triclosan in soils in Australia. In Sweden, triclosan was detected in just over half of surface soil samples (i.e. 4 out of 7) at concentrations ranging from <3 to $15 \text{ } \mu\text{g/kg}$ (Remberger et al., 2002). Similarly in Australia, no field monitoring data on the absorption of triclosan by plants or fish from contaminated water is available, though triclosan has been measured in muscle of wild-caught freshwater fish at $\leq 3.4 \text{ ng/g}$ ($\mu\text{g/kg}$; wet wt) overseas. Therefore, overseas data suggest that public exposure to triclosan via food and soil is expected to be low.

The US EPA estimated triclosan residues in food due to its migration from contact with food-contact paper, paperboard use, adhesive use, ice-making equipment, cutting boards, counter tops and conveyor belts. Based on the FDA methodology for calculating the estimated daily intake and daily dietary doses, none of these indirect food contact scenarios appeared to exceed the Agency's level of concern (US EPA, 2007).

16. Data on Environmental Exposure

Triclosan is a widely applied antimicrobial agent used in human domestic, commercial, agricultural and industrial applications for approximately 30 years. Use of triclosan in Australia involves widespread and diffuse emissions since the substance is present in a wide range of personal care and consumer products used throughout Australia.

The majority of the triclosan imported to Australia is used as a minor component in domestic/commercial situations (e.g. personal care and consumer products, textiles, plastics). Therefore, the use of triclosan in Australia results in widespread exposure to the general public. After its use, a high proportion is eventually washed off or discharged with wastewater to the Australian sewerage system. Sewage is treated at municipal sewage treatment plants (STPs) situated throughout Australia. Treated effluent is discharged mostly to the aquatic environment.

In many instances, treated STP effluent is re-used (reclaimed water) in irrigation (urban, commercial, agricultural) or industrial applications. Solid wastes containing triclosan, such as unsaleable products, off-cuts, emptied containers with residues of products containing triclosan or products at the end of their useful life, are mostly sent to landfill for disposal.

16.1 Fate and transformation processes

This section describes the potential transformation processes that may act upon triclosan in the environment including hydrolysis, chlorination, photolysis, adsorption, mobility, biodegradation and methylation, reactions with metals and combustion.

16.1.1 Water solubility and hydrolysis

With solubility in water of 10 mg/L at 20°C (Ciba-Geigy Limited, 1990c), triclosan is considered slightly to moderately soluble in water at 20°C. Water solubility increases with increasing temperature (40 mg/L at 50°C). Triclosan is readily soluble in sodium hydroxide solution and organic solvents (Ciba Specialty Chemicals, 1998a).

Triclosan is hydrolytically stable in water at pH 4, 7 and 9 at 50°C, and it has a half-life longer than 1 year at 25°C in waters of pH 4, 7 and 9 (Ciba-Geigy Limited, 1990f). After 15 hours in a 3N alcoholic sulphuric acid solution no hydrolysis occurred and <0.5% occurred in a solution of 5N caustic soda (Ciba Specialty Chemicals, 1998a).

16.1.2 Chlorination

Disinfection of wastewaters using aqueous chlorine is undertaken at many municipal STPs and potentially other waste water treatment plants (WWTPs). Some STP operations include dechlorination of effluent prior to discharge. In addition, the use of many products containing triclosan involves mixing in water from a reticulated water supply, which then generally contains chlorine used as a disinfectant. Chlorination may occur during disinfection and deodorisation of

triclosan-containing solutions with bleach (sodium hypochlorite is a domestic bleach agent).

Triclosan concentrations and formed product concentrations after bleaching of textiles impregnated with triclosan were reported by Kanetoshi et al. (1987). These studies demonstrate the formation of 3 chlorinated derivatives (Figure 16.1), with derivative IV (2',3,4,4',5-pentachloro-2-hydroxydiphenyl ether) being formed in higher amounts than the other two derivatives (Table 16.1).

Table 16.1 - Formation of chlorinated derivatives of triclosan (TCS) following bleaching with sodium hypochlorite.

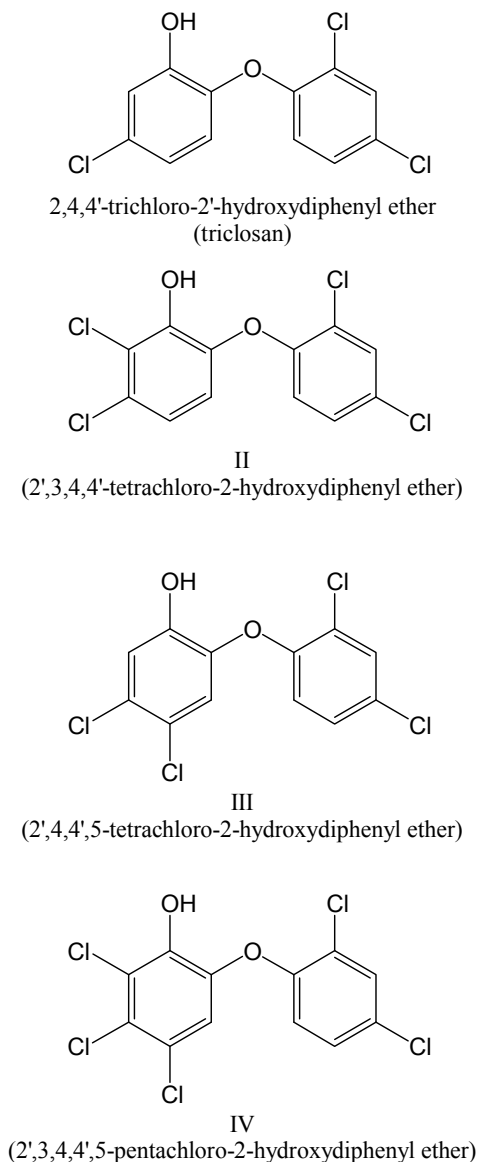
Sample No.	Untreated (µg/g)				Treated with 0.02% available chlorine (µg/g)				Treated with 0.2% available chlorine (µg/g)				
	TCS	II	III	IV	TCS	II	III	IV	TCS	II	III	IV	
1	1320	ND	ND	ND	F	495	18	14	67	474	20	10	62
					A	102	35	8	55	203	18	7	26
2	365	ND	ND	ND	F	152	4	3	48	234	14	10	55
					A	2	6	1	22	48	7	2	13
3	367	ND	ND	ND	F	5	ND	ND	5	5	ND	ND	3
					A	ND	6	ND	2	2	ND	ND	1
4	493	ND	ND	ND	F	530	3	2	8	441	25	36	18
					A	ND	ND	ND	ND	ND	ND	ND	1
5	515	2	3	ND	F	197	9	6	34	130	12	11	38
					A	ND	ND	ND	4	ND	ND	ND	1

Source: Kanetoshi et al. (1987). Bleaching was carried out at 45°C for 30 minutes. F = fabric (socks). A = aqueous. Compounds: II = 2',3,4,4'-tetrachloro-2-hydroxydiphenyl ether; III = 2',4,4',5-tetrachloro-2-hydroxydiphenyl ether; and IV = 2',3,4,4',5-pentachloro-2-hydroxydiphenyl ether. ND = not detected (<1 µg/g). Analysis by HPLC.

Canosa et al. (2005b) investigated the degradation of triclosan in chlorinated water. Chlorination of the phenolic ring and cleavage of the ether bond were identified as the main triclosan degradation pathways. Both processes led to the production of two tetra- and penta-chlorinated hydroxylated diphenyl ethers in agreement with Kanetoshi et al. (1987) described above. However, the tetracosans were detected only for short reaction times therefore suggesting they are further chlorinated to produce the pentacosan. In addition, concentrations of 2,4-dichlorophenol (2,4-DCP) were found to increase at a steady rate with the reaction time until 40-60 minutes, then decrease slowly. This product could be formed through rupture of the ether bridge contained in triclosan, the tetracosans or the pentacosan. In addition, significant amounts of 2,4,6-trichlorophenol (TCP) were noticed, with concentrations increasing slowly but steadily with the reaction time. This was the most abundant metabolite for long reaction times. Separately to this experiment, 2,4,6-TCP has been shown to be produced from chlorination of 2,4-DCP. All of these five compounds were also identified when triclosan was added to tap-water samples with free chlorine concentrations <1 mg/L. Minor amounts of three dihydroxylated phenols, containing from one to three chlorines in their structures, were also identified as unstable by-products. The analysis of several raw wastewater samples showed the co-existence of important concentrations of triclosan and its most stable by-products (2,4-DCP and 2,4,6 TCP), reinforcing the

potential occurrence of the described transformations when products containing triclosan are mixed with chlorinated tap water.

Figure 16.1. Chlorinated derivatives of triclosan.



Rule et al. (2005) describe a further study undertaken to characterize the kinetics and products of triclosan and free chlorine reactions under conditions typical of drinking water treatment. Initial free chlorine concentrations were 0.192-0.177 mg/L as Cl_2 with initial triclosan concentrations of 0.72-8.0 mg/L. It was shown that triclosan and free chlorine readily react and the kinetics is a function of the pH. In the absence of triclosan, loss of free chlorine was negligible, and in the absence of free chlorine, triclosan was stable. Reaction rates increased as pH increased from 3.5 to 6.5, then decreased as pH increased above 8. This effect can be rationalized on the basis of the pH dependent speciation of both free chlorine and triclosan. Overall, second-order kinetics were observed, first-order in free chlorine and first-order in triclosan. It was determined that the pH effect indicates

that the dominant reaction in the test system used was between the ionized phenolate form of triclosan and hypochlorous acid (HOCl). The overall second-order rate coefficient was determined to be $5.40 (\pm 1.82) \times 10^3 \text{ M}^{-1} \text{ s}^{-1}$ resulting in a triclosan half-life of 0.19 minutes. Three chlorophenoxy phenols (5,6-dichloro-2-(2,4-dichlorophenoxy) phenol (II); 4,5-dichloro-2-(2,4-dichlorophenoxy) phenol (III) and 4,5,6-trichloro-(2,4-dichlorophenoxy) phenol (IV)) were identified and two chlorophenols were identified. 2,4-DCP was detected under all reaction conditions, forming via ether cleavage of triclosan. In experiments with excess free chlorine, 2,4,6-TCP was formed via electrophilic substitution of 2,4-DCP. Chloroform formation was observed when an excess of free chlorine was present.

It is further stated in Rule et al. (2005) that while the use of free chlorine in wastewater treatment to disinfect the final effluent should suggest rapid removal of triclosan based on their results, the high levels of ammonia present in wastewater effluent effectively cause formation of chloramines. These are generally weaker oxidants than free chlorine and it is therefore expected these would react with triclosan at a much slower rate. This was investigated by Greyslock and Vikesland (2006) where triclosan reactivity in chloraminated waters was examined over the pH range of 6.5-10.5. It was shown that triclosan reacts in the presence of monochloramine, but the reaction occurs over a longer time frame than observed with free chlorine (reaction rate some 2-4 orders of magnitude slower). As observed with the free chlorine experiments, there was an increase in the triclosan loss rate with a decrease in pH over the tested range. By-products of these reactions included three chlorinated triclosan by-products as well as 2,4-DCP and 2,4,6-TCP. Low levels of chloroform were detected after one week at pH values of 6.5 and 7.5. The authors conclude that the slow reactivity of triclosan in the presence of chloramines explains the recalcitrance of this species in nonnitrified wastewater effluents. The potential for hypochlorous acid to act as a reactive species was also evaluated by conducting chloramination experiments under elevated ammonia conditions and described in this publication. At high ammonia concentrations, the production of hypochlorous acid is significantly repressed making it possible to isolate the reactivity of mono- and dichloramine. Triclosan was shown to decay at a much slower rate in the elevated ammonia experiments supporting the hypothesis that hypochlorous acid formation enhances triclosan loss. Further, the slow but still significant decay of triclosan under excess ammonia conditions suggests that mono- and dichloramine also react with triclosan.

16.1.3 Photolysis

Agrisearch Inc (1993) investigated the photolytic potential of triclosan in water under laboratory conditions according to US EPA Pesticide Assessment Guidelines and Good Laboratory Practice Standards. Radiolabelled ^{14}C -triclosan (4.42 ppm, purity >99%) was added to sterile buffer (pH 7; filtered, deionised, distilled tap water) and subjected to continuous artificial light (xenon arc lamp rated at 400-765 W/m^2 and a UV filter to remove radiations $\leq 290 \text{ nm}$), considered equivalent to natural sunlight, at $25.4 \pm 0.6^\circ\text{C}$ for 3 hours. Control samples were similarly dosed but held within foil-wrapped containers in the dark during the test, and control showed no significant transformation of triclosan. Triclosan and products were analysed by HPLC and radiocarbon analysis using liquid scintillation counting. The detection limit for the buffer solution was $23 \mu\text{g}/\text{L}$. Within 3 hours, the triclosan concentration reduced from an initial parent concentration of 98.4% to 1.2% of applied dose. There was a corresponding increase mean concentration of

2,4-dichlorophenol (95.2% in 3 hours). The aqueous photolysis half-life of triclosan in water at pH 7 under irradiated conditions was ~41 minutes with a rate constant of 1.68×10^{-2} /minute.

As part of a wider experiment, Latch et al. (2005) considered triclosan decay kinetics. When photolyzed under Hg-vapour lamps ($\lambda > 300$ nm), the triclosan phenolate anion rapidly degraded whereas the parent phenol form displayed much slower photodegradation kinetics. Triclosan dissolved in deionised water, was photodegraded by natural sunlight with a half-life (corrected for the lens effect) of 5 h. The quantum yield measured with sunlight irradiation was lower than that measured under Hg-vapour lamps (0.12 under natural sunlight compared to 0.21 to 0.74 under the lamps) reflecting differences in the light sources.

Factors affecting photolysis

However, other laboratory experiments show that triclosan (phenolic or molecular form) is relatively photostable, with the deprotonated phenolate (anionic) form of triclosan relatively more photodegradable and able to rapidly degrade (orders of magnitude faster) when exposed to sunlight (Poiger et al., 2003). The equilibrium between triclosan and triclosan (phenolate) in water is pH dependent, with a dissociation constant (pKa) of 8.14 (Ciba-Geigy Limited, 1990e). Therefore at pH 8.14, an approximate 50:50 ratio of triclosan and triclosan (phenolate) is expected. At pH 7 (e.g. freshwaters), triclosan is expected to dominate while at pH 9 the phenolate form will dominate. As such, the rate of loss of triclosan through photolysis is expected to be relatively greater in alkaline solutions.

Based on data from Poiger et al. (2003), which showed changes in surface water concentrations of triclosan over time, the rate of photolysis of triclosan under natural conditions is potentially seasonal, with lower aquatic concentrations corresponding to seasons of greater sunlight intensity and/or duration. However, other factors not considered may have also influenced the loss of triclosan from the surface waters (e.g. sedimentation, biodegradation, bioaccumulation).

Tixier et al. (2002) quantified the phototransformation of triclosan in water under laboratory conditions using artificial UV light and sunlight irradiation and pH 7-9. The results were used to model vertical concentration profiles of triclosan in Lake Greifensee, Switzerland. The pH of surface freshwaters (commonly pH 7-9) determines the speciation of triclosan (pKa 8.1) and therefore its absorption of sunlight. Direct photochemical degradation of the anionic form with a quantum yield of 0.31 (laboratory conditions at 313 nm) was found to be the dominant photochemical degradation pathway. First order rate constants (s^{-1}) derived by Tixier et al. (2002) at different pH were:

- $3.8 (\pm 0.6) \times 10^{-4}$ (pH 5.9, 1% anionic form);
- $6.9 (\pm 0.5) \times 10^{-3}$ (pH 8.0, 48% anionic form);
- $1.1 (\pm 0.2) \times 10^{-2}$ (pH 9.1, 91% anionic form); and
- $1.2 (\pm 0.3) \times 10^{-2}$ (pH 11.0, 99.9% anionic form).

Modelling the photochemical and environmental parameters indicated that phototransformation during summer potentially accounted for 80% of the observed elimination of triclosan from the lake's surface waters, with outflow from the lake being the other major loss pathway (17%). Daily average half-lives varied from 2-2000 days, depending on latitude and season (Tixier et al., 2002). Sedimentation

and biodegradation were expected to be minor loss pathways in this particular lake at the time sampled. Nevertheless, triclosan accumulation has been identified in the sediments of the lake (Singer et al., 2002).

Various factors affect the rate of triclosan phototransformation in the environment including sunlight availability and water pH (Tixier et al., 2002; Arnold et al., 2003). Half-lives at pH 6 are about 19 times longer than at pH >10.

The availability of sunlight to surface waters is affected by several factors including latitude, season, time of day, climatic conditions affecting the transmission of the atmosphere, average ozone layer thickness, shading and water absorption (e.g. turbidity, dissolved organic matter, suspended particulate matter, surface vegetation). At latitudes of 0-20°, seasonal change in triclosan half-life is restricted to within a factor of ~2. However, at 40° latitude, there is a 9-fold increase in the half-life of triclosan from summer to winter, and at 60°, the increase is 160-fold (Tixier et al., 2002). The half-life of triclosan in natural water at 40° latitude in the protonated form is expected to be 2.55 hours in summer, and 5.5 days in the winter. In the deprotonated form, the half-life of triclosan is expected to be 6.15 min in summer and 5.35 hours in the winter (Arnold et al., 2003).

Increasing water column depth potentially reduces the rate of phototransformation and increases the half-life of triclosan, due to the inability of sunlight to penetrate deeper waters. Dissolved organic carbon (DOM, e.g. humic and fulvic acids) affects the phototransformation of triclosan by acting as a light absorber and potentially as a photosensitiser or scavenger of reaction intermediates. DOM (2 mg/L) in nanopure water decreased the phototransformation rate by ~20% under test conditions (Tixier et al., 2002).

Mechanism of photolysis

Research indicates that triclosan is subject to reaction with hydroxyl radicals (Latch et al., 2005; Arnold et al., 2003). The second order rate constant for triclosan is 5.4×10^9 /Mol/seconds. In natural near-surface waters, hydroxyl radical concentration may range from 10^{-16} M (in agriculturally impacted waters containing high nitrate levels) to 10^{-18} M (pristine waters) (Brezonik and Fulkerson-Brekken, 1998; Mill, 1999). Based on these steady-state concentrations, the half-life of triclosan by this route may range widely from 15.1 days to 4.1 years in surface waters.

Direct photolysis occurs rapidly for triclosan when present in the deprotonated phenolate form. Triclosan also reacts with singlet oxygen in a pH dependent reaction (Latch et al., 2005; Arnold et al., 2003). The dissociated form of triclosan has been found to quickly react with singlet oxygen ($k_{rxn} = 1.07 \times 10^8$ /M/s at pH 10). 2,4-Dichlorophenol and another insoluble product are formed during the singlet oxygen reaction. However, preliminary study results indicate that direct photolysis is the dominant photo-initiated loss process. During darkness, photolysis would be absent and other loss mechanisms (e.g. deposition) would dominate.

Ferrer et al. (2004) investigated the photolytic half-life of triclosan in spiked (7 mg/L; pH 8.0), UV irradiated (solar light), filtered wastewater samples collected from an urban STP, Almeria, Spain. Samples were analysed for triclosan by liquid chromatography/electrospray ionization time-of-flight mass spectrometry (LC/ESI-TOFMS). A half-life of 23 h was determined, and triclosan was practically all

degraded after 4 days of irradiation. Photolysis was more rapid in filtered wastewater than in reagent water.

As a treatment process, some STPs include UV disinfection of effluent. There is a potential for photolysis of triclosan and formation of derivatives following this process; however, this could not be verified on the basis of the data available.

Products of photolysis

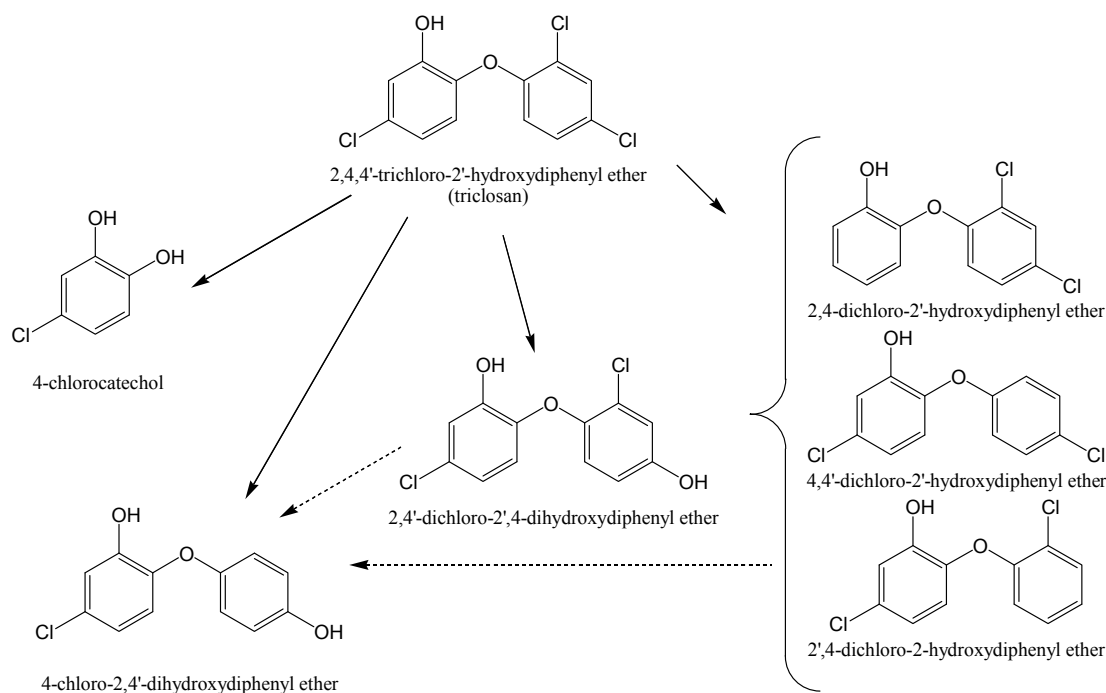
Photolysis of triclosan results in the formation of various products by dechlorination (replacing Cl with OH), and/or photo-induced hydrolysis of one of the aromatic rings through the cleavage of the C-O bond, leading to a phenol structure (refer Figure 16.2).

When triclosan was irradiated for 3 hours in reagent water (filtered, deionised, distilled, pH 7), 2,4-dichlorophenol (2,4-DCP) was identified as the major product formed (Agriseach Inc, 1993). However, Ferrer et al. (2004) did not identify 2,4-DCP but instead identified the structurally similar 4-chlorocatechol and several other products. Latch et al. (2005) showed that triclosan photodegrades to form 2,4-DCP in natural waters. In this experiment, irradiation of 100 μM triclosan (pH 8.2) with Hg-vapour lamps resulted in a yield of 3.1% 2,4-DCP and a quantum yield of formation of 0.023.

Ferrer et al. (2004) analysed samples by LC/ESI-TOFMS to quantify in greater detail the photodegradation products of triclosan in wastewater. Figure 16.2 illustrates the proposed products of photolysis. The analytical method used a derivitisation step to identify some of the polar products of triclosan. The software (Data Explorer; Applied Biosystems, USA) was used to process spectra generated. Samples of filtered (0.45 μm) wastewater collected from an urban STP, Almeria, Spain, were spiked with triclosan (7 mg/L; pH 8.0) and UV irradiated (solar light) for 1-2 days prior to analysis. The full scan chromatogram after one day exposure to sunlight (minus the background mass spectrum) revealed three major peaks (the deprotonated triclosan molecule $[\text{M}-\text{H}]^-$, $[\text{M}-\text{H}+2]^-$ and $[\text{M}-\text{H}+4]^-$), representing the characteristic chlorine signature for a three-chlorine chemical structure, and several minor peaks.

After two days exposure to sunlight Ferrer et al. (2004) identified the triclosan molecule and four new peaks at different retention times were observed as compared to the blank samples taken at time zero. Two of the degradation products presented a one-chlorine signature and the other two a two-chlorine signature. This particular chromatogram was reconstructed using a narrow range (50 mDa) rather than the more conventional 1 mDa window. The first major product was 4-chlorocatechol, a product of photo-induced hydrolysis of triclosan leading to the loss of one aromatic ring. Two other products included 4-chloro-2,4'-dihydroxydiphenyl ether and 2,4'-dichloro-2',4-dihydroxydiphenyl ether. The fourth major peak was further investigated and three peaks corresponding to dichlorinated isomers were observed representing 2,4-dichloro-2'-hydroxydiphenyl ether, 4,4'-dichloro-2-hydroxydiphenyl ether and 2'4-dichloro-2-hydroxydiphenyl ether. The replacement of a chlorine atom by a hydroxyl group was identified as the preferred pathway, therefore the major product was the compound yielding the $[\text{M}-\text{H}]$ ion (i.e. 2,4'-dichloro-2',4-dihydroxydiphenyl ether).

Figure 16.2. Proposed photolysis products of triclosan



All of the degradation products were monitored in aliquots taken at different times, and intensities were plotted versus time. All degradation products identified in this study for triclosan were found to be unstable and their concentrations decreased over time, like that of triclosan. Ferrer et al. (2004) hypothesized that these products may be metabolites for the formation of other products including 2,7-dichlorodibenzo-p-dioxin (2,7-DCDD) and 2,8-DCDD.

Parallel experiments with triclosan in solution held in the dark and analysed at different times indicated that hydrolysis was a negligible degradation pathway for triclosan (Ferrer et al., 2004).

Ferrer et al. (2004) proposed that triclosan photolytically degrades to one of at least seven products including 4-chlorocatechol, 4-chloro-2,4'-dihydroxydiphenyl ether and 2,4'-dichloro-2',4-dihydroxydiphenyl ether, which degrades to 4-chloro-2,4'-dihydroxydiphenyl ether. The other products, including 2,4-dichloro-2'-dihydroxydiphenyl ether, 4,4'-dichloro-2'-hydroxydiphenyl ether and 2',4-dichloro-2-hydroxydiphenyl ether, are formed but also degrade to 4-chloro-2,4'-dihydroxydiphenyl ether (Figure 16.2).

Sanchez-Prado et al. (2006) further investigated the photolysis products of triclosan using photo-solid-phase microextraction (photo-SPME). In photo-SPME, photodegradation is carried out on the SPME fibre containing the target compound. Triclosan was extracted from aqueous solutions by use of polydimethylsiloxane SPME fibres and these were subsequently exposed to UV irradiation (power 8 W, wavelength 254 nm) for different times (from 2 to 60 min). The photodegradation kinetics of triclosan were investigated, the photoproducts generated were tentatively identified, and the photochemical behaviour of these products was

studied by use of this on-fibre approach followed by gas chromatographic-mass spectrometric analysis. Eight photoproducts were tentatively identified, and they included dichlorophenol, monochlorophenol, monochlorohydroxydiphenyl ether, three dichlorohydroxydiphenyl ethers, 2,8-DCDD and a possible dichlorodibenzodioxin isomer or dichlorohydroxydibenzofuran. The effect of pH on triclosan degradation and on triclosan-to-dioxin conversion was also investigated. Triclosan degradation occurred, and generation of 2,8-dichlorodibenzo-p-dioxin was confirmed, throughout the pH range studied (from 3 to 9).

Dioxin formation

When irradiated by UV light in the solid state or in aqueous solution, some triclosan is converted to 2,8-DCDD (Latch et al., 2005; Mezcua et al., 2004; Arnold et al., 2003; Latch et al., 2003; Kanetoshi et al., 1987, 1992).

Mezcua et al. (2004) investigated the photolysis of triclosan in water and wastewater (filtered 0.45 μm ; Almeria urban WWTP, Spain) and spiked at 8 $\mu\text{g/mL}$ under natural sunlight irradiation and variable pH. The WWTP includes primary treatment. Test solutions were placed in stoppered 5 L pyrex bottles and agitated at $\leq 35^\circ\text{C}$ during irradiation (UV transmission $>80\%$ between 320-400 nm). Aliquots were sampled (125 mL) at different times during the experiment and analysed by solid phase extraction and GC/MS. 2,7/2,8-DCDD was detected in irradiated reagent and wastewater samples. In distilled water, photolysis of triclosan was much greater at pH 7 than pH 5 and 2,7/2,8-DCDD was only detected in samples at the higher pH. In irradiated reagent water (pH 7) and wastewater (pH 8) spiked with 8.1 μg triclosan/mL, removal of triclosan was greater in the wastewater and 2,7/2,8-DCDD formation was more rapid. In this experiment, 2,7/2,8-DCDD concentrations were not quantified. Influent and effluent samples (filtered 0.45 μm) were also collected from the WWTP between June 2002 and March 2003, with detection of triclosan and 2,7/2,8-DCDD in all samples. 2,7/2,8-DCDD concentrations in influent and effluent ranged from 0.02-3.7 $\mu\text{g/L}$ and 0.004-0.4 $\mu\text{g/L}$, respectively. Filter media was sampled and only triclosan was detected (up to 195 $\mu\text{g/L}$); however, the authors indicated that 2,7/2,8-DCDD may also have been present but not extracted effectively.

In both buffered aqueous solution and natural waters (Mississippi River), triclosan is directly photolysed to 2,8-DCDD with yields of 1%-12% under a variety of conditions (Latch et al., 2003). Yields in Mississippi water (pH 7.8-9.0) ranged from 1.2%-3.7%. In this study, aqueous solutions (25-50 mL) of triclosan (3.5-76 μm) exposed to air were irradiated with filtered light (>280 , >290 and >320 nm) from a medium-pressure Hg-lamp (450 W). Dioxins were analysed by GC-MS, HPLC and NMR spectroscopy by comparison to standards. No 2,8-DCDD was detected in the initial triclosan sample. Ring closure and formation of 2,8-DCDD was observed in solutions buffered at pH 8 or above. In another study, the direct photolysis of triclosan at pH >8.0 led to the formation of 2,8-DCDD in yield ranging from 1%-10% under experimental conditions (Arnold et al., 2003).

Photolysis of chlorinated derivatives and methyl-triclosan

Several studies have reported the photolysis of chlorinated derivatives of triclosan. Latch et al. (2003) reported that formation and decay of the product 2,8-DCDD indicated that the compound was an intermediate species. Irradiation of 2,8-DCDD

indicates that it is photoreactive, with degradation quantum yields 2-20 times lower than the apparent quantum yields. In general, dioxins are known to undergo photochemical degradation. Latch et al. (2003) did not identify the degradation products of 2,8-DCDD; however, these may include dechlorinated congeners. Nilsson et al. (1974) reported PCDD formation following irradiation of 2',3,4,4',5-pentachloro-2-hydroxydiphenyl ether when in a methanol solution. Kanetoshi et al. (1987) irradiated (UV) the chlorinated derivatives of triclosan for 20 hours (3.2 J/m²/s), finding various chlorinated products (Table 16.2).

Methyl-triclosan (MTCS, 5-chloro-2-(2,4-dichlorophenoxy)anisole; CAS No. 4640-01-1), which does not dissociate in water, behaves like undissociated triclosan, and is not, or only very slowly, photolysed in surface waters at low and high pH (Poiger et al., 2003; Latch et al., 2003; Tixier et al., 2002; Singer et al., 2002; Balmer et al., 2004).

Table 16.2 -Products from UV irradiation of triclosan (TCS) and chlorinated derivatives

Parent compound *	Products of photolysis *	% of parent compound
TCS	TCS (residual parent compound)	19
	Di-CDD	1
	Dichlorohydroxydibenzofuran	---
	II	---
II	II (residual parent compound)	16
	TCS (formed via dechlorination)	2
	Tri-CDD	Trace
	III	---
	IV	---
	Tetrachlorodihydroxybiphenyl	---
	Pentachlorodihydroxybiphenyl	---
III	III (residual parent compound)	12
	Tri-CDDs	Trace
	TCS	---
	TCS isomer	---
	II	---
	Isomer of II or III	---
IV	IV (residual parent compound)	22
	II	---
	III	---
	Isomer of II or III	---
	hexachlorohydroxydiphenyl ether	---

Source: Kanetoshi et al. (1987). --- = percent not quantified. Compounds: II: 2',3,4,4'-tetrachloro-2-hydroxydiphenyl ether; III: 2',4,4',5-tetrachloro-2-hydroxydiphenyl ether; IV: 2',3,4,4',5-pentachloro-2-hydroxydiphenyl ether. * Refer to Figure 16.1 for chemical structures.

Atmospheric photooxidation

No experimental data for degradation in the atmosphere were provided. However, this was considered through modelling.

The rate constant for reactions of triclosan with OH radicals (photochemical oxidative degradation) in the atmosphere was calculated using the AOP program [AOPWIN Program (Atmospheric Oxidation Program for Microsoft Windows 3.1) Version 1.51, Syracuse Research Corp. 1988-97]. The SMILES notation of triclosan (pure) as entered into the program was: O(c(c(O)cc(c1)Cl)c1)c(c(cc(c2)Cl)Cl)c2.

First, the rate constant k_{OH} of the active substance was estimated based on the chemical structure. The resulting value was

$$k_{OH} 16.1147 \times 10^{-12} \text{ cm}^3/\text{molecule}\cdot\text{s}$$

The half-life of this process is calculated by the following equation:

$$t_{1/2} = \ln 2/k' = \frac{\ln 2}{k_{OH}} \times [\text{OH radicals}]$$

The diurnally and seasonally averaged concentration of tropospheric hydroxyl radicals used by the AOP program is $1.5 \times 10^6 \text{ cm}^{-3}$. Therefore, half-life for the degradation of triclosan by hydroxyl radicals was calculated to be 7.96 hours.

16.1.4 Adsorption and mobility

Soils

ABC Laboratories Inc. (1997a) has investigated the adsorption of ^{14}C -triclosan to suspended solids (49.6 mg/L) obtained from deactivated sewage sludge with a total organic carbon (TOC) content of 45.5% (initially 22.6 mg C/L). The test procedure followed US FDA Technical Assistance Document 3.08, Sorption/Desorption. The aqueous phase consisted of well water (buffered pH 6.5-7.0), and the triclosan concentrations (nominal) were 15, 40, 100 and 250 $\mu\text{g/L}$. Adsorption of triclosan to the solid matrix was determined to be 53.7% at 8 hours. The K_d and K_{OC} values were estimated to be 21592 and 47454 L/kg, respectively, at a solids suspension pH of 6.55 (measured at initiation of tests). Based on these results, a major portion of triclosan is expected to partition to STP and WWTP solids in the effluent. Triclosan in the protonated form (OH) should bind more strongly than when in the deprotonated phenolate form (O⁻). HPLC analysis of aqueous adsorption phases from the highest test concentration verified the stability of triclosan under the conditions of the isotherm test.

Due to its hydrophobic nature, triclosan is expected to have a high affinity for organic-rich sediments (and soils), and to have low mobility when adsorbed (Mensink et al., 1995). When saturated or binding capacity is reached, mobility may potentially increase, and mass movement of triclosan-adsorbed particles (e.g. erosion) may also result in the migration of triclosan.

Impregnated plastics and textiles

Leaching of triclosan from various consumer products was investigated by Junker and Hay (2004) including 50 acrylonitrile-butadiene-styrene (ABS) plastic coupons

(7.5 × 2.5 × 0.3 cm) containing 5% w/w or 5000 mg/kg of triclosan, a shower curtain and dishtowel. Desorption was examined in triplicate by adding 4.7 g of the test materials each in 100 mL of sterile, deionised and distilled water. The suspension was shaken (150 rpm) at 22°C for 50 hours. Samples of water were taken at 0, 22 and 50 hours for analysis by GC/MS. A standard curve of 6 concentrations of triclosan was generated for comparative purposes. Full data were not reported. The concentration of triclosan detected from the ABS, shower curtain and dishtowel were ~12, 18 and 1100 µg/L, respectively. By mass balance, the mass of triclosan in the ABS was 23500 µg and the mass released into the water was 1.2 µg, representing a total desorption of ~0.005%. A similar trend was found by Junker and Hay (2004) using a bioavailability assay with ¹⁴C-triclosan and the bacterial strain *Sphingomonas*, which is capable of degrading triclosan to CO₂. This assay measured the induction of mineralisation of the triclosan by this strain, which was known to occur in concentrations ≥250 µg/L. From this study, it is clear that desorption of triclosan from plastic and textiles can occur. However, the initial concentrations of triclosan in the plastic shower curtain and dishtowel were not reported and no comparative analysis of the relative desorption capability in this media can be made.

16.1.5 Biodegradation and methylation

Sewage sludge micro-organisms

Aerobic conditions

The biodegradability of triclosan by wastewater micro-organisms has been investigated in several studies based on OECD and non-standard test protocols (Table 16.3). In general, the rate of biodegradation is very slow under anaerobic conditions relative to aerobic conditions.

With the possible exception of the first result listed, there is no evidence to indicate that triclosan is readily biodegradable within the classification of the OECD. However, several non-standard tests undertaken indicate that triclosan is biodegraded over time by sewage micro-organisms, suggesting that it may be inherently biodegradable.

Laboratory studies indicate that the rate of biodegradation is inversely proportional to the triclosan exposure concentration, with greater inhibition occurring at higher exposure concentrations (refer to Section 21). However, microbial community adaptation to triclosan has been demonstrated, and removal efficiency is independent of triclosan concentration in adapted microbial populations. Lengthening the duration of exposure enables relatively greater removal of triclosan by biodegradation to occur, even at relatively higher exposure concentrations.

Based upon results from tests using methods OECD 301B (CO₂ Evolution, Modified Sturm Test), triclosan is not considered inherently or readily biodegradable (Ciba-Geigy Limited, 1989). However, the test concentrations used (i.e. 10000-20000 µg/L) are likely to have inhibited microbial growth. In other studies, high biodegradation, particularly through mineralisation to CO₂, has been demonstrated in tests involving activated sludge micro-organisms at more realistic triclosan concentrations.

Table 16.3 - Aerobic and anaerobic biodegradation of triclosan

Triclosan Conc. (µg/L)	Conditions	Duration of Test (days)	Percent triclosan degradation	Reference
10	Aerobic	28	70%	Hansveit and Hamwijk (2003)
10	Aerobic	28	52.1	Stasinakis et al., (2008)
1000-5000	Aerobic	21	50%	Voets et al. (1976)
10000	Aerobic	28	37%	Ciba-Geigy Limited (1989)
20000	Aerobic	28	18%	
20	Aerobic	71	31%	Federle et al., (2002)
100			45%	
200			52%	
500000	Aerobic	91	35%	Hay et al. (2001)
200	Anaerobic	147	10%	Springborn Laboratories Inc. (1994a)
1000-5000	Anaerobic	21	50%	Voets et al. (1976)

Most recently, the biodegradability of triclosan was evaluated using OECD method 301F (manometric respirometry test) and activated sludge as inoculum. Manometric respirometry tests were carried out in the Sensomat system (AQUALYTIC[®] ZN, Tintometer GmbH, Germany), which is based on a manometric principle. Owing to microbial activity, oxygen is taken from the gas phase of the hermetically sealed reaction vessels, while carbon dioxide released from respiration is absorbed by KOH in a small tube and the resulting reduction in air pressure inside the closed system is measured.

After an initial lag phase of 16.5 ± 3.5 days, triclosan was aerobically biodegraded at a percentage equal to $52.1 \pm 8.5\%$ ($n = 3$) and a half-life equal to 1.8 ± 0.5 days. Experiments in the co-presence of a readily biodegradable compound showed the absence of co-metabolic phenomena during triclosan biodegradation. Toxicity tests using marine bacterium *Vibrio fischeri* showed that biodegradation of triclosan is a simultaneous detoxification process (Stasinakis et al., 2008).

Hansveit and Hamwijk (2003) reported data from two laboratory-based die-away studies. The test reports were not sighted during this assessment. The studies investigated the potential degradation of triclosan in STP effluents after mixing with effluent and river water. Both studies used ¹⁴C labelled triclosan at a concentration of 10 µg/L incubated at ambient temperature for up to 35 days. The tests indicated that CO₂ evolution reached a level of 70% within 28 days, and within 14 days in some tests. Half-lives of triclosan in river water ranged from 2.5-3.6 days (first order rate constants of 0.19 and 0.28 day⁻¹).

Hay et al. (2001) identified an activated sludge (Neyland municipal STP, Knoxville TN, USA) microbial consortium capable of using triclosan as a sole source of carbon and energy. After 13 weeks of growth on 500 mg/L triclosan (28°C) approximately 35% of the triclosan was mineralised and captured as CO₂.

Mineralisation proceeded almost immediately when inoculated with 10% (v/v) of an exponential phase culture; however, active growth of sludge organisms did not occur until after a lag phase of 1-2 days. With an inoculum volume of <5% (v/v), bacterial growth on triclosan required a long lag phase and was occasionally lost.

Bester (2005) concluded that STPs with activated sludge mechanisms eliminate triclosan with relatively high efficiency. This followed an experiment in Germany sampling effluents from two STPs, one with a two-stage biological process to eliminate easily degradable carbon and one with just a single-stage process. The plant operating the two stage biological (activated sludge) process removed triclosan more efficiently than the second plant with a combination of physical and activated sludge process. The elimination rates for triclosan were 87% and 95% respectively.

The biodegradation potential of triclosan has been investigated by Federle et al. (2002). Activated sludge (Avondale STP, USA) was screened (2 mm) and suspended solids adjusted to 2500 mg/L. Triplicate samples (1 L) were dosed with test chemical (20, 100 and 200 µg ¹⁴C-triclosan /L) and incubated in 2 L flasks, mixed continuously on a shaker table at 22±1.5°C in the dark. The headspace of each flask was purged with CO₂-free air and the effluent gas was collected in CO₂ traps (KOH) and analysed by liquid scintillation counting (LSC) to determine the amount of ¹⁴CO₂ evolved (i.e. mineralisation of triclosan). In addition, subsamples of the mixed liquor were filtered (0.45 µm) and filter residue and filtrate were analysed by LSC. Mineralisation to CO₂ began at the initiation of the tests and final ¹⁴CO₂ recovery after 71 days averaged 30.9%, 44.7% and 52.3% for the 20, 100 and 200 µg/L treatments, respectively. To assess adaptational response, two of the 200 µg/L test systems were dosed with 1 mg/L and mineralisation followed for 52 days. The third replicate was used as a control. After a lag period of 3-10 days, mineralisation occurred more rapidly and extensively (~80% ¹⁴CO₂ recovery) than with the unadapted microbes (Federle et al., 2002). Batch conditions enabled mineralisation of a proportion of the triclosan over time, and acclimation of the sludge micro-organisms enhanced mineralisation. Identification of triclosan metabolites other than CO₂ was not performed. Batch tests indicated that a prolonged residence time was required (e.g. 50-70 days) to achieve high mineralisation rates.

Anaerobic conditions

In a relatively old study, Voets et al. (1976) investigated the degradation of triclosan under aerobic and anaerobic conditions with synthetic sewage sludge, reporting 50% degradation under both aerobic and anaerobic conditions after 21 days exposure to an initial nominal triclosan concentration of 1000-5000 µg/L. Degradation was estimated based on analytical testing of triclosan using the 4-amino antipyrine method. Cometabolism was the proposed method of biodegradation. However, the rate of anaerobic biodegradation is much faster than reported in a later study by Springborn Laboratories Inc. (1994a). No bacteria actively metabolising triclosan were isolated from the activated sludges; however, the higher triclosan concentrations used in the tests may have inhibited microbial growth. Residual toxicity (cell growth) of triclosan in effluent from the activated sludge system to *Bacillus subtilis* was examined using a modified method of Bringmann (1973). The effluent was found to inhibit growth of *B. subtilis*. The sensitivity limit (inhibition of bacterial growth by 25%) for triclosan was reported at a concentration of 600 µg/L.

Springborn Laboratories Inc. (1994a) investigated the anaerobic biodegradation of ^{14}C -triclosan at a test concentration of 200 $\mu\text{g/L}$ in inoculum consisting of primary anaerobic sludge from a domestic wastewater treatment plant. Approximately 90-92% of the extractable residues remained as ^{14}C -triclosan after 147 days of incubation with anaerobic inoculum and anaerobic conditions. The percent extractable decreased steadily with time, but with no appearance of triclosan metabolites it is unlikely that mineralisation to CO_2 and methane occurred. Microbial analysis of the sludge during the study indicated that the sludge microbes remained viable. No evidence of anaerobic biodegradation was observed in this study.

Further information on the microbiological treatment of triclosan is presented in Section 16.3.1.

Several studies highlight the production of methyl-triclosan during wastewater treatment, probably due to microbial methylation. Bester (2003) estimates a conversion rate of 1% of triclosan to methyl-triclosan during STP (secondary) treatment. Methylation of triclosan may also continue post-treatment in the receiving environment.

Laboratory-scale continuous activated sludge systems

The biodegradation potential of triclosan has been investigated in laboratory-scale continuous activated sludge (CAS) systems using acclimated sewage micro-organisms (Roy F. Weston Inc., 1992, 1998; Federle et al., 2002).

In one CAS study, six CAS units were used, with nominal concentrations of 6.0 (background control), 7500, 11000, 20000 and 50000 ng/L (Roy F. Weston Inc., 1998). Each CAS unit has a mixing container where wastewater and test feed solution were mixed with overflow to an aeration basin containing 6 L of screened (2 mm) activated sludge (Downington Regional Water Pollution Control Center) adjusted to 2500 mg/L suspended solids. The activated sludge amendment provided the equivalent of 6000 ng triclosan/L and treatment concentrations were amended accordingly. Given this background triclosan level, the microbial population was pre-exposed and probably adapted to triclosan, which was added using ^{14}C -labelled and unlabelled triclosan in varying proportions. The aeration basins discharged to 2 L clarifiers (mixed 2 rpm) fitted with facilities for recycling and effluent discharge. The influent flow rate to each aeration basin was 1 L/min (0.91 mL/min wastewater and 0.09 mL/min feed solution). Following establishment, all CAS units only received wastewater for 24 hours initially. This was followed by a stabilisation phase for 14 days in which the units received wastewater and feed solutions containing unlabelled triclosan at the nominal treatment concentrations. During this phase, the control received wastewater and deionised water. Stabilisation was followed by an equilibrium period for one month during which the test units continued operation but received a proportion of the triclosan as ^{14}C -triclosan. After the equilibrium phase, testing was conducted for one week. The CAS units were operated with a hydraulic residence time of 6 h, and solids retention time was 11 d. Percent removal was established by assaying the ^{14}C level in the test feed, effluent, influent and mixed liquor. Disappearance of ^{14}C -triclosan and the formation of metabolites were determined with thin layer chromatography (RAD-TLC) analysis. No adverse effect on the overall CAS system performance was observed during any phase of the study. Over the five-day monitoring period, >98.2% of the triclosan was removed. A summary of the data is

presented in Table 16.4. Triclosan removal was independent of triclosan influent concentration. Several (4) metabolites of triclosan were detected during the study but not identified.

Previously, Roy F. Weston Inc. (1992; reported in Federle et al., 2002) had undertaken a similar CAS study to the above but at higher nominal test concentrations of 40, 100, 200, 500, 1000 and 2000 µg/L. The study was conducted in six phases with concentrations increasing incrementally from 40 to 2000 µg/L. A 7th phase included consisted of a test period using unadapted solids and a high level dosing experiment. Activated sludge was obtained from the Avondale STP. Both ¹⁴C labelled and unlabelled triclosan was used. Following establishment, the CAS units were stabilised for 11 days (the units received wastewater and deionised water only). The source of activated sludge was not analysed for triclosan. If present, adaptation of sludge microbes used in the test to triclosan may potentially have occurred.

Table 16.4 - Removal of triclosan (TCS) from wastewater in a laboratory-scale continuous activated sludge (CAS) study

Influent TCS (ng/L)	Overall TCS removal from influent (%) ^a	Mineralisation to CO ₂ (%)	Mean TCS in solids; ng/L (%)	Mean TCS in effluent, ng/L (%)
7500	96.7±0.12	73.9	130 (1.78)	110 (1.45)
11000	97.4±0.39	75.6	210 (1.92)	70 (0.64)
20000	97.2±0.61	76.6	390 (1.94)	180 (0.9)
50000	97.9±0.28	76.7	690 (1.38)	360 (0.72)

Source: Roy F. Weston Inc. (1998) and Federle et al. (2002). Percentages reported as a percentage of influent.

a. Overall removal by primary biodegradation = 100 – (% adsorbed + % in effluent).

Following stabilization an acclimation period was conducted for each test substance concentration, lasting until removal of the test substance equilibrated. During acclimation, influent, aeration mixed liquor and effluent samples were collected and analysed. A five-day removal period was conducted for each test substance concentration following the acclimation period. The CAS units were operated with a hydraulic residence time of 6 h, and solids retention time was 4-12 d. During this time, samples of influent, mixed liquor and effluent (unfiltered) were assayed on 5 consecutive days for ¹⁴C using LSC and one overnight composite sample was analysed by HPLC. In addition, aliquots were filtered (0.4 µm) and constituents in filtrate and remaining on the filter were assayed by LSC. No adverse effect on the overall CAS system performance was observed during any phase of the study.

Several polar intermediates (extractable to ethyl acetate) and very polar intermediates (non-extractable to ethyl acetate) of triclosan were detected during the study but not identified. As the experiment progressed and concentration

increased, the abundance of very polar intermediates compared to polar intermediates tended to increase. No radioactivity in the effluent co-eluted with 2,4-dichlorophenol, a postulated biodegradation intermediate.

For each treatment concentration, over the 5-day period overall removal of parent triclosan was >98.5% (Table 16.5). Triclosan was not detected in the effluent (detection limit <1.5%) and ~75%-88% of the influent loading was removed by mineralisation to CO₂ or was incorporated into biomass. Approximately 30%-63% of the ¹⁴C recovered in solids was triclosan and, based upon specific analysis, 5.4%-12.5% of the initial triclosan in the wastewater was removed by adsorption to solids. Removal of triclosan was independent of triclosan concentration in influent.

Roy F. Weston Inc (1992; reported in Federle et al., 2002) also investigated the biodegradation of triclosan with apparently unacclimated sludge using the control; however, the activated sludge was not tested for triclosan and may have contained background level, as found by Roy F. Weston Inc. (1998). Triclosan was added to the CAS at a nominal concentration of 35 µg/L for 15 days. Influent, mixed liquor and effluent samples were collected and assayed daily for ¹⁴C. The dose was increased to 750 µg/L for 4 hours, then reduced to 35 µg/L, but increased to 750 µg/L 2 days later. The shock load was equivalent to a release over a 4 hour period of 3.1 kg of triclosan in a STP treating 25 ML/d. Prior to shock loading, triclosan removal was ~97% of influent, with 3% in effluent (~1.05 µg/L). After each pulse, removal efficiency of triclosan was reduced to ~94%-95%, followed by a return to baseline treatment conditions. After dosing to 750 µg/L, with a removal efficiency of 94%-95%, triclosan concentration may have approximated 37.5-45 µg/L. Other operational parameters of the CAS units were unaffected (i.e. suspended solids, chemical oxygen demand, biological oxygen demand, ammonia, and nitrate in effluent) by the pulse of triclosan. During pulse conditions, reduction in STP efficiency to degrade triclosan relative to baseline conditions may be expected.

Table 16.5 - Removal of triclosan (TCS) from wastewater in a laboratory-scale continuous activated sludge (CAS) study

TCS in influent (µg/L)	Overall TCS removal from influent (%) ^a	Mineralisation to CO ₂ or in biomass (%)	Mean TCS adsorbed onto solids; (%)	Estimated maximum TCS in effluent; µg/L ^b (%)
40	>98.5	74.7	9.1	0.6 (<1.5)
100	>98.5	75.5	12.5	1.5 (<1.5)
200	>98.5	85.7	7.0	3.0 (<1.5)
500	>98.5	76.3	9.8	7.5 (<1.5)
1000	>98.5	87.8	5.4	15 (<1.5)
2000	>98.5	87.1	8.3	30 (<1.5)

Source: Roy F. Weston Inc. (1992) and Federle et al. (2002). Percentages reported as a percentage of influent.

a. Overall removal by primary biodegradation = 100 – (% adsorbed + % in effluent). b. Estimated maximum concentration = 1.5% of nominal influent concentration.

Federle et al. (2002) also reported the results of a CAS experiment conducted at an influent concentration of 10 µg/L (nominal) over a 15 day period. CAS units were operated with a hydraulic residence time of 6 hours and solids retention time of 11 days. At steady state, ~94.7% of the triclosan was removed. Approximately 79.1% of the triclosan was mineralised to CO₂, 1.0% was partitioned to solids, 6.0% was in biomass and 5.3% (0.53 µg/L) was partitioned to effluent. Analysis of the effluent revealed the presence of at least two polar intermediates in addition to triclosan.

Resistant micro-organisms

A bacterium most similar to an auxotrophic *Sphingomonas*-like organism, Strain Rd1, was identified in the activated sludge consortium as capable of partially mineralising triclosan when grown on complex media (Hay et al., 2001). Based on closest 16S rRNA gene match, other bacteria isolated from the triclosan-degrading consortium are thought to include *Pseudomonas mendocina*, *P. aeruginosa*, *Alcaligenes xylooxidans* and *Rhodanobacter lindanoclasticus*, which may have a minor role in triclosan degradation. Failure to isolate a single strain capable of completely mineralising triclosan indicates that co-metabolic steps by several consortium bacteria are required to completely mineralise triclosan. Unlike the study by Hundt et al. (2000; reported below), 2,4-dichlorophenol was not detected as a product from the bacterial consortium or the isolated Rd1 strain. Several triclosan-resistant bacteria have been isolated from diluted municipal STP wastewater plated onto triclosan-enriched (20, 50 and 100 µg/L) agar (Reither, 2003). Species included *Aeromonas caviae*, *A. media*, *Ralstonia eutropha*, *Pseudomonas nitroreducens/azelaica*, and *Achromobacter xylooxidans*.

Soil micro-organisms

Biodegradation and mineralisation to CO₂ may not be the only microbial processes by which a compound is removed from the environment. *O*-methylation of halo-substituted phenols, where the carbon skeleton remains intact, has also been demonstrated as an alternative process, and methylated products (halo-anisoles) have also been detected in various environmental media and biota (Hagglblom et al., 1989). These are of ecological relevance due to their similar toxicity to aquatic organisms and their potential to bioaccumulate (Allard et al., 1987). The *O*-methylation reaction dominates only under aerobic conditions and de-*O*-methylation dominates in anaerobic conditions (e.g. anaerobic sediments) (Allard et al., 1987; Remberger et al., 1986).

Springborn Laboratories Inc. (1994b) reported aerobic biodegradation of ¹⁴C-radiolabelled triclosan in sewage sludge-amended soils under laboratory conditions using the Carbon Dioxide Evolution Method in accordance with US FDA Technical Assistance Document, S. 3.12. Soils used in the study were Arkansas Silt Loam, Kansas Loam and Wisconsin Sandy Loam. Prior to use, all soils were sieved (2 mm). Moisture contents of the soils ranged from 13.3%-15.5%, but were kept above 20% of field moisture capacity by remoisturising with reagent water. A 200 µg/kg (nominal) concentration of ¹⁴C-triclosan was tested rather than the protocol-specified 10 mg carbon per 50 g soil (200 mg C/kg soil) due to the microbiocidal properties of triclosan. The concentration tested approximates 1% of the IC₅₀ (i.e. 20000 µg/L) obtained during an activated sludge inhibition study (Ciba-Geigy Limited, 1990g). Actual concentrations were measured on Day 0 and throughout the tests. Soils were amended with triclosan-acclimated activated sludge obtained

from an industrial sewage treatment plant receiving triclosan in the waste stream. While the test results indicate aerobic biodegradation of triclosan in sewage sludge-amended soils, this scenario is unlikely to occur in the environment, except where biosolids are applied to soil. The test protocol did not include determination of the taxa undertaking the biodegradation. Soils were incubated for 64 days in the dark at 23°C to 27.5°C. A control (¹⁴C-radiolabelled glucose) was also tested. Plate counts of bacterial density in the three test soils at initiation were 3.3-5.2x10⁶ cfu/g, and at Day 64 were 7.5-15x10⁶ cfu/g. Test results are presented in Table 16.6.

The results indicated transformation of triclosan through methylation and, to a lesser extent, ultimate mineralisation to CO₂, under the aerobic test conditions. Between 77%-93% of the triclosan added to the soils was removed after 64 days of testing. Between 7%-23% remained in the soils after 64 days testing. A major metabolite was identified in all soils tested, particularly the Wisconsin soil. By mass spectral plotting, a 302 g/mole-molecular weight metabolite was identified as methyl-triclosan. In support of other aerobic studies, it is noteworthy that the Wisconsin sandy loam soil had the relatively higher removal rate. Other metabolites were present in minor concentrations in the soils but were not identified. Thus, *O*-methylation was a primary process, transforming up to ~62%, 70% and 80% of the triclosan in the Arkansas, Kansas and Wisconsin soils, respectively. About 14%-20% of the triclosan removed was mineralised as the mean cumulative radiolabelled CO₂ evolution rates were 20.1% (Arkansas), 11.9% (Kansas) and 13.6% (Wisconsin). Half-lives for triclosan in Arkansas, Kansas and Wisconsin soils were 35.2, 29.1 and 17.4 days, respectively.

Table 16.6 - Reduction in triclosan in sewage sludge-amended soils

Soil Type	Phys/Chem	Time	Triclosan Conc. µg/kg (mean±SD)	Reduction (%)
Arkansas Silt Loam	35% sand	Day 0	114 ±10.3	77.3
	51% silt	Day 14	80.7	
	14% clay	Day 28	72.8 ±23.6	
	1.6% OM	Day 42	58.1 ±1.61	
	pH 5.9	Day 56	46.8 ±3.51	
	CEC 9.8 meq/100 g	Day 64	25.8 ±4.84	
Kansas Loam	31% sand	Day 0	166 ±6.81	79.3
	43% silt	Day 14	102	
	26% clay	Day 28	97.5 ±6.07	
	3.7% OM	Day 42	50.1 ±3.65	
	pH 6.5	Day 56	45.1 ±6.39	
	CEC 22.4 meq/100 g	Day 64	34.4 ±3.17	
Wisconsin Sandy Loam	59% sand	Day 0	158 ±21.5	93.1
	29% silt	Day 14	51.3	
	12% clay	Day 28	22.6 ±1.02	
	5.7% OM	Day 42	13.6 ±3.08	
	pH 7.5	Day 56	12.7 ±4.62	
	CEC 17.1 meq/100 g	Day 64	10.9 ±2.54	

Source: Springborn Laboratories Inc. (1994b).

Meade et al. (2001) isolated bacteria with high levels of triclosan resistance from garden compost. Two bacteria (*Pseudomonas putida* triRY and *Alcaligenes xylooxidans* subsp. *denitrificans* TR1) were able to use triclosan as a sole carbon source and clear particulate triclosan from agar.

Triclosan can be degraded by two species of white rot fungi (*Trametes versicolor*, *Pycnoporus cinnabarinus*; Hundt et al., 2000). *T. versicolor*, which grows naturally in dead wood, produced the metabolites; 2-*O*-(2,4,4'-trichlorodiphenyl ether)- β -D-xylopyranoside, 2-*O*-(2,4,4'-trichlorodiphenyl ether)- β -D-glycopyranoside, and 2,4-dichlorophenol. In contrast to other diphenyl ethers, no ring cleavage products were formed from triclosan by *T. versicolor*. *P. cinnabarinus* converted triclosan to 2,4,4'-trichloro-2'-methoxydiphenyl ether through methylation of the hydroxy group, and the glucoside conjugate known from *T. versicolor*; 2-*O*-(2,4,4'-trichlorodiphenyl ether)- β -D-glycopyranoside. Each of the conjugates showed much lower cytotoxic and microbiocidal activity than triclosan when tested using the neutral red test with fibroblast-like cells according to the method of Kusnick (1998).

In an earlier study, Voets et al. (1976) investigated the biodegradation of triclosan under aerobic and anaerobic laboratory conditions in mineral solutions consisting of soil extract. The tests were performed according to OECD methods for the biodegradability testing of detergents (Anon., 1971). Triclosan was dissolved in a mineral solution, inoculated with soil extract and incubated in air (aerobic) or under vacuum (anaerobic) conditions. The soil extract was prepared using 10 g of fertile field soil suspended and mixed in 100 mL of tap water prior to filtration. Samples of test media were analysed daily over a 3-week period, with triclosan test solution concentrations in the range of 1-5 mg/L (nominal). Products and metabolites produced during the tests were not identified. No degradation of triclosan was observed under aerobic or anaerobic conditions after 21 days exposure using only the soil extract. These results suggest that triclosan may not be biodegraded or only degraded at a very slow rate over time in oligotrophic aquatic or terrestrial systems (i.e. systems low in nutrients, organic matter and primary production).

Aerobic soil degradation

European soils

The route and rate of degradation of ^{14}C -triclosan has been studied in three European soils incubated under aerobic conditions at 20°C for a period of 124 days (Adam 2007). The study was conducted according to OECD Guidelines for Testing Chemicals: Aerobic and Anaerobic Transformation in Soil, Guideline 307. The following soils were used: soil I (Speyer 5M, sandy loam), soil II (Senozan, clay loam) and soil III (Gartenacker, loam). In order to investigate the influence of temperature on the degradation of Triclosan, one of the selected soils (soil I, Speyer 5M) was additionally incubated at 10°C. The properties of the soils are summarised in Table 16.7.

The freshly sampled soils were passed through a 2 mm sieve before use. Aliquots of 100 g dry soil were then treated with the ^{14}C -labelled test item at the maximum expected environmental concentration of 0.2 mg/kg dry soil. The treated soil samples were incubated at $20 \pm 2^\circ\text{C}$ or $10 \pm 2^\circ\text{C}$ in the dark under continuous ventilation with moistened air. The exit air was passed through a trapping system

consisting of flasks of sodium hydroxide and ethylene glycol in series. Prior to treatment and at the end of the incubation period, the microbial biomass was determined for each soil. The results showed that the soils were viable during the study.

Table 16.7 –Properties of soil used to study degradation of triclosan in soils

Parameters	Soils		
	I Speyer 5M	II Senozan	III Gartenacker
Site location:	Germany	France	Switzerland
Batch:	F5M4806	12/06	12/06
Soil characteristics:			
pH (CaCl ₂)	7.10	6.85	7.30
Organic carbon % (g/100 g soil)	1.39	1.04	1.73
Organic matter* (g/100 g soil) %	2.4	1.79	2.98
Cation exchange capacity (meq/100 g soil)	13.0	19.5	10.1
Nitrogen % (g/100 g soil)	n.a.	0.12	0.15
CaCO ₃ (g/100 g soil) %	n.a.	0.70	6.8
Soil type (according to USDA):	Sandy loam	Clay loam	Loam
Particle size analyses (mm) USDA:			
clay (< 0.002) %	10.7	28.4	10.1
silt (0.002-0.05) %	28.9	51.2	47.6
sand (> 0.05) %	60.4	20.4	42.3
Max. water holding capacity (MWC) (g water/100 g soil)			
at pF 1.0	41.6	52.3	62.8
at pF 2.0	n.a.	30.6	39.5
at pF 2.5	n.a.	22.8	25.0
Biomass (mg microbial C/100 g dry soil)			
Start of incubation	16.9	19.7	17.7
End of incubation	10.6	10.0	10.8

*Calculated based on the equation: %OM = %OC x 1.724

Duplicate samples per soil incubated at 20°C were taken for extraction and analysis immediately after treatment (time 0), and after 1, 2, 3, 7, 14, 28, 61 and 124 days of incubation. For the 10°C part (soil I), duplicate samples were taken on days 0, 3, 7, 14, 28, 61 and 124 only. All soil samples were exhaustively extracted with acetonitrile/water (4:1; v/v). From the second interval onwards, additional Soxhlet extraction using the same solvent mixture for four hours was performed. The extracts were then concentrated under reduced pressure and analysed by HPLC and/or 2D-TLC for the test item and degradation products. In order to investigate the non-extractable residues, the samples from day 124 (20°C) were submitted to additional reflux extraction using acidic conditions followed by organic matter fractionation.

A total balance of radioactivity, the nature of extracted radioactivity and pattern of metabolites were established for each sampling interval.

One major characterised degradation product was formed, methyl-triclosan. Present from day 2 onwards, methyl-triclosan reached peak levels of 18% (day 28), 24% (day 28) and 13% (day 14) in soils I, II and III, respectively. In soil I incubated at

10°C, its rate of formation was slower, with methyl-triclosan reaching its peak of 15% on day 61. Thereafter, it steadily decreased in all three soils.

The following DT50 (dissipation time for 50%), DT75 and DT90 values were calculated for ¹⁴C-Triclosan and its major metabolite, methyl-triclosan, based on first-order two-compartment or consecutive first-order kinetics.

Table 16.8 – DT50, DT75 and DT90 values for triclosan and methyl-triclosan in the three soils

Soil	Temp. [°C]	Triclosan			Methyl-triclosan		
		DT50 [days]	DT75 [days]	DT90 [days]	DT50 [days]	DT75 [days]	DT90 [days]
I	20	2.46	6.16	19.1	96.7	193	321
II	20	3.27	7.65	19.9	153	307	509
III	20	2.68	9.26	21.6	39.2	78.3	130
I	10	10.7	57.1	231	-	-	-
Kinetic model used		First-order two-compartment			Consecutive first-order		

- Not calculated due to an insufficient number of data points.

All other radioactive fractions were transient, not exceeding 5% of the applied radioactivity at any sampling interval. The percentage of ¹⁴CO₂ released during the study reached 14.0, 16.2 and 11.5 at the end of the study for Soils I, II and III, respectively.

The study indicates that primary degradation of triclosan is rapid in soils with some slowing over time.

Australian soils

Ying *et al.* (2008) have reported the biodegradation behaviour of triclosan in a loam soil with pH value of 7.4 (the soil contained 52.1% of sand, 11.6% of silt, 34.7% of clay and 1.3% of organic carbon and was collected from an agricultural land) by laboratory degradation experiments and environmental fate modelling. Quantitative structure activity relationship (QSAR) analyses showed that triclosan has a tendency to partition into soil or sediment in the environment. Fate modelling suggests that triclosan ‘does not degrade fast’ with its primary biodegradation half-life of ‘weeks’ and ultimate biodegradation half-life of ‘months’.

For aerobic experiments, 5 g of soil was weighed into each scintillation vial (20 mL). The moisture level in each vial was adjusted using sterile water to 50% MWHC (maximum water holding capacity). Triclosan at a concentration of 1 mg/L in acetone was added into each vial to make 1 mg/kg in the soil. Lids were left open for 1 h to allow acetone to evaporate. Each vial was mixed well and incubated under darkness at 22°C in a constant temperature room. Half of the vials were sterilised by autoclaving at 120°C under 300 kPa chamber pressure for 30 min for three times within 3 days before adding triclocarban or triclosan, and used as sterile controls. Each vial was opened weekly to let the air in to maintain its aerobic conditions during the incubation.

For anaerobic experiments, preparation was carried in an anaerobic incubation chamber filled with nitrogen gas. Five grams of soil and 1 mL of sterile water was weighed into each Hungate anaerobic culture tube. Half of the tubes were taken out for autoclaving, and after sterilisation these tubes were placed back into the anaerobic chamber. Triclosan at a concentration of 1 mg/L in acetone was spiked into each tube to make 1 mg/kg in the soil. Lids were opened for some time to allow acetone to evaporate. Resazurin was added at a concentration of 0.0002% into two tubes as a redox indicator. Reducing conditions within the tubes were indicated by the disappearance of the red resazurin colour. All Hungate tubes were incubated under darkness at 22°C. Concentrations of each compound in the samples were monitored at certain intervals (0, 1, 7, and weekly to 70 days) by utilising three samples from each treatment. Triplicate sterile controls were also monitored at the same time.

The results of the laboratory experiments showed that triclosan were degraded in the aerobic soil with a half-life of 18 days. No negative effect of the antimicrobial agent on soil microbial activity was observed in the aerobic soil samples during the experiments. However, triclosan persisted in the anaerobic soil within the 70 days of the experimental period.

Aerobic aquatic degradation

The fate of triclosan has been investigated in two aquatic systems (river and pond) at 20°C in the dark (Adam 2006). The test item was applied to the water phase of the water/sediment systems at a dose of 0.109 mg/L.

The water/sediment systems were sampled from a river (Rhine river/Mumpf AG Switzerland) and from a pond (Möhlin BL, Switzerland) and consisted of natural water filtered through a 0.2 mm sieve and the uppermost 5-10 cm of the sediment sieved through a 2 mm mesh.

The test systems were acclimated under aerobic conditions in the dark for about two weeks prior to treatment. During this time, the measured values for pH, oxygen concentration and redox potential in water and pH and redox potential in sediment had reached constant values.

In the river system, the pH value of the water phase of the treated samples during incubation was on average 8.1. The corresponding value for the oxygen concentration was 8.3 mg/L. The mean value for the redox potential was 119 mV in water and -117 mV in the sediment). Virtually identical values were obtained for the untreated control samples (Table 16.9).

In the pond system, the pH value of the water phase of the treated samples during incubation was on average 8.0. The corresponding value for the oxygen concentration was 6.4 mg/L. The mean value for the redox potential in water was 122 mV and -124 mV in the sediment. Very similar values were found in the untreated controls indicating that the test item had no measurable effect on the physico-chemical parameters of the test system (Table 16.10).

In both systems the water was aerobic but the sediment was anaerobic according to the definition in OECD TG 308 (ie once the redox potential reaches -100 mV it is regarded as anaerobic).

Table 16.9 – Physical-chemical characteristics of the river aquatic system treated with ¹⁴C-Triclosan during incubation

Incubation Time (d)	Redox Potential (mV)		Oxygen Conc. Water (mg/L)	pH Water	Room Temp.
	Water	Sediment			
-1*	130 to 189	-147 to -80	5.9 to 8.6	7.30 to 8.35	
0	139	-123	7.1	7.60	
1	131	-135	8.7	8.13	
7	117	-114	8.0	8.13	
14	108	-118	6.8	7.96	20
28	110	-114	9.1	8.31	
56	112	-98	8.5	8.26	
104	121	-121	10.1	8.33	
Average	119	-117	8.3	8.10	
± SD	12	11	1.1	0.26	

*: Ranges of fluctuation in redox potential, oxygen and pH measured in the individual flasks one day before treatment of the test system.

SD: standard deviation

Note: Values represent the mean of duplicate samples

Table 16.10 – Physical-chemical characteristics of the pond aquatic system treated with ¹⁴C-Triclosan during incubation

Incubation Time (d)	Redox Potential (mV)		Oxygen Conc. Water (mg/L)	pH Water	Room Temp.
	Water	Sediment			
-1*	129 to 193	-153 to -96	2.3 to 7.7	6.87 to 8.07	
0	137	-144	4.5	7.71	
1	119	-137	8.6	8.19	
7	120	-120	7.6	8.12	
14	113	-158	4.8	7.73	20
28	99	-139	8.6	8.30	
56	97	-95	8.7	8.48	
104	107	-114	9.9	8.42	
Average	122	-124	6.4	8.01	
± SD	23	22	3.0	0.48	

*: Ranges of fluctuation in redox potential, oxygen and pH measured in the individual flasks one day before treatment of the test system.

SD: standard deviation

Note: Values represent the mean of duplicate samples

Following the acclimation period, the ¹⁴C-test item was applied to the water surface of each sample at a concentration of about 109 µg ¹⁴C-Triclosan per litre of water. During the incubation period, a stream of air was allowed to pass through the samples. Organic volatiles and ¹⁴C-carbon dioxide were collected in ethylene glycol and sodium hydroxide traps, respectively. During the entire incubation period, the samples were incubated in the dark and aerated by gentle agitation of the water layer so that the sediment remained undisturbed.

Duplicate samples of each system were taken for analysis after 0, 1, 7, 14, 28, 56 and 104 days of incubation. For each system, the water and sediment phases were

separated and the sediments were extracted with acetonitrile/water (4/1 v/v). Soxhlet extraction was additionally performed on selected samples. The radioactivity in the water phases and sediment extracts was determined by LSC followed by chromatographic analysis of concentrated aliquots with HPLC and 2D-TLC. A total radioactivity balance and the distribution of radioactivity was established for each interval.

Total recoveries of the applied radioactivity (material balances) averaged $94.1 \pm 2.6\%$ and $95.4 \pm 1.5\%$ in the river and pond systems, respectively.

The radioactivity in the water phase decreased continuously, from mean amounts of 96.9% (river) and 95.2% (pond) immediately after application to 7.9% and 11.4% of the applied radioactivity, respectively, within 14 days of incubation. At the end of incubation (day 104), only 1.7% and 2.7% of the applied radioactivity was detected in the river and pond water phases, respectively.

The extractable radioactivity from sediments increased reaching maximum mean amounts of 75.1% after 7 days (river) and 78.7% of the applied radioactivity after 14 days (pond). Corresponding values for day 104 were 34.7% and 27.6%, respectively. Soxhlet extractions recovered up to 6.1% of the applied radioactivity in both systems.

The amount of non-extractable radioactivity steadily increased during incubation. At the end of incubation, means of 32.4% and 33.0% of the applied radioactivity remained unextracted from the river and pond sediments, respectively.

The mineralisation of the test item (dichloro-phenyl ring moiety) was significant with CO_2 reaching maximum mean amounts of 21.4% (river) and 29.1% (pond) of the applied radioactivity after 104 days of incubation. Other organic volatile compounds did not exceed 0.6% of the applied radioactivity in both systems.

Further harsh extractions using acidic conditions under reflux extracted a maximum of 3.5% of the applied radioactivity from the sediment on day 104. Subsequent organic matter fractionation of the non-extractable residues indicates that in both sediments the major part of the non-extractable radioactivity was bound to the immobile humin fraction amounting to mean amounts of 17.5% and 20.2% of the applied radioactivity for river and pond, respectively. Corresponding values for the fulvic acids were 7.5% and 5.0% and for the humic acids 4.0% and 6.0%.

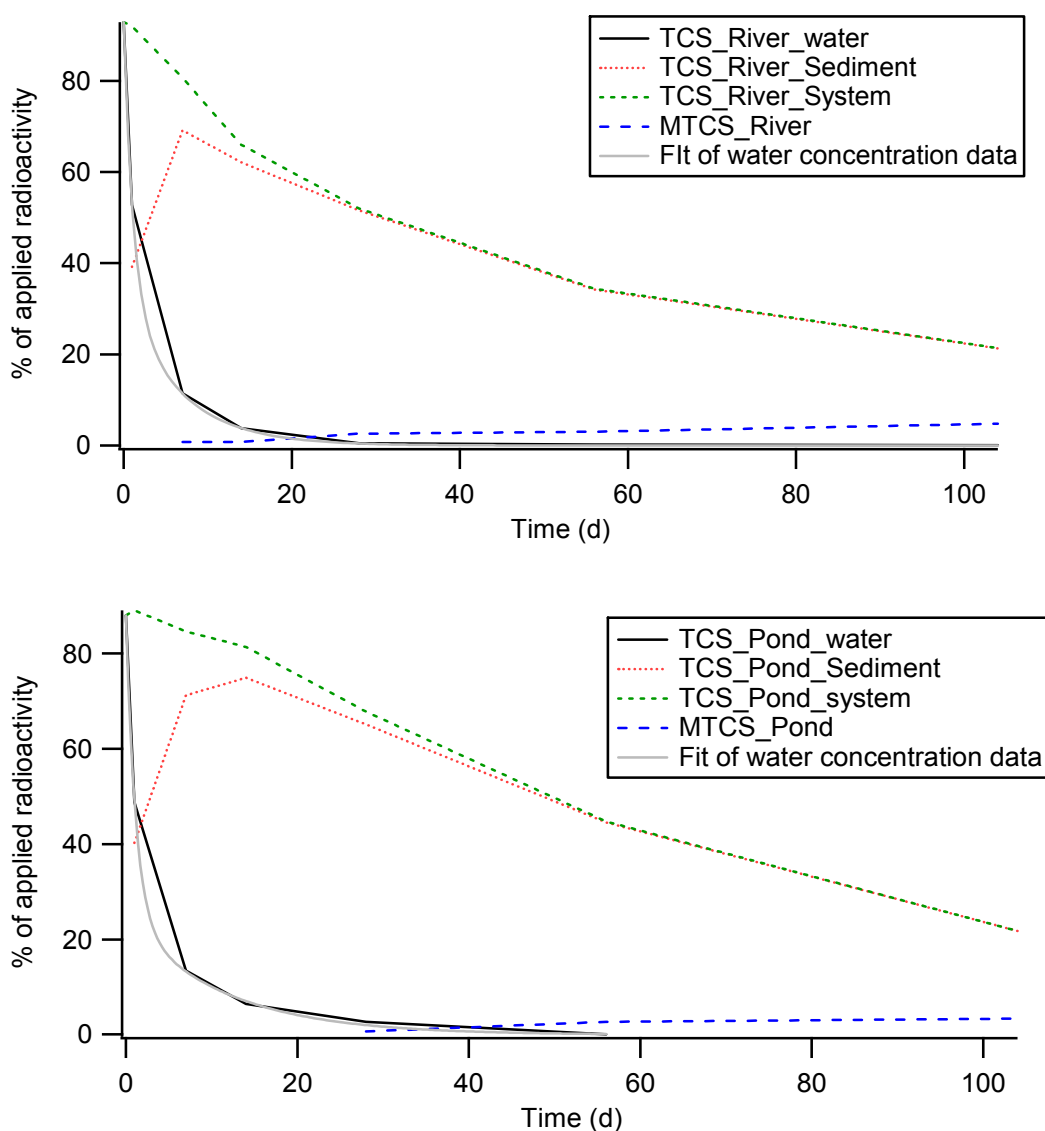
In both aquatic systems ^{14}C -Triclosan dissipated very rapidly from the water phase to the sediments. The concentration of the test item in the water phases, represented on average 92.9% (river) and 88.0% (pond) immediately after application decreasing to 3.8% and 6.5% within 14 days of incubation. At the end of incubation, ^{14}C -Triclosan in the water phase reached mean amounts of 0.1% and below the detection limit. In the sediment, the test item represented a maximum mean amount of 69.2% (river) and 74.9% (pond) of the applied radioactivity after 7 and 14 days, respectively. Thereafter, its concentration declined continuously to about 21% of the applied radioactivity after 104 days.

Besides the test item, up to sixteen minor metabolites were observed, one of which was identified by co-chromatography using HPLC and 2D-TLC as methyl-triclosan (highest amounts of 4.8% on day 104 in river system). All of the other minor metabolites reached at highest 6.5% (M8 at day 56 in River) of the applied

radioactivity in the water phases or sediments of both systems. At the end of the study their amounts were $\leq 5.5\%$. For further analysis, their amounts were too low.

The concentration of ^{14}C -Triclosan in the total river and pond systems represented initially 92.9% and 88.0% and decreased to 21.4% (river) and 21.8% (pond) on day 104. Degradation of the test item was observed in both compartments, but was more pronounced in the aqueous phases than in the sediments (Figure 16.3).

Figure 16.3. Measured concentrations of triclosan (TCS) and methyl-triclosan (MTCS) in the water sediment systems.



The dissipation times (DT50 and DT90) for the parent compound ^{14}C -Triclosan from the water phase, sediment and total system were calculated using first order kinetics. The values are listed in the table below. Note the data presented below are a result of analysis of the raw data and are not the values presented in the report, as the report analysed the data for all compartments using first order kinetics.

Table 16.11 – DT50, and DT90 values for triclosan in water sediment systems

Dissipation Time	¹⁴ C-Triclosan		
	Water Phase	Sediment	Total system
River			
DT50 (days)	1.2	56.8	48.5
DT90 (days)	11.5	188.7	161.0
Model used	First-order two-compartment	First-order	First-order
Pond			
DT50 (days)	1.3	53.7	50.6
DT90 (days)	8.3	178.5	168.1
Model used	First-order two-compartment	First-order	First-order

In aerobic aquatic systems, ¹⁴C-Triclosan dissipates rapidly from the water phase by degradation and adsorption to the sediment. In both compartments, it degrades to numerous minor metabolites, bound residues and radioactive carbon dioxide.

16.1.6 Reaction with metals

Reaction of triclosan with some metal oxides in soils and sediments may affect other environmental transformation processes particularly when conditions are not conducive to biodegradation or photochemical degradation (Zhang and Huang, 2003). In general, oxides of manganese, iron and aluminium in soils are able to facilitate abiotic reactions of some organic compounds via hydrolysis, oxidation or reduction. Rapid reaction of triclosan with manganese dioxide (MnO₂), similar to species found in soils and sediments (e.g. birnessite and manganite MnOOH), was observed and yielded Mn²⁺ ions. Both the reaction rate and adsorption of triclosan to oxide surfaces increased as pH decreased. The pH dependence of the reaction rate is attributed to the effect of pH on the adsorption of triclosan to the oxide surface and on electron-transfer reaction. Protonated triclosan, dominant at pH 5-8, adsorbs more strongly to MnO₂ than the deprotonated phenolate form (dominant at pH >8). Competition with dissolved ions (Mn²⁺, Zn²⁺, Ca²⁺) for MnO₂ decreased the reaction rate, as did the addition of organic (humic) matter derived from the Suwannee River. Reaction rate is slowed as the available oxidation sites are saturated. A slower reaction rate was observed in Suwannee River water, probably due to a combination of inhibitory effects from dissolved metal ions, natural organic matter, and other inorganic anions such as phosphate. Reaction with MnO₂ was faster than with MnOOH. This is likely due to the larger surface area and more accessible active surface sites. Analysis of products indicated triclosan oxidation at the phenol moiety, yielding primarily coupling and p-(hydro)quinone products of triclosan including 2-chloro-5-(2,4-dichlorophenoxy)-[1,4]benzoquinone (<5% of triclosan loss) and 2-chloro-5-(2,4-dichlorophenoxy)benzene-1,4-diol (<5% of triclosan loss). A small quantity (<1% of triclosan loss) of 2,4-dichlorophenol was also produced, indicating bond breaking of the ether linkage of triclosan (Zhang and Huang, 2003). PCDD/Fs were not formed during this reaction. Other products

were present but were not described. Zhang and Huang (2003) indicated that MnO₂ also promotes dimerisation and potentially polymerisation of triclosan, likely by radical reactions. Assuming a soil of pH 6 and 10 µm manganese, the half life of triclosan was estimated to be <21 hours; however, the presence of other ions in the soil is likely to slow the reaction. Dimerisation and polymerisation of triclosan is likely to lead to more hydrophobic products of potentially lower mobility, bioavailability and toxicity.

16.1.7 Products from combustion of triclosan and derivatives

Products of triclosan (including dioxins)

Products and materials potentially containing triclosan are combusted either intentionally or accidentally. For example, some sewage sludges (e.g. Lower Molonglo STP, Canberra) are incinerated at ~1000°C to produce ash that is used in agricultural soil conditioning applications. Medical wastes are typically incinerated and municipal solid wastes are sometimes incinerated either in commercial waste incinerators or at landfill sites.

Triclosan is thermally stable below 300°C and the thermal cyclization of triclosan and other polychlorophenoxyphenols to PCDD/Fs is established and occurs readily for triclosan above 300°C (Latch et al., 2003). Thermal degradation of triclosan produces di-CDDs (i.e. 2,8-CDD; Nilsson et al., 1974; Kanetoshi et al., 1988a). Kanetoshi et al. (1988a) demonstrated that pyrolysis of triclosan at 400°C for 10 minutes resulted in the conversion of 42% of the triclosan to Di-CDD (refer Table 16.12) and a trace amount of 2,4-DCP was also detected (Kanetoshi et al., 1988a).

Table 16.12 - Formation of PCDDs from combustion of triclosan and chlorinated derivatives

Compound combusted	Dioxin formed (% and range)					Total PCDDs *
	Di-CDD	Tri-CDD	Tetra-CDD	Penta-CDD	Hexa-CDD	
Triclosan	42 (39-42)					42%
II		22 [2] (17-22)	46 [3] (44-47)			68%
III		44 [2] (31-56)	25 [2] (23-27)	1 (trace-1)		70%
IV			16 [2] (11-20)	Trace	40 [4] (35-45)	56%

Source: Kanetoshi et al. (1988a). * Calculated on the initial amounts of triclosan and its chlorinated derivatives. Values in square brackets [] are the numbers of isomers detected. Triclosan provided as Irgasan DP 300. Chlorinated derivatives: II = 2',3,4,4'-tetrachloro-2-hydroxydiphenyl ether; III = 2',4,4',5-tetrachloro-2-hydroxydiphenyl ether; and IV = 2',3,4,4',5-pentachloro-2-hydroxydiphenyl ether. Refer to Figure 16.1 for chemical structures.

The combustion of textile materials impregnated with triclosan potentially also forms PCDD/Fs, particularly di-CDDs (Kanetoshi et al., 1988a). The conversion rates of triclosan to di-CDDs were determined, using a textile product containing 515 ppm of triclosan, to be 26% (range 20-32), 43% (38-48) and 24% (21-26) (averages from two experiments) at combustion temperatures of 400, 600 and

800°C, respectively. Combustion of four other textile products yielded di-CDD conversion rates of 19%-43% (Table 16.13).

Ciba Geigy has investigated the PCDD/F toxicity equivalency (TEQ) following combustion (800°C, residence time 2 seconds) of triclosan-containing fibres including polypropylene, polyacrylonitrile and cellulose acetate (0.5% triclosan) and polyvinyl chloride (1% triclosan). The TEQ refers to the toxicity of higher chlorinated PCDD/Fs and does not include di- or tri-CDD/Fs. TEQ values for combusted fibres containing triclosan did not increase compared to controls.

Table 16.13 - Formation of Di-CDD following combustion of commercial triclosan-impregnated textiles

Textile	Material	Triclosan Conc. (µg/g)	Di-CDD formed (µg/g)	Conversion rate (%) *
Bath mat	Acrylic	515	194 (172-216)	43
Men's socks	Cotton Nylon	5890	999 (627-1370)	19
Men's shirt	Cotton	747	182 (109-255)	28
Slip	Acrylic	463	132 (129-135)	33

Source: Kanetoshi et al. (1988a). * Calculated from the initial amounts of triclosan. Triclosan provided as Irgasan DP 300.

Chlorinated derivatives of triclosan

Pyrolysis of the chlorinated derivatives of triclosan also give rise to various PCDD/Fs. Nilsson et al. (1974) indicated that 2',3,4,4',5-pentachloro-2-hydroxydiphenyl ether is converted to 1,2,3,8-tetra-CDD when heated. In addition, the perchlorinated analogue of triclosan has been reported to form octachlorodibenzo-*p*-dioxin (OCDD) at the heated inlet of analytical GCs (Rappe and Nilsson, 1972). As indicated in Table 16.12 (Kanetoshi et al., 1988a), combustion of compound II gave 2 isomers of tri-CDDs (e.g. 1,2,8-tri-CDD; 22%), at least three tetra-CDD isomers (46%) and compound III residues. Combustion of compound III gave a rise to 2,3,7-tri-CDD (44%), several tetra-CDD isomers (25%), penta-CDD (1%) and compound III residues. Combustion of penta-IV gave rise to 2 tetra-CDD isomers (e.g. 1,2,3,8-tetra-CDD; 16%), a trace of penta-CDDs and three hexa-CDD isomers (e.g. 1,2,3,6,7,8-hexa-CDD; 40%).

Similar PCDD/Fs were also detected following combustion of chlorinated derivatives of triclosan absorbed onto cotton gauze (Table 16.14).

In addition, combustion experiments following sodium hypochlorite bleaching of textile (men's socks) containing triclosan also produced several PCDD/Fs (Table 16.15; Kanetoshi et al., 1988a).

Data in Table 16.14 and Table 16.15 indicate that combustion of triclosan-impregnated textile produced di-CDDs; however, chlorination followed by combustion also gave rise to tri- and tetra-CDDs due to the formation of, and subsequent combustion of, the chlorinated derivatives of triclosan formed following chlorination with 0.02% available chlorine at 45°C for 30 minutes (Kanetoshi et al., 1988a).

Table 16.14 - Formation of PCDDs from chlorinated derivatives of triclosan adsorbed onto cotton gauze upon combustion at 600°C

Compound	Dioxin formed (µg)			Total PCDDs formed (%)*
	Di-CDD	Tri-CDD	Tetra-CDD	
II	9 (6.4-11)	61 (57-64)	ND	8
III	19 (18-19)	102 (80-124)	ND	14
IV	6 (3-8)	18 [3] (11-25)	70 (48-92)	11

Source: Kanetoshi et al. (1988a). Triclosan provided as Irgasan DP 300. * Calculated on the initial amounts of triclosan derivatives. ** Values in [] brackets are the numbers of isomers detected. ND = Not detected (<0.5 µg). Chlorinated derivatives: II = 2',3,4,4'-tetrachloro-2-hydroxydiphenyl ether; III = 2',4,4',5-tetrachloro-2-hydroxydiphenyl ether; and IV = 2',3,4,4',5-pentachloro-2-hydroxydiphenyl ether.

Table 16.15 - Formation of chlorinated derivatives of triclosan and PCDDs from a triclosan-impregnated textile (men's socks) after bleaching with sodium hypochlorite and combustion at 600°C

Sample	Amount formed after bleaching (µg/g)*			Amount formed after combustion (µg/g)**			
	Triclosan	II	III	IV	di-CDD	tri-CDD	tetra-CDD
Untreated	5890	ND	ND	ND	999 (627-1370)	ND	ND
Treated with 0.02% AC	2580 (2380-2780)	458 (421-494)	215 (194-236)	1180 (1080-1280)	268 (254-282)	132 [3] (121-142)	93 (81-104)

Source: Kanetoshi et al. (1988a). Triclosan provided as Irgasan DP 300. * ND = Not detected (<1 µg/g). ** ND = Not detected (<0.5 µg/g). AC = available chlorine. Values in [] brackets are the numbers of isomers detected. Values are averages of two experiments, with ranges of the data in parentheses. Chlorinated derivatives: II = 2',3,4,4'-tetrachloro-2-hydroxydiphenyl ether; III = 2',4,4',5-tetrachloro-2-hydroxydiphenyl ether; and IV = 2',3,4,4',5-pentachloro-2-hydroxydiphenyl ether.

16.2 Environmental exposure

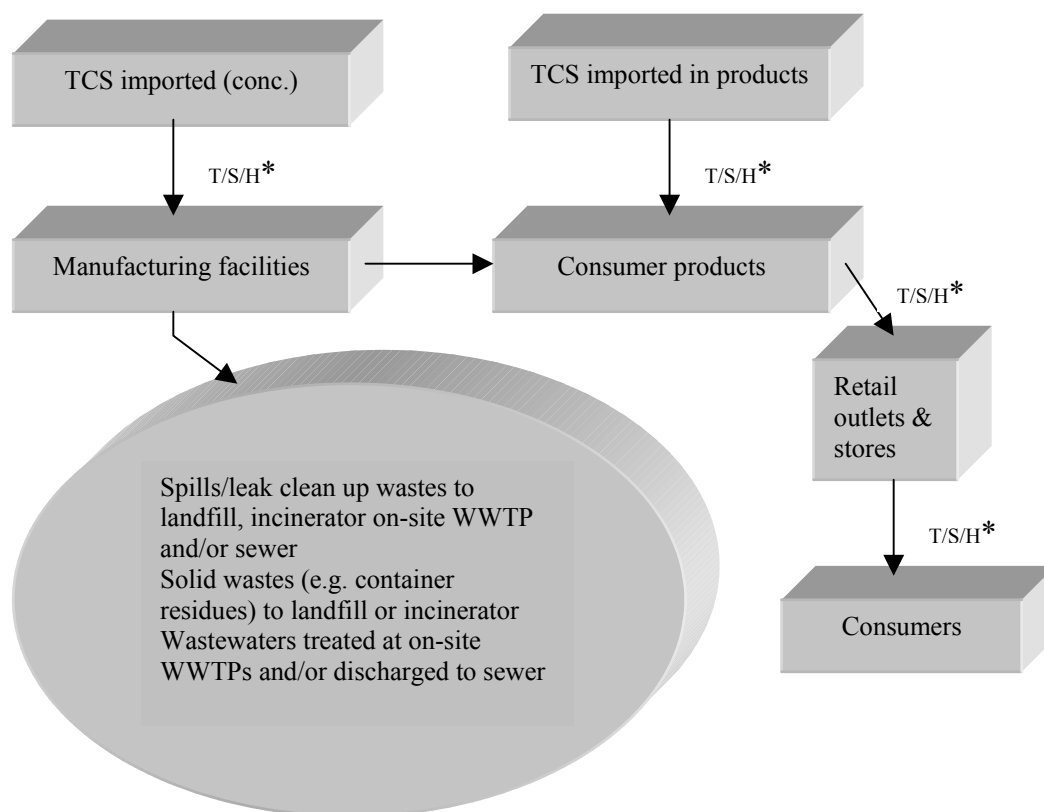
Triclosan has not been manufactured in Australia, and consequently, there is no Australian environmental release or exposure resulting from manufacturing operations of the substance itself.

16.2.1 Import and manufacture

Direct release of imported triclosan (concentrate) or products containing triclosan to the environment may potentially occur from spills and leaks as a result of accidents or incidents during transportation, storage, handling (T/S/H) and manufacturing (Figure 16.4). However, the environmental impact of these events is likely to be limited, being managed through established spill incident response mechanisms (i.e. MSDS). Some manufacturing facilities claim to have on-site

wastewater treatment plants (WWTPs) to treat spills prior to discharge of wastewater to sewer.

Figure 16.4. Conceptual exposure model for triclosan (TCS) in Australia: Importation and Manufacture of Products (T/S/H* = transportation, storage, handling).



Manufacturing facilities that use triclosan in their products are likely to generate wastewaters containing relatively small quantities of triclosan compared to the quantity used in products manufactured overseas. These wastewaters may be treated at on-site WWTPs and/or discharged to sewer. WWTP sludge is typically dried and sent to landfill for disposal via licensed waste disposal contractors.

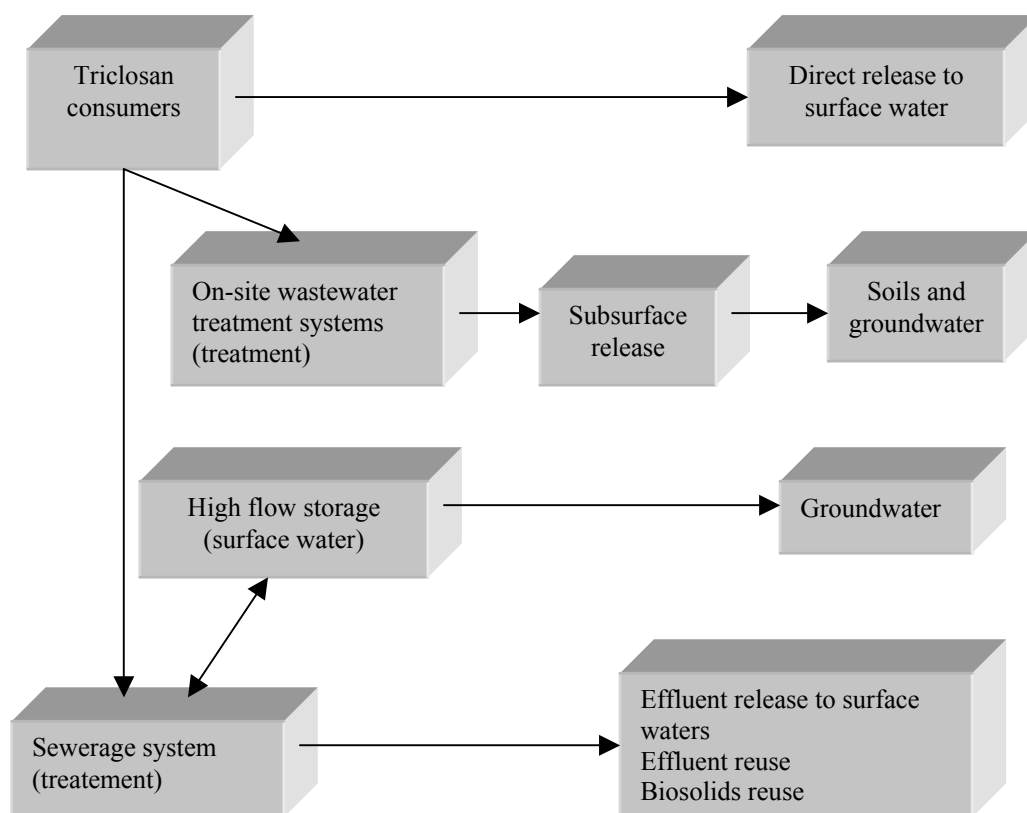
After being emptied, imported containers may contain small residues of products (e.g. 1% - 5% of initial contents) containing triclosan. These residues, along with other solid wastes containing triclosan (e.g. off-spec stock), are mostly sent to landfill for disposal; however, at some facilities these wastes may go to industrial incinerator for disposal via waste contractor.

16.2.2 Uses, releases and disposal

Triclosan is a widely applied antimicrobial agent used in domestic, commercial, hospital, agricultural and industrial applications for ~30 years. The use and disposal pattern is widespread throughout Australia. Each use pattern generates solid and liquid wastes containing triclosan. Solid wastes (e.g. container residues, impregnated textiles and plastics) may be sent to landfill, or less often, commercial incinerator for disposal or potentially to plastics recycling facilities. Aqueous wastes are typically treated at on-site WWTPs and/or disposed of to sewer. Figure

16.5 presents a conceptual model of the triclosan use pattern and potential environmental release pathways.

Figure 16.5. Conceptual exposure model for triclosan use, release and disposal



Direct release to surface waters

During recreational activities such as swimming at waterways and beaches, personal care products, disinfectants, creams and insect repellents that have been applied to skin that potentially contain triclosan may be washed off directly into the water. No information or estimate is available on the actual quantity dissolved directly into the water and its environmental impact.

Disposal into the sewerage system

Following its use, the majority (~96%, Ciba Specialty Chemicals, 1998a) of the triclosan used in Australia is washed off or disposed of into the Australian sewerage system (including municipal STPs and domestic on-site wastewater treatment systems) in association with various products and uses. These products containing triclosan potentially include many types of soaps, washes, disinfectants, dishwashing liquids and powders, deodorants, disinfectant skin creams and lotions, medicated insect repellents, body and foot powders, oral hygiene products (toothpastes and mouthwashes) and shampoos (for humans and domestic animals).

Although triclosan is used in textile and plastic articles, many of which have uses associated with water, leaching studies indicate that only a small proportion of the impregnated triclosan may be dissolved and released to sewer, with most eventually going to landfill within the articles.

The use in oil-based paints is not expected to result in significant releases of the imported triclosan to the aquatic compartment as it is anticipated that the overwhelming majority of the triclosan is expected to be contained within the cross linked inert paint matrix and share its fate. This is likely to be disposed of to landfill (either as paint dust resulting from sanding back the painted surface or bound to the surface) at the end of its useful life time. As it will be bound within the inert paint matrix leaching from landfill is not expected and it will slowly degrade through a mixture of biotic and abiotic processes. The use of the tile paint in shower cubicles gives rise to the potential release of triclosan to the environment through leaching from the paint. However, the rate of leaching is expected to be extremely low and hence, the releases from this to source is expected to be insignificant.

As an alternative to disposal to the Australian municipal sewerage system, a small proportion of domestic wastewater is discharged to on-site wastewater systems, of which there are many proprietary types (e.g. cesspools or privies, septic tank/soakage, septic tank/low pressure soakage, sand filters/evapo-transpiration, special media filters/evapo-transpiration, aerobic wastewater systems/evapo-transpiration), after which effluent may be discharged to decentralised or centralised disposal systems or are regularly pumped out (pump-out systems) with no on-site discharge. These are particularly common in rural and regional Australia. Septic systems traditionally comprise a bioreaction chamber (anaerobic), which receives untreated wastewater, and a subsoil drain field where aerobic biodegradation of discharged effluent occurs. Septic and pump-out systems, which can achieve ~40% and ~90% solids removal, respectively, are subject to operational deficiencies, such as poor treatment efficiency and overflow if not properly located and maintained. Pump-out systems are commonly not pumped out resulting in overflow, waterlogging and discharge to surface waters. Centralised systems include conventional gravity systems (CGS), common effluent drainage (CED) and septic tank effluent pumping or drainage (STEP, STED) where partially treated wastewater is treated in a communal facility.

Degradation and partitioning in the sewerage system

Triclosan in wastewater collected at municipal STPs, hospitals or other wastewater treatment plants, or septic systems may be degraded or modified through several processes (e.g. biodegradation, methylation). Triclosan may also bind to solids and partition to sludge and only a fraction may remain in the aqueous phase (e.g. dissolved or adsorbed to suspended solids or dissolved organic matter) and pass through the STP in effluent. The degree of treatment, partitioning to sludge or effluent by triclosan is a function of the processes used to treat the wastewater. The efficiency of wastewater treatment processes has been described in Section 16.3.1.

Releases from the municipal sewerage system

Wastewater (sewage) entering the sewerage system is mostly collected and treated in the system at municipal STPs. However, a fraction of untreated wastewater in the sewerage system is lost prior to reaching the STP through sewer overflows (emergency relief structures; ERS), transmission network leaks and uncontrolled discharges resulting in the contamination of soils, groundwater and/or surface waters (Figure 16.6). Sewerage system overflows may occur during low or high flows (e.g. storm events and stormwater ingress), power outages (pump failure) and transmission line blockages (e.g. chokes, mainly due to tree roots).

Sewerage system overflows and leaks

Sewer overflows occur regularly in the Australian sewerage system and in all sewerage systems worldwide; however, information on the quantity released is largely unknown. The Sydney sewerage system, managed by Sydney Water Corporation, contains approximately 6000 discharge points (Cadden and West, 1995), comprising 3000 design overflow points as well as additional surcharge points such as access chambers (Sydney Water Corporation, 2000a).

In 2002-03, there were 19620 field verified raw sewage overflows from this system, an increase of 25% from 2001-02. In 2002-3, Sydney's newly constructed Northside Sewerage Tunnel collected and diverted 5580 ML of overflow from entering Port Jackson, representing ~86% of the total overflow volume from the particular overflow points involved. However, ~0.93 ML of raw sewage flowed from these overflow points to Port Jackson during this period (Sydney Water Corporation, 2003).

Sydney Water has reported that as 2005-06 was a relatively dry year, the number of wet weather overflows remained low, and a total of 1% of untreated wastewater overflowed in either dry or wet weather conditions. With a total of 432 542 ML (where 1 ML = 1 000 000 L) of wastewater collected in 2005-06, this would equate to untreated overflow volumes of 4 325 420 000 L in several events over the year. Apparently the number of dry weather sewage overflows increased by 18% from 2004-05, although the number of properties affected was below their Operating Licence limit.

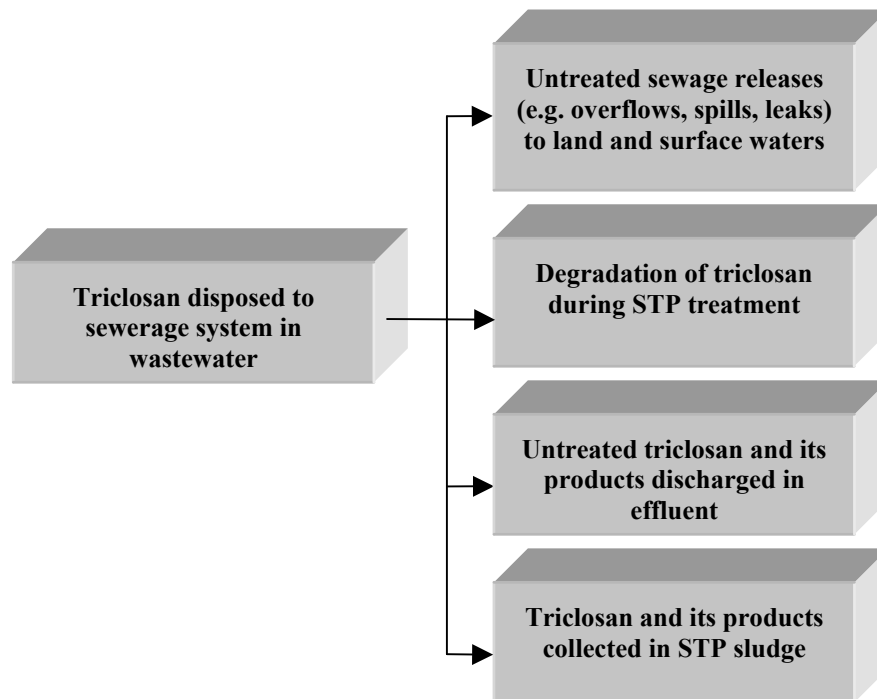
Sewer overflows also occur in regional areas. For example, in 2001-02 in the Gosford Shire, NSW, there were 677 sewage discharges to the environment; however, <1% were not contained at source (Gosford City Council, 2002). In the Yarra Valley sewerage system, Victoria, in 2000-01, sewage spills to the environment accounted for 0.05% (62 ML) of the total sewage treated (Yarra Valley Water, 2001).

To address the issue of sewer overflows and wastewater releases, modern sewerage systems include emergency response protocols for managing sewer overflows and programs for upgrading systems are underway in many areas (e.g. Sydney Water Corporation SewerFix Program).

Disposal of untreated sewage to the aquatic environment, potentially containing triclosan, may also occur from ships and other marine craft that do not utilise land-based sewage pump out facilities.

No Australian environmental monitoring data were available on the effect of these uncontrolled releases of untreated wastewater to potential receiving environments including land, groundwater and surface waters (Wilkison et al., 2002). Closure of recreational activities is a common consequence from significant sewer overflows due to exceedances of health-based water quality criteria, which predominantly relate to microbial contamination, in surface waters where pollution events are detected. The probable immediate drivers of concern in raw wastewater are BOD and ammonia.

Figure 16.6. Conceptual model for triclosan for sewer disposal route



Use of treated effluent, sludge and biosolids

Appendix A provides a description of the Australian sewerage system, wastewater generation rates, and re-use strategies for STP products (effluent, sludge/biosolids).

Beneficial products from STPs include treated effluent and sludge (biosolids). Throughout Australia, treated effluent is increasingly being utilized in a range of agriculture (irrigation), agroforestry and industrial applications. For example, all biosolids captured by Sydney water, which collects more than 1.2 billion litres of wastewater a day, are used for agricultural or horticultural purposes (Sydney Water Corporation 2006). Reported occurrences of triclosan in treated effluent are described in Section 16.3.1.

A proportion of the triclosan entering STPs will partition from the wastewater to suspended solids. Depending on STP design and operating conditions, solids may be collected as sludge (primary, secondary, digested). Biosolids are nutrient rich organic matter derived from stabilised sewage sludge, which are applied to soils as a soil fertility conditioner. Reported occurrences of triclosan in various STP sludge are provided in Section 16.3.2.

Release to groundwater

Triclosan is unlikely to be used in a manner resulting in its intentional release to groundwater; however, untreated wastewater or treated effluent potentially containing triclosan may be released intentionally or otherwise to land, waterways and groundwater. Potential sources include high-flow storage ponds, pipeline leaks,

sewer overflows, effluent infiltration ponds and domestic on-site wastewater treatment systems.

- During periods of high inflow, some municipal STPs store untreated wastewater in storage ponds for later treatment through the STP. These holding ponds create a potential source of groundwater contamination via infiltration and percolation.
- Sewer overflows and pipeline leaks occur throughout the Australian sewerage system. These leaks provide an avenue for direct release of untreated wastewater potentially to soil, groundwater and surface water.
- Several Western Australian STPs discharge ~2 gallons/year of treated effluent to infiltration channels with the potential for percolation to groundwater. In particular, 840 ML of effluent from Halls Head STP has been discharged to infiltration ponds for subsequent reclamation through groundwater extraction for irrigation.
- Domestic on-site wastewater treatment systems are used in parts of Australia, and these typically discharge to a subsurface trench or centralised treatment facility, with a potential for contamination of groundwater by these discharges.

Overall, groundwater contamination by triclosan is unlikely except in localised conditions of saturation as described above due to its high affinity to soils/sediments, organic matter and low water solubility. However, no field monitoring data are available to suggest groundwater contamination by triclosan has occurred.

Atmospheric release

While release of triclosan to the atmosphere will occur, it has a very low vapour pressure (4×10^{-6} mmHg; Ciba-Geigy Limited, 1990d) at environmentally relevant temperatures of 20°C to 25°C. With a Henry's Law Constant of $\sim 10^{-2}$ Pa.m³/mole, triclosan is essentially non-volatile from water surfaces at these temperatures and the rate of partitioning of triclosan to the atmosphere is likely to be low compared to other environmental compartments and degradation processes.

Triclosan is more volatile in steam. When a suspension of 1000 mg of triclosan in 800 mL water is distilled, 180-200 mg of triclosan (18%-25%) is found in the initial 500 mL of the distillate (Ciba Specialty Chemicals, 1998a). This has greater relevance where triclosan is used in combination with hot water (e.g. certain industrial applications, steam cleaning, showers, dish-washing and cleaning). However, this is unlikely to be a significant source of atmospheric release of triclosan.

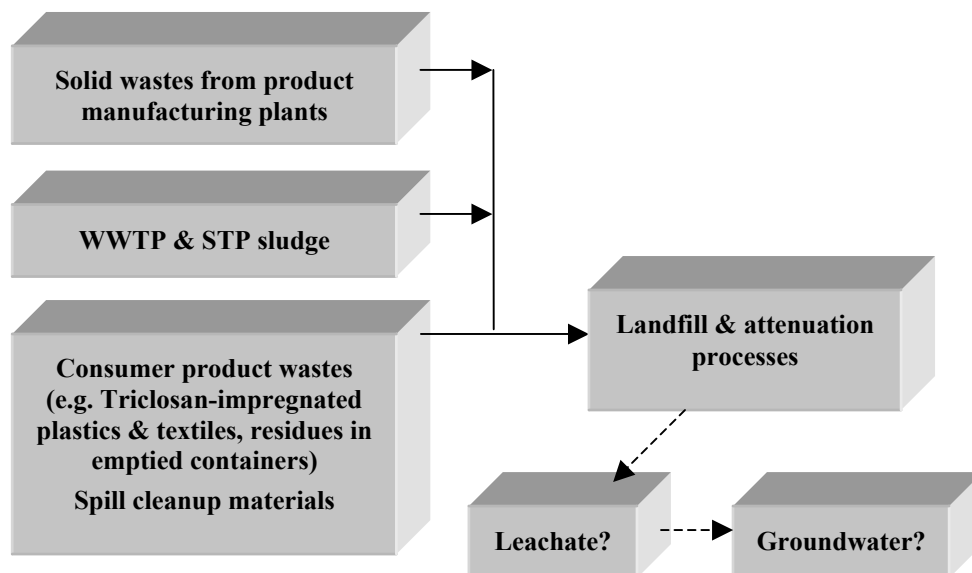
No vapour pressure data were available for methyl-triclosan or chlorinated derivatives of triclosan with which to assess their potential for volatilisation to the atmosphere.

Landfill disposal

A proportion of the triclosan used in Australia is sent to landfill for disposal (refer Figure 16.7). These wastes derive from triclosan-impregnated plastics, textiles, residues in emptied containers and sludges from some municipal STPs and other WWTPs. The fate of triclosan in the landfill environment has not been investigated.

Solid wastes containing triclosan, and emptied containers with residues of products containing triclosan, are mostly sent to landfill for disposal. Use of triclosan in Australia involves widespread and diffuse emissions since the substance is present in a wide range of personal care and consumer products.

Figure 16.7. Conceptual model for landfill disposal route



16.3 Occurrence in wastewater and the sewerage system

This section provides a summary of the reported occurrence of triclosan in wastewater systems in Australia and internationally.

16.3.1 Untreated and treated wastewater

Australian municipal STP data

Ying and Kookana (2007) Study

The presence of triclosan in Australian wastewater has recently been reported (Ying and Kookana, 2007). In a screening study, the level of triclosan in 19 effluents from sewage treatment plants across Australia was examined. After the screening study in 2004, a triclosan fate study was conducted in five sewage treatment plants (STPs) (A, B, C, D, E). In both parts of the investigation, water samples were collected in duplicate using pre-cleaned, 1 L brown glass bottles and preserved by acidifying to pH 3 with 5M sulfuric acid. Two blank samples were also collected during sampling process. For this, two bottles filled with Milli-Q water were taken to the field to check for potential contamination. After collection, samples were transported on ice to the analytical laboratory, and then stored in a cold room (4 C) until extraction. Water samples were normally extracted within a week. Biosolid samples were collected in plastic buckets, and kept at -20°C in a freezer until extraction. After clean up, both substrates were subjected to GC-MS analysis.

Sampling was conducted in 2004 (screening study) and 2005 (fate study). Final effluents (19 treated wastewaters) and biosolids (17 digested sludges; discussed further in Section 16.3.2) for the screening study were collected from STPs around Australia in 2004.

The concentrations of triclosan in nineteen effluents from the screening study ranged from 23 ng/L to 434 ng/L with mean and median concentration of 142 and 108 ng/L, respectively. Details of the STPs from which these samples were collected are not available although a breakdown of the states in which the plants were located were provided (8 from South Australia, 5 from Queensland, 2 from Australian Capital Territory, 1 from Western Australia and 3 from Victoria). Influent samples were not collected at these STPs and consequently no information on plant performance can be inferred. However, in a follow up study, some details of the STPs used in the fate study were provided and are summarised in Table 16.16.

Table 16.16 - Details of STPs where fate studies were conducted by Ying and Kookana (2007)

STP	Location	Population served	Treatment Level	Treatment	Discharge	Overall Removal
A	Urban (SA)	1 300 000	Tertiary	Activated sludge with 6 lagoons	Ocean	93%
B	Urban (WA)	300 000	Tertiary	Activated sludge with sand filtration	Ocean	72%
C	Rural (SA)	3300	Tertiary	10 lagoons in series (2 anaerobic followed by 8 aerobic lagoons)	Creek	85%
D	Rural (SA)	7377	Secondary	Activated sludge (3 bioreactors with UV)	Creek	89%
E	Rural (SA)	5000	Secondary	Biological treatment (2 oxidation ditches)	Creek	92%

Triclosan was found in the influents (raw wastewaters) from plants A, B, C, D and E with concentrations ranging from 573 ng/L to 845 ng/L. The concentrations in the final effluents (secondary or tertiary effluents depending on the STP) ranged from 60.5 ng/L to 159 ng/L.

This study provides an excellent first step in determining the range of concentrations of triclosan in Australian STPs. However, these five STPs are not likely to be representative of the full range likely at Australian STPs. In addition, given that some of these plants have extensive lagoon systems, they are likely to have much higher retention rates than the average STP.

The total removal rates for triclosan in the five STPs used for the fate study were 93%, 72%, 85%, 89% and 92% for plants A, B, C, D and E, respectively. In the two urban STPs, removal by primary treatment was 41% for plant A and 7% for plant B. Significant loss of triclosan was seen at each stage of the treatment process for plant A, and the removal rates were 41%, 41%, 11% for primary, secondary and tertiary (lagoons) treatments, respectively. Although both plants A and B are activated sludge systems, the triclosan removal rate was lower in plant B than in plant A. Only a small loss was observed for plant B during primary treatment (primary sedimentation) and tertiary treatment (sand filtration and chlorination). A gradual decrease in triclosan concentration was observed in Plant C, which consists of a series of lagoons. The triclosan concentrations changed from 586 ng/L in raw wastewater, 344 ng/L in the 4th lagoon, 182 ng/L in the 6th lagoon and 90 ng/L in the 10th lagoon. There was a good removal from lagoon to lagoon. In the first two anaerobic lagoons, loss of triclosan could be attributed to settling with sludge and possibly little anaerobic degradation as this process was previously found not significant for triclosan removal (McAvoy et al., 2002). Except for the first two anaerobic lagoons, the rest of the eight lagoons were all aerated. Therefore, aerobic biodegradation of triclosan occurred in the STPs.

The other two rural STPs (plant D with two oxidation ditches, and plant E with three bioreactors) gave triclosan removal rates of 89% and 92%. A rapid drop in triclosan concentration was observed in plant D from 805 ng/L in the sewage inlet to 121 ng/L in the clarifier. A similar trend was also found in plant E, decreasing from 791 ng/L in the sewage inlet to 69 ng/L in the clarifier. Little removal occurred in the final stage of treatment (UV disinfection and chlorination for plant D, and chlorination for plant E).

The authors concluded that biological degradation was the predominant removal mechanism for triclosan in the STPs. However, adsorption onto sludge also played a role in the removal of triclosan in the STPs.

Other Australian data

The only other data available was collected in 1996 from effluent treated in Sydney, Melbourne and Wagga Wagga (described below).

Apart from these two sets of data, a survey of major sewerage treatment operators throughout Australia undertaken during this assessment found that triclosan is not routinely monitored in STP influent, effluent, sludge or biosolids or in discharge receiving environments. Concentrations or loadings (percentile, average annual, maximum) of triclosan from Australian STPs have otherwise not been investigated or reported.

Sydney

Ciba Specialty Chemicals (2003a) briefly reported the results of a limited investigation comprising the collection and analysis of grab samples of high flow primary-treated effluent from major STPs operated in the Sydney region (Malabar, Bondi, North Head) in 1995-96. Each of these STPs currently provides relatively limited (high flow primary) wastewater treatment.

Sampling data from laboratory test reports by Australian Government Analytical Laboratory (AGAL) indicated the presence of triclosan in sampled high flow primary treated effluent at concentrations ranging as follows:

- Malabar STP <0.100-0.74 µg/L (≤ 740 ng/L; 8 samples);
- Bondi STP 0.13-0.46 µg/L (≤ 460 ng/L; 4 samples); and
- North Head STP 0.13-0.32 µg/L (≤ 320 ng/L; 5 samples).

The limited sampling data, and paucity of background information, lack of reporting of quality assurance and quality control procedures and age of the study (1995-96) limits the utility of the data for this assessment. As well, the lower use levels of triclosan at the time indicates that levels in the influent are likely to be currently higher. No information was available on specific sampling locations, methods of sampling, sampling containers used, sample preservation and handling, chain-of-custody procedures, laboratory analytical method, field or laboratory quality assurance and quality control procedures. No results for field or laboratory blanks, field or laboratory duplicates, matrix spikes, surrogates or certified reference materials were reported. No data were available on triclosan loading (e.g. kg/ML), methyl-triclosan, chlorinated derivatives of triclosan, or dissolved or particulate-bound triclosan in wastewater or effluent.

Furthermore, operational conditions at the STPs at the time of sampling were not described (e.g. relative flow rate), limiting the ability to use this data for modelling purposes. The effluent concentrations refer to triclosan usage at the time of the study, which was approximately 15000 kg in 1995. The average import volume of 26.8 tonnes per annum for the period 2001-2005 which is approximately double that used in 1995, indicates that the effluent triclosan concentration may also have doubled during this time (e.g. up to 1500 ng/L). The recent Ying and Kookana (2007) results are within or even below the above ranges, with the maximum concentration (740 ng/L) for the Malabar STP well above that (434 ng/L) of the 19 STPs sampled. However, the Malabar STP, which has only limited primary treatment, is significantly different from the secondary and tertiary-treated plants tested by Ying and Kookana (2007) and is therefore likely to have a much lower removal rates. Consequently, it is possible that the levels in Malabar would be significantly higher now when compared with 1995-96. In addition, flow rates through plants like Malabar have also increased significantly since 1995-96 and consequently retention times have decreased, indicating that removal rates may be lower than they were in 1995-96.

Melbourne and Wagga Wagga

Ciba Specialty Chemicals (2003a) noted data from secondary treated STP effluents (sample data unknown) from Melbourne (South Eastern Purification Plant, Victoria) and Wagga Wagga (regional NSW) indicating triclosan concentrations of <100 ng/L [note these levels are below the effluent mean concentration of 142 ng/L from 19 STPs of Ying and Kookana (2007)]. No sampling or laboratory analytical report was provided to verify these results.

Australian manufacturing facility data

Manufacturing facilities using triclosan in products provide a potential source of triclosan-containing solid and liquid wastes. However, very limited wastewater

monitoring data were available from Australian manufacturing facilities using or blending triclosan into products.

International data

In considering the available studies, it should be noted that it is not possible to directly compare measured concentrations of triclosan in water between filtered and unfiltered samples. This is because unfiltered samples may contain triclosan bound to suspended solids, which can increase the measured concentration. Filtered samples are more likely to reflect the actual level of triclosan dissolved in the water column as triclosan bound to suspended material will be removed through filtration.

Canada

Hing-Biu et al. (2005) describe an optimised method for the extraction of phenols and acids in sewage samples using an anion exchanger with subsequent elution to fractionate the compounds. This method was applied to composite influent and effluent samples collected from May to July 2004 from STPs located in Burlington, Galt, Guelph, Mississauga, Toronto (3 plants) and Waterloo in southern Ontario. All samples were mixtures of residential and industrial wastewaters in various proportions. Prior to extraction, the samples were filtered through a 90 mm GF/C filter (1.2 µm retention) under slight vacuum. Triclosan was one of 21 phenols considered. Influent concentrations ranged from 0.87 to 1.83 µg/L with a median concentration in influent of 1.35 µg/L. Effluent concentrations ranged from 0.05 to 0.36 µg/L with a median effluent concentration of 0.14 µg/L. Overall removal ranged from 68% to 96% with a median removal efficiency of 88%.

Denmark

Paxeus (2004) identified triclosan in secondary treated effluent from the Avedores STP (domestic/industrial, 25 Mm³/annum) at a concentration of 90 ng/L. Treatment includes activated sludge and biological nutrient removal. The samples, collected in 2002-03, were filtered (1.2 µm glass-fibre) and analysed by GC/MS. Triclosan removal rate was 88% due to the treatment process. An influent triclosan concentration of 750 ng/L has been estimated for this STP based on effluent triclosan and removal efficiency.

In June-July 2002, samples of wastewater and effluent were collected from 2 STPs in Denmark (Renseanlaeg Lynetten, RL, Renseanlaeg Damhusaen, RD; Pedersen and Nielsen, 2003, reported in Danish Environmental Protection Agency, 2003b). Both STPs use activated sludge processes with nitrogen and phosphorus removal, and both serve the Copenhagen region. The data, reported in Table 16.17, indicate influent concentrations in the range of 1600-3000 ng/L (lower on weekends) and primary and secondary effluent concentrations of 1400-1800 and <1000 ng/L, respectively. The analytical methodology included GC/MS analysis after dichloromethane extraction.

Table 16.17 - Triclosan in influent and primary and secondary (activated sludge) effluent from two Danish STPs

STP	Equivalent population	Sample Date	Influent triclosan (ng/L)	Primary effluent (ng/L) (% removal)	Secondary effluent (ng/L) (% removal)
RL	750000	Week 26 (workdays)	2600	1800 ^a (31%)	<1000 (>62%) ^b
		Week 27 (workdays)	2400	1400 ^a (42%)	<1000 (>58%) ^b
		Week 26 (weekend)	1600	---	---
		Week 27 (weekend)	1800	---	---
RD	350000	Week 26	2700 ^a	---	---
		Week 27	3000 ^a	---	---

Source: Pedersen and Nielsen (2003, reported in Danish EPA, 2003b). a = analysis of composite (week) sample.

--- = not analysed. RD = Renseanlaeg Damhusaen STP. RL = Renseanlaeg Lynetten STP. b = Actual value not reported.

Eriksson et al. (2003) undertook an intensive study of triclosan in greywater from an urban block of flats in Copenhagen, Denmark in 2000. Here greywater is defined as wastewaters derived from sources other than toilets, bidets, or heavily polluted process waters (e.g. showers, hand basins). The study included an inventory of personal care products used by 30 of the 38 tenants (22 adults; 16 children). Daily greywater production averaged 750 L. Semi-quantitative analysis indicated triclosan in grey water samples (unfiltered) at a concentration of 600 ng/L, which was discharged to sewer.

France

Paxeus (2004) identified triclosan in STP effluents in the range of 170-430 ng/L (Table 16.18). The samples, which consisted of 24 h averaged flow-proportional samples collected in February-March 2001, were filtered (1.2 µm glass-fibre) and analysed by GC/MS. The triclosan removal rate was 55% at Chatillon-sur-Chalaronne STP due to the treatment process. An influent triclosan concentration of 378 ng/L has been estimated for this STP based on effluent triclosan and removal efficiency.

Germany

Quintana and Reemtsma (2004) investigated triclosan concentrations in 24 h composite samples of untreated wastewater and treated wastewater from a municipal activated sludge treatment plant and surface waters from Lake Tegal (situated within Berlin), which receives wastewater discharges. Samples (100 mL) were collected in May 2003. All samples were filtered (0.45 µm cellulose acetate filters) and stored frozen at -20°C. Samples were analysed by LC/ESI/MS (i.e. ion-pair liquid chromatography; IP-LC, with electrospray ionization; ESI, tandem mass spectrometry; MS, in the negative ion mode). A solid phase extraction (SPE) procedure was also used to further reduce detection limits.

Table 16.18 - Triclosan in secondary treated STP effluent, France

Location	Level of Treatment	Triclosan Concentration (ng/L)
Chatillon-sur-Chalaronne STP Domestic/industrial discharges 0.5 Mm ³ /annum.	AS	170
Pierre Benite STP Domestic/industrial discharges 48 Mm ³ /annum	AS	430

Source: Paxeus (2004). AS = Activated sludge (secondary).

The study developed an alternative method to the more commonly used methods of GC/MS, LC/MS and LC/MS-MS in order to obtain a similar or lower detection limit but with smaller sample volume. With SPE, the LOQs and detection limits for triclosan in wastewater, treated wastewater and surface water were 9.4, 11.2-24 and 11 ng/L, respectively, which were significantly higher than for all of the other pharmaceutical compounds also analysed. Recoveries (expressed as relative standard deviation - RSD%) for triclosan spiked at various concentrations in pure water (1 µg/L), pure water (0.05 µg/L), wastewater (5 µg/L) and treated wastewater (5 µg/L) were low (~43%-53%) indicating incomplete (~50%) ability to measure triclosan, and the authors attributed this to incomplete elution of the SPE cartridge. Triclosan was not detected in influent or effluent (~ <50 ng/L) or surface water samples (~ <22 ng/L) assuming incomplete recoveries as indicated above.

Bester (2003) reported a 5 day mass balance study of triclosan at a German STP (Dortmund; 200 000 m³ (200 ML)/day from ~350000 people; 50% domestic). The plant is fitted with primary settlement basins, activated sludge treatment basins, sludge separation basins, anaerobic sludge digesters and a clarifier. Samples (unfiltered) were collected between 8-12 April 2002 and were analysed by GC-MS. Inflow averaged 184 000 m³ (184 ML)/day. Overall inflow (untreated wastewater) concentrations (5 days) averaged 1200 ± 80 ng/L (range 1100-1300 ng/L) and outflow (treated wastewater) concentrations averaged 50 ± 7.7 ng/L (range 43-59 ng/L), indicating an overall triclosan removal efficiency of 95-96 ± 0.5% and an effluent breakthrough of 4-5 ± 0.4%. Sludge concentrations averaged 1200 ± 130 ng/g (~30%). Daily 5 day mass balance results are presented in Table 16.19.

Bester (2005) reports much higher concentrations in inflow to two further STPs in Germany. Both operated in the Rhine-Ruhr region discharging into the Rhine River. Both plants operate on a mixture of industrial and household wastewater and have inhabitant equivalents of around 1.1 million. Concentrations in the inflow of one of the STPs ranged near 7300 ng/L, with day to day variation of 1500 ng/L. This STP operated a two-stage biologic process and the overall removal rate in the plant was >95% with effluent having mean triclosan concentrations of 300 ng/L. The second plant had a one stage biologic process. Inflow concentrations ranged near 4800 ng/L with a daily variation of 550 ng/L. Concentrations after primary sedimentation were 3300 ± 950 ng/L. Removal was less efficient than the two stage biologic STP at around 87% and the final concentrations in effluent were reported as 620 ng/L (±1500 ng/L), with the variation attributed to daily variation.

Table 16.19 - Mass balance study of triclosan in a German activated sludge STP

Day	Inflow ng/L & (g)	Outflow ng/L & (g)	Sludge g & (%)	Balance (g)	Balance (%)
1	1300 (240)	59 (11)	69 (29%)	160	66
2	1200 (230)	58 (11)	49 (22%)	170	74
3	1100 (200)	43 (8)	67 (33%)	130	63
4	1200 (210)	50 (9)	91 (43%)	110	53
5	1100 (200)	43 (8)	47 (25%)	140	72
% of Influent	---	4.3%	30%	---	---
Mean (\pm SD)					
Conc (ng/L)	1200 \pm 80	51 \pm 7.7	---	---	---
Mass (g/d)	(216 \pm 18)	(9.4 \pm 1.5)	64.6 \pm 17.9	-142 \pm 24	-65.6 \pm 8

Source: Bester (2003). Samples of effluent were not filtered.

Bester (2003) estimated that methylation of triclosan accounted for 0.1%-1% of the triclosan concentration in wastewater inflow, with ~1.2-12 ng/L methyl-triclosan found in the secondary treated effluent. The author indicated that >50% of the triclosan inflow is transformed to unknown products, potentially dehalogenated products such as less chlorinated biphenyl ethers. However, experiments by Federle et al. (2002) suggest that the majority triclosan lost may be explained by mineralisation to CO₂.

Wind et al. (2004) investigated the concentration of triclosan in the treated effluent from the STP at Solingen-Ohligs, Germany (~86000 population, 13 gallons/year) in October 2000. One grab sample (unfiltered) was analysed for triclosan using GC/MSD, providing a value of 180 ng/L (refer Table 16.40).

Greece

Paxeus (2004) identified triclosan in STP effluents in the range of 130-190 ng/L (Table 16.20). The samples were filtered (1.2 μ m glass-fibre) and analysed by C/MS. Triclosan removal rate was 94% at Patras STP due to the treatment process. An influent triclosan concentration of 2167 ng/L has been estimated for this STP based on effluent triclosan and removal efficiency.

Table 16.20 - Triclosan in secondary treated STP effluent, Greece

Location	Level of Treatment	Triclosan Concentration (ng/L)
Iraklio STP Domestic discharges 7.3 Mm ³ /annum	AS	190 ^a
Patras STP Domestic discharge 5.1 Mm ³ /annum	AS	130 ^b

Source: Paxeus (2004). AS = Activated sludge. A. Grab samples collected Feb-Mar 2001. b. 24 h flow-proportional composite sample collected Sept-Mar 2002-3.

Italy

Paxeus (2004) identified triclosan in STP effluents in the range of 370-700 ng/L (Table 16.21). The samples were filtered (1.2 µm glass-fibre) and analysed by GC/MS. Triclosan removal rate was 73% at Naples STP due to the treatment process. An influent triclosan concentration of 1370 ng/L has been estimated for this STP based on effluent triclosan and removal efficiency.

Table 16.21 - Triclosan in secondary treated STP effluent, Italy

Location	Level of Treatment	Triclosan Concentration (ng/L)
Latina STP Domestic discharges 6.9 Mm ³ /annum	AS	580 ^a
Roma STP Domestic/industrial 73 Mm ³ /annum	AS	700 ^a
Naples STP Domestic discharges 69.5 Mm ³ /annum	AS	370 ^{a, b}

Source: Paxeus (2004). AS = Activated sludge. A. Grab samples collected Feb-Mar 2001. b. Grab samples collected Sept-Mar 2002-3.

Norway

Weigel et al. (2004) present the first research on the occurrence of triclosan in sewage in Norway. The study was conducted concurrently with a marine surface water sampling program (refer section 16.3.2 below). Triclosan was measured in sewage influent and effluent collected from various municipal sewerage systems at Tromso, Norway, that either involved no treatment processes and discharge directly to sea, or involved mechanical filtration (primary treatment; Table 16.22). In addition, samples were collected from Breivikia Hospital sewer, which is untreated and discharges into a public sewerage system. For comparison, samples of sewage effluent were also collected from the Hamburg (Germany) STP after primary clarification and secondary (biological) treatment processes. Samples were stored at 4°C for ≤24 h prior to filtration (1.2 µm GF/C - grade glass fibre). The filtrate was adjusted to pH 7 with H₂SO₄ and, following an extraction procedure, analysed by GC/MS (limit of quantitation of 0.24 ng/L). No sewage sludge samples were collected. The analytical results, presented in Table 16.22, show detection of triclosan in all sewage samples with concentrations in the Tromso sewerage system ranging from 160-480 ng/L, comparable to the samples collected in November 2002 from Hamburg (influent 380 ng/L and effluent 180 ng/L, this study) and from Sweden of ≤500 ng/L (Paxeus, 1996). Samples of influent and effluent were similar, reflecting the minimal effect of the primary treatment processes on triclosan attenuation. Sewage samples collected from hospital and public sewers showed triclosan concentrations up to 2380 ng/L.

Table 16.22 - Triclosan concentrations reported in untreated wastewater in Norway

Sample Location	Sample date	Concentration (ng/L)*
Tromsø STP Influent	18 April 2002	430
Tromsø STP Effluent	18 April 2002	480
“	23 April 2002	440
“	25 April 2002	160
“	8 October 2002	470
Breivika Hospital sewer	18 April 2002	690
Breivika mixed sewer	18 April 2002	2380
Asgard sewer	18 April 2002	1680

Source: Weigel et al. (2004). * Grab samples.

Spain

Mezcua et al. (2004) investigated triclosan in influent and effluent from the Almeria urban WWTP, Spain, between June 2002 and April 2003. The WWTP includes primary treatment for solids removal. The results, presented in Table 16.23, highlight the effect of treatment in reducing triclosan concentration, temporal variation of triclosan concentration between sampling events and variable removal rate. No clear relationship between removal rate and triclosan influent concentration could be ascertained from the data available. Samples were filtered (0.45 µm) and triclosan in solution was directly proportional to triclosan retained on the filter throughout the range of concentrations tested.

Table 16.23 - Concentration of triclosan in influent and effluent samples, Almeria WWTP, Spain

Month sampled	Influent (ng/L)	Primary Effluent (ng/L)	% Reduction
June 2002	173600	109500	37
July 2002	29900	6700	78
Aug 2002	3700	300	92
Oct 2002	4900	700	86
Nov 2002	9700	400	96
Jan 2003	562000	269000	52
Feb 2003	163000	40800	75
Mar 2003	6200	2800	55
Apr 2002	2300	100	96
<i>Range</i>	<i>2300-562000</i>	<i>100-269000</i>	<i>37-96</i>

Source: Mezcua et al. (2004). Samples were filtered (0.45 µm) prior to analysis.

Aguera et al. (2003) reported triclosan concentrations in primary effluent from two municipal STPs from Almeria, Spain, collected in 2002 (refer Table 16.24). In each STP, wastewater is subjected to primary treatment for solids removal. As an indication of STP operational capacity, about 85% of influent BOD is removed

during the process. Samples (filtered) were collected for analysis from the influent to aerobic digestion and of the treated effluent, which is discharged to the Mediterranean Sea. For comparison, samples were analysed by liquid chromatography (LC-ESI/MS/MS) and GC/MS after solid phase extraction by three methods (Isolute, Oasis, C₁₈) and pressurised liquid extraction (PLE). Analytical recovery was highest for C₁₈ cartridge (84%). The triclosan removal rate (influent to effluent) was in the range of 35%-69%, and the lower rate of removal with high influent concentrations may be due to microbial inhibition although a range of other factors may have also led to this result.

Table 16.24 - Variation in triclosan concentration in a municipal STP influent and primary effluent, Almeria, Spain

Month sampled	Influent (ng/L)	Primary Effluent (ng/L)	% Reduction
April 2002	1300	400	69
May 2002	2600	800	69
June 2002	37800	22100	42
July 2002	30100	19600	35

Source: Aguera et al. (2003).

Sweden

Palmquist and Hanaeus (2005) investigated triclosan in Swedish greywater (household water without any input from toilets) and blackwater (toilets) in 2001. Greywater (66.4 L/person/day) samples (unfiltered) were collected from 47 households (Vibyasen North, population 169; 112 adults and 57 children). Blackwater (28.5 L/person/day) was collected in samples (unfiltered) from a nearby housing area (Vibyasen South, population 141 people, 92 adults, 49 children). Grab samples (3 collected hourly) were composited and analysed by GC/MS (detection limit 0.500 µg/L). Triclosan was detected in greywater and blackwater at concentrations of 560-5900 ng/L and <500-3600 ng/L, respectively.

Paxeus (2004) identified triclosan in STP effluents in the range of 130-160 ng/L (Table 16.25). The samples were filtered (1.2 µm glass-fibre) and analysed by GC/MS. Triclosan removal rates were 58% at Kallby STP and 73%-91% at Ryaverket STP to the treatment process. Influent triclosan concentrations of 381 ng/L and 481-1444 ng/L, respectively, have been estimated for these STPs based on effluent triclosan and removal efficiency.

Treated effluents (flow proportional daily composite samples) from the three largest municipal STPs in Sweden (Hendriksdal STP, Stockholm; Goteborg STP; Sjolunda STP) were sampled in December 1993 and analysed for the presence of triclosan (Paxeus, 1996). Water treatment included mechanical treatment (primary settling) and biological activated sludge (aeration and settling) processes. Samples were filtered (0.5 µm glass fibre) prior to analysis. Estimated triclosan concentrations ranged up to 0.5 µg/L. As only one sample was analysed per STP and due to the high analytical limit of detection (i.e. µg/L range), little useful information can be extracted from this study.

Table 16.25 - Triclosan in secondary treated STP effluent, Sweden

Location	Level of Treatment	Triclosan Concentration (ng/L)
Ryaverket STP Domestic, industrial, hospital discharges, 120 Mm ³ /annum	AS/T	130 ^a
Kallby STP Domestic/hospital 12 Mm ³ /annum	AS	160 ^b

Source: Paxeus (2004). AS = Activated sludge. T = biological nutrient removal. A. Flow-proportional samples collected between Feb 2001 and March 2003. b. 24 h flow-proportional sample collected Sept-Mar 2002-3.

Paxeus (unpublished, reported in Danish Environmental Protection Agency, 2003b) investigated the concentrations of triclosan in six Swedish STPs in 1995. Each STP used a biological treatment process. Samples consisted of 1-month composite samples, consisting of combined daily random samples or daily flow-proportional samples. The data, reported in Table 16.26, indicate influent and effluent concentrations in the ranges of 100-1500 and not detected-200 ng/L, respectively, and removal efficiencies in the range of 0-100%. The study report was not available for this assessment and the quality of the data cannot be verified.

Table 16.26 - Triclosan in Swedish STP influent and secondary treated effluent

STP	Size	Wastewater Sources	Biological Process	Influent triclosan (ng/L)	Effluent (ng/L)	% Removal
Olmanas	Small	Domestic wastewater	AS	100	100	0
Donso	“	“	AS	200	100	50
Lerum	Medium	Domestic wastewater, small industries, workshops, hospitals	AS	300	200	33
Skansverket (Uddevalla)	“	“	AS	400	ND	100
Goteborg (GRYAAB)	Large	Domestic wastewater, industries, car washing facilities	SBR (~AS)	200	100	50
Hendriksdal (Stockholm)	Large	“	AS	1500	ND	100

Source: Paxeus (unpublished, reported in Danish EPA, 2003b). AS = activated sludge. SBR = Sequencing batch reactor. ND = not detected (detection limit not stated).

Switzerland

In seven samples from five Swiss municipal STPs (Maur, Pfaffikon, Uster, Wetzikon, Gossau, 3 samples) collected 1997-2001, triclosan was consistently detected in primary effluent (concentration range 500-1300 ng/L). Methyl-triclosan, probably formed due to microbial methylation, was detected at concentrations of ≤ 4 ng/L in primary effluent. Concentrations of triclosan in secondary effluents from these STPs were in the range of 70-650 ng/L (Table 16.27). This represents a reduction in triclosan concentration between primary and secondary treatments of 34%-92%. No details on the type of treatment at these plants were provided; however, they are described as modern 3- or 4-stage mechanical/biological/chemical plants. The concentrations of methyl-triclosan (up to 11 ng/L) were similar or increased (by a 4.4-fold increase in one municipal STP) during secondary treatment (Poiger et al., 2003; Lindstrom et al., 2002). The unaccounted remainder of the triclosan was probably either biodegraded (mineralised to CO₂) or partitioned to sludge.

Singer et al. (2002) analysed 72 hour composite samples of effluent from seven Swiss municipal STPs (Uster, Wetzikon, Egg, Gossau, Hinwil, Maur, Moenchaltorf), collected in June 1999. Treatment processes at each STP consisted of mechanical clarification, biological treatment (nitrification), and flocculation filtration. The effluent was not disinfected by chlorination. At two of the STPs, biological treatment was supplemented with an anoxic zone for denitrification. In failure-free operation, all of these STPs remove at least 85% of influent COD and at least 95% of the influent BOD. The final filtration stage leads to suspended solids concentration of ~ 10 mg/L, as indicated by analysis of effluent samples. Triclosan concentrations in treated effluents from the seven municipal STPs ranged from 42-213 ng/L and the corresponding triclosan loads were 0.2-3.2 g/day (30-210 mg triclosan/1000 inhabitants per day assuming households were the only source of triclosan).

Table 16.27 - Triclosan (TCS) and methyl-triclosan (MTCS) in Swiss municipal STP influent and effluent

STP	Population $\times 1000$	Date	Flow (Mega L/d)	Primary effluent (ng/L) ^a		Secondary Effluent (ng/L)	
				TCS	MTCS	TCS & (% loss) ^c	MTCS
Maur	4.5	Mar 2001	2.94	980	<1	650 (34)	<2
Pfaffikon	9.2	Feb 2001	3.2	1044	4	250 (76)	4
Uster	36	Feb 2001	14.25	1300	2.5	110 (92)	11
Wetzikon	19	Mar 2001	15	584	<1	183 (69)	<2
Gossau	11	Jan 2001	3.45	970	<1	136 (86)	3.5
Gossau	10.5	Oct 1997	3.2	1000	(b)	100 (90)	b
Gossau	10.5	Dec 1997	3.9	500	(b)	70 (86)	b

Source: Poiger et al. (2003) and Lindstrom et al. (2002). a. Influent to the biological stage (effluent following primary sedimentation). b. All samples were methylated, precluding differentiation between triclosan and methyl-triclosan. c. Percent reduction in triclosan concentration between primary effluent concentration and secondary effluent concentration. Wastewater samples were centrifuged prior to extraction and analysis. Influent concentration of triclosan was not reported.

For detailed flux mass balance modelling, additional samples were collected by Singer et al. (2002) from the outlet of the Gossau municipal STP (primary and secondary) sedimentation in June 1999. This plant consists of mechanical treatment, activated sludge treatment with a preceding denitrification step, and phosphate precipitation with filtration of the effluent. A grab sample from the activated sludge tank indicated triclosan concentrations of 580 ng/g (dry matter) adsorbed (c_s) and 35 ng/L dissolved (c_w), respectively. A value for K_{OC} of 4.7×10^4 L/kg was derived using the equation: $c_s = K_{OC} \times c_w \times f_{OC} (1 + 10^{(pH-pK_a)})^{-1}$, and considering an organic carbon fraction (f_{OC}) of the sludge particles of 0.4 and a measured pH of 7.3. The average dissolved concentration of triclosan in the weekly flow-proportional composite samples ranged from 520 ng/L in the primary clarified effluent to 45 ng/L in the secondary effluent. Over the 7 day survey, 79% of the triclosan was biologically degraded and 15% was removed with the excess sludge. About 6% of the triclosan entering the plant left in the final effluent after the filtration stage, with effluent containing an average of 42 ng/L.

The Netherlands

Triclosan has been detected in filtered samples (0.45 μ m glass fibre) from a municipal STP effluent from the Netherlands; however, the concentration was not quantified (van Stee et al., 1999).

United Kingdom

Wastewater influent, primary effluent and final effluent concentrations of triclosan were analysed from two municipal STPs in the United Kingdom; Slough (Berkshire; population ~126 000) and Chertsey (Surrey; population ~62000), by Ciba Specialty Chemicals (1999). Slough and Chertsey have activated sludge and trickling filter secondary treatment processes, respectively. Analyses were performed using an internal laboratory method (B18 solid phase extraction, derivitisation, isotope dilution, HRGC/HRMS). Quantitation was achieved using spiked ^{13}C -triclosan as internal standard, which was spiked into samples. Recoveries on the spiked sample (~43%-86%) were within the normal range. The data (Table 16.28) indicate low removal of triclosan after primary treatment (~2%-51%) but higher overall removal (~91%-94%) in the secondary treated activated sludge (AS) and trickling filter (TF) effluents. The data highlight the inability of the STPs to remove all of the triclosan from the wastewater prior to discharge of effluent to the receiving environment, with effluent concentrations containing 470-1100 ng/L. No data were available for methyl-triclosan or chlorinated derivatives of triclosan from this study.

Concentrations of triclosan in influent, primary-treated wastewater and secondary effluent from municipal STPs in the River Aire Basin, Yorkshire UK, were reported by Sabaliunas et al. (2003). Crofton STP (activated sludge) serves ~9000 people and the wastewater flow was 1.385 ML/day (~156 L/capita/day). Meltham STP (trickling filter) serves ~7900 people and has an average flow of 4.14 ML/day (524 L/capita/day). Meltham STP operates two consecutive series of trickling filters and may be considered an advanced secondary treatment plant. In both plants, >98% of the wastewater is derived from domestic sources. Samples (hourly time-proportional composites) of influent, primary effluent and final effluent were collected over a 24-hour period in September 2000. Wastewater samples were analysed by GC/MSD in a single ion monitoring (SIM) mode. Sampling results from Sabaliunas et al. (2003; Table 16.29) show low triclosan removal rates after

primary treatment (21%-39%), but higher removal (~95% of influent) in final effluents after secondary treatment. Although both plants achieved ~95% reduction of triclosan, the results demonstrate the inability of both types of commonly used secondary treatment processes to remove all of the triclosan in the influent, with final effluent triclosan concentrations of 340 ng/L (TF) and 1100 ng/L (AS). There was high variability (3 times) in influent triclosan concentrations between the two STPs. No data were available for methyl-triclosan or chlorinated derivatives.

Table 16.28 - Triclosan in some municipal STP influent and effluent in the UK

Solution	Slough STP (AS)		Chertsey STP (TF)		
	Triclosan (ng/L)	% Reduction	Triclosan (ng/L)	% Reduction	
Influent	7510	---	11980	---	
Primary Effluent	7350	2.1	5080	57.6	
Secondary Effluent	470	93.6 ^(a)	1100	78.3 ^(a)	90.8 ^(b)

Source: Ciba Specialty Chemicals (1999). a. Final effluent triclosan as a percentage of primary effluent triclosan. b. Final effluent triclosan as a percentage of influent triclosan.

Table 16.29 - Triclosan in municipal STP influent, primary and secondary treated effluent, River Aire Basin UK

Sewage Treatment Plant	Effluent triclosan (ng/L)	% Reduction	
Meltham (TF) STP			
Influent	7500	0	
Primary effluent	5900	21.3	
Secondary effluent	340	94.2 ^(a)	95.5 ^(b)
Crofton (AS) STP			
Influent	21900	0	
Primary effluent	13350	39	
Secondary effluent	1100	91.7 ^(a)	95 ^(b)

Source: Sabaliunas et al. (2003). a. Final effluent triclosan conc. As a percentage of primary effluent triclosan. b. Final effluent triclosan conc. As a percentage of influent triclosan (total removal).

The occurrence of triclosan in influent and effluent from six STPs in the United Kingdom was investigated in late autumn and early winter of 2001 by Kanda et al. (2003). The STPs were not named in the article. Samples (unfiltered) were collected as time-weighted composites, and analyses were performed using GC-MS following extraction. Analytical quality assurance confirmed the acceptability of the data. The limit of detection was 17 ng/L. Kanda et al. (2003) detected triclosan in all of the municipal wastewaters sampled. The sampling data indicated triclosan concentrations up to 3100 ng/L in influent from a domestic catchment. Triclosan removal efficiency varied from 0-100%; however, removal efficiencies for individual treatment processes could not be determined as analytical data were not fully reported.

United States

Thomas and Foster (2005) monitored influent, and primary, secondary and final effluent triclosan concentrations at three STPs in the United States in January 2004. Final treatment after secondary treatment included phosphorus removal, gravity filtration and disinfection (Cl, UV). Samples consisted of: 24 h flow- and time-integrated composite samples (STP1) or grab samples (STP2 and 3). Samples were filtered (8 & 1 µm, glass fibre) prior to analysis by GC/MS after solid phase extraction. The results, presented in Table 16.30, indicate percent reduction of triclosan for primary and secondary levels of treatment of 10%-45% and 97%-98%, respectively, with final effluent containing 1%-2% of initial triclosan. Influent and effluent concentrations ranged from 3000-3600 ng/L and 28-72 ng/L, respectively (Thomas and Foster, 2005).

Morrall et al. (2004) analysed grab samples (unfiltered) of treated effluent from the Cibolo municipal STP, South Central Texas (~9.5 ML/day flow) in Spring 1999, finding a concentration of 785 ng/L. Triclosan was determined by GC-MS (detection limit 10 ng/L).

Table 16.30 - Triclosan (TCS) in influent and effluent from three STPs, USA

Solution	STP 1			STP 2			STP 3		
	TCS (ng/L)	% Reduction		TCS (ng/L)	% Reduction		TCS (ng/L)	% Reduction	
Influent	3000	A	B	3300	A	B	3600	A	B
Primary	2700	10	---	1800	45	---	3000	17	---
Secondary	82	97	97	54	97	98	65	98	98
Effluent	72	12	98	47	13	99	28	57	99

Source: Thomas and Foster (2005). Activated sludge biological nutrient removal process. STP 1: Arlington County Water Pollution Control Plant (38.9 ML/d). STP 2: City of Alexandria Sanitation Authority (13.8 ML/d). STP 3: Norman M Cole Water Pollution Control Plant (15.9 ML/d). A = Reduction as a percentage of previous level of treatment. B = Reduction as a percentage of initial influent concentration.

Boyd et al. (2003) reported triclosan concentrations in treated effluent from the Jefferson Parish East Bank Municipal STP, Louisiana, collected February-March 2002. The STP, which discharges treated effluent into the Mississippi River, uses conventional secondary treatment, and treated effluent samples were collected prior to the chlorination process. The triclosan concentration in treated effluent samples (filtered 1.0 & 0.2 µm glass fibre) ranged between 10-21 ng/L.

Arnott (2003) reported triclosan concentrations in STP effluent samples (filtered) from four municipal STPs (Charlottesville, Lexington, Lynchburg, Roanoke) collected November 2001 and July 2002, USA (Table 16.31). Detail on the level of treatment of wastewater at these plants was not reported. Samples were analysed by HPLC after C₁₈ solid phase extraction and methanol:water elution. Arnott (2003) also referred to other studies that indicated municipal STP average influent and effluent triclosan concentrations of 4700-10350 ng/L and 1410-1500 ng/L, respectively (all study reports not available for review).

Table 16.31 - Triclosan in effluent from four municipal STPs, USA

STP	Sample date and mean triclosan conc. (ng/L)	
	Effluent (Nov, 2001)	Effluent (July 2002)
Charlottesville	3800	1000
Lexington	8100	NS
Lynchburg	15500	2200
Roanoke	2200	1300

Sources: Arnott (2003) and Reither (2003). NS = Not sampled. Samples were filtered prior to analysis.

Activated sludge treatment represents the largest portion of treated wastewater flow in the US (~75% of flow). Trickling filter represents a small (~5%) and variable treatment process. McAvoy et al. (2002) investigated triclosan removal and formation of several chlorinated derivatives from wastewater at several municipal STPs in Ohio USA, including activated sludge treatment plants (two; Columbus, Loveland) and two trickling filter plants (two; Glendale, West Union). All plants studied received mainly domestic wastewater. Samples were collected in 1996, with the Western Union site being sampled twice. Samples were not filtered prior to analysis. The results indicate overall reductions in triclosan concentrations of 58%-96.2% between raw influent and final treated effluent (Table 16.32). Activated sludge removal was relatively high and consistent (95.4%-96.2%). These results are in close agreement with laboratory-based data from a continuous activated sludge process (Federle et al., 2002). The results for trickling filter treatment were lower and more variable with removal ranging between 58%-86.1%. Influent concentrations varied from 3800-16600 ng/L, based on variations in per capita water usage. Triclosan concentrations in primary treated effluent ranged from 3380-8000 ng/L, whereas final effluent values were 240-410 ng/L (activated sludge) and 1610-2700 ng/L (trickling filter), highlighting the relatively greater removal by the activated sludge process. Removal by primary treatment varied from 7%-48%. Samples from West Union showed that the sand-filter tertiary treatment process removed a negligible amount of triclosan from the wastewater compared to primary and secondary treatment.

As indicated in Table 16.32, chlorinated derivatives were sometimes present but not always quantifiable due to the low concentrations present. At the time of the study, the Columbus municipal STP was the only STP disinfecting effluent by chlorination, with no apparent effect on chlorinated derivative generation. The quantifiable samples were generally <300 ng/L. As little or no change in concentration was detected throughout the treatment processes, the treatment process is unlikely to have increased the formation of chlorinated derivatives. Methyl-triclosan was only qualitatively detected in influent samples, and no formation was evident during the treatment process.

Jungclaus et al. (1978) reported triclosan concentrations in wastewaters from a specialty chemicals manufacturing facility, USA. The facility, located adjacent to the Pawtuxet River (Rhode Island), was not named in the study. Four wastewater samples (grabs; unfiltered) were collected from an on-site WWTP from flow after a clarification process during 1975-76. Samples were analysed by GC/MS. Triclosan concentrations in treated effluent ranged from 6000-14000 µg/L. Later, Lopez-

Avila and Hites (1980) sampled the same effluent and found triclosan at a concentration of 4000 µg/L.

Table 16.32 - Triclosan (TCS), methyl-triclosan (MTCS) and chlorinated derivatives in influent and secondary effluent (ng/L) from four municipal STPs, USA

Site/sample	TCS (ng/L) & (% Reduction)	MTCS	II	III	IV
Columbus (AS)					
Raw influent	5210	NQ	(10)	(20)	(20)
Primary effluent	3380 (35%) ^a	NQ	ND	(<10)	(<20)
Secondary effluent	240 (95%) ^b	NQ	ND	ND	ND
Loveland (AS)					
Raw influent	10700	NQ	(30)	80	50
Primary effluent	7000 (35%)	NQ	40	80	50
Secondary effluent	410 (96%)	NQ	ND	(30)	ND
Glendale (TF)					
Raw influent	3830	NQ	ND	ND	(10)
Primary effluent	3560 (7%)	ND	ND	ND	ND
Secondary effluent	1610 (58%)	ND	ND	ND	ND
West Union A (TF)					
Raw influent	16600	NQ	270	150	310
Secondary effluent	2300 (86%)	NQ	(40)	(20)	(60)
Tertiary effluent	2100 (87%)	NQ	(10)	(10)	(10)
West Union B (TF)					
Raw influent	15400	NQ	620	250	190
Primary effluent	8000 (48%)	NQ	340	160	160
Secondary effluent	2700 (83%)	NQ	290	70	70

Source: McAvoy et al. (2002). NQ: not quantifiable (signal/noise <10). Limit of quantitation = 100 ng/L. Methyl-triclosan was qualitatively detected in all liquid samples but the method was not validated for quantification below 100 ng/L. Recovery of methyl-triclosan was acceptable (50%-70%). The concentration of methyl-triclosan was estimated at 2-50 ng/L. ND: Not detected. The detection limit was 10 ng/L. Compounds: II: 2',3,4,4'-tetrachloro-2-hydroxydiphenyl ether; III: 2',4,4',5-tetrachloro-2-hydroxydiphenyl ether; IV: 2',3,4,4',5-pentachloro-2-hydroxydiphenyl ether; Refer to Figure 16.1 for chemical structures. a = Percent removal by primary treatment. b = Percent removal after primary and secondary treatment.

Summary of untreated and treated wastewater concentrations

Triclosan

The international occurrence of triclosan in urban wastewaters is evident through numerous monitoring studies undertaken of grey water, black water, industrial and municipal wastewaters (refer Table 16.33). In addition, monitoring data from several studies undertaken in 2000-01 indicate triclosan concentrations in greywater and blackwater from residential premises in Sweden and Denmark in the range of 560-5900 ng/L and <500-3600 ng/L, respectively (Palmquist 2003; Eriksson et al., 2003). Furthermore, the widespread occurrence of triclosan in treated municipal STP effluents is confirmed, with no evidence of any municipal

STP or on-site WWTP capable of complete removal of triclosan from the aqueous or solid phases prior to discharge to the environment.

Table 16.33 presents a collation of available information of the reported occurrence of triclosan in municipal STP influent, primary and secondary or higher treated effluents. As the data in Table 16.33 are derived from a range of studies of STPs incorporating different processes and conditions, the data are not directly comparable but are provided as a general indication only of triclosan concentrations.

As noted previously, it is not possible to directly compare measured concentrations of triclosan in water between filtered and unfiltered samples. This is because unfiltered samples may contain triclosan bound to suspended solids, which can increase the measured concentration. Filtered samples are more likely to reflect the actual level of triclosan dissolved in the water column as triclosan bound to suspended material will be removed through filtration.

The available Australian data indicates that triclosan is present in influent and treated effluent at levels which are within the range of overseas data but at the lower end of the observed range (see table 16.33).

In summary, the recorded concentrations of triclosan in influent, primary effluent, and secondary or higher treated effluent triclosan range from 100-562000 ng/L, <100-269000 ng/L and 10-2700 ng/L, respectively.

Table 16.33 - Occurrence of triclosan in untreated wastewater and treated effluent

Country, No. of STPs sampled & (year sampled)	Influent (ng/L)	Primary Effluent (ng/L)	Secondary or Higher Treated Effluent (ng/L)	Reference
<u>Australia</u>				
19 Effluents (2004)	---	23-434 (level of treatment unclear but likely to be secondary or higher)		Ying and Kookana (2007)
5 STPs (2005)	573- 845		60.5-159	Ying and Kookana (2007)
5 STPs (1995-6)	---	<100-740	---	Ciba Specialty Chemicals (2003a)
<u>Canada</u>				
8 STPs (2004)	0.87-0.83	0.05-0.36 (level of treatment unclear)		Hing-Biu et al. (2005)
<u>Denmark</u>				
1 STPs (2002-3)	750 ^c	---	90 (AS)	Paxeus (2004)
2 STPs (2002)	1600-3000	1400-1800	<1000 (AS)	Pedersen and Nielsen (2003; reported in Danish EPA, 2003b)
<u>France</u>				
2 STPs (2001)	378 ^c	---	170-430 (AS)	Paxeus (2004)

Country, No. of STPs sampled & (year sampled)	Influent (ng/L)	Primary Effluent (ng/L)	Secondary or Higher Treated Effluent (ng/L)	Reference
<u>Germany</u>				
1 STP (2003)	ND (<9.4) ^a	---	ND (<24) ^a	Quintana and Reemtsma (2004)
1 STP (2002)	1100-1300 (1200±80)	---	43-59 Mean 50±7.7	Bester (2003)
1 STP (2004)	7300 (±1500)	---	300 (±100)	Bester (2005)
1 STP (2004)	4800 (±550)	---	260 (±1500)	Bester (2005)
1 STP (2000)	---	180	---	Wind et al. (2004)
1 STP (2002)	380	---	180	Weigel et al. (2004)
<u>Greece</u>				
2 STPs (2002-3)	2167 ^c	---	130-190 (AS)	Paxeus (2004)
<u>Italy</u>				
3 STPs (2002-3)	1370 ^c	---	370-700 (AS)	Paxeus (2004)
<u>Norway</u>				
3 STPs & hospital (2002).	430-2380	160-480	---	Weigel et al. (2004)
<u>Spain</u>				
1 STP (2002-3)	2300-562000	100-269000	---	Mezcua et al. (2004)
2 STP (2002)	1300-37800	400-22100	---	Aguera et al. (2003)
<u>Sweden</u>				
3 STPs (1993)	---	---	≤500	Paxeus (1996)
6 STPs (1995)	100-1500	---	≤200	Paxeus (cited in Danish EPA, 2003b) ^b
2 STPs (2001-3)	381-1444 ^c	---	130-160 (AS)	Paxeus (2004)
<u>Switzerland</u>				
5 STPs (1997-2001)	---	500-1300	70-650	Poiger et al. (2003); Lindstrom et al. (2002)
7 STPs (1999)	---	520	42-213	Singer et al. (2002)
<u>United Kingdom</u>				
6 STPs (2001)	≤3100	---	---	Kanda et al. (2003)

Country, No. of STPs sampled & (year sampled)	Influent (ng/L)	Primary Effluent (ng/L)	Secondary or Higher Treated Effluent (ng/L)	Reference
2 STPs (2000)	7500-21900	5900-13350	340 (TF) 1100 (AS)	Sabaliunas et al. (2003)
2 STP (1999)	7510-11980	5080-7350	470 (AS) 1100 (TF)	Ciba Specialty Chemicals (1999)
<u>United States</u>				
3 STPs (2004)	3000-3600	1800-3000	54-82 (AS) 28-72 (final)	Thomas and Foster (2005)
1 STP (2002)	---	---	10-21	Boyd et al. (2003)
5 STPs (2001-2)	---	---	1000-15500	Arnott (2003)
	4700-10350	---	1410-1500	Cited in Arnott (2003) ^b
1 STP (1999)	---	---	785 (TF)	Morrall et al. (2004)
4 STPs (1996)	3830-16600	3380-8000	240-410 (AS) 1610-2700 (TF)	McAvoy et al. (2002)
<i>Range</i>	<i>100-562000</i>	<i><100-269000</i>	<i>10-2700</i>	

--- = No data available. AS = activated sludge. TF = trickling filter. Values are presented as concentrations ranges and mean \pm SD. ND = not detected. ^a = matrix spike recoveries in these samples were low (~50%) and actual concentrations in these media are likely to have been higher. ^b = Test report not available for review. ^c = Influent concentration estimated from reported effluent concentration and removal efficiency.

Reported triclosan removal rates for various treatment processes are presented in Table 16.34. Although the removal efficiency of triclosan from wastewaters by municipal STPs varies according to treatment type and operating regime, triclosan is mostly removed from wastewater by aerobic biological treatment processes as indicated by biodegradation studies and field monitoring of wastewater triclosan throughout the STP process. Secondary treatment removes a much greater proportion of wastewater triclosan than primary treatment. The data available indicates that some conventional tertiary treatment processes (e.g. sand filtration) provide only a minor removal process compared to secondary biological treatment processes. However, monitoring data are very limited for other tertiary treatment processes, and advanced treatment techniques such as reverse osmosis would be likely to have a greater effect on removing triclosan from the aqueous phase. In general, the monitoring data available indicates that activated sludge (secondary) treatment (or equivalent) enables greater removal of triclosan than trickling filter (secondary) treatment.

Triclosan degradation products

Reported concentration ranges of several chlorinated derivatives of triclosan in STP influent and effluent are presented in Table 16.35.

Methyl-triclosan

Methyl-triclosan in primary treated effluent has been detected in the concentration range of ≤ 4 ng/L. Marginally higher concentrations of methyl-triclosan, up to 4.4-fold increase at one STP (12 ng/L), were evident in secondary treated effluent. Methyl-triclosan's occurrence is probably due to microbial methylation of triclosan during biological treatment processes.

Table 16.34 - Extent of removal of triclosan from wastewater for various levels of treatment

Influent to Primary (%)	Primary to secondary (%)	Influent to secondary (%)	Reference
7-41%	41	72-93% ^a	Ying and Kookana (2007)
---	34-92 ^b	---	Poiger et al. (2003)
---	---	0-100 (AS/SBR) ^c	Paxeus (cited in Danish EPA, 2003b)
---	---	55-94 (AS)	Paxeus (2004)
10-45	97-98 (AS)	97-98 (AS)	Thomas and Foster (2005)
---	---	96 (AS)	Bester (2003)
37-96	---	---	Mezcua et al. (2004)
35-69	---	---	Aguera et al. (2003)
31-42	---	>58 (AS) ^a	Pedersen and Nielsen (cited in Danish EPA, 2003b)
35	---	95-96 (AS)	McAvoy et al. (2002)
2	---	94 (AS)	Ciba Specialty Chemicals (1999)
39	---	95 (AS)	Sabaliunas et al. (2003)
---	---	94-97 (CAS)	Federle et al. (2002)
---	---	98-99 (CAS)	Roy F. Weston (1998)
7-48	---	58-86 (TF)	McAvoy et al. (2002)
58	---	91 (TF)	Ciba Specialty Chemicals (1999)
21	---	96 (TF)	Sabaliunas et al. (2003)
<i>Range</i>			
2-96%	34-98%	58-96% (TF) 55-99% (AS)	

--- = No data available. AS = activated sludge treatment. TF = trickling filter. SBR = Sequencing Batch Reactor. CAS = Continuous activated sludge (laboratory-scale study). a = 3 (of 5) were tertiary treatment plants, including the lowest of the range. b = type of secondary treatment not described. c = Accurate removal rate not defined, test report not available for review and data quality not verifiable.

Photolytic products

No data were available for the potential products of photolysis including 2,4-DCP or 4-chlorocatechol; however, photolysis is unlikely to occur in the sewer or during STP treatment, with the potential exception of STP effluents that are disinfected by ultraviolet irradiation. In one study (Mezcua et al., 2004), 2,7/2,8-DCDD concentrations in influent and primary effluent ranged from 0.02-3.7 µg/L and 4-400 ng/L, respectively. In this study, triclosan influent and effluent concentrations ranged from 2300-562000 and 100-269000 ng/L, respectively, with 2,7/2,8-DCDD representing ≤31% and ≤7% of the influent and effluent triclosan concentrations, respectively.

Chlorinated derivatives

Several chlorinated derivatives of triclosan may potentially arise in wastewater due to the reaction of triclosan-containing products with residual chlorine in wastewater, chlorinated reticulated water supply, or due to reaction with chlorine used to disinfect treated effluent. Several chlorinated derivatives of triclosan have been identified in wastewaters.

Table 16.35 - Chlorinated derivatives of triclosan in STP influent and effluent

Chlorinated compound	Untreated (raw) effluent (ng/L)	Primary effluent (ng/L)	Secondary effluent (ng/L)	Tertiary (AS)/Final effluent (ng/L)
II	≤620	≤340	≤290	≤10
III	≤250	≤160	≤70	≤10
IV	≤310	≤160	≤70	≤10

Chlorinated compound: II: 2',3,4,4'-tetrachloro-2-hydroxydiphenyl ether; III: 2',4,4',5-tetrachloro-2-hydroxydiphenyl ether; IV: 2',3,4,4',5-pentachloro-2-hydroxydiphenyl ether. Refer to Figure 16.1 for chemical structures.

McAvoy et al. (2002) reported no net increase in the formation of chlorinated derivatives due to STP processes, and the data available would indicate a general decline in concentration with level of treatment.

16.3.2 Sewage sludge and biosolids

Australian data

Limited data is available for the levels of triclosan in Australian biosolids. The level of triclosan in biosolids has been reported in three studies (Luke et al., 1996; Luke, 1999; Ying and Kookana 2007). A survey of biosolid contaminants from a sewage treatment plant in Victoria detected a polychlorinated biphenyl in all samples from a large biosolids pile (Luke et al., 1996). The compound was identified as triclosan using GC/MS. The levels of triclosan in the biosolids and soils treated some years earlier with these biosolids was in the mg/kg range. A follow up study reported triclosan in samples of biosolids from two sewage treatment plants (Luke, 1999). Triclosan was measured at 50 and 3400 ng/g in the two samples. No details of the origin of the samples were reported. In the most recent study, Ying and Kookana (2007) reported the concentration of triclosan in biosolids from 17 Australian STPs. The concentrations in the biosolids ranged from 90 to 16790 ng/g on dry weight basis with a mean concentration of 5580 ng/g and a

median concentration of 2320 ng/g. All biosolid samples were anaerobically digested sludges except for one sample that was aerobically digested. The triclosan concentration in this aerobically digested sample was 220 ng/g.

International data

No data were available on triclosan or products in biosolids. Following is a summary of data on triclosan in biosolids (otherwise known as sewage sludges).

Canada

In Canada, most STPs employ primary and secondary treatment processes. A survey of 35 STP sludges from throughout Canada collected between 1994 and 2000 identified triclosan in all samples. The median triclosan concentrations (dry wt.) in raw (primary) and digested sludges (1999-2001 samples) were 11600 ng/g (range 3400-17900) and 19200 ng/g (range 5400-28200), respectively. Only 3 of 35 samples contained <5000 ng/g, and 7 of 8 pairs of raw and digested sludge samples collected at the same time from the same STPs had higher triclosan concentrations (increases of 8%-65%) in the digested sludge (Lee and Peart, 2002).

Data from Lee and Peart (2002) indicate triclosan concentration in raw (1998-2001) and digested (1994-2001) sludges in Canada have generally increased in recent years by ~4 and ~2 times, respectively. However, the wide concentration ranges reported among STPs reflect variability in sampling, local use pattern, treatment processes or other factors.

Germany

Bester (2003) reported a five day average triclosan concentration in sludge analysed from a German STP of 1200 ± 130 ng/g (\pm SD). The STP consisted of primary settlement basins, activated sludge treatment basins, sludge separation basins, anaerobic sludge digesters and a clarifier before effluent was discharged to a river. The sludge sampled was collected from trucks loaded with 'sludge' for off-site disposal; and it is likely to consist of anaerobically-digested sludge. The samples contained ~60% moisture content when collected and data are apparently reported on a wet weight basis (i.e. dry weight values would be higher).

Data from a further 20 German STPs (North Rhine-Westphalia) of various designs and operating capabilities indicated sludge triclosan concentrations in the range of 400-8800 ng/g (Bester, 2003); however, it is not known whether these data are reported on a wet or dry weight. The lowest concentration was from a rural STP, whereas the highest concentration was reported from an urban STP.

Sweden

In 2001-02, Svensson (2002) investigated the triclosan concentrations in sludge from 19 Swedish STPs of various size and operation (refer Table 16.36). Only one sample was collected from each sludge type. As indicated in Table 16.36, triclosan concentrations ranged from 28-6400 ng/g (dry wt; average 1239 ± 1832 ng/g; \pm SD), with the lowest concentration reported from an activated sludge treatment plant with chemical precipitation. Concentrations in sludge from activated sludge processes ranged from 200-3700 ng/g. The highest sludge triclosan concentration was found at an STP using a trickling filter process.

Remberger et al. (2002; cited in Danish Environmental Protection Agency, 2003b) reported triclosan concentrations in samples of anaerobically digested sludge collected in 2001 from 4 Swedish STPs in the range of 2800-4400 ng/g (dry wt). Details on the type of STP treatment processes used were not reported.

Table 16.36 - Triclosan in sludge (ng/g dry weight) from 19 Swedish STPs

STP	Equivalent Population	Process	Triclosan in sludge (ng/g dry wt)
Lysekil	8000	MB1C (TF)	1200*
Ulricehamn	8725	MB1C (TF)	5100*
Alingsås	23930	MB1C (TF)	6400*
Vara	6360	MCB2C (AS)	450*
Amal	10000	MB2C (AS)	28*
Skara	14000	MB134C (AS)	380*
Uddevalla	38000	MCB2C (AS)	180*
Ryaverket	605530	MB2C (AS)	35*
Bohus-Malmon	400	MC (Primary)	2100
Donso (Goteborg)	2000	MB1C (TF)	470
Munkedal	4000	MB1C (TF)	530
Bralanda (Vanersborg)	2250	MB2C (AS)	340
Ravlanda	2600	MB2PC (AS)	3700
Herrljunga	3880	MB2C (AS)	350
Tranemo	5000	MCB2 (AS)	340
Karlsborg	5200	MB2C (AS)	180
Stenungsund	14500	MB4PC (AS)	200
Skene	17220	MB2C (AS)	260
Lidköping	28160	MB4C (AS)	1300

Source: Svensson (2002).

Process: M = mechanical; C = chemical; B = biological; P = biological phosphate removal; Primary = primary treatment; 1 = Trickling filter (TF); 2 = activated sludge (AS); 3 = Sequential batch reactor (SBR); 4 = Activated sludge (aerobic and anoxic treatment); * Process includes anaerobic digestion of sludge.

Switzerland

Singer et al. (2002) reported sludge triclosan concentration from the Gossau municipal STP (primary and secondary activated sludge sedimentation) collected in June 1999. A grab sample from the activated sludge tank indicated triclosan concentrations of 580 ng/g (dry wt) adsorbed to sludge particles and 35 ng/L in the aqueous phase.

United States

Triclosan concentrations in municipal STP sludges reported by McAvoy et al. (2002) have been presented in Table 16.37.

Table 16.37 - Triclosan (TCS), methyl-triclosan (MTCS) and chlorinated derivatives in sludges (ng/g dry weight) from activated sludge and trickling filter STPs, USA

Site/sample	TCS	MTCS	II	III	IV
Columbus (AS)					
Primary sludge	8750	260	180	220	420
Secondary sludge	900	310	(50)	(20)	(60)
Loveland (AS)					
Primary sludge	14700	50	40	100	70
Secondary sludge	4200	1030	60	40	90
Glendale (TF)					
Primary sludge	7500	NQ	ND	ND	ND
(AN) Digested sludge	15600	130	110	100	(90)
West Union A (TF)					
Primary sludge	11700	200	<40	<40	ND
(AER) Digested sludge	530	170	ND	ND	ND
West Union B (TF)					
Primary sludge	12200	140	70	120	120
Secondary sludge	7300	450	90	50	80
(AER) Digested sludge	1500	130	ND	ND	ND

Source: McAvoy et al. (2002). AN = anaerobic. AER = Aerobic. NQ: not quantifiable (signal/noise <10). Limit of quantitation of 70 ng/g sludge (dry wt). West Union STP was sampled twice. NQ indicates that the standard injection gas chromatography-mass spectrometry acceptable criteria were not fulfilled. ND: Not detected. The detection limit was 40 ng/g. Chlorinated compound: II: 2',3,4,4'-tetrachloro-2-hydroxydiphenyl ether; III: 2',4,4',5-tetrachloro-2-hydroxydiphenyl ether; IV: 2',3,4,4',5-pentachloro-2-hydroxydiphenyl ether. Refer to Figure 16.1 for chemical structures. AS = activated sludge. TF = trickling filter.

The data indicate primary sludge triclosan concentrations in the range of 7500-14700 ng/g (dry wt), and in secondary activated sludge in the lower range of 900-4200 ng/g. In aerobically digested sludge, triclosan concentrations ranged from 530-1500 ng/g, whereas, in anaerobically digested sludge the concentration was higher (e.g. 15600 ng/g; Ciba Specialty Chemicals, 1998a). This supports other data that triclosan is poorly biodegraded under anaerobic conditions and that anaerobic digestion has the effect of concentrating triclosan in the sludge. Methyl-triclosan concentrations ranged up to 260 ng/g (primary sludge), 310-1030 ng/g (secondary sludge) and 130-170 ng/g (digested sludge; McAvoy et al., 2002). No enrichment of sludges by chlorinated derivatives was evident during the STP process.

Summary of municipal STP sludge concentrations

Triclosan in STP sludges

Table 16.38 presents a summary of monitoring data for triclosan in various STP sludges.

Table 16.38 - Summary of mean triclosan concentrations (ng/g dry weight) in municipal STP sludges

Location & date	Primary (raw) sludge	Secondary sludge		Digested sludge		Reference
		TF	AS	Anaerobic	Aerobic	
<u>Australia</u> 2 STPs (1999)	---	---	---	50-3400*		Luke 1999
17 STPs (2004)	---	---	---	90-16790	220	Ying and Kookana (2007)
<u>Canada</u> 35 STPs (1999-2001)	(11600) 3400-17900	---	---	(19200) 5400-28200 _P	---	Lee and Peart (2002)
<u>USA</u> 4 STPs (1996)	7500-14700	---	900-4200	15600 ^P	530 ^P 1500 ^{AS}	McAvoy et al. (2002)
<u>Germany</u> 1 STP (April 2002)	---	---	---	(3000)**	---	Bester (2003)
<u>Switzerland</u> 7 STPs (June 1999)	---	---	580	---	---	Singer et al. (2002)
<u>Sweden</u> 19 STPs	2100	470-530	180-3700	1200-6400 ^{TF} 28-450 ^{AS}	---	Svensson (2002)*
4 STPs	---	---	---	2800-4400†	---	Remberger et al. (2002)
<i>Range</i>	<i>2100-17900</i>	<i>470-530</i>	<i>180-4200</i>	<i>5400-28200_P</i> <i>1200-6400^{TF}</i> <i>28-450^{AS}</i>	<i>530^P</i> <i>1500^{AS}</i>	

All values are in ng/g dry weight unless specified otherwise. Values in parentheses refer to mean concentrations and other values refer to concentration range. P = primary treated. TF = trickling filter. AS = activated sludge. *Details of treatment level not reported. † Reported in Danish EPA (2003b) and details of treatment level not reported. ** Converted to dry weight based on a reported value 1200 ng/g (wet wt) and 60% moisture and density of 1 kg/L.

Although influent concentrations will vary temporally and spatially (e.g. by STP and country) and affect sludge content, primary sludges (≤ 17900 ng/g) and anaerobically-digested sludges (≤ 28200 ng/g dry wt) show higher triclosan

concentrations relative to secondary sludges (≤ 4200 ng/g) and aerobically-digested sludges (≤ 1500 ng/g), indicative of the greater potential for aerobic microbial degradation of triclosan. Several studies (e.g. Lee and Peart, 2002; Ciba Specialty Chemicals; 1998a) identified a concentrating effect of triclosan when sludges are anaerobically digested. From limited evidence, levels within Australian samples seem to reflect those from overseas.

Triclosan Degradation Products in STP sludges

Methyl-triclosan

Data from one United States study of municipal STP sludges (McAvoy et al., 2002) reported methyl-triclosan concentrations in the ranges as follows:

- Primary (raw) sludge: 50-260 ng/g;
- Secondary (activated sludge; AS): 310-1030 ng/g;
- Secondary (trickling filter; TF): 450 ng/g;
- Digested sludge (TF/aerobic): 130-170 ng/g; and
- Digested sludge (primary, anaerobic): 130 ng/g.

Where comparative data were available from primary and secondary treated sludge processes (3 STPs), triclosan showed a general decrease in concentration with treatment; however, methyl-triclosan increased (~200-fold increase from 5 to 1030 ng/g at one STP) as treatment progressed from primary to secondary.

Chlorinated derivatives of triclosan

As indicated in Table 16.39, several of the chlorinated derivatives of triclosan (compounds II, III, and IV) may be detected in various STP sludges; however, concentrations in sludge from secondary treatment (i.e. biologically treated effluent) and aerobically digested sludge were relatively low compared to primary or anaerobically digested sludge (McAvoy et al., 2002).

At one STP, chlorinated derivatives were not detected in primary or secondary sludges. However, they were detected in anaerobically digested sludge, highlighting the potential concentration of these compounds during the anaerobic digestion process.

No data were available for the potential products of photolysis of triclosan; 2,4-DCP, 4-chlorocatechol or DCDD compounds (e.g. 2,7/2,8-DCDD) in STP sludge. However, treatment processes prior to clarification and sludge collection are unlikely to involve photolysis and their presence in sludge is unlikely.

16.4 Occurrence in the natural environment

This section describes the occurrence of triclosan and its products in various environmental media (surface waters, sediments, aquatic biota, soils, terrestrial biota, and groundwater) based on field studies, undertaken mostly in other countries.

Table 16.39 - Occurrence of chlorinated derivatives of triclosan in STP sludge

Site/sample	Compound II	Compound III	Compound IV
Primary sludge	ND-180	ND-220	<70-420
Secondary			
Activated sludge (AS)	50-60	20-40	60-90
Trickling filter (TF)	90	50	80
Digested sludge	≤110 (P & AN) ND (P & TF/AER)	≤100 (P & AN) ND (P & TF/AER)	≤90 (P & AN) ND (P & TF/AER)

Source: McAvoy et al. (2002). All values in ng/g (dry weight). Chlorinated compounds: II: 2',3,4,4'-tetrachloro-2-hydroxydiphenyl ether; III: 2',4,4',5-tetrachloro-2-hydroxydiphenyl ether; IV: 2',3,4,4',5-pentachloro-2-hydroxydiphenyl ether. Refer to Figure 16.1 for chemical structures. AS = activated sludge. TF = trickling filter. P = primary digested sludge. AER = aerobic sludge digestion. AN = anaerobic sludge digestion. ND = not detected. Detection limit 40 ng/g (sludge).

16.4.1 Surface waters and sediments

As indicated above, triclosan has the potential to be released in to the environment. Products of triclosan include methyl-triclosan and several chlorinated derivatives. No surface water, sediment or biological tissue residue data were available for chlorinated derivatives of triclosan.

Surface waters

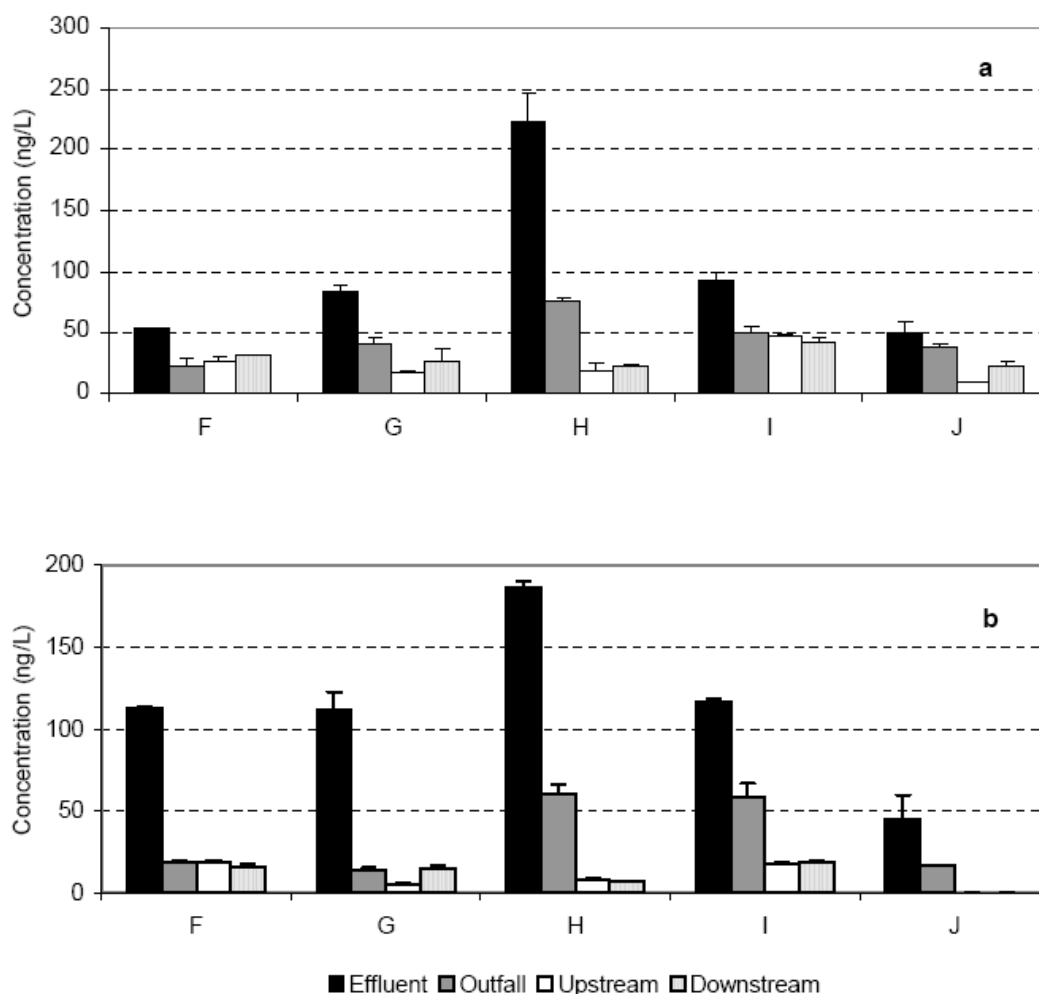
Australia

The occurrence of triclosan in Australian waters has recently been reported by Ying and Kookana (2007). Triclosan at concentrations up to 75 ng/L was detected in surface waters (outfall, upstream, and downstream) from five rivers receiving effluent discharge from STPs in Queensland. A survey conducted during this assessment of major wastewater treatment utilities throughout Australia found that none routinely monitor triclosan levels in raw untreated sewage, treated effluent or surface waters in effluent receiving environments.

Triclosan was detected in surface waters of the five rivers associated with wastewater discharge that were sampled in 2004 and 2005. The triclosan concentrations in surface waters collected from the outfall (near the effluent discharge point) of the sewage effluent ranged from 21 to 75 ng/L for 2004 and from 14 to 60 ng/L for 2005 (Figure 16.8). At the same time, triclosan was also measured for the effluent samples from the five STPs, they ranged between 51 and 222 ng/L for 2004 and between 45 and 187 ng/L for 2005. The variation in triclosan concentrations between 2004 and 2005 was found to be very small for the effluents and surface waters from outfalls.

Triclosan concentrations in surface water ranged from 9 to 47 ng/L upstream (about 200 m) from the outfalls and 21 to 43 ng/L downstream (also about 200 m) from the outfalls in 2004. But relatively lower triclosan concentrations in surface waters from both upstream and downstream were observed in 2005 ranging from below the detection limit (<3 ng/L) to 19 ng/L. This is said to have probably been caused by faster degradation of triclosan in summer due to the higher temperatures.

Figure 16.8. Triclosan concentrations in surface waters near five STPs (F, G, H, I and J) that discharge effluent into the rivers. (a) Data from sampling in October 2004. (b) Data from sampling in February-March 2005 (Ying and Kookana 2007)



Photodegradation has been found to be responsible for the rapid removal of triclosan in surface waters in summer (Tixier et al., 2002, Lindstrom et al., 2002). Effluents from plants G and J are discharged into a freshwater environment, while those from plants F, H and I are discharged into an estuarine environment. No significant difference in triclosan concentrations was found between upstream and downstream for estuarine discharges. This is believed to be due to samples taken from the estuarine environment being mixed due to tidal movement. For the two freshwater sites (plants G and J), the triclosan concentrations in the upstream samples were lower than in downstream samples. However triclosan was below the limit of detection both upstream and downstream of plant J in year 2005.

Although the highest triclosan concentration measured in the streams was 75 ng/L, the authors suggested that higher concentrations could be expected in some streams, particularly during dry conditions when almost all water in some streams comprises effluent from STPs. This would be taken into account in the risk assessment where the DEW default is no dilution in freshwater receiving waters. However, examination of Fig 16.8 shows, with the exception of J in 2004, at least a 50% (1:1) dilution was achieved.

Canada

In Canada, raw water samples were collected in January 2002 from the inlet and outlet of the A.H. Weeks Water Treatment Plant, Windsor Ontario, which relies on the Detroit River as its source (Boyd et al., 2003). The drinking water treatment plant uses ozonation, conventional treatment (alum, and Percol LT22 as coagulants) and chlorination prior to distribution. Triclosan was not detected in any water samples above the method detection limit of 0.2 ng/L.

Hua et al., (2005) examined the presence and UV-treatment effects on triclosan in effluent from the major STP servicing the City of Windsor, Ontario and its fate in surface waters of the upper Detroit River. Triclosan in the Little River STP decreased 22% after final UV treatment to a mean concentration of 63 ng/L at the point of release. Surface water samples (0.5 L grab samples) were taken from shoreline sites on the Canadian side of the Detroit River at 0.7 m. With a detection limit of 4 ng/L, triclosan was detected at one site (~600 m downstream of the STP) at around 8 ng/L and was still detected at around the LOQ of 4 ng/L at a second site some 2 km downstream.

Germany

A computer simulation of the potential environmental concentration of triclosan in the river Itter, a 19.2 km long tributary of the river Rhine, Dusseldorf, has been undertaken by Wind et al. (2004) using the geo-referenced exposure model GREAT-ER (Geo-referenced Regional Environmental Assessment Tool for European Rivers, version 1.03; ECETOC, 1999). Three STPs (~90% municipal and ~10% industrial sources) discharge into the river and the overall water flow (0.74 m³/s) is comprised mostly (~66%) of treated effluent. The triclosan concentration in effluent from one of the STPs (Solingen-Ohligs) was 180 ng/L (other two STPs not sampled; refer Table 16.40). The simulation was used to derive a predicted environmental concentration (PEC) profile in surface waters within the entire catchment (45 km²) on a regional and local (hot spot) scale. The simulation was based on consumption figures for triclosan in the year 2000 (40 tonnes per annum or 0.5 g/person/year) which were equilibrated to the catchment population, STP removal rate of triclosan (86.5%-99.5%), sewer removal rate (25%) and an in-stream removal rate of 0.144 h⁻¹ (t_{1/2} of 4.8 h; based on photolysis and aerobic biodegradation). The simulation was evaluated using measured concentrations in samples (automated 24 h composite and grab; unfiltered) collected under dry weather conditions in October 2000 from various locations up and downstream of STP discharge points (refer Table 16.40). Samples (unfiltered) were analysed by GC/MSD (LOQ 5 ng/L).

GREAT-ER predicted catchment and initial concentrations of 70 ng/L (range 21-94 ng/L) and 130 ng/L, respectively, approximating the measured range of 30-90 ng/L. Deviations were less than a factor of 1.2 from measured concentrations and the calculated 90th percentile concentration was not exceeded in measured samples. Partitioning of triclosan from surface water to sediment was not estimated or measured.

Table 16.40 - Predicted triclosan concentration in surface waters of the river Itter, Germany

Sample location (upstream to downstream)	Estimated/Measured triclosan concentration (ng/L)
STP Solingen-Graefrath	Not determined
Kuckesburg (8.8 km)	30
STP Solingen-Ohligs	180
Trotzhilden (10.1 km)	90
Hilden (15.2 km)	69
STP Hilden	Not determined
Itter confluence (19.1 km)	65

Source: Wind et al. (2004).

Norway

Weigel et al. (2004) present the first research on the occurrence of triclosan in marine waters in Norway. The study was conducted concurrently with a sewage sampling program (refer to section 16.4.1). Grab samples of seawater were collected from 12 locations in April 2002 from the Tromso Sound, located adjoining municipal and hospital STP outfalls (e.g. in the sewage plume to 300 m offshore from the sewage plume). Samples were collected from a boat using a submersible stainless steel sampler operated with 2.5 L glass solvent bottles. Samples were stored at 4°C for ≤24 h prior to filtration (1.2 µm GF/C glass fibre). The filtrate was adjusted to pH 7 with H₂SO₄ and, following an extraction procedure, analysed by GC/MS (limit of quantitation of 0.24 ng/L). No triclosan was detected in any of the surface water samples. No sediment samples were collected.

Sweden

Remberger et al. (2002, reported in Danish Environmental Protection Agency, 2003b) analysed samples of ocean surface waters for triclosan collected from three locations at Stenungsund, Sweden. Details of sampling procedures and analytical test methods were not reported. The region represents an area of chemical manufacturing and heavy industry. Triclosan was detected in one sample (160 ng/L).

Switzerland

Poiger et al. (2003) and Lindstrom et al. (2002) reported the presence of triclosan and methyl-triclosan in surface waters in Switzerland. Surface water samples (grabs; unfiltered) were collected from several lakes (Greifensee, Zurichsee, Jorisee) and a river (Glatt) between 1998-2001. Semi-permeable membrane devices (SPMDs) were also used to sample the surface waters. The results are presented in Table 16.41. Lake Jorisee (altitude 2450 mASL) is remote from human activities and as expected, no triclosan or methyl-triclosan was detected (<0.4 ng/L). Seasonal variation of triclosan concentration in surface waters was recorded, thought to be due to differential photolysis of triclosan; however, other factors may have been involved.

Table 16.41 - Triclosan and methyl-triclosan in surface water samples, Switzerland

Samples	Triclosan		Methyl-triclosan	
	Grab (ng/L)	SPMD (ng/g)	Grab (ng/L)	SPMD (ng/g)
Lake Greifensee	≤14*	ND	ND-0.8	33
Lake Zurichsee	≤3	ND	ND-0.8	16
River Glatt	74	ND	2	---

Source: Poiger et al. (2003 and Lindstrom et al. (2002). ND – not detected <1 ng/L); * With seasonal pattern (lower in summer) potentially due to photolysis but also other possible factors.

Through modelling, Poiger et al. (2003) estimated that photolysis is a significant transformation process for triclosan; however, the more photostable methyl-triclosan is likely to be less affected by photolysis. Thus, due to its relatively greater persistence, methyl-triclosan may accumulate reaching concentrations in the epilimnion of ~30% of the parent compound triclosan, even through the initial effluent discharge ratio of triclosan to methyl-triclosan was ~2% in their estimation. As indicated in Section 16.3.1, treated effluent concentrations of methyl-triclosan and triclosan of up to 12 ng/L and 2700 ng/L have been recorded, although the average concentration is probably much lower.

Singer et al. (2002) reported surface water concentrations of triclosan in two Swiss rivers (Aa Uster and Aabach Moenchaltorf). Surface waters were also collected from seven depths from Lake Greifensee, Switzerland, from a small eutrophic lake with regular deep mixing over winter (from December to March) and a mean water residence time of 408 days. Surface waters were sampled in October 1999. Weekly flow proportional effluent samples collected by Singer et al. (2002) in August to October 1999 from municipal STPs at Uster, Maur and Moenchaltorf showed a relatively constant triclosan concentration in outflows. However, concentrations in the Aa Uster River increased by a factor of 5 (up to 100 ng/L) during high flow events, probably due to the discharge of untreated sewage from sewer overflows. For the Aabach Monchaltorf River, the impact of untreated sewage from sewer overflows is less as a relatively constant triclosan concentration of ~20 ng/L (range ~12-35 ng/L) was recorded for the same time period.

Surface water samples from two depth profiles from Lake Greifensee collected in August and October 1999 showed slightly lower triclosan concentrations in the surface to 10 m of the lake (e.g. 5-10 ng/L) and highest concentrations (10-15 ng/L) in the depth range of 10-30 m (lake bottom; Singer et al., 2002).

Singer et al. (2002) modelled the fate of triclosan in surface water from Lake Greifensee, Switzerland, by examining its mass balance over a 3 month period. The triclosan input to the lake was estimated to be 720 g (input by 2 rivers and 3 municipal STPs discharging directly into the lake). The total amount of triclosan in the lake surface water, determined from the vertical depth profiles at the beginning and end of the study period, decreased from 1450 to 1290 g (or by 160 g). Furthermore, 130 g of triclosan was flushed by the River Glatt. An overall elimination/degradation of 750 g of triclosan over the assessment period was calculated. This overall elimination rate of 0.03 d⁻¹ (0.0013 h⁻¹) for triclosan in the lake water column is the sum of the different transport and transformation processes and does not include the flushing rate of 0.006 d⁻¹ (0.00025 h⁻¹) through

the lake outflow. Singer et al. (2002) suggested that photolysis, and to a lesser extent sedimentation of particulate-bound triclosan, were the most important processes affecting triclosan in the surface water of the lake.

Balmer et al. (2004) sampled surface waters in several lakes in Switzerland (Jorisee, Huttensee, Zurichsee, Greifensee and Limmat) in 2002 using SPMDs (≥ 1 /site) exposed to surface waters for 18-41 days. Data are reported in Table 16.42.

Table 16.42 - Methyl-triclosan (MTCS) in surface water samples, Switzerland

Location	MTCS (ng/SPMD)	Estimated MTCS in surface water (ng/L)
Jorisee	<1	<0.02
Huttensee	~1	<0.02
Zurichsee	25, 28 and 32	0.4-0.5
Greifensee	56 and 85	0.8-1.2
Limmat	87 and 137	Not determined

Source: Balmer et al. (2004).

The Netherlands

Limited data were available on triclosan concentrations in surface waters in The Netherlands. Leonards (as reported in van Wezel and Jager, 2002) measured triclosan in SPMDs at concentrations of 150-540 ng/g triolein. Surface water concentrations were estimated from SPMD data at 2.1-7.7 ng/L. No further information on sampling or analytical methodology was available.

United Kingdom

In September 2000, Sabaliunas et al. (2003) undertook surface water monitoring of triclosan concentrations in a 3.5 km section of a freshwater stream (Mag Brook, 0.13-0.18 m³/s, 0.05-0.57 m depth) receiving treated effluent from the Meltham trickling filter STP, Yorkshire UK. Effluent from the Meltham STP has been sampled once by Sabaliunas et al. (2003) and found to contain 340 ng triclosan/L; however, time and flow-dependent variability in triclosan concentration from this STP has not been investigated. No additional inflows to the 3.5 km section of river were observed; however, unobservable inputs (e.g. groundwater ingress) cannot be discounted. One SPMD was set at each sampling site for a period of 5 weeks. In addition, a grab sample of surface water was collected at each sampling location. Rhodamine dye was used as a tracer for the sampling program. Five sampling sites were selected downstream of the STP discharge point (20 m, 0.75 km, 1.5 km and 3.5 km); however, data from the 3.5 km site was not recoverable as sediment buried the SPMD. River water samples were analysed by GC/MS. Methyl-triclosan was not measured in river waters during this study, and river sediments were not sampled for triclosan or its products.

The sampling results (Table 16.43) highlight the presence of triclosan in surface waters upstream of the STP due to unknown sources, and elevated concentrations (+220%) compared to upstream sources at least 1.5 km downstream from the STP discharge point. More than 50% of the initial concentration of triclosan was present after ~ 2.7 hours at a distance of 1.5 km downstream from the STP. Triclosan was

also detected in SPMD samples 3.5 km downstream. The rate of reduction of triclosan in the first 150 m downstream (~34%) was about double that in the following 750 m section of river (~19%), indicating a reduction in the rate of loss of triclosan from the surface water with distance downstream. The full distance travelled by triclosan was not determined in this study.

Table 16.43 - Triclosan in surface waters of Mag Brook, Yorkshire UK

Site	Travel time (mins)	Grabs (<i>n</i> =3) TCS (ng/L)	% Change (Grab samples)			SPMD (ng/3 units)
			(a)	(b)	(c)	
50 m upstream	---	19 ± 1.4	(a)	(b)	(c)	93
20 m downstream	0	80 ± 15	+421	0	---	489
0.75 km downstream	~60	53 ± 3.2	+278	-33.8	0	423
1.5 km downstream	~160	43 ± 5.6	+220	-46.3	-18.8	205

Source: Sabaliunas et al. (2003). a. Percent change (increase) relative to background concentration. b. Percent reduction relative to triclosan concentration 20 m downstream of STP. c. Percent reduction relative to triclosan concentration 0.75 km downstream from STP.

United States

Over a six month period in 2003, Boyd et al. (2004) investigated the occurrence of triclosan in surface waters in several water bodies in New Orleans. These surface waters and results are as follows; two stormwater canals (Orleans, London; 0-29 ng/L), Bayou St. John (<0.2 ng/L), Lake Pontchartrain (1.6-14.9 ng/L) and the Mississippi River (<0.2-3.1 ng/L). Grab samples (4 L) were filtered at least twice (1.6 and 0.2 µm glass fibre), solid-phase extracted and then analysed using selection ion monitoring (SIM) on a GC/MS. The canals receive only stormwater and are not used to receive effluent from STPs; however, the occurrence of triclosan is attributed to non-point source sewage contamination from the ageing New Orleans sewerage system. In the canals, triclosan was detected in 70% of samples and triclosan concentration increased with rainfall. Triclosan was primarily detected in the winter months. The Lake and River receive waters from the canals and probably other sources in the catchment.

In an earlier study, Boyd et al. (2003) reported triclosan concentrations in surface water samples (filtered 1.0 & 0.2 µm glass fibre) from the Mississippi River at locations beyond the direct influence of discharge points of known private or municipal STPs, and from Lake Pontchartrain, central Gulf Coast, Louisiana, collected September-November 2001. Triclosan was not detected in river or lake samples above the method detection limit of 0.2 ng/L. Water samples were collected from various stages of the Jefferson Parish East Bank drinking water treatment plant, Louisiana, which relies on the Mississippi River as its raw water source (Boyd et al., 2003). The facility applies conventional water treatment including coagulation (alum and cationic polyelectrolyte polymer), flocculation, sedimentation and disinfection by chlorination prior to filtration and chloramination prior to distribution. Triclosan was not detected in any water samples above the method detection limit of 0.2 ng/L.

Kolpin et al. (2002) undertook an extensive survey of triclosan in freshwater streams across 30 States throughout the United States between 1999-2000.

Sampling locations were biased towards areas known or suspected of contamination by organic wastewater contaminants such as triclosan (e.g. downstream of urbanised areas), but were representative of stream conditions. Water samples were filtered (0.7 µm baked glass fibre) prior to extraction and analysis by capillary column GC-MS (analytical reporting level 50 ng/L). Triclosan was commonly detected in surface waters (56 of 85 samples), with recorded median and maximum concentrations of 140 and 2300 ng/L, respectively. No sediment or biological samples were collected.

The fate of triclosan in surface water in a freshwater stream (Cibolo Creek, South Central Texas) was investigated by Morrall et al. (2004; Table 16.44). The stream had a mean width of 6-26 m, mean depths of 0.4 m in riffles and 1.5 m in pools and mean velocities of 0.2 m/s in riffles and 0.007 m/s in pools (average flow 0.1 m³/s). Triclosan was analysed from grab samples collected 200 m upstream of the Cibolo Creek STP, from effluent from the STP, and downstream from the STP (200 m, ~2 km and ~8 km) in Spring 1999. The STP is a trickling filter plant with tertiary treatment in the form of a dual media filtration. The plant has two above ground trickling filters with an intermediate clarifier in between and primary and secondary clarifiers both operating at 50% of design capacity. Less than 5% of inflow is derived from industrial sources. The biological oxygen demand (BOD₅) and total suspended solids (TSS) removal efficiency by the STP were 97.8% and 98.4%, respectively, indicating that the STP was operating within specifications. Bromide (Br⁻) was used as a tracer in the stream in order to follow and sample a specific body of water as it flowed down river. Travel time between 200 m and 8 km was 23 h based on the bromide tracer.

The sampling data from Morrall et al. (2004), presented in Table 16.44, indicate the presence of triclosan in treated effluent (785 ng/L) and about 25% remaining present in surface water a distance of at least 8 km (~23 hours after discharge) downstream from the discharge point, highlighting the persistence of triclosan in this freshwater environment. The full distance travelled by triclosan downstream was not determined during this study. The triclosan concentration 8 km downstream was ~300% higher than detected upstream of the STP. The first order loss rate of triclosan from the water column was calculated from measured data (0.06 h⁻¹). Potential contributions of downstream sources of triclosan and/or flow into the river (e.g. groundwater ingress, run-off) on triclosan concentration and dilution were not identified or accounted for in the modelling of triclosan removal.

Through modelling, loss of triclosan over 8 km was attributed to adsorption and settling of solids (~19% depending on stream reach), biodegradation and photolysis, although these were not measured. The rate of loss of triclosan from the surface waters slowed with distance downstream. As the triclosan concentration in the surface water dropped by ~52% in the first 1.8 km, but took a further 5.8 km to fall a further ~25%. Due to turbidity in the stream, photolysis was not considered a significant loss pathway. No sediment sampling was conducted as part of this study to verify sedimentation, sediment accumulation or the potential for mobilisation of historically deposited and accumulated triclosan from sediments into the water column.

The Morrall et al. (2004) study also highlights the presence of triclosan in waters upstream from the Cibolo STP (34 ng/L) from unknown sources.

Table 16.44 - Triclosan in Cibolo Creek, Texas

Site	Travel time (min)	Triclosan (ng/L)	% Change		
200 m Upstream of STP	---	34	(a)	(b)	(c)
STP Effluent	0	785	---	---	---
200 m downstream of STP	115	431	+1268	0	---
2 km downstream of STP	585	223	+656	-48	---
8 km downstream of STP	1485	104	+305	-76	-53

Source: Morrall et al. (2004). a. Percent increase relative to triclosan concentration 200 m upstream from STP. b. Percent reduction relative to triclosan concentration 200 m downstream from STP. c. Percent reduction relative to triclosan concentration 2 km downstream from STP.

Wilkison et al. (2002) investigated the effects of municipal STP discharges and sewer overflows to triclosan levels in Blue River, Brush Creek and Indian Creek, Kansas/Missouri USA. Blue River and Indian Creek received nearly continuous base flows of STP effluent. Brush Creek did not receive STP effluent but received untreated sewage from sewer overflows during intermittent storm events. The sampling program was conducted between July 1998 and October 2000 included at least 10 storm events. Surface water grab samples were not filtered prior to analysis. STP efficiencies for triclosan removal were 40% (Blue River) and 97% (Tomahawk Creek STP located near the confluence with Indian Creek). Triclosan was detected in almost every base-flow (dry weather) sample (97% of samples). Median concentrations of triclosan in samples from Indian Creek (800 ng/L) and Blue River (values not reported) were significantly higher ($p < 0.001$) than in samples from Brush Creek (~110 ng/L). In particular, the monitoring data highlight the occurrence of triclosan in waterways receiving either STP effluent or sewer overflows.

Jungclaus et al. (1978) reported triclosan concentrations in surface water in a US river (Pawtuxet) receiving a treated wastewater discharge from a specialty chemicals manufacturing facility containing 6-14 mg/L of triclosan. Seven water samples (grabs; unfiltered) were collected from the river up- and downstream from the facility in 1975-76. Samples were analysed by GC/MS. Triclosan concentrations reported in river surface water ranged from 0.012-0.30 mg/L (12000-300000 ng/L). Triclosan was not detected in up-river surface water samples. A more detailed study of triclosan in the receiving waters downstream of this facility was undertaken by Lopez-Avila and Hites (1980). Surface water samples (unfiltered) collected in 1977-78 from the Pawtuxet River, Pawtuxet Cove and the Providence River contained 10-40 µg/L (10000-40000 ng/L), 10-20 µg/L (10000-20000 ng/L) and 0.6-5 µg/L (600-5000 ng/L) of triclosan, respectively.

Summary

Triclosan and methyl-triclosan have been reported in natural waters from Australia and several North American and European countries (refer Table 16.45). Considering that the Australian data were collected within 200 m of the outfalls, levels are generally similar or lower to those from other countries, in particular the relatively high levels from the US/Canada.

Table 16.45 - Occurrences of triclosan and methyl-triclosan in natural waters

Country	Triclosan range (ng/L)	Methyl-triclosan range (ng/L)	Reference
Australia	<3-71 2 FW, 3 EW	---	Ying and Kookana (2007)
Germany	30-90 FW	---	Wind et al. (2004)
Norway	ND MW	---	Weigel et al. (2004)
	160 MW	---	Remberger et al. (2002)
Switzerland	≤3-74 FW	ND-2 FW	Poiger et al. (2002)
	5-100 FW	---	Singer et al. (2002)
	---	ND-1.2 FW	Balmer et al. (2004)
The Netherlands	2.1-7.7 FW	---	Wezel and Jagar (2002)
United Kingdom	19-80 FW	---	Sabaliunas et al. (2003)
United States/Canada	ND FW	---	Boyd et al. (2003)
	4-8 FW	---	Hua et al. (2005)
	ND-2300 FW	---	Kolpin et al. (2002)
	34-785 FW	---	Morrall et al. (2004)
	110-800 FW ^a	---	Wilkison et al. (2002)
	12000-300000 FW ^b	---	Junclaus et al. (1978)
	600-40000 FW ^b	---	Lopez-Avila and Hites (1980)
<u>Range</u>			
FW	≤2300 300000 ^b	≤2	
MW	≤160	---	

--- = No data available. ND = Not detected (limit of quantitation varied among studies). FW = Freshwater. EW = Estuarine waters. MW = Marine waters. a. = Median values reported. b. = Samples collected downstream from specialty chemicals manufacturing facility discharge outlet.

Sediments

Australia

No Australian sediment triclosan data were available for this assessment. A survey conducted during this assessment of major wastewater treatment utilities throughout Australia found that none monitor triclosan levels in sediments in effluent receiving environments.

Germany

Kronimus et al. (2004) investigated the occurrence of methyl-triclosan and other organic contaminants in sediments of the Lippe river, a tributary of the Rhine river, Germany. Triclosan and methyl-triclosan are considered markers of municipal effluent. The catchment includes urban, rural and industrial land uses, with fewer activities in the upper catchment. There are 15 STPs that discharge into the river, 6

of which service >50000 people. Sampling of surficial sediments was conducted at nine selected sampling locations along the river on four occasions between 1999 and 2001. Samples were collected from stagnant water zones directly at the riverside with a high-grade steel scoop. Samples were stored in glass vessels with PTFE seals at 4°C. Samples were mostly clay or silt, but at sample location 1, sand content ranged from 45%-75%. Samples were analysed by GC/MS (acetone/hexane extraction) linked to a HRGC. A reference standard of methyl-triclosan was synthesised by addition of triclosan with dimethylsulphate and analytical recovery was 35%±7 (SD). All concentrations reported were recovery corrected and normalised on a dry weight basis (detection limit 0.1 ng/g).

The results, presented in Table 16.46, indicate that methyl-triclosan was detected above the detection limit during all four sampling events, in 29 of 36 samples. The highest concentration detected was 450 ng/g and the river-wide average was ~47 ng/g. Concentrations varied widely both temporally and spatially; however, this may be a sampling artefact due to the small number of samples collected at each site rather than representative of actual rapid changes in concentration in the surface sediment, particularly as the sediments sampled were deposited over several years. Concentrations of triclosan in the sediments were not reported.

Table 16.46 - Methyl-triclosan in sediments of the Lippe river, Germany (1999-2001)

Site	Sampling Date and Methyl-triclosan Concentration (ng/g dry wt)				Mean (range)
	Aug. 1999	Feb. 2000	Aug. 2000	March 2001	
1	220	250	1	32	126 (1-250)
2	49	ND	6	2	14.3 (ND-49)
3	32	70	<0.5	20	30.6 (<0.5-70)
4	34	30	ND	4	17.0 (ND-34)
5	ND	450	34	<0.5	121.1 (ND-450)
6	28	280	20	2	82.5 (2-280)
7	18	16	4	<0.5	9.6 (<0.5-18)
8	29	50	ND	<0.5	19.8 (ND-50)
9	<0.5	ND	ND	ND	0.1 (<0.5)
Mean (max)	46 (ND-220)	127 (ND-450)	7.3 (ND-34)	6.8 (ND-32)	46.7 (ND-450)

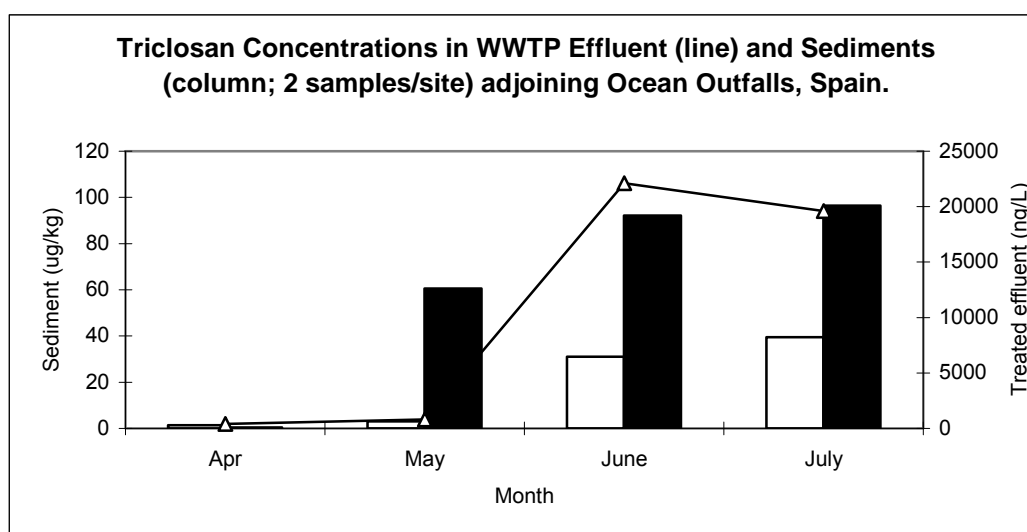
Source: Kronimus et al. (2004). Values are in ng/g (dry weight) and adjusted for 35% analytical recovery. Site 9 = upstream. Detection limit 0.1 ng/g. <0.5 = concentration was below the limit of quantitation and above the detection limit. For estimation of mean, not detected (ND) and <0.5 ng/g values are assumed at half the limit of detection and 0.25 ng/g, respectively.

A further sediment core from a floodplain of the Lippe River was taken in October 2001 (Heim et al. 2004). The core of 166 cm length was divided into 4 cm segments. The sediment was characterized as loamy fine sand with distinct bedding and with evident colour variation. The concentrations in the sediment core of methyl-triclosan ranged between 1 and 28 ng/g. The first occurrence of methyl-triclosan was detected at a depth of 46 cm with very low values. The concentration maximum was reached at a depth between 14 and 6 cm.

Spain

Aguera et al. (2003) reported triclosan concentrations in Mediterranean Sea surface sediments (depth not reported) collected in 2002 at the effluent discharge points of two municipal STPs at Almeria, Spain. Three samples were collected covering an area of 20 m to the south, east and west of each final effluent discharge point (ocean outfall). Divers collected the sediment samples (method not reported) in water depths of 20-45 m. Influent and effluent from the STPs also contained triclosan in the range 1300-30100 ng/L and 400-22100 ng/L, respectively, when sampled. The results, presented in Figure 16.9, suggest monthly average surface sediment concentrations (0.3-97 ng/g) varying in proportion with monthly effluent concentrations, potentially varying due to unidentified seasonal changes.

Figure 16.9. Triclosan in sediments adjoining primary treated effluent outfalls, Mediterranean Sea, Spain (after Aguera et al., 2003)



Sweden

Remberger et al. (2002, reported in Danish Environmental Protection Agency, 2003b) analysed samples of ocean sediments for triclosan collected from three locations at Stenungsund, Sweden. Details of sampling procedures and analytical test methods were not reported. The region represents an area of chemical manufacturing and heavy industry. Triclosan was detected in all three sampling locations (8-17 ng/g dry wt; 0-0.25 cm). Sediment samples (0.25 and 10-15 cm depth) were also collected near a former wood preservation plant at Boro, Vetland, and triclosan concentrations of up to 25 ng/g (dry wt) were detected. In a reference site at Boro, the sediment triclosan concentration was <2 ng/g (dry wt).

Switzerland

Singer et al. (2002) reported the occurrence of triclosan in sediment collected centrally from Lake Greifensee, Switzerland, in 1998. Depth-based dating of the core sample (from bottom to top surface) indicated an increase in triclosan concentration between 1960 (<5 ng/g) to 1974-75 (~73 ng/g), a decline in sediment concentration between 1974-75 and 1982-83 (~30.9 ng/g), followed by an increase to 1992-93 (~53 ng/g). The initial increase in triclosan concentration coincides with

the discovery and increased use of triclosan in the region. The decline from the mid-1970s to mid-1980s reflects the introduction of biological wastewater treatment stages in STPs that discharge treated effluent to the lake and/or tributaries in the surrounding catchment.

The popularity and increased use of triclosan is reflected in the increase in triclosan concentration in surface sediments since 1982-83. This analysis is based on the assumption of triclosan persistence, which has not been adequately investigated in sediments; however, the high concentrations reported in ~30 year old subsurface sediments, approximately dating to the initial use and discharge of triclosan, highlight the slow degradation in the sediments, which are likely to be anaerobic. The surface sediment concentration (53 ng/g) is the same order of magnitude as the modelled triclosan concentration in sinking particles (125 ng/g), assuming 10 ng/L in the hypolimnion and a pH of 7.8.

The results of Singer et al. (2002) highlight the ability of triclosan to accumulate in sediments that are distant from catchment sources, as well as the persistence of triclosan in sediments. Other studies indicate a low capacity for anaerobic biodegradation and high stability in the absence of sunlight.

United States

Miller et al.(2008) examined contaminant profiles in ¹³⁷Cs/⁷Be-dated sediment cores taken near wastewater treatment plants (WWTPs) in the, Maryland Jamaica Bay (JB), New York and Chesapeake Bay watershed (CB). In JB, triclosan occurrences tracked the time course of usage and wastewater treatment strategies employed, first appearing in the 1960s, and peaking in the late 1970s (0.6 and 0.8 mg/kg). Reductions in the levels of the sediments deposited since the mid 1980s is ascribed to the introduction of full activated sludge treatment to the JB WWTPs in 1978. In contrast, triclosan concentrations were low or not detectable in the CB core, where the time of sediment accumulation was not as well constrained by ¹³⁷Cs depth profiles.

Hale et al. (2000) reported triclosan at a concentration of 160 ng/g in surface sediment collected using a Smith-MacIntyre grab near a decommissioned STP (Virginia USA). The STP samples were collected in 1998 and the STP was decommissioned in the 1970s. Details on the STP treatment process were not available; however, Hale et al. (2000) indicated that the STP operated at low treatment efficiency. The presence of triclosan in sediments for ~20 years highlights the persistence of triclosan in the sediment environment.

Jungclaus et al. (1978) reported triclosan concentrations in surface sediments from the Pawtuxet River (USA) receiving wastewater discharges from a specialty chemicals manufacturing facility containing 6-14 mg/L of triclosan. Five sediment samples (dredge-type sampler grabs) were collected from the river downstream from the facility in 1976 and analysed by GC/MS. Triclosan concentrations reported in the sediments ranged from 1.2-5 mg/kg (1200-5000 ng/g). Jungclaus et al. (1978) derived a sediment accumulation factor for triclosan of ~30 by dividing the geometric mean sediment concentration (2 mg/kg) by the geometric mean river water concentration (0.06 mg/L).

Lopez-Avila and Hites (1980) has undertaken a more detailed study of triclosan in the surface sediments (0-6 cm; cores) downstream of the facility investigated by Jungclaus et al. (1978). Sediment samples collected in 1977-78 from the Pawtuxet

River contained triclosan in the range 20000-100000 ng/g, higher than previously reported; however, triclosan was not detected (detection limit ~100-500 ng/g) in sediment samples from the downstream Pawtuxet Cove, the Providence River and Narragausett Bay.

Summary

Triclosan has been reported in sediments from natural waterways from several North American and European countries (refer Table 16.47). No monitoring studies have been undertaken in Australia.

Table 16.47 - Occurrences of triclosan and methyl-triclosan in natural sediments

Country	Triclosan range (ng/g)	Methyl-triclosan range (ng/g)	Reference
Germany	---	ND-450 FS	Kronimus et al. (2004)
	---	1-28	Heim et al. (2004)
Spain	0.3-97 MS	---	Aguera et al. (2003)
Sweden	ND-25 MS	---	Remberger et al. (2002)
Switzerland	ND-73 FS	---	Singer et al. (2002)
United States	ND-800000	---	Miller et al. (2008)
	160 FS	---	Hale et al. (2000)
	≤5000 FS ^a	---	Junclaus et al. (1978)
	≤100000 FS ^a	---	Lopez-Avila and Hites (1980)
<u>Range</u>			
FS	ND-160 ≤100000 ^a	ND-450	
MS	ND-97	---	

Values are presented on a dry weight basis. --- = No data available. ND = Not detected (limit of quantitation varied among studies). FS = Freshwater sediments. MS = Marine sediments. a = Samples collected downstream from specialty chemicals manufacturing facility discharge outlet.

16.4.2 Bioaccumulation in aquatic biota

Laboratory studies

General

With a log $P_{\text{octanol:water}}$ of 4.7 - 4.8 (Ciba-Geigy Limited, 1990b; Boehmer et al., 2004), triclosan is lipophilic and is readily taken up by exposed aquatic organisms from waters, sediments and food (Poiger et al., 2003). Ciba-Geigy Limited (1990b) measured the octanol water partition co-efficient using OECD TG 107 (shake flask procedure), deriving a Log $P_{\text{octanol:water}}$ of 4.8 (pH 6.7, 25°C). Three reference compounds tested validated the test results.

Triclosan and other chlorinated phenolic compounds can be biologically methylated to methyl ether derivatives (Valo and Salkinoja-Salonen, 1986;

Hagblom et al., 1989; Allard et al., 1987; Neilson et al., 1988), and methyl-triclosan has been detected using GC-MS in freshwater fish (carp *Carassius carassius* and goby spp.) and shellfish from the Tama River and the Tokyo Bay in Japan (Miyazaki et al., 1984), as well as other studies (Balmer et al., 2004; Alaei et al., 2003; Remberger et al., 2002). With an estimated log $P_{\text{octanol:water}}$ of 5.0-5.2 (Valo and Salkinoja-Salonen, 1986; Boehmer et al., 2004, estimated using KowWin Version 1.67), methyl-triclosan has a potentially greater affinity for octanol than triclosan (Poiger et al., 2003; Boehmer et al., 2004) and consequently a greater potential to bioaccumulate in aquatic organisms. This is supported by fish tissue monitoring studies (e.g. Boehmer et al., 2004).

Bioconcentration tests

Ciba-Geigy Ltd (1991) and Orvos et al. (2002) reported on the bioconcentration and depuration of ^{14}C -triclosan in zebra fish (*Brachydanio rerio*). The test followed the method of OECD TG 305C. The fish (30 per concentration; mean wt. 0.33 g) were exposed to a blank control and two triclosan concentrations (3 and 30 $\mu\text{g/L}$ nominal; 3.18 and 27.66 $\mu\text{g/L}$ measured) for 5 weeks in a continuous flow-through system (5 L/h or 10 mL triclosan/h), and depuration was monitored for 2 weeks post-exposure. Test vessels consisted of 30 L glass aquaria containing 20 L of control or test solution. Test solutions were aerated. The stock solutions were prepared by addition of triclosan in ethanol made to volume in dechlorinated tap water (hardness 9.5°dh, chlorine <0.1 mg/L). Fish mortality, test concentration, pH (7.7-8.0), temperature (22.3°C to 24.3 °C) and dissolved oxygen (63%-97% saturated) in the test vessels were monitored daily. The tests were conducted under 12 hours light and 12 hours dark photoperiod. Analyses were performed weekly on 3 fish per treatment to determine the concentration of triclosan accumulated in the fish. The method of analysis of water and fish was not reported and no evaluation of analytical data quality can be made. No fish mortality occurred during the period of the tests.

Reported fish (whole) triclosan concentrations and BCFs are presented in Table 16.48. In accordance with OECD test guidelines, presumably analytical data are presented on a wet weight basis. Maximum BCF values were reached after 3 weeks.

Table 16.48 - Triclosan accumulation in zebra fish (whole body)

Exposure (water)	Average Conc. In Fish ($\pm\text{SD}$, $\mu\text{g/kg}$ wet wt)	Conc. Range in Fish ($\mu\text{g/kg}$ wet wt)	5-week Average BCF	Maximum BCF
3.18 $\mu\text{g/L}$	12881 \pm 2440	10687-16492	4157	5337
27.66 $\mu\text{g/L}$	68793 \pm 15275	51041-92504	2532	3408

Source: Ciba-Geigy Ltd (1991). Test solution pH was 7.7-8.0.

Selected fish tissues were analysed (2 fish per treatment) after 5 weeks exposure to triclosan. As indicated in Table 16.49, most of the triclosan (5-9 times greater) was detected in the intestines relative to the other tissues analysed. This tissue was not described and it is not clear whether organs or fluids (e.g. bile) were included in the samples. The author indicates that triclosan apportioned in fish tissues as follows: ~75% intestines and 9%-13% in fillet. As maximum accumulation of triclosan was

achieved after 3 weeks exposure, the concentrations reported below may not represent the maximum concentrations achieved in the fish tissues.

The depuration of triclosan was monitored by placing triclosan-exposed fish in aquaria containing no triclosan. Two fish per treatment (whole) were collected and analysed for triclosan at the end of weeks 6 and 7 (Table 16.50).

As indicated in Table 16.50, triclosan was detected in the fish two weeks post-exposure although concentrations had declined by $\geq 98\%$ from levels experienced during the exposure period. Depuration rate constants at 3 and 30 $\mu\text{g/L}$ were reported by Orvos et al. (2002) as 0.142 d^{-1} and 0.141 d^{-1} , respectively. Depuration is relevant to the environment where spills, pulse emissions occur or where exposure is intermittent, such as when fish migrate.

Table 16.49 - Triclosan accumulation in tissues of zebra fish after 5 weeks exposure

Exposure (water)	Tissue analysed	Tissue triclosan Conc. ($\mu\text{g/kg}$ wet wt)	BCF
3.18 $\mu\text{g/L}$	Head/scales	4963	1561
	Fillet	2878	905
	Intestines	25158	7911
27.66 $\mu\text{g/L}$	Head/scales	49618	1794
	Fillet	53112	1920
	Intestines	298145	10779

Source: Ciba-Geigy Ltd (1991).

Table 16.50 - Depuration in zebra fish (whole) 1-2 weeks post-exposure to triclosan

Pre-depuration exposure concentration	Week	Triclosan Conc. ($\mu\text{g/kg}$ wet wt)	BCF	Percent decline from Week 5
3.18 $\mu\text{g/L}$	6	359.15	113	97%
	7	131.51	41	99%
27.66 $\mu\text{g/L}$	6	2413.16	87	95%
	7	893.54	32	98%

Source: Ciba-Geigy Ltd (1991).

Bioconcentration of triclosan in zebra fish, and potentially other fish species, is water pH-dependent, with higher uptake at low pH. With exposure to 35-50 μg triclosan/L for 250 days in waters of different pH, BCF values were as follows (Schettgen et al., 1999):

<u>pH</u>	<u>BCF</u>
9	3700
8	6350
7	8150
6	8700

After termination of exposure, triclosan was eliminated at a rate (half-life) of 16.8 to 19.9 hours. Although the uptake rate is pH dependent, the elimination rate is pH independent (Schettgen, 2000).

Field studies

A limited number of field monitoring studies from Germany, Japan, Sweden, Switzerland, the Netherlands and the United States confirm the presence of triclosan and methyl-triclosan in aquatic organisms. No environmental monitoring data were available on levels of triclosan in terrestrial plants, vertebrates or invertebrates.

Australia

No data describing triclosan or metabolites in Australian aquatic organisms were available for this assessment. A survey conducted during this assessment of major wastewater treatment utilities throughout Australia found that none monitor triclosan or metabolite levels in aquatic biota in effluent receiving environments.

Germany

Boehmer et al. (2004) retrospectively investigated the levels of triclosan and methyl-triclosan in bream (*Abramis brama*) collected from several rivers in Germany between 1994-2003, providing temporal and spatial information. Bream were caught annually after spawning between mid-July and mid-October. At least 20 fish aged 8-12 years were sampled at each site. Muscle samples (10 g) were pooled, ground and stored (-150°C) under nitrogen as a homogenized powder in the German Environmental Specimen Bank.

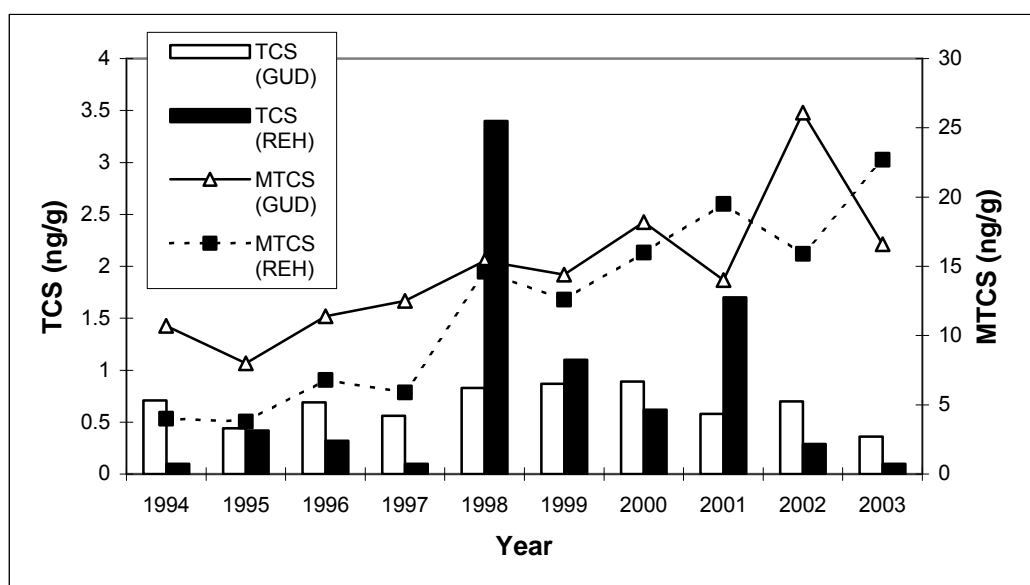
Samples were collected from:

- river Elbe near Prossen (km 13), Fehren (km 93), Barby (km 296), Cumlosen (km 470) and Blankenese (km 632);
- river Elbe tributaries of Mulde (Dessau, near the mouth) and Saale (Wettin);
- river Rhine near Weil (km 174), Iffezheim (km 334), Koblenz (km 590) and Bimmen (km 865);
- river Saar near Gudingen (km 54), and Rehlingen (km 91; Figure 16.9);
- river Danube near Ulm (km 2.593), Kelheim (km 2.404) and Jochenstein (km 2.210); and
- Lake Belau (low polluted reference site).

Fish sample extracts were analysed for methyl-triclosan and triclosan by GC/MS/MS and GC/NCI-MS (negative chemical ionization), respectively. All data are presented on a wet weight basis. The limit of quantification (LOQ) for methyl-triclosan and triclosan were 0.25 ng/g and 0.10 ng/g. Blank samples analysed showed triclosan and methyl-triclosan concentrations of <0.20 ng/g and <LOQ, respectively (effective LOQ 0.20 ng/g).

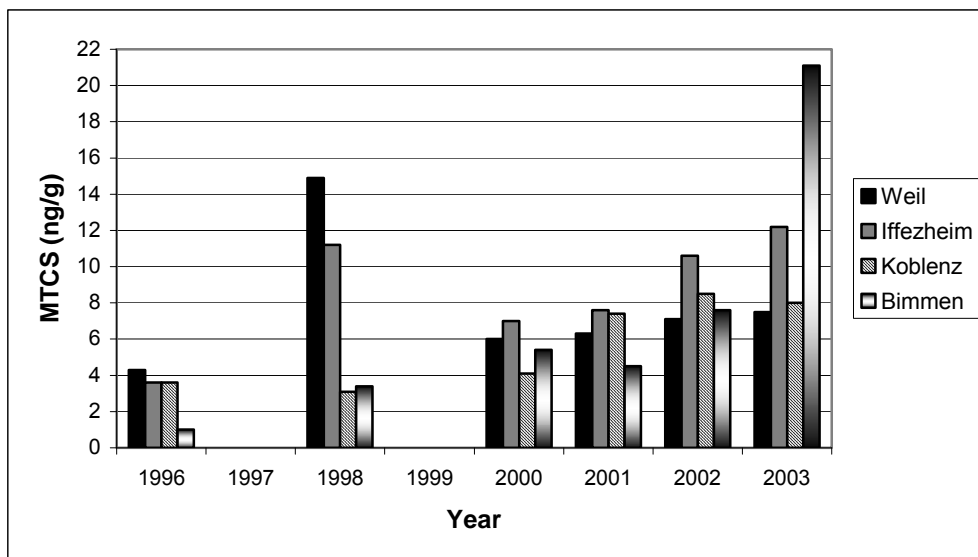
As indicated in Figure 16.10, triclosan was detected only in a few fish samples, mainly from the river Saar, while methyl-triclosan was detected in all samples from all rivers. No triclosan or methyl-triclosan was detected in the samples from Lake Belau. Relatively low concentrations of methyl-triclosan were identified in fish (2002-3 samples only) from the river Danube (i.e. 2-5 ng/g), and concentrations of triclosan were <LOQ. Triclosan concentrations in the samples from the river Saar ranged from <LOQ to 3.4 ng/g, whereas in the same locations, methyl-triclosan concentrations are much higher (range 4-26.1 ng/g). Between 1994 and 2003, concentrations of triclosan were relatively constant over time at Gudingen (0.4-0.9 ng/g) and Rehlingen (<LOQ-3.4 ng/g), reaching a peak at Rehlingen in 1998; however, methyl-triclosan in bream has increased since the mid-1990s.

Figure 16.10. Retrospective monitoring of triclosan (TCS - column) and methyl-triclosan (MTCS - line) in bream muscle in the River Saar at Gudingen (open) and Rehlingen (solid), Germany (Boehmer et al., 2004)



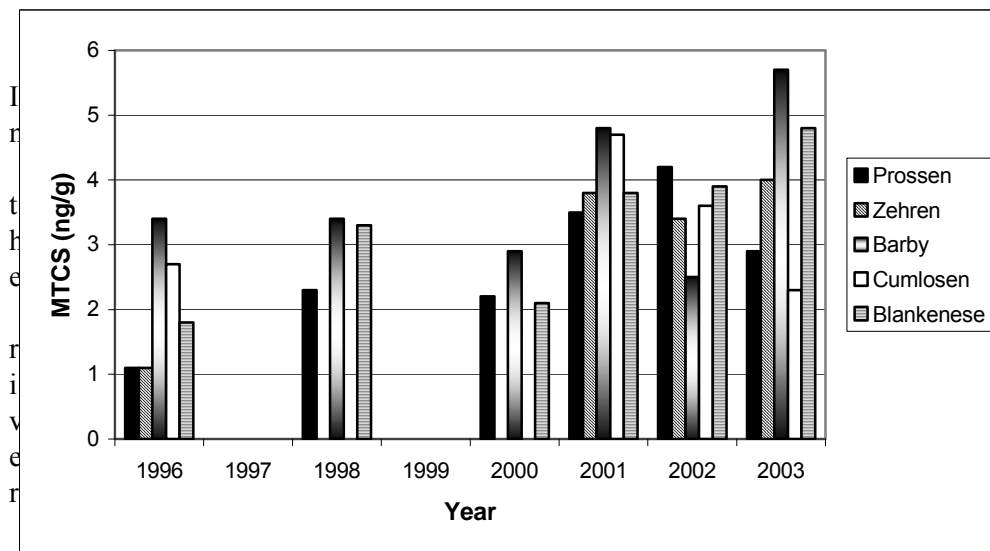
Bream muscle methyl-triclosan data from river Rhine bream (Figure 16.11) indicate concentrations in the range of 1-21.1 ng/g, similar to the river Saar (Figure 16.10). Concentrations of methyl-triclosan have increased since the 2000 sampling at all sites. Triclosan concentrations ranged up to 0.7 ng/g at Weil and Iffezheim, but were <LOQ at the other two sites.

Figure 16.11. Retrospective monitoring of methyl-triclosan (MTCS) in bream muscle in the River Rhine at 4 sites (Boehmer et al., 2004)



In the river Elbe, triclosan levels in bream were <LOQ of 0.2 ng/g, and methyl-triclosan levels were all <6 ng/g (Figure 16.12). The author reported a slight increase in methyl-triclosan over time.

Figure 16.12. Retrospective monitoring of methyl-triclosan (MTCS) in bream muscle in the River Elbe (Boehmer et al., 2004)



In the river Elbe tributaries of Saale (Wettin) and Mulde (Dessau), triclosan levels in bream muscle were relatively low (e.g. ~1 ng/g) in annual samples from 1995-2003 when compared to methyl-triclosan. Methyl-triclosan levels were comparable in these tributaries in 1995-96 (both ~2 ng/g); however, since then concentrations have increased in the Saale bream to levels of 14-33 ng/g while concentrations in the Mulde bream have increased but by a relatively lower rate (~4.5 ng/g in 2003). Levels of methyl-triclosan in the Saale tributary bream are much higher than detected in river Elbe bream (i.e. <6 ng/g) but comparable to levels detected in river Rhine and river Saar bream samples.

The research from Boehmer et al. (2004) indicates that triclosan concentrations have remained largely unchanged over time; however, methyl-triclosan concentrations in bream, which are significantly higher than triclosan, have generally increased in recent years. Methyl-triclosan concentrations in German bream are in the range of those reported from Tokyo Bay and Swiss lakes (Balmer et al., 2004; Miyazaki et al., 1984).

Sewer slimes from German sewerage systems have been collected and analysed for triclosan (Sauer et al., 1997). Triclosan was detected in slimes at a concentration up to 38800 ng/g. The slimes provide a biological indicator for the presence of contaminants in the effluent.

Japan

Methyl-triclosan was first reported in wild-caught fish collected from Tokyo Bay, Japan in 1984. Miyazaki et al. (1984) collected 10 fish (freshwater Topmouth goby *P. parva*; probably *Valenciennesa parva*) and estuarine yellowfin goby (*Acanthogobius flavimanus*) and 4 shellfish samples from 11 sampling locations on the Tama River and Tokyo Bay in September 1981.

The concentration of methyl-triclosan in *P. parva* ranged from 1 to 38 ng/g (wet weight; mean 11.6 ng/g; whole body) and 1 to 2 ng/g in *A. flavimanus*. Concentrations recorded in shellfish were: short-necked clam *Tapes philippinarum* 3 ng/g, thin-shelled surf clam *Macra veneriformis* 5 ng/g, oyster *Crassostrea gigas* 13 ng/g, and blue mussel *Mytilus edulis* 20 ng/g. It is unclear whether methylation had occurred in the fish prior to or following uptake by the fish, or whether triclosan was also accumulated. Concurrent concentrations of triclosan and methyl-triclosan in surface waters and sediments from the sampling locations were not available to derive bioconcentration factors (BCFs) or biota-sediment accumulation factors (BSAFs) for the various biota sampled (Miyazaki et al., 1984).

Sweden

Balmer et al. (2004) reported fish tissue methyl-triclosan concentration in lake trout caught in August 2000 from the isolated lake Habberstjärnen. No methyl-triclosan was detected above the detection limit of 1 ng/g lipid (<0.2 ng/g wet weight; Table 16.52).

Remberger et al. (2002, reported in Danish Environmental Protection Agency, 2003b) analysed samples of different Swedish aquatic species for triclosan, finding triclosan in 11 of 12 samples at concentrations ranging from <0.1 to 13 ng/g wet weight. Further information on sampling and analytical method was not available.

Triclosan occurrence in the aquatic environment has been examined in bile from rainbow trout (*Oncorhynchus mykiss*) held in cages in the receiving waters adjacent to a small municipal STP (Grabo), and held in tanks containing treated effluent from two large municipal STPs (Ryaverken and Henriksdal; Adolfsson-Erici et al., 2002). Wild fish were also caught and bile analysed for triclosan. Samples were analysed by GC/MS. Grabo STP (3500 person capacity; domestic wastewater) is a conventional STP with chemical precipitation and aerobic treatment but with no anaerobic digestion. Ryaverken and Henriksdal STPs include chemical precipitation, anaerobic and aerobic digestion, and Henriksdal also includes sand filtration. At Henriksdal, rainbow trout (60 per tank, 45 g each) were exposed online for 3 weeks in 70 L tanks to treated effluent before and after sand filtration

(flow rate 1 L/min). At Ryaverken, rainbow trout were exposed online for 4 weeks to treated wastewater in 17 L tanks (flow rate 0.5 L/min, 15 fish per tank, 45 g each). Trout (60 g each) were caged (20 per cage) for 3 weeks upstream and adjoining the Grabo STP discharge point and 1 and 2 km downstream from the Grabo STP outfall.

The contribution of effluent to creek flow was about 50%. Wild living fish collected and analysed included roach (*Rutilus rutilus* 2.5 km downstream of Grabo), eelpout (*Zoarces viviparus* 1 and 2 km downstream of Ryaverken) and perch (*Perca fluviatilis* 2 km downstream of Henriksdal outlet). Wild-living fish were also caught from reference sites. Fish bile results, presented in Table 16.51, highlight the occurrence of triclosan in captive and wild-living fish and a strong correlation with triclosan discharges from STPs. Caged fish had much higher triclosan bile concentrations (up to 120 µg/g) than wild living fish (≤4.4 µg/g) probably due to the much higher exposure concentrations of caged fish, and there was a distinct reduction in trout bile concentration of ~64% occurred between 0 and 2 km downstream of the Grabo STP.

Table 16.51 - Triclosan concentrations in fish bile

STP	Exposure	Fish species	Distance from discharge (km)	Triclosan conc. in bile (µg/g wet wt)
Grabo	Cages in river	Rainbow trout	Upstream	0.71
			0	47
			1	25
			2	17
	Wild-living	Roach	Reference site	<0.01
		2.5	4.4	
Ryaverken	Control	Rainbow trout	NA	<0.08
	Sewage water		Tank	35-53
	Wild-living	Eelpout	Reference site	<0.01
			1	0.63-0.90
		2.5	0.24-0.37	
Henriksdal	Control	Rainbow trout	Tank	<0.08
	Sewage water		Tank	83-120
	Sand filtered & sewage water		Tank	59-94
	Wild-living	Perch	Reference site	<0.01
		2.5	0.44	

Source: Adolfsson-Erici et al. (2002). NA – not applicable.

In general, conjugates of non-polar organics are mainly excreted via bile into the intestine. While the presence of triclosan in bile indicates exposure and bio-uptake of triclosan by fish from the effluent receiving environment, the data are of limited value in predicting bioaccumulation or concentrations in whole fish or other tissues. The data also highlight the potential for excretion of unmetabolised triclosan by fish.

Switzerland

In several Swiss lakes influenced by STP effluent, the occurrence of triclosan and/or methyl-triclosan was observed (Poiger et al., 2003; Lindstrom et al., 2002; Singer et al., 2002; Tixier et al., 2002), and methyl-triclosan levels of up to 35 ng/g (wet weight; highest at Lake Greifensee; 365 ng/g lipid basis) were detected in fish from these lakes (Balmer et al., 2004).

Balmer et al. (2004) collected and analysed fish from several lakes in Switzerland including lakes Greifensee, Pfaffikersee, Zurichsee and Thunersee. The first 3 lakes are located in the Swiss midland region while the latter is located in the pre-alpine region. All 4 lakes receive STP effluent. In addition, fish were sampled from remote lakes in Switzerland (Huttensee) and Sweden (Habberstjärnen). Fish analysed included white fish (*Coregonus* sp.), roach (*Rutilus rutilus*) from Zurichsee and Greifensee, white fish from Pfaffikersee and Thunersee, roach from Huttensee and lake trout (*Salmo trutta*) from the Swedish lake. Fish species differed due to geographical location, and sampling date varied. Fish collected were weighed and sealed in aluminium foil and plastic bags on the day of catch and kept frozen (-20°C) until analysed. All fish sampled were >2 years old. Samples of fish muscle (fillet; skin partly or all removed; 25 g) were analysed by GC/MS and some by MS/MS. The analytical data reported in Table 16.52 indicate that methyl-triclosan was detected in all fish sampled, except from the remote lakes sampled in 2000 and 2002. Concentrations were slightly higher in roach than white fish.

Concurrently, surface waters in several lakes in Switzerland (Zurichsee and Greifensee) were sampled by Balmer et al. (2004) using semi-permeable membrane devices (SPMDs; refer to Section 16.3.1) and these data were used to derive a bioconcentration factor (BCF) for methyl-triclosan. The concentration in lipids exceeded the SPMD-derived concentrations in the water of the respective lakes by a factor of up to 2.6×10^5 , and a log BCF_{lipid} of 5.0-5.4 was derived. Assuming an average fat content in the fish of 2%, the BCF for methyl-triclosan on a wet weight basis was estimated to be 2000-5200 L/kg (log BCF 3.3-3.7).

The Netherlands

The occurrence of triclosan in the bile of wild-caught fish (male bream *Abramis brama*) from three rivers in The Netherlands has been investigated in 1999 by Houtman et al. (2004). Triclosan in bile was analysed by GC/MS-MS. Bile was evaluated for estrogenic activity using the ER-CALUX method (Legler et al., 2002) and a toxicity identification and evaluation (TIE) method that uses bioassay-directed fractionation of estrogenic compounds was performed. Sample locations included lake Bergumermeer, River Drommel and Amsterdam North Sea Canal, and each represents the receiving water for industrial and STP effluent. Triclosan was detected in samples from the latter two sites; North Sea Canal (14 µg/mL of bile) and River Drommel (80 µg/mL of bile, ~80 µg/g). Triclosan, which was extracted into the non-polar fraction of bile, did not show any estrogenic activity at concentrations up to 0.1 mM indicating that this compound is not or is very weakly estrogenic relative to other polar compounds also detected in the bile during this study (e.g. 17β-estradiol).

United States

Triclosan and methyl-triclosan have been detected in the plasma of fish from a North American river at concentrations up to 10.4 ng/g and 0.0132 ng/g, respectively (Alaee et al., 2004).

In what may be the same research, Valters et al., (2005) report levels of triclosan and methyl-triclosan among other contaminants in the plasma of seven benthic and six pelagic feeding fish species from the highly contaminated Detroit River corridor. Triclosan was detected in plasma from all 13 species at 0.75 to >10 ng/g wet weight. Methyl-triclosan was also detected in the neutral fractions from all 13 fish plasma samples but was 2-4 orders of magnitude lower than triclosan in fish plasma.

Coogan and La Point (2008) have quantified snail bioaccumulation factors (BAFs) for triclosan, and methyl-triclosan at the outfall of Pecan Creek (TX, USA), the receiving stream for the city of Denton (TX, USA) STP. *Helisoma trivolvis* (Say) is ubiquitous and thrives under standard laboratory conditions, leading to its choice for this bioaccumulation study in conjunction with *Cladophora* spp. Along with providing substrate for epiphytic growth, *Cladophora* spp. provide a source of food and shelter for *H. trivolvis*. After being caged for two weeks, algae and snails were collected from the STP outfall, along with water-column samples, and analyzed by isotope dilution gas chromatography–mass spectrometry for triclosan and methyl-triclosan. Algal and snail samples were analyzed before exposure and found to be below practical quantitation limits for all antimicrobial agents. Triclosan and methyl-triclosan in water samples were at low-ppt concentrations (40–200 ng/L). Triclosan and methyl-triclosan were elevated to low-ppb concentrations (50–300 ng/g fresh wt) in caged snail samples and elevated to low-ppb concentrations (50–400 ng/g fresh wt) in caged algal samples. Resulting snail and algal BAFs were approximately three orders of magnitude (Table 16.52), which support rapid bioaccumulation among algae and adult caged snails at this receiving stream outfall.

Table 16.52 – Bioaccumulation triclosan in algae and snails

Contaminant	Medium	Results (ppb)	Standard error	BAF
Triclosan	Water	0.112	4.00×10^{-3}	
	Snails	58.7	3.39	500
	Algae	162	17.6	1,400
Methyl-triclosan	Water	0.041	9.00×10^{-4}	
	Snails	49.8	2.49	1,200
	Algae	50.4	5.21	1,200

Summary

Both triclosan and methyl-triclosan are considered to have a high to very high bioconcentrating potential (i.e. BCF 1000 to >5000; Mensink et al., 1995), and both of these analytes have been detected in caged and wild-caught fish and shellfish in international monitoring studies.

Table 16.53 - Methyl-triclosan (MTCS) concentrations reported in fish muscle, Switzerland

Lake	Fish sp.	Catch date	Wt (g)	Fat (%)	MTCS (ng/g lipid)
Zurichsee	White fish	14/11/2001	86	7.5	55
	“	“	133	6.8	38
	“	“	237	5.5	47
	“	18/1/2002	270	2.6	48
	“	“	275	0.8	32
	<i>Average</i>				<i>44±9.0</i>
	Roach	18/1/2002	272	3.1	46
	“	“	298	5.2	40
	“	5/6/2002	136	1.1	62
	“	15/8/2002	145	1.6	56
	“	338	1.3	46	
	<i>Average</i>				<i>50±8.8</i>
Greifensee	White fish	30/1/2002	470	0.9	165
	“	“	453	1.1	211
	<i>Average</i>				<i>188±32.5</i>
	Roach	30/1/2002	373	1.6	307
	“	“	366	0.4	365
	“	9/8/2002	338	0.3	200
	“	192	0.8	300	
	<i>Average</i>				<i>293±68.5</i>
Thundersee	White fish	22/1/2002	177	7.6	5.5
	“	“	170	8.6	4.2
	“	“	170	1.1	6.4
	<i>Average</i>				<i>5.4±1.1</i>
Pfaffikersee	White fish	1/9/2002	651	2.8	43
	“	“	561	4.8	56
	<i>Average</i>				<i>49.5±9.2</i>
Huttensee	Roach	8/9/2002	268	0.2	<5
	“	“	412	0.2	<2
Habberstjärnen (Sweden)	Lake trout	8/2000	---	1.4	<1

Source: Balmer et al. (2004). All data are presented in ng/g on a lipid basis.

16.4.3 Soils

No environmental monitoring data were available on concentrations of triclosan or its products in soils in Australia.

In soils, subsurface infiltration and migration of triclosan from surface application is unlikely to occur due to its adsorptive properties; however, the extent of soil contamination would depend on the quantity and duration of release, the soil type and environment factors.

Sweden

Sampling results reported by Remberger et al. (2002) identified triclosan in soils at concentrations from <3 to 15 µg/kg, and triclosan was detected in 4 of 7 surface soil samples.

16.4.4 Bioaccumulation in soil biota and higher organisms

No laboratory bioaccumulation studies or field monitoring data were available on the concentrations of triclosan or products in soil organisms (animals, plants, fungi) that may be exposed through contact with land-applied STP sludge or biosolids or irrigated STP effluent.

16.4.5 Landfill leachate and groundwater

No environmental monitoring data were available on concentrations of triclosan or its products in landfill leachate or groundwater in Australia.

16.4.6 Atmosphere

Very limited environmental monitoring data were available on concentrations of triclosan or its products in the atmosphere.

Sweden

Air monitoring data reported by Remberger et al. (2002) identified triclosan in urban air and deposition. Urban air concentrations ranged from <0.003-0.17 ng/m³, and triclosan was detected in 8 of 13 samples. Triclosan concentrations in deposition ranged from 0.38-20 ng/m²/d, with detection in 4 or 6 samples (detection limit 0.2 ng/m²/d).

16.4.7 Summary of monitoring studies

Review of Australian and international environmental monitoring data from several developed countries that use triclosan (presented above) indicates triclosan and products in various environmental media within the concentration ranges described in Table 16.54.

In the environment, triclosan and its products are potentially subject to transformation processes and the concentration detected will vary temporally and spatially. The data reported in Table 16.54 provide an indication of environmental media concentrations only, and the original data should be reviewed to obtain a greater appreciation of the circumstances under which those data were collected.

Table 16.54 - Overall summary of reported concentration ranges of triclosan and products in various environmental media

Media & Units	Triclosan	Methyl-triclosan	Chlorinated derivatives			
			II	III	IV	DCDD
STP influent (ng/L)	<100-562000	≤4	≤620	≤250	≤310	20-3700
STP effluent (ng/L)						
Primary	100-269000	---	≤340	≤160	≤160	4-400
Secondary	10-2700	1-12	≤290	≤70	≤70	---
Tertiary/final	28-72	---	≤10	≤10	≤10	---
STP sludge (ng/g dry wt)						
Primary	3400-17900	50-260	≤180	≤220	≤420	---
Secondary	580-4200	310-1030 ^(AS)	≤60	≤40	≤90 ^(AS)	---
Digested ^(AN)	5400-28200	≤450 ^(TF)	≤90	≤50	≤80 ^(TF)	---
Digested ^(AER)	530-1500	130 ^(P/AN)	≤110 ^(P/AN)	≤100 ^(P/AN)	≤90 ^(P/AN)	---
		130-170 ^(TF)	<40 ^(P&TF)	<40 ^(P&TF)	<40 ^(P&TF)	---
Aquatic environments (ng/L)						
Freshwaters	≤2300	<1-2	---	---	---	---
Marine	300000*					
	≤160	---	---	---	---	---
Sediments (ng/g dry wt)	0.3-160	<0.5-450	---	---	---	---
	100000*					
Biota						
Fish (bile) (µg/g wet wt)	≤80 (wild) ≤47 (caged) ≤120 (tank)		---	---	---	---
Fish (whole) (ng/g wet wt)	---	≤38	---	---	---	---
Fish Muscle (ng/g wet wt)	≤3.4 (wild)	≤35.5	---	---	---	---
Fish lipid (ng/g lipid)	---	≤365	---	---	---	---
Fish (ng/g plasma)	10.4	0.0132	---	---	---	---
Shellfish (ng/g wet wt)	---	≤20	---	---	---	---
Terrestrial environments						
Soils	---	---	---	---	---	---

16.5 Predicted environmental concentrations in Australia

This section provides estimates of triclosan and products in municipal wastewater and various environmental media in Australia based on mass balance modelling. These estimates have been compared to triclosan and product concentrations in various environmental media have been reported from Australia and similarly developed countries (e.g. Canada, Denmark, France, Germany, Greece, Italy, Japan, Norway, Spain, Sweden, Switzerland, USA).

Triclosan may be expected to occur at relatively higher concentrations in the environment where materials containing triclosan are spilled, leaked or deposited including STP effluent and sludge receiving environments and reclaim areas, solid waste landfills and industrial facilities that incorporate triclosan into manufactured products.

It is likely that most of the triclosan used in Australia is sent to sewer for disposal after use, with the remainder sent to landfill for disposal. Ciba Specialty Chemicals (1998a) suggested a ratio of 96:4 for the proportion of triclosan discharged to sewer and sent to landfill, and this ratio has been adopted for this assessment.

Based on use data presented in Section 3 (Table 3.6), ~26.0 tpa of triclosan is estimated to be discharged to sewer after use of products containing triclosan (based on the average import volume of 26.8 tonnes/annum for the period 2001-2005 presented in Table 3.3). This comprises ~97% of the triclosan introduction level in Australia. The estimate assumes all personal care products, therapeutic and ag/vet products are discharged to sewer, as well as 1% of triclosan used in textiles and plastics (via leaching from products or from aqueous waste generated during the manufacture of products).

Triclosan occurs in the Australian aquatic environment, given that triclosan has been detected in the Australian sewerage and river systems. It is difficult to determine the source of the triclosan as multiple sources may be involved. However, this is of limited consequence in terms of cumulative environmental risk. From an administrative perspective, as indicated in Table 3.6, ~16 tonnes/annum (~59%) of the ~27 tonnes/annum of triclosan introduced into Australia is administered under the jurisdiction of NICNAS. Most of this triclosan is discharged in wastewater to sewer after use, with a fraction either sent to landfill or incinerated with the products in which triclosan is contained. The majority of the remaining quantity introduced into Australia (~11 tonnes/annum or ~41%) in products designated for therapeutic uses, administered by the Therapeutic Goods Administration, is expected to follow a similar use and disposal pattern to the triclosan in products administered under NICNAS. The calculations in the following sections therefore cover the total amount of triclosan imported into Australia.

16.5.1 Untreated wastewater triclosan

International monitoring data, presented in Table 16.54, provides an indication of the triclosan and product concentration ranges found in untreated wastewaters, which are influents to STPs. Data from several sources indicate influent triclosan concentrations may vary widely (range ND-562000 ng/L).

Australian monitoring data from 1995 show high-flow primary treated effluent concentrations up to 740 ng triclosan/L. Recent data available for five STPs have

found triclosan influent concentrations ranging from 573 ng/L to 845 ng/L (Ying and Kookana, 2007). No Australian data are available for triclosan degradation product concentrations in wastewater.

Estimation of the national average triclosan concentration in wastewater has been undertaken using a mass balance model (refer Table 16.55). Model input parameters include:

- Proportion of the total quantity of triclosan used in Australia that is disposed of to sewer, which is estimated at ~97% of annual import quantity; and
- Projected annual wastewater generation (refer Appendix A).

Based on the analysis presented in Table 16.55, untreated municipal wastewater in Australia in 2001-05 may potentially have contained an average triclosan concentration in the range of ~14500-17400 ng/L. No degradation within the sewerage system prior to receipt at STPs (or equivalent) is assumed in this estimation, and spatial and temporal variability about this average range is expected due to geographical changes in use pattern and environmental conditions. The derived range for Australian conditions is within the range reported from other countries. Environmental discharges of untreated wastewater, such from sewer overflow points or pipeline leaks, may potentially contain triclosan within this concentration range. However, the measured concentrations of Ying and Kookana (2007) only relate only to 4 STPs in SA and one in WA; three of which were small rural STPs. These are likely to differ from concentrations in the extremely large STPs of Sydney and Melbourne.

Table 16.55 - Estimated Australian average triclosan concentration in influents (2001-2005 period)

Parameter	Value	Comment
Triclosan import quantity	~26.8 tonnes/annum	Average of 2001-2005 import volumes Range 21-30 tonnes/annum
Proportion of triclosan to sewer	96%-97%	
Quantity to sewer	26.0 tonnes/annum	
Wastewater generation (refer Section 8.2.2)	1496.5 Gallons/annum 1790.5 Gallons/annum	Environment Australia (2003) ASTE (2004) and Dillon (2000)
Estimated average wastewater concentration ^a	17400 ng/L 14500 ng/L	Environment Australia (2003) ASTE (2004) and Dillon (2000)
Highest Measured Australian Concentration	845 ng/L	Ying and Kookana (2007)

a. Concentration = (introduced level × proportion to sewer) ÷ wastewater volume.

16.5.2 Treated effluent triclosan

As indicated above, the limited amount of municipal STP effluent monitoring data from Australia in 1995-1996 detected triclosan concentrations of <100-740 ng/L. In more extensive sampling Ying and Kookana (2007) have recently reported triclosan effluent concentrations ranging from 23 to 434 ng/L from 19 STPs from around Australia. As noted, these results are unlikely to be representative of all Australian conditions, such as NSW STPs or larger STPs, as these were not sampled.

In general, methods available for estimating effluent triclosan concentration include:

- Extrapolation from international studies; and
- Mass-balance modelling without and with triclosan removal based on physico-chemical parameters of triclosan and/or chemical-specific removal rates for different levels of treatment found at various types of STPs.

Several studies demonstrate that triclosan removal efficiency by STPs depends on the type and level of treatment provided. Australian STPs provide various levels of wastewater treatment. Consequently, predicted effluent triclosan concentrations have been developed for the broad categories of primary and secondary levels of treatment.

International data from other developed countries are available and have been used for comparative purposes only. The latter approach provides greater accuracy for Australian conditions and has been used to estimate effluent triclosan concentrations.

International data on effluent triclosan concentrations

International monitoring data, presented in Table 16.54 also provides an indication of triclosan concentrations in treated wastewater. Various sources of information have reported effluent triclosan in the following concentration ranges:

- Primary effluent 100-269000 ng/L; and
- Secondary/final effluent 10-2700 ng/L.

Mass-balance modelling

More detailed estimation of effluent triclosan has been undertaken using a mass balance STP model with input parameters including estimated wastewater triclosan concentration (refer to above) and expected removal rates for different levels of treatment (e.g. primary, secondary, tertiary).

Treatment-specific wastewater triclosan removal rates

In general, the level of treatment provided will affect the level of triclosan removal from wastewater (i.e. effluent triclosan concentration). In Australia, wastewater treatment varies among STPs (and within based on operating conditions) prior to environmental release or reclamation and re-use.

Several approaches to determining triclosan removal rates are available including:

- Estimation with an STP model; and

- Direct STP monitoring of triclosan removal rates.

Modelling of STP removal rate is limited by model availability and only one model representing an activated sludge treatment process (i.e. SimpleTreat) was available.

STP Model: SimpleTreat

Chemical removal rate during STP treatment may be estimated using the SimpleTreat 3.0 model (Struijs, 1996; EC, 2003b). This model is a multi-compartment box model, calculating steady-state concentrations in an averaged sized STP, consisting of a primary settler, an aeration tank and a liquid-solid separator. The model assumes a medium sludge loading rate of 0.15 kg BOD/kg dry weight/day, a hydraulic retention time (HRT) of 7.1 hours and a sludge retention time (SRT) of 9.2 days. Model input parameters consist of the partition co-efficient (i.e. $\log K_{ow} = 5$ at 20°C), Henry's Law constant ($H = 1.4 \times 10^{-2} \text{ Pa}\cdot\text{m}^3\cdot\text{mol}^{-1}$, based on vapour pressure of $4 \times 10^{-6} \text{ mmHg}$ ($5.3 \times 10^{-4} \text{ Pa}$ at 20°C, $\log H$ of -1.8), and the results of biodegradation tests as input parameters.

The SimpleTreat model is reliant on the results of ready or inherent biodegradation tests obtained using standard OECD/EU methods. There is no evidence to indicate that triclosan is readily biodegradable; however, the ready biodegradability test was conducted at test concentrations that were likely to have inhibited the sludge microorganisms. The data from several non-standard tests at more realistic concentrations indicates that triclosan will undergo aerobic biodegradation during, for example, the activated sludge treatment process. Given this uncertainty regarding biodegradation potential, the SimpleTreat model has been used assuming no biodegradation and inherent biodegradation (refer Table 16.56).

Table 16.56 - SimpleTreat activated sludge model output

Partitioning	No biodegradability ^a	Inherently Biodegradable ^a
Air	0%	0%
Effluent	39%	28%
Sludge	61%	56%
Biodegraded	0%	17%
Total Removal	61%	72%

a. Values for triclosan assume $\log K_{ow}$ of 5 and $\log H$ of -2.

As indicated in Table 16.56, the two scenarios regarding biodegradation have a minor effect on the effluent triclosan concentration, with 28%-39% of influent triclosan remaining in treated effluent. Based on the above estimation of untreated wastewater triclosan concentration, an average effluent triclosan concentration in the range of 4060-6770 ng/L for the period 2001-2005, has been derived (Table 16.57).

Table 16.57 - Predicted STP effluent triclosan concentration using the SimpleTreat model and the estimated Australian triclosan introduction quantity

Parameter	Environment Australia (2003) STP model		ASTE (2004) and Dillon (2000) model	
	Estimated influent wastewater concentration (ng/L)	17400		14500
Fraction in effluent based on SimpleTreat model (%)	28 ^b	39 ^a	28 ^b	39 ^a
Estimated Effluent triclosan concentration (ng/L) *	4860	6770	4060	5660

* The SimpleTreat model output refers only to an activated sludge treatment process. a. = Assumes no biodegradation. b. = Assumes inherently biodegradable.

Direct STP monitoring of triclosan removal rates

Several studies have reported triclosan removal rates for broadly defined levels of treatment (i.e. primary, secondary, tertiary). Whereas the SimpleTreat model provides an analysis of the cause of attenuation, the method of removal is non-specific for monitoring data (e.g. partitioning to sludge, biodegradation, etc). These removal efficiency rates provide a general guide for Australian conditions only as the data available represents a relatively small sample, and in practice a much broader range of treatment plant processes are utilised in Australia for which no triclosan treatment efficiency data are available. The monitoring data available (refer Section 16.3) report triclosan removal rates for several STP processes as follows:

- Primary treatment: 2% to 96% (mostly <58%)
- Secondary (trickling filter): 58% to 96%
- Secondary (activated sludge): 55% to 99% (mostly >90%)
- Tertiary 87% to potentially ≥99%

Table 16.58 provides an estimation of the triclosan content of STP effluent after several levels of treatment using the range of internationally-reported triclosan removal rates obtained through STP monitoring programs.

As indicated in Table 16.57 and Table 16.58, after the activated sludge process the various models used predict an effluent triclosan concentration in the range of 174-7300 ng/L, depending largely on removal efficiency. The SimpleTreat model estimates a removal rate (61%-72%) that is within the range reported from monitoring studies (55%-99%); however, the majority of the monitoring studies available indicate a secondary-treatment removal rate for triclosan of >90%, suggesting that the SimpleTreat model may overestimate of the triclosan remaining in the effluent under most conditions. This indicates that in most instances, the actual effluent concentration is more likely to be in the lower end of the range scale. Several continuous activated sludge (CAS) studies indicate triclosan removal from effluent in the range of 97%-99% (~94% after shock loading); however, it is

difficult to extrapolate these ideal laboratory-scale test conditions to STP conditions.

Table 16.58 - Predicted STP effluent triclosan concentration using reported triclosan removal rates and the estimated Australian triclosan introduction quantity

Level of Treatment and reported removal rate	Environment Australia (2003) STP model (ng/L)	ASTE (2004) and Dillon (2000) model (ng/L)
Estimated wastewater triclosan concentration (ng/L)	17400	14500
Primary Treatment 2-96%	695-17000	581-1420
Secondary Treatment		
Trickling Filter 58%-96%	695-7300	581-6100
Activated Sludge 55%*-99%	174-7820	145-6530
Tertiary treatment 87%-≥99%	≤174-2260	≤145-1890

* The slightly lower value for activated sludge treatment relative to trickling filter treatment is probably an artefact of the sample of studies available, as in most instances the activated sludge process is reported to provide a greater level of treatment and removal of triclosan than the trickling filter process.

Comparison with Australian data

The range of 4060-6770 ng/L for the period 2001-2005 derived in Table 16.57 is about an order of magnitude above the range (23-740 ng/L) measured in over 20 Australian STPs from 1995-2005. If the SimpleTreat removal assumptions are applied to the influent concentration range of 573-845 ng/L from 5 local STPs, the predicted 160-330 ng/L still overestimates the effluent range of 60.5-159 ng/L found. Therefore SimpleTreat does not appear to model these 5 STP plants well.

Likewise the ranges predicted in Table 16.58 for secondary and tertiary treatment seem to overestimate triclosan levels when compared with the range of 23-434 ng/L found in 19 Australian STPs, although it is again noted that these 19 STPs do not include larger STPs and may not be representative of conditions across Australia. This also appears to be the case for the predicted range (581-17000 ng/L) for primary treatment, compared with <100-740 ng/L for the 3 known local STPs tested with only this level of treatment.

16.5.3 Sludge and biosolids from municipal STPs

The level of triclosan in Australian biosolids has been quantified in two reports. Luke (1999) reported triclosan at 50 and 3400 ng/g in the two samples, while Ying and Kookana (2007) found triclosan concentrations in the 17 biosolid samples (all except one anaerobically digested) ranging from 90 to 16790 ng/g on a dry weight basis.

In this section sludge triclosan concentrations have been estimated using the procedures described above for effluent triclosan.

International data on sludge triclosan concentrations

International monitoring data, presented in Table 16.54, indicate STP sludge triclosan concentrations in the following concentration ranges (dry wt.):

- Primary sludge 3400-17900 ng/g;
- Secondary/final sludge 580-4200 ng/g;
- Digested (anaerobic) 5400-28200 ng/g; and
- Digested (aerobic) 530-1500 ng/g.

The data available indicates that anaerobic digestion of STP sludge has the effect of concentrating the triclosan. While the organic matter component of the sludge undergoes degradation, the triclosan is relatively resilient under these conditions.

Mass-balance modelling

As undertaken above for effluent, a more detailed estimation of the sludge triclosan content has been undertaken using a mass balance approach with input parameters including estimated wastewater triclosan concentration (refer to above) and expected removal rates for different levels of wastewater treatment (e.g. primary, secondary).

STP Model: SimpleTreat

Using the SimpleTreat model, between 55%-61% of the influent quantity of triclosan is estimated to partition to suspended solids and accumulate in sludge (i.e. ~13.2-14.6 tonnes/annum; Table 16.59). On this basis, the estimated average activated sludge triclosan concentration in the range of 89000-121000 ng/g (dry weight) has been derived using this approach. This assumes 0.1 tonnes of sludge (dry weight) is generated per mega litre of wastewater treated (Environment Australia, 2003).

Based on the information available, aerobic digester conditions of this sludge may result in the degradation of the triclosan to a lower concentration; however, under anaerobic sludge digester conditions, the triclosan concentration may increase as organic material in the matrix is degraded. In addition, some triclosan would be expected to break down and become mineralised.

Direct STP monitoring of sludge triclosan partitioning rate

As described in Table 16.58, several studies have investigated the overall triclosan removal rate from wastewater; however, in most instances, the partitioning and degradation processes involved have not been investigated and the removal may be due to one of several processes (e.g. biodegradation, sedimentation, photolysis). Consequently, use of these removal rates to estimate partitioning to sludge alone will likely over-estimate the triclosan concentration in sludge.

The partitioning of triclosan to STP sludges has been investigated at the laboratory-scale using continuous activated sludge (CAS) units. Although sludge retention rates for triclosan of 2%-12.5% were observed, which is significantly lower than estimated using SimpleTreat, it is difficult to extrapolate these rates obtained under ideal laboratory conditions to STP conditions. However, using these removal rates, the estimated activated sludge triclosan concentration (range ~3000-25000 ng/g)

more closely approximates actual STP monitoring results reported in several international studies (e.g. 580-4200 ng/g).

Table 16.59 - Predicted STP sludge triclosan concentration using the SimpleTreat model and the estimated Australian triclosan introduction quantity

Parameter	Environment Australia (2003) STP model		ASTE (2004) and Dillon (2000) model	
	Estimated quantity of triclosan to sewer (kg/y)	26000		26000
Estimated quantity of triclosan to sewer (mg/y)	2.60×10^{10}		2.60×10^{10}	
Estimated fraction in sludge based on SimpleTreat model (%)	55% ^a	61% ^b	55% ^a	61% ^b
Estimated quantity of triclosan in sludge (mg/y)	1.43×10^{10}	1.59×10^{10}	1.43×10^{10}	1.59×10^{10}
Estimated wastewater generation rate (ML/y)	1.50×10^6		1.79×10^6	
Sludge generation per year (kg) ^c	1.50×10^8	1.50×10^8	1.79×10^8	1.79×10^8
Estimated sludge triclosan conc. (mg/kg dry wt)	96.5	106	79.9	88.6
Estimated sludge triclosan conc. (ng/g dry wt)	96500	106000	79900	88600

Notes: The SimpleTreat model output refers only to an activated sludge treatment process. a. = Assumes no biodegradation. b. = Assumes inherently biodegradable. c. = Based on a sludge generation rate of 100 kg/ML of wastewater.

Comparison with Australian data

Again the range of 77900-106000 ng/g dry weight for sludge predicted using the SimpleTreat model (Table 16.59) is an order of magnitude above the range of 90-16790 ng/g dry weight found for 17 treated Australian biosolid samples. However, the latter is much closer to the international data range of 530-17900 ng/g, and that predicted from sludge partitioning of ~3000-25000 ng/g, particularly the upper end.

16.5.4 Effluent and sludge from septic and household systems

No field monitoring data or information on the fate of triclosan or its products in domestic on-site wastewater treatment systems was available for this assessment. Septic systems provide treatment of wastewater within a bioreaction chamber (solids collection to form primary sludge) under anaerobic conditions followed by treatment in a drain field (e.g. soil adsorption trench, leaching trench, seepage pit)

or communal lagoon. In a few instances, septic tank effluent is contained in a holding tank that is pumped out and transported to sewer.

Although no data are available on triclosan concentrations in septic tank sludge or drain field effluent, the influent triclosan concentration is likely to be comparable to untreated municipal wastewater sourced from domestic households (i.e. 14500-17400 ng/L) as calculated above (Table 16.58). Due to the limited anaerobic biodegradation of triclosan, effluent and sludge triclosan concentrations may approximate primary treated effluent and primary sludge, respectively (e.g. 581-17000 µg/L for effluent see Table 16.58 and 79900-106000 ng/g for sludge, see Table 16.59). However, anaerobic digestion of the sludge may potentially increase the triclosan concentration in the sludge.

16.5.5 Aquatic environments

Surface waters

Australian data

Ying and Kookana (2007) have measured surface water concentrations of 14-75 ng/L from near the outlet of 5 STPs in Queensland, or within 200 m upstream or downstream of the rivers into which they discharged. These compare with the effluent sample range of 45-222 ng/L measured at the same time, suggesting about a 1:4 dilution effect, and are at the lower end of the international range (below).

International data

Several international studies report triclosan concentrations in surface waters as follows:

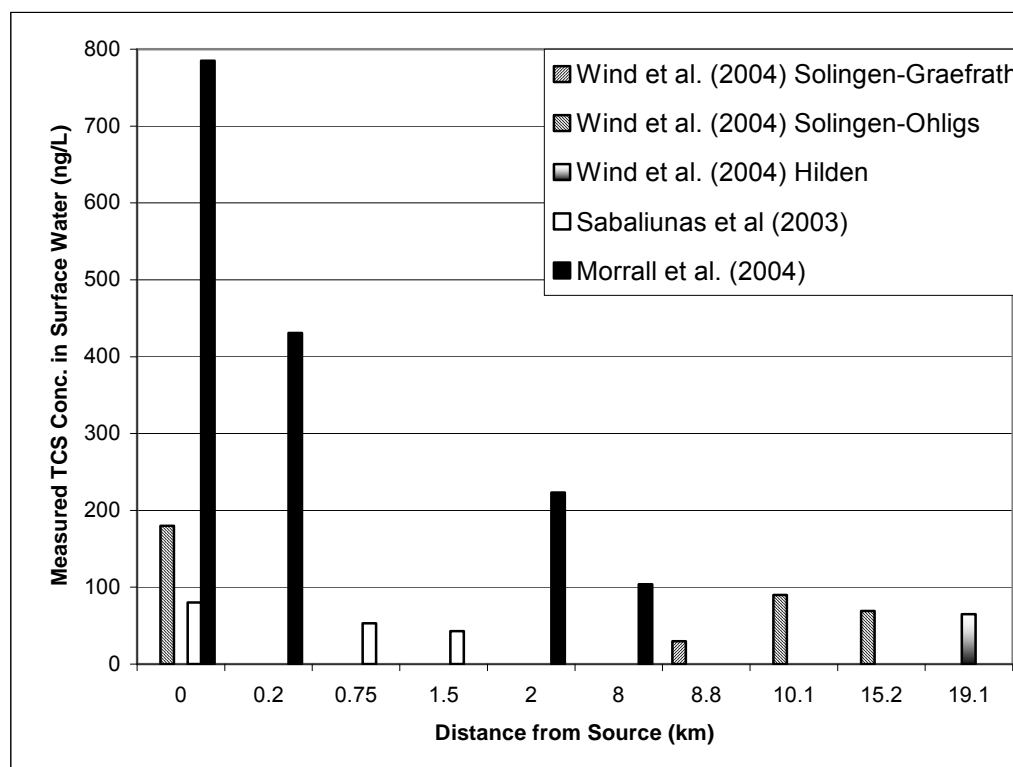
- Freshwaters ≤2300 ng/L (300000 ng/L near an industrial source); and
- Marine ≤1600 ng/L.

Removal of triclosan from surface waters

Estimation of a predicted environmental concentration (PEC) for triclosan in surface waters will vary according to several factors including the source load, distance from source, climate and receiving environment conditions. Several studies indicate that triclosan, initially discharged in the water column, will partition to suspended matter and accumulate in sediments and into biota, and will undergo degradation over time due to biotic and abiotic processes to form methylated (e.g. methyl-triclosan) and chlorinated derivatives, and oxides of carbon and water.

Figure 16.13, which contains stream monitoring data from several studies, illustrates the removal of triclosan from surface water with distance downstream of STP sources of triclosan potentially due to abiotic (sedimentation, photolysis, dilution) and biotic (bioaccumulation, biodegradation) processes. Nevertheless, triclosan may be present at concentrations >50 ng/L approximately 20 km downstream from a source.

Figure 16.13. Selected stream monitoring data and triclosan (TCS) concentrations with distance from STP source



Mass-balance modelling

Surface water triclosan PECs have been estimated using the procedures described above for STP effluent and sludge triclosan (refer Table 16.60).

Table 16.60 - Predicted surface water triclosan concentrations using SimpleTreat, reported triclosan removal rates, various levels of wastewater treatment and the estimated Australian triclosan introduction quantity

Level of Treatment	Removal rate (%)*	PEC Freshwater (triclosan, ng/L)	PEC Marine (triclosan, ng/L)
Untreated wastewater	---	14500-17400	1450 - 1740
Primary Treatment	2-96	581-17000	58 - 1700
Secondary Treatment			
Trickling Filter	58-96	581-7300	581 - 730
Activated Sludge	55-99	145-7820	14.5 - 782
Activated sludge (SimpleTreat)	61-72	4070-6780	407 - 678
Tertiary treatment	87-≥99	≤145-2260	≤14.5 - 226

* Removal rate obtained from literature sources. Freshwater and marine PEC values obtained by dividing the estimated effluent concentration by receiving environment dilution factors of 1 and 10, respectively.

In accordance with the STP model developed by Environment Australia (2003), dilution factors of 1 and 10 will apply to freshwater and marine receiving environments for STP effluent discharges. The PEC values in Table 16.60 represent estimated concentrations within the 'mixing zone' of the receiving environment. Although STP effluent can in some instances form 100% of stream flow (e.g. dry weather flows), a reduction in triclosan concentration in the surface water is expected with distance from the source due to natural attenuation processes (refer Figure 16.13). Several studies have estimated stream removal rates from surface water (e.g. 0.144 h^{-1} or $t_{1/2}$ of 4.8 h Wind et al., 2004; 0.0013 h^{-1} Singer et al., 2002; 0.06 h^{-1} Morrall et al., 2004).

More accurate estimation of estimated triclosan concentrations in surface water in Australia, such as by using detailed catchment-based computer modelling methods, is not possible. However, applying the dilution factors of 1 and 10 to the available range of effluent concentrations measured in Australia by Ying and Kookana (2007) and by Ciba Specialty Chemicals (2003a) gives PECs ranges for freshwater of 23-740 ng/L, and for marine waters of 2.3-74 ng/L. While these freshwater PECs based on measured effluent concentrations are greater than levels measured in surface waters of five rivers in Queensland near the STP outlet (14-75 ng/L, see above), it is unlikely that the five surface water samples cover the full range of Australian conditions.

Sediments

There are no data available on the occurrence of triclosan in sediments in the Australian environment.

International data

The limited data available report sediment triclosan concentrations (dry wt) as follows:

- Freshwaters $\leq 160 \text{ ng/g}$ ($\sim 100000 \text{ ng/g}$ near an industrial source); and
- Marine $\leq 97 \text{ ng/g}$.

Methyl-triclosan has been detected in river sediment samples at a concentration range of $\leq 450 \text{ ng/g}$ dry wt.

The concentration in sediment has been estimated using equilibrium partitioning methodology as described in the EU TGD (EC, 2003b) with relevant default values taken from the Mackay Level III model (publicly available from <http://www.trentu.ca/cemc/models/models.html>). These default values include a fraction of organic carbon in suspended matter ($F_{oc,susp}$) of 0.2, sediment composition of 20% solids and 80% water, a bulk density of solids of 2400 kg/m^3 and therefore, a density of sediments of 1280 kg/m^3 .

The first step to estimating the $PEC_{sediment}$ is to determine the partition coefficient for solid-water in suspended matter. This is the $F_{oc,susp} \times K_{oc}$. A K_{oc} value of 47454 L/Kg ($\log K_{oc} = 4.68$) has been used based on the measured data described in Section 16.1.4. [Note, this study measured adsorption of ^{14}C -triclosan to suspended solids (49.6 mg/L) obtained from deactivated sewage sludge with a total organic carbon (TOC) content of 45.5% and therefore may not be a good representation of soil K_{oc} . However, there were no measured soil K_{oc} results available. EPI estimates a $\log K_{oc}$ value of 4.265]. A $K_{p,susp} = 9490 \text{ L/kg}$ is

derived. This value represents the concentration of the substance sorbed to solids (mg/kg) divided by the concentration dissolved in porewater (mg/L).

The next step is to convert this value to the whole sediment compartment. In sediment, solids are assumed to account for 20% of the sediment compartment. Therefore, the sediment whole compartment Kp must be converted to account for the make up of the sediment (80% water, density 1000 kg/m³; and 20% solids, density 2400 kg/m³). The whole compartment partition coefficient is the concentration in solids (mg/m³) divided by the concentration in water (mg/m³).

Therefore, the K_{susp-water} is $0.8 + 0.2 \times \frac{K_{\text{susp}}}{1000} \times 2400 = 4556.4 \text{ m}^3/\text{m}^3$

The final step is to convert the PEC_{water} to a PEC_{sediment} based on the K_{susp-water} partition coefficient, and the density of the sediment compartment (1280 kg/m³). This is achieved as follows:

$$\text{PEC}_{\text{sediment}} = \frac{K_{\text{susp-water}}}{\text{Density}_{\text{sed}}} \times 1000 \times \text{PEC}_{\text{water}}$$

The results for predicted sediment concentrations using this approach are as presented in Table 16.61.

It should be noted that highly adsorptive substances might not be considered adequately with this approach, as they are often not in equilibrium distribution between water and suspended matter due to their cohesion to the suspended matter. However, they may be desorbed after ingestion by benthic organisms. In the case when release to the surface water predominantly occurs as particles, this calculation may underestimate the sediment concentration (EC, 2003b). This will be considered in further evaluation below when comparing the PEC with monitoring data for existing chemicals, and if necessary, in the risk characterization.

Table 16.61 - Predicted average sediment triclosan concentrations based on Equilibrium Partitioning

Level of Treatment prior to discharge	PEC _{river sediment} (mg/kg, wet weight)	PEC _{marine sediment} (mg/kg, wet weight)
Untreated wastewater	51.7 - 61.8	5.17 - 6.18
Primary Treatment	2.07 - 60.5	0.207 - 6.06
Trickling Filter	2.07 - 26	0.207 - 2.6
Activated Sludge	0.517 - 27.8	0.0517 - 2.78
Activated sludge (SimpleTreat)	14.5 - 24.1	1.45 - 2.41
Tertiary treatment	≤0.517 - 8.04	0.0517 - 0.804

Aquatic organisms

BCF-based

With log Pow values of 4.8 and 5.2, respectively, both triclosan and methyltriclosan have a high potential to bioaccumulate in aquatic organisms. Bioaccumulation potential is also evident from laboratory-scale bioconcentration factor (BCF) studies and field monitoring studies. With an exposure concentration of ~3000 ng/L, BCF values (whole body) for triclosan have been estimated in the

range of 5337 (whole body) and 905 (fillet). The bioconcentration of triclosan is dependent on water pH (greater accumulation at lower pH) and exposure concentration.

Using these BCF values, PEC values for fish have been estimated using the worst case PEC values calculated for freshwater and marine environments (refer Table 16.62). As a comparison, in laboratory-scale BCF tests, whole fish triclosan concentrations of up to 16492 µg/kg (whole fish wet wt) and 2878 µg/kg (muscle wet wt) have been measured after 3 weeks exposure to ~3000 ng/L under laboratory test conditions.

Table 16.62 - Predicted maximum triclosan concentrations in freshwater and marine fish (whole body and fillet) calculated using BCF values of 5000 (whole body) and 900 (muscle) and estimated surface water PEC values

Level of Treatment prior to discharge	PEC freshwater fish (triclosan, µg/kg wet wt)		PEC marine fish (triclosan, µg/kg wet wt)	
	Whole Fish	Fillet	Whole Fish	Fillet
Untreated wastewater	86873	15637	8687	1564
Primary Treatment	85000	15300	8500	1530
Trickling Filter	36500	6570	3650	657
Activated Sludge	39100	7038	3910	704
Activated sludge (SimpleTreat)	33900	6102	3390	610
Tertiary treatment	11300	2034	1130	203

Depuration is rapid, and losses of 95%-97% have been measured after 7 days from cessation of exposure. However, the use pattern for triclosan indicates that environmental release and exposure may be continuous rather than intermittent.

International data

Field monitoring data are available from several international studies for different components of fish (whole, bile, muscle, lipid) and shellfish and different experimental procedures. Field data represent intake from one or more exposure routes (e.g. dissolved, sediment, food) of varying bioavailability.

No data are available for triclosan in whole fish; however, triclosan has been measured in muscle of wild-caught freshwater fish at ≤3.4 ng/g (µg/kg; wet wt).

Several studies report a higher concentration of methyl-triclosan than triclosan in aquatic organisms, and temporal data indicate increases in methyl-triclosan over time. Whole fish, fish muscle and shellfish methyl-triclosan concentrations of 38, 35.5 and 20 ng/g (wet wt) have been reported internationally.

Although triclosan is likely to accumulate in sediments, no sediment-biota accumulation factor (BSAF) is available for this assessment.

16.5.6 Landfill

No landfill leachate or groundwater monitoring data was available for triclosan. While a fraction of the triclosan used in textiles and plastic materials may be

leached and enter the aqueous compartment (e.g. sewer), the majority of the triclosan in these materials is expected to eventually be sent to landfill for disposal at the end of product life. In addition, other sources of landfill include residues of products containing triclosan in emptied containers, manufacturing solid wastes, etc. Within a landfill environment, triclosan is expected to slowly release from these articles as they degrade. Triclosan will likely degrade through abiotic and biotic processes over time to form simpler compounds containing carbon and chlorine. Based on adsorption properties and water solubility, triclosan in the landfill environment is not likely to be mobile and will partition to the organic phase. The potential for release from the landfill environment is further reduced as most landfills that generate leachate have groundwater monitoring programs, leachate collection and treatment processes.

16.5.7 Soils

Apart from localised spill incidents involving triclosan, application of STP sludge (biosolids) to soils as a soil conditioner potentially provides a pathway for transfer of triclosan from the sewerage system to soils. In addition, septic tank maintenance involves pumping out of accumulated sludge, and the sludge requires further treatment to render it acceptable for disposal or re-use as a soil conditioner. Direct application to land, disposal in trenches at STPs and disposal to landfill are methods that have been used in Australia to manage sludge (Patterson, et al., 1998).

Irrigation of treated effluent, which may also contain triclosan, provides an additional pathway for release of triclosan and products to soils.

A predicted environmental concentration (PEC) of triclosan in soil has been derived using the STP model developed by Environment Australia (2003) and estimates of triclosan in secondary (activated sludge) treated effluent (i.e. irrigation) and sludge (soil conditioning), with partitioning to sludge and effluent based on the SimpleTreat model. For calculation of a soil PEC from application of biosolids, it is assumed that the sludge is applied to soil (0-0.1 m depth) of bulk density 1300 kg/m³ at a rate of 10 tonnes/ha/year. For calculation of a soil PEC from irrigation of treated effluent, it is assumed that the effluent is applied to soil at a rate of 1 m/ha/year. In both instances, accumulation without triclosan degradation is assumed. PEC values are shown in Table 16.63.

Using the same assumptions Ying and Kookana (2007) estimated a maximum PEC of 0.131 mg/kg from the application of biosolids in the range they measured. Similarly using the same assumptions and assuming a 1 m depth of effluent with triclosan in the range of 23-740 ng/L was irrigated to soil per year, a PEC range of 0.18-5.7 µg/kg is predicted. Both are considerably lower than those estimated in Table 16.63, particularly the latter.

16.5.8 Atmosphere

No air monitoring data were available for triclosan; however, given the very low volatility of the compound, partitioning to air is not expected to be a significant migration pathway and concentrations in air are likely to be very low.

Table 16.63 - Soil PECs resulting from use of biosolids and a soil conditioner and treated effluent for irrigation

Parameter	Environment Australia (2003) STP model		ASTE (2004) and Dillon (2000) model		Measured Australian Data Ying and Kookana (2007)	
Estimated quantity of triclosan to sewer (kg/year)	26000		26000		-	
Estimated quantity of triclosan to sewer (mg/year)	2.60×10^{10}		2.60×10^{10}		-	
Estimated fraction in sludge based on SimpleTreat model (%)	55% ^a	61% ^b	55% ^a	61% ^b	-	-
Estimated sludge triclosan conc. (mg/kg dry wt)	95.6	106	79.9	88.6	0.09	16.79
Soil Application Rate tonnes/ha/year			10			
PEC _{Soil} biosolid application (mg/kg dry wt)	0.735	0.815	0.614	0.681	0.0007	0.129
Influent Concentration (µg/L)	17400	17400	14500	14500	-	-
Overall Removal Rate (%)	61% ^a	72% ^b	61% ^a	72% ^b	-	-
Concentration in effluent (µg/L)	6.78	4.86	5.66	4.07	0.023	0.740
Waste water application rate to land (m/ha/year)			1.0			
PEC _{Soil} irrigation (mg/kg dry wt)	0.0521	0.0374	0.0436	0.0313	0.0018	0.0057

Notes: The SimpleTreat model output refers only to an activated sludge treatment process. a. Assumes no biodegradation. b. Assumes inherently biodegradable.

16.5.9 Groundwater

No landfill leachate or groundwater monitoring data was available for triclosan. Potential sources of triclosan to the groundwater include leakage from pipelines, sewer overflows, infiltration from wastewater and effluent storage lagoons, trenches and septic system effluent.

16.5.10 Wildlife exposure

This section describes the potential exposure to triclosan by various wildlife species in the Australian environment. In the absence of actual environmental monitoring data, exposure has been estimated using an exposure modelling

approach (refer Appendix B). Estimates for wildlife intake of triclosan by oral routes of exposure are presented in Table B-2 and B-3 (birds) and B-4 and B-5 (mammals) of Appendix B.

Summary of potential wildlife exposures

Drinking water

Wildlife triclosan intake rates by birds and mammals during drinking have been estimated using PEC surface water values (e.g. ≤ 17400 ng/L) and the abovementioned wildlife exposure model equations for surface water ingestion. Using this method, the maximum bird and mammal intake rates of triclosan by the drinking water exposure route are ≤ 0.004 mg/kg bw/day.

Sediment consumption

Wildlife triclosan intake rates by birds and mammals from incidental or intentional sediment ingestion have been estimated using PEC sediment (e.g. 7.2-55.4 mg/kg wet wt) and the abovementioned wildlife exposure model equations for sediment ingestion. Using this method, the maximum bird and mammal intake rates of triclosan by the sediment exposure route are ≤ 3.2 mg/kg bw/day.

Food consumption

Triclosan in the aquatic environment has the potential to bioaccumulate in aquatic organisms and foodchain exposure by wildlife may occur. Estimated wildlife dietary intake of triclosan has been presented in Tables B-2, B-3, B-4 and B-5 (Appendix B). Dietary exposure to triclosan is estimated in the range of 2.9-113 mg/kg bw/day (freshwater) and 0.3-11.3 mg/kg bw/day (marine) depending on taxa, weight and the discharge source. The foodchain potentially provides a significantly greater level of exposure than other routes of exposure evaluated. A similar scenario may be expected for methyl-triclosan. Methyl-triclosan can occur at relatively higher concentrations in biota than triclosan.

Platypus exposure

The major route of environmental exposure of triclosan is to the aquatic compartment. Because of this the exposure to platypuses has been estimated, given their dependence on the aquatic compartment. The estimate is based on the exposure through consumption of contaminated biota and sediment. The exposure through consumption of water during foraging has been ignored given the relatively small magnitude of this exposure route when compared to biota and sediment exposures (see Tables B-2 – B-5). The dietary intake of platypuses is based on the work of Krueger et al. who determined that the mean daily food consumption by platypus in captivity has been found to vary between 14.9%-21.2% of body weight throughout the year (Krueger et al. 1992). The estimated platypus exposure is given in Table 16.64. The PEC food exposure and PEC sediment exposure have been determined based on the methodology outlined in Appendix B.

Table 16.64 - Estimated triclosan exposure to platypuses based on food daily food consumption of between 14.9%-21.2% of body weight after varying levels of wastewater treatment

Effluent Source	Maximum Freshwater PEC (ng/L)	Freshwater Biota PEC ^a (mg/kg wet weight)	PEC Food Exposure ^b (mg/kg bw/d)	PEC Sediment (mg/kg wet weight)	PEC Sediment Exposure ^c (mg/kg bw/d)	Total PEC ^d (mg/kg bw/d)
Untreated wastewater	17400	86.9	12.9 - 18.4	61.8	1.84 - 2.62	14.8 - 21
Primary Treatment	17000	85.0	12.7 - 18	60.5	1.8 - 2.6	14.5 - 20.6
Trickling Filter	7300	36.5	5.44 - 7.74	26.0	0.77 - 1.1	6.21 - 8.84
Activated Sludge	7820	39.1	5.83 - 8.29	27.8	0.83 - 1.18	6.66 - 9.47
Activated sludge (Simple Treat)	6780	33.9	5.05 - 7.19	24.1	0.72 - 1.02	5.77 - 8.21
Tertiary treatment	2260	11.3	1.68 - 2.4	8.04	0.24 - 0.34	1.92 - 2.74
Measured Australian Data Ying and Kookana (2007)	740 ^e	3.7	0.55 - 0.78	2.63 ^f	0.08 - 0.11	0.63 - 0.90

a. BCF value used = 5000; b. Wildlife exposure is calculated by multiplying the body weight-normalised food intake rate for each consumption rate by the food concentration (Biota PEC); c. Based on the sediment forming 20% of dietary intake; d. Determined by summing the water food and sediment exposure; e. Based on maximum effluent level measured by Ying and Kookana (2007); f. Calculated from maximum effluent level of Ying and Kookana (2007) as for Table 16.55.

17. Kinetics and Metabolism

17.1 Absorption

17.1.1 Animal studies

Inhalation

There are no direct absorption studies on triclosan following inhalation exposure. However, on the basis of severe clinical signs of toxicity, such as muscle spasms, seen in a rat 21-day inhalation study (see section 18.4.1) it is assumed that absorption via the respiratory tract would occur and will be dependent on particle size. Additionally, the partition coefficient of 4.8 indicates the potential for absorption across the respiratory tract epithelium. Data do not allow a quantitative assessment of the absorption of triclosan for the inhalation route.

Dermal

Rat

Groups of 3 female rats (strain not reported) were placed in metabolic cages, 100 μ L of 64.5 mM of ^3H -labelled triclosan in ethanol/water (9:1 v/v) applied to the animals' back (non-occlusive dressing) and animals sacrificed up to 24 h later (Moss et al., 2000). Radioactivity was measured in washings from the skin surface as well as in the urine, faeces, blood, skin, stratum corneum, carcass, cage wash, and application cover by high performance liquid chromatography (HPLC). Recovery of radioactivity after 24 h exposure was 90.46% of the administered dose. Absorption as determined by the combined radioactivity in urine and faeces over 24 h and in the blood and carcass at 24 h was 20.46% of the administered dose. Furthermore, 4.31% of the administered dose remained bound in the skin with an additional 36.33% in the stratum corneum.

The dermal absorption of triclosan was determined by liquid scintillation counting of the urine and faeces in a number of experiments in Wistar and SIV-50 rats (Ciba-Geigy Limited, 1976a). All experiments were for a single application of triclosan. Four SIV-50 males received ^3H -labelled triclosan solution in ethanol at a dose of 0.61 mg/kg bw and 2 SIV-50 males ^{14}C -labelled triclosan solution in acetone at a dose of 5 mg/kg bw. Additionally, one Wistar male rat received ^3H -labelled triclosan in a cream at a dose of 5 mg/kg bw and 4 SIV-50 females ^3H -labelled triclosan in Vaseline at a dose of 37 mg/kg bw. Over 96 h combined radioactivity in urine and faeces was 68.9% after application of triclosan in ethanol solution and 91.7% after application of triclosan in acetone solution, while over 48 h it was 23.1% after application of triclosan in cream and 42.8% after application of triclosan in vaseline.

In an experiment by Hong et al. (1976), 2 male rats (strain not reported) received a single topical application of 400 mg/kg bw ^{14}C -labelled triclosan in 5% soap solutions to the back of the neck under occlusive dressing and were kept in a 'breath chamber' for 72 h. Recovery of radioactivity was 91.7%. Over 72 h, mean absorption of the applied dose as determined by the combined radioactivity in urine

and faeces along with that in blood, organs and carcass at 72 h was 22.4%, while a further 5.5% remained bound in the skin.

In a further experiment by Hong et al. (1976) no significant difference was seen in the level of free triclosan in the blood of rats (5 per group, strain and sex not reported) 3 h after a single topical application of 200 mg/kg ¹⁴C-labelled triclosan in water (mean 16 ppb), or 200 or 400 mg/kg bw ¹⁴C-labelled triclosan in 5% soap solution (mean 20 ppb).

The dermal absorption of triclosan was determined in rats by liquid scintillation counting of the urine and faeces following application of ³H-labelled triclosan in ethanol, in a shampoo or in an aerosol deodorant (Black and Howes, 1975). The results are not considered reliable because of the difficulty in administering a standard accurate dose for deodorant application and hence, are not presented here.

For triclosan in ethanol, a group of 12 female Colworth-Wistar rats received a topical application of 162 µg ³H-labelled triclosan and animals were killed up to day 4 post-application. Plasma levels of triclosan ranged from 0.07 to 0.36 µg/mL with maximum concentrations reached about 6 h after application. The total amount of triclosan absorbed over 48 h as determined in 4 animals was 27.6% of the applied dose.

For triclosan in shampoo, groups of 3 to 12 'lightly' anaesthetised female Colworth-Wistar rats received a topical application of 0.1 or 0.2 mL of 0.05%, 0.1%, 0.5%, 1.0% or 2.0% ³H-labelled triclosan in shampoo for 4, 10 or 20 min. The total amount of triclosan absorbed over 48 h ranged from 2.8% to 4.1% of the applied dose for the various doses, concentrations and exposure durations employed.

The results for the deodorant were not considered reliable by the authors because of the difficulty in administering a standard accurate dose and hence, are not presented here.

A study in Crl:CDBR rats (5 per sex per dose) conducted primarily to investigate repeat dose toxicity showed a dose related increase in mean plasma triclosan levels (Burns, 1997b). This study provides very limited qualitative information and no quantitative absorption data and therefore is not summarised further here.

Mice

In a study in CD-1 mice (5 per sex per dose) conducted primarily to investigate repeat dose toxicity (Burns, 1997a), a daily topical application of 0 (untreated control), 0 (acetone vehicle control), 0.3, 0.6, 1.5, 3.0 or 6.0 mg/day triclosan for 14 days resulted in a dose related increase in mean plasma triclosan levels in males (0, 0, 33, 63, 99, 148 and 173 µg/mL, respectively) and generally in females (0, 0, 63, 125, 144, 124 and 295 µg/mL, respectively). Triclosan was determined in the blood by gas chromatography using electron-capture (GC/EC) detection. A further study in mice also showed a dose related increase in mean plasma triclosan levels (Burns, 1996), while absorption was seen in a study primarily conducted to investigate toxicokinetic endpoints other than absorption (Kanetoshi et al., 1992). However, as these studies provide only limited qualitative information and no quantitative absorption data they are not summarised further here.

Guinea-pig

Groups of five male Dunkin-Hartley guinea-pigs received either a single application (2 min of lathering then wash) of 0.5 mL of a super-fatted soap containing 0.1%, 1% or 2% of ³H- or ¹⁴C-labelled triclosan or a non-soap detergent containing 1% ³H-labelled triclosan (Black et al., 1975). Additionally, groups of five male Dunkin-Hartley guinea-pigs received 2 applications a day of 0.5 mL super-fatted soap containing 1% of ³H-labelled triclosan for a total of 9 applications. Animals were kept in metabolic cages.

Autoradiography and/or scintillation counting (of skin samples) indicated that triclosan remained primarily on the stratum corneum, with small amounts in the epidermis, dermis, hair follicles and sebaceous glands. Repeated application did not increase localisation in the skin, though increasing concentrations resulted in increased triclosan deposition throughout the skin depth with no particular localisation. Similar results were seen with the two radiolabels used. Blood levels of triclosan ranged from 2 to 6 ppb after a single wash with the super-fatted soap containing 1% ³H-labelled triclosan increasing to 19 ppb after the ninth wash. Absorption of triclosan was low as indicated by 80% to 90% recovery of ³H-labelled triclosan from the application site in rinse water after a single application and a mean of 95% after nine applications.

Rabbit

The dermal absorption of triclosan was determined by liquid scintillation counting of the faeces and/or urine in a number of experiments in blue Vienna and silver fawn rabbits (Ciba-Geigy Limited, 1976a). The following experiments were for a single application of triclosan. Three blue Vienna males received ³H-labelled triclosan solution in either propylene glycol at a dose of 6.0 mg/kg bw, dimethyl sulfoxide (DMSO) at a dose of 8.6 mg/kg bw or nickethamide at a dose of 10.7 mg/kg bw. A single silver fawn female received ¹⁴C-labelled triclosan solution in hexane at a dose of 0.42 mg/kg bw. Additionally, in experiments in blue Vienna rabbits with a cream containing ³H-labelled triclosan, 3 and 2 males received a dose of 3 mg/kg bw over 64 cm² or 24 cm² skin respectively, and 1 male a dose of 0.3 mg/kg bw over 24 cm².

Over 72 h, radioactivity in urine was 49.1%, 47.3% and 49.7% of the applied dose after application of triclosan in propylene glycol, DMSO and nickethamide solution respectively, and 78.4% in urine and faeces combined after application of triclosan in hexane solution. Over 48 h, combined radioactivity in urine and faeces was 48.6% and 28.1% following application of 3 and 0.3 mg/kg triclosan in cream to 24 cm² skin respectively. The radioactivity in the urine over 72 h of 48.4 and 28.6% following application of 3 mg/kg bw to 64 cm² and 24 cm² skin respectively indicates that the amount excreted in the urine is inversely dependent on the quantity of cream applied per unit of area (i.e. the degree of absorption diminished with trebling of the surface dose).

An experiment was conducted to investigate absorption of ¹⁴C-labelled triclosan following single and repeated application of a soap solution containing 0.1% triclosan (Ciba-Geigy Limited, 1976a). An area of skin measuring 56 cm² was treated for 5 min once or for 5 consecutive days in 1 and 2 animals respectively. Absorption as determined by combined radioactivity in urine, faeces, and carcass

was 1.4% over 96 h for a single application and 10.0% over 10 days for repeated application.

A study exposing rabbits to urine soaked diapers treated with fabric softener containing triclosan provides no reliable absorption data and consequently is not discussed further here (Ciba-Geigy Limited, 1977a).

Dog

Three Beagle dogs (sex not reported) received a daily application of 200 mg/kg bw triclosan in water for up to 4 months (Hong et al., 1976). Triclosan was determined in the blood by gas-liquid chromatography using electron-capture detection (GLC/EC). Mean triclosan levels in blood increased from 7 (129 ppb) to 14 days (249 ppb) when exposure was ended in 2 dogs as they were emancipated. In the remaining animal, triclosan levels decreased from day 76 (195 ppb) to 4 months (132 ppb).

Monkey

Two 3-day old Rhesus monkeys (sex not reported) were washed with a soap solution containing 1 mg/mL triclosan and blood samples taken up to 24 h later (Parkes, 1978a). Triclosan was determined in blood by HPLC. No free triclosan was detected. Conjugated triclosan was detected in the blood at the first sampling time of 1 h post-washing and reached peak levels after 8 to 12 h (maximum concentration 0.68 ppm). In this study a further bathing experiment is reported in Rhesus monkeys, however, no results are provided and consequently this study is not discussed further.

A 90-day repeat dose bathing study that determined plasma triclosan levels in 5 male and 5 female infant Rhesus monkeys is available. Monkeys were bathed daily for 5 min with 15 mL of a soap solution containing 0.1% triclosan (i.e. 1 mg/mL) (Parkes, 1979). Concentrations of triclosan and its conjugates in plasma were determined by GLC/EC with a detection limit of 0.04 ppm. No triclosan was detected, however, triclosan conjugates were detected from the earliest sampling time of day 1. Levels ranged from 0.17 to 0.98 ppm and steady state concentrations were reached within 15 days of treatment.

Summary

Following dermal exposure, the data in animals demonstrate that triclosan is readily absorbed. The available quantitative data indicate that absorption is dependent on the formulation in which triclosan is delivered with greater absorption seen following delivery in a solution than in cream or Vaseline, the duration of exposure and the dose applied per unit of surface area. Triclosan did not appear to accumulate in the skin. Overall, a number of studies in the rat indicate that absorption was approximately 21% to 28% in ethanol/water, soap solution or a cream, though higher values have been reported in some studies.

Oral

Rat

A well-conducted study determining absorption in male rats following single and repeated oral dose administration is available (van Dijk, 1996). Groups of 5 male

BRL-HAN Wistar rats received a single oral (gavage) dose of approximately 2 or 200 mg/kg bw ¹⁴C-labelled triclosan and radioactivity determined in urine and faeces over 96 h and in plasma, organs, carcass and cage wash at 96 h by liquid scintillation counting. Mean recovery of radioactivity was 95.3% and 98.3% in low and high dose animals respectively. Absorption of the administered dose, as determined by the combined mean radioactivity in urine over 96 h along with that in blood, organs (excluding intestinal tract), carcass and cage wash was 14.2% in low dose animals and 15.9% in high dose animals. The remaining radioactivity (over 80% for both dose levels) was detected in the faeces.

In the same study using groups of 4 male BRL-HAN Wistar rats and the same concentrations (van Dijk, 1996), radioactivity was determined in the plasma over 96 h following a single gavage dose, and up to 96 h after administration of ¹⁴C-labelled triclosan in the diet on day 14 following 13 days of unlabelled triclosan feed.

For single administration of the low dose, radioactivity was detected in the plasma at the earliest sampling time of 30 minutes and increased after 1 h (mean concentration of 4.77 µg/g) with a second mean maximum concentration at 4 h (4.46 µg/g). Radioactivity levels decreased thereafter. At about 90 times higher dose levels the calculated 'area under the curve' (AUC) data increased only 51 times for the high dose compared to the low dose (64 and 3237 mg/kg x hour respectively). The increase reflects the ~30- to 40-fold increase in maximum plasma levels of triclosan. Taking into account the similar half lives (10.0 to 12.6 h), the results indicate that the process of absorption is saturated at the high dose level of 200 mg/kg bw.

For the repeated dose schedule for both low and high dose treatment, the AUC values, maximum plasma triclosan levels and half-lives were found to be similar to those following single treatment indicating that repeated exposure to the low dose did not induce significant changes in absorption. The data again indicated absorption was saturated at the high dose level following repeated exposure.

A study investigated the absorption of 5 mg/kg bw triclosan in groups of 2 to 3 male Sprague-Dawley rats administered a single dose of unlabelled triclosan in aqueous solution or a slurry of toothpaste in water, or ¹⁴C-labelled triclosan in aqueous solution (Lin and Smith, 1990). This study employed GC and liquid scintillation counting as methods of detection.

For all groups receiving unlabelled triclosan, conjugates of triclosan were detected in the plasma at the earliest sampling time of 30 min post dosing and levels were more than 200-fold greater than detected for triclosan. Radioactivity was also detected in the plasma at the earliest sampling time. For ¹⁴C-labelled triclosan aqueous solution, absorption of the administered dose as determined by the combined mean radioactivity in urine over 72 h along with that in organs (excluding intestinal tract) and carcass was 6.9%. Absorption of unlabelled triclosan in aqueous and slurry solution was 3.2 and 1.3% over 72 h respectively. For all three groups the majority of the administered dose was detected in the faeces (mean of 57.3% to 83.7%).

The absorption of ³H-labelled triclosan was determined in a number of experiments by Stierlin (1972a). A group of 4 male and 4 female SIV-50 rats received 0.38 mg/kg bw and 3 male Wistar rats 5 mg/kg bw and the mean absorption of the administered dose, as determined by the combined radioactivity in urine over 168

h, was 3.3%, 17.1% and 3.0% respectively (with corresponding mean values in faeces of 78.0%, 68.1% and 91.3%).

Additionally, radioactivity in the plasma was determined over 24 h following oral or intravenous (iv) administration of 5 mg/kg bw ³H-labelled triclosan to groups of 4 or 5 rats (Stierlin, 1972a). Radioactivity was detected at the earliest sampling time of 30 min post administration, which was when the mean maximum concentrations were seen (4.0 µg/mL after oral administration). Based on AUC's for oral and iv administration the author reports that 70% to 80% of the dose was absorbed following oral administration.

A group of 4 male rats (strain not reported) received an oral dose of 50 mg/kg bw ¹⁴C-labelled triclosan (Hong et al., 1976). Absorption as determined by measuring radioactivity in urine over 96 h from dosing together with that in the carcass and organs (excluding intestine and stomach) at 96 h was 4.3%.

A study in male RA rats provides qualitative evidence of absorption (Ciba-Geigy Limited, 1977b). Twenty-four hours following a single or 14 consecutive daily oral doses of 5 mg/kg bw ¹⁴C-labelled triclosan to groups of 4 male RA rats radioactivity in the blood calculated as free triclosan were 0.34 and 0.64 µg/g respectively. Using the same methodology and animal numbers, corresponding values following single or repeated administration of 30 mg/kg bw ¹⁴C-labelled triclosan were 2.74 to 3.69 µg/g respectively.

Plasma concentrations of triclosan, determined by GC were undertaken in groups of 3 to 20 Sprague-Dawley rats per sex per group after 13, 26, 52, 78 and 104 wks administration of triclosan in the diet at dose levels equivalent to 0, 12, 40 or 127 mg/kg bw/day in males and 0, 17, 56 or 190 mg/kg bw/day in females (Parkes, 1986). Practically all the test material in the blood was conjugated with less than 1% seen as free triclosan. The amount of free and conjugated triclosan combined, detected in plasma was proportional to the feeding level in both sexes. Plasma levels generally remained constant in females, while in males a gradual and continual decrease was seen with time. As this study provides no quantitative absorption data it is not discussed further here.

Mice

A well-conducted study by van Dijk (1995) is available in groups of up to 15 male and 15 female Crl: CD-1 mice that employed the same methodology and dose levels as used in male rats for determining absorption of triclosan (van Dijk, 1996).

Following a single oral (gavage) dose of approximately 2 or 200 mg/kg bw/day ¹⁴C-labelled triclosan, mean recovery of radioactivity was 96.6% to 97.9% and 93.5% to 100.1% in low and high dose animals respectively. Absorption of the administered dose, as determined by the combined radioactivity in urine over 96 h along with that in plasma, bile, organs (excluding intestinal tract), carcass and cage wash at 96 h was 21.1% and 34.5% in males and 20.2% and 15.0% in females, in low and high dose animals respectively. The majority of radioactivity was detected in the faeces for both sexes.

In contrast to the study by van Dijk (1996) in rats, this study also determined the absorption of the applied dose following repeated administration to groups of 15 male and 15 female Crl: CD-1 mice as done for a single dose (van Dijk, 1995). Mean recovery of radioactivity was 95.2% to 97.1% and 92.4% to 93.4% in low

and high dose animals respectively. Absorption was determined to be 28.0% and 43.2% in males and 20.7% and 39.1% in females, in low and high dose animals respectively. The majority of radioactivity was detected in the faeces for both sexes.

For single administration of the low and high dose to groups of 36 male and 35 female Crl: CD-1 mice, radioactivity was detected in the plasma at the earliest sampling time of 30 min in both sexes and reached a mean maximum concentration at 4 h in males (19.5 and 212.8 µg/g in the low and high dose groups respectively), and at 4 and 2 h in low (7.7 µg/g) and high (267.2 µg/g) dose females respectively. Radioactivity levels decreased thereafter in both sexes for both dose levels.

Further investigations in groups of 23 male Crl: CD-1 mice showed that for repeated exposure the low dose maximum mean plasma concentration at 4 h (5.0 µg/g) was 3-fold lower than after a single low dose (14.3 µg/g), suggesting some saturation in plasma after repeated administration of the low dose (van Dijk, 1995). Similarly, results with the high dose suggest partial saturation in absorption after repeated administration (i.e. maximum mean plasma concentrations at 4 h of 276.1 and 100.6 µg/g following single and repeated administration respectively).

The study by van Dijk (1995) also investigated the absorption of ¹⁴C-labelled triclosan in Crl: CD-1 mice following a single iv dose and after iv administration of ¹⁴C-labelled triclosan on day 14 following 13 days of unlabelled triclosan in the diet. No significant differences were seen in elimination patterns (i.e. in the urine and faeces) between oral and iv administration (both single and repeated), indicating that absorption was virtually complete after oral administration.

The absorption of triclosan was determined by liquid scintillation counting of the urine over 24 h following administration of 188 and approximately 200 mg/kg bw ¹⁴C-labelled triclosan to groups of 6 male and 6 female Swiss (Howes et al., 1989a) and C-57 (Howes et al., 1989b) mice respectively. Urine was collected over 0.5, 1, 2, 4, 8 and 24 h post dosing from a single of each sex that was then sacrificed. Assuming that cage rinsings and spital debris were radioactive by contamination with urine, absorption in Swiss mice over 24 h was determined to be 44% and 28% from single male and female animal respectively. Corresponding values in C-57 mice were 26% and 42%. Due to the small number of animals and conflicting results seen in males and females between the two strains of mouse, no significance can be reliably attached to the reduced rates of excretion seen between the two sexes.

In a study primarily undertaken to determine disposition and excretion of triclosan and its derivatives (Kanetoshi et al., 1988b), the mean percentage of radioactivity recovered in the urine of 3 male ddY mice over 96 h was 25%.

Hamster

A well-conducted study by van Dijk (1994) is available that used groups of 5 male and 5 female Syrian golden hamsters and the same methodology and dose levels as used for determining absorption in male and female mice (van Dijk, 1995).

One hundred and sixty-eight hours after administration of a single oral (gavage) dose of approximately 2 or 200 mg/kg bw/day ¹⁴C-labelled triclosan, mean recovery of radioactivity was 95.7% to 97.2% and 99.3% to 101.6% in low and high dose animals respectively. Absorption of the administered dose, as determined

by the combined radioactivity in urine over 168 h post dosing along with that in plasma, bile, organs (excluding intestinal tract), carcass and cage wash at 168 h was 68.2% and 88.6% in males and 81.4% and 84.2% in females, in low and high dose animals respectively. For the same determination following repeated exposure, the mean recovery of radioactivity was 102.5% to 102.8% and 98.2% to 101.2% in low and high dose animals respectively and absorption was determined to be 67.7% and 73.2% in males and 68.4% and 74.1% in females, in low and high dose animals respectively.

For single administration of the low and high dose to groups of 12 male and 12 female Syrian hamsters, radioactivity was detected in the plasma at the earliest sampling time of 30 min in both sexes and reached a mean maximum concentration at 1 h in males (7.7 and 359.2 µg/g in the low and high dose groups respectively) and in females (7.4 and 384.9 µg/g in the low and high dose groups respectively). Radioactivity levels decreased thereafter in both sexes for both dose levels.

Further investigations in males only (groups of 16) showed that for the low dose groups the maximum mean plasma concentration at 1 to 2 h was similar following single (4.9 µg/g) and repeated (5.0 µg/g) administration (van Dijk, 1994). In contrast, for repeated exposure the high dose maximum mean plasma concentration at 1 to 2 h (155.1 µg/g) was approximately 50% less than after a single high dose (347.7 µg/g), suggesting partial saturation in absorption after repeated administration.

As undertaken with mice (van Dijk, 1995), van Dijk investigated the absorption (distribution and excretion) of 2.0 mg/kg bw ¹⁴C-labelled triclosan in Syrian golden hamsters following iv administration (van Dijk, 1994). No significant differences were seen in elimination patterns between oral and iv administration (both single and repeated), indicating that absorption was virtually complete after oral administration.

Plasma concentrations of triclosan, determined by GC/EC analysis, were undertaken in groups of 10 Syrian hamsters per sex per group after 52 and 90 to 95 wks administration of triclosan in the diet at dose levels equivalent to 0, 0 (duplicate control group), 12.5, 75 or 250 mg/kg bw/day (Chasseaud et al., 1999). The authors state that plasma concentrations of triclosan were generally below the limit of quantification (< 5 ng/mL) in control animals at the interim kill (52 wks) and study termination. Though plasma concentration of triclosan appeared to increase by more than would be predicted from a linear relationship in both sexes at study termination this was only statistically significant in males (p=0.007). As this study provides no quantitative absorption data it is not discussed further here.

The absorption of triclosan was determined by liquid scintillation counting of the urine collected up to 24 h after administration of approximately 130 mg/kg bw ¹⁴C-labelled triclosan to groups of male and female Syrian hamsters (Howes and Moule, 1989). Assuming that radioactivity in cage rinsings was from urine, absorption over 24 h was determined to be 66% and 75% from a single male and female animal respectively.

Rabbit

The absorption of triclosan was determined by liquid scintillation counting of the urine over 72 h following administration of 5 or 50 mg/kg bw ³H-labelled triclosan to groups of 3 male rabbits (Stierlin, 1972a). Mean absorption was determined to

be 60.4% and 74.1% following administration of 5 and 50 mg/kg bw respectively. It is reported that the low recovery of radiolabel in low dose animals was due to the inadequacy of the metabolic cages used.

Dog

The absorption of triclosan was determined by liquid scintillation counting of the urine over 120 h following administration of 5 mg/kg bw ¹⁴C-labelled triclosan to 2 male beagle dogs firstly by iv then 14-days later by ingestion of a gelatine capsule (Stierlin, 1972a). Mean absorption was determined to be 8.3% to 8.8% and 12.9% to 17.7% following oral and iv administration respectively, while the large majority of radiolabel was detected in the faeces (69.8% to 71.4% and 67.4% to 70.1% respectively). Comparing the elimination patterns between oral and iv administration the author calculated that 50% to 65% of the dose was absorbed following oral administration. For oral administration, radioactivity was detected in the plasma of both animals 1 h after dosing with maximum concentrations seen after 2 to 4 h (mean of 4.3 µg/mL), while the higher values seen following iv administration support the calculated absorption value.

The absorption of triclosan was also determined by liquid scintillation counting of the urine over 144 h following administration of a gelatine capsule containing 5 mg/kg bw ¹⁴C-labelled triclosan to 2 male beagle dogs (Ciba-Geigy Limited, 1977b). Mean absorption was determined to be 12.2%. Furthermore, radioactivity was detected in the plasma at the earliest sampling time of 1 h post dosing, with maximum concentrations reached after 2 to 8 h (mean of 8.1 µg/mL).

A study primarily undertaken to develop analytical procedures to differentiate and quantitate triclosan conjugates in the blood (Ciba-Geigy Limited, 1976b), reported that 'only a few percent of the administered dose' were found in the urine of beagle dogs following administration of 5 mg/kg bw ¹⁴C-labelled triclosan.

Data is available from a 30-day oral study in dogs (Hohensee and Berke, 1991). However, experimental details are lacking (including dose levels administered), and as this study provides no reliable quantitative data it is not discussed further.

Monkey

The absorption of triclosan was determined by liquid scintillation counting of the urine following administration of a gelatine capsule containing 5 mg/kg bw ¹⁴C-labelled triclosan to 2 male baboons (Ciba-Geigy Limited, 1977b). For the 72 h the animals were in metabolic cages the mean absorption was determined to be 55.4%. Radioactivity was detected in the plasma at the earliest sampling time of 2 h post dosing, with maximum concentrations reached after 12 to 24 h (mean of 2.5 µg/mL).

Absorption, as a measure of urinary excretion, was also determined in Rhesus monkeys (Parkes, 1978b). Three males and 1 female received 5 mg/kg bw triclosan and levels of free triclosan and its conjugates determined in blood, urine and faeces by gas chromatography using electron capture analysis. Recovery of triclosan and its conjugates in urine and faeces over 5 days accounted for 83% to 99% of the administered dose with 43.2% to 60.8% (mean 52.2%) detected in urine. Triclosan was not detected or at 'trace levels' only in the plasma. Maximum concentrations of triclosan and its conjugates combined were detected 3 to 5 h after dosing (mean of 2.9 ppm).

In a study primarily undertaken to develop analytical procedures to differentiate and quantitate triclosan conjugates in the blood (Ciba-Geigy Limited, 1976b), absorption as determined by the mean recovery of radioactivity in urine over 72 h following administered 5 mg/kg bw ¹⁴C-labelled triclosan to 2 male baboons was 32%. This study provides no further useful absorption data and hence is not discussed further. Similarly, a briefly reported study in baboons during the final phase of a 1-year dietary study provides no useful absorption data and, hence, is not discussed further (Caudal et al., 1975).

Summary

Following oral administration, absorption from the gastrointestinal tract is rapid and extensive. Comparative studies of oral and iv administration are available in the rat, mouse, hamster and dog. Similar patterns of elimination (in the urine and faeces) following oral and iv administration indicate that absorption was 'virtually complete' in the mouse and hamster, while absorption was calculated to be 70% to 80% in the rat and 50% to 65% in the dog.

17.1.2 Human studies

Inhalation

No data are available. Although a potential for absorption across the respiratory tract epithelium is assumed, this will depend on particle size. No quantitative assessment of the absorption of triclosan via the inhalation route can be made.

Dermal

Absorption data are also available from studies that investigated the toxicokinetics of triclosan following topical application of triclosan containing products/formulations. In the majority of studies no free triclosan was detected in the plasma or, was at levels below the limit of detection, and the values reported related to a conjugated form that was often not specified.

The dermal absorption of triclosan was determined by liquid scintillation counting of the urine and faeces following a single 24 h topical application of a cream containing 3% radio labelled triclosan (Stierlin, 1972b). Blood samples were also taken to determine the level of radiolabel. In this study, a cream containing ³H-labelled triclosan was applied to the site of a psoriatic lesion on the elbow of a 67-year old woman, then a month later to 'intact' skin on the forearm. Additionally, a 75-year old woman received a cream containing 3% triclosan ¹⁴C-labelled triclosan to intact skin of the forearm. All application sites were covered by an occlusive dressing and urine and faeces samples collected over 72 h. For intact skin 2.7% – 2.8% of the radioactive label was recovered in the urine and faeces combined, while for psoriatic skin it was 9.0%. Total recovery of radioactivity (i.e. levels in the cleaning materials, dressing, skin strip-offs, urine and faeces combined) was approximately 75% and 100% for the ³H- and ¹⁴C-label respectively. Assays for radioactivity in the blood were reported to yield values of background levels. The results of this study suggest that skin diseases can result in an increased dermal absorption of triclosan.

Two briefly reported studies are also available that determined triclosan absorption by analysis of the urine of six healthy male volunteers following a single topical application of a cream or soap containing triclosan. In one study (Caudal et al.,

1974), volunteers received the cream at a dose equivalent to 150 mg triclosan and urine collected over 48 h and analysed for free triclosan and triclosan glucuronide by GC/EC detection. Results indicate that a minimum of 2.5% to 6.5% triclosan (mean of 3.9%) was absorbed in volunteers. In the other study (Maibach, 1969), urine was collected over 5 days following topical application of a soap containing ¹⁴C-labelled triclosan. The results indicate a minimum of 5.8% to 15.0% triclosan (mean of 8.9%) was absorbed in volunteers. However, the absence of information on how triclosan was analysed in the urine, limits the significance that can be attached to the values from this study.

The absorption of 2% triclosan in a 10%, 15% and 15% soap solution was determined by spectrophotometric measurement of triclosan in test and control solutions prior to and after a 6 h exposure (Schenkel and Furia, 1965). However, as there is limited confidence in the method of analysis and subsequent quantitation employed, no further details of this study are presented here.

Triclosan absorption was investigated in a series of experiments by Thompson et al. (1975a; 1975b; 1976). In these experiments, triclosan concentration was determined in blood and urine samples by GC/EC detection analysis. The limit of detection for free triclosan and free and conjugated triclosan combined was 3 ng/mL and 15 ng/mL respectively. It is reported that volunteers were instructed not to use products containing triclosan 1 month prior to and during the experiments.

In a study primarily undertaken to validate GC/EC detection analysis as the analytical method for measurement of triclosan (Thompson et al., 1975a), 4 healthy male volunteers washed their hands and forearms twice consecutively with 5 mL of a skin cleanser containing 0.75% triclosan for a total of 8 min. Peak total triclosan (i.e. triclosan and its conjugates combined) plasma concentrations of 15 to 31 ng/mL were seen after 8 h. Mean total urinary excretion of triclosan was 627 µg over 48 h. Plasma and urine concentrations of free triclosan ranged from < 3 to 4 ng/mL and < 3 to 16 ng/mL respectively.

A further experiment was undertaken to compare triclosan absorption in intact skin, abraded skin and intact skin following occlusive dressing of the application site (Thompson et al., 1975b). Four healthy male volunteers received topical application of 1.0 mL of a patient skin prep containing 0.5% triclosan (i.e. 5 mg triclosan) for 12 h to intact skin, skin abraded by application and removal of cellulose tape and intact skin that was initially covered with an occlusive dressing for the first 2 h. Applications were undertaken 1 month apart. Absorption as determined by total triclosan concentration in the urine over 72 h was not markedly increased by abrasion but was following the use of an occlusive dressing. For non-occlusive application sites 6% to 14% of the applied dose was detected in the urine and 40% to 58% following occlusive dressing. For occlusive dressing, the maximum total triclosan plasma concentrations ranged from 112 to 192 ng/mL, 4 to 8 h after topical application, while in the absence of an occlusive dressing levels were below the limit of detection in 3 of the 4 subjects.

Thompson et al. (1976) also compared the absorption of triclosan following single and repeated use of a surgical scrub containing 0.5% triclosan. Six healthy male volunteers washed their hands and forearms twice consecutively with 5mL per wash of a skin cleanser containing 0.5% triclosan (i.e. total dose of 50 mg triclosan) for a total of 5 min. An additional group of 6 male volunteers repeated this procedure three times daily for 7 consecutive days with a final wash on day 8.

For the single exposure, measurable triclosan concentrations were noted 2 to 4 h after hand washing. The peak total plasma concentrations ranged from 62 to 143 ng/mL between 10 and 24 h post exposure (mean 89 ng/mL at 19 h). Absorption as determined by total triclosan concentration in the urine over 96 h following a single exposure was at least 2.6% to 6.6%.

For the repeated schedule, total triclosan concentrations in the plasma were still increasing on day 8 in 5 volunteers and ranged from 490 to 1780 ng/mL. Within this range it was seen that 4 Caucasian volunteers had maximum plasma concentrations of 490 to 715 ng/mL compared to 1640 and 1780 ng/mL in 2 Negroid volunteers. Plasma concentrations of free triclosan ranged from < 3 to 13 ng/mL and were similar for Caucasian and Negroid volunteers. Therefore, it can be seen that steady state plasma levels were not achieved over 8 days of washing with this surgical scrub.

The two Negroid volunteers from the above study had also participated in a further multiple scrub study (Thompson, 1975). This study was conducted in 5 and 6 Caucasian and Negroid volunteers respectively (sex not reported). The study used the same detection analysis, surgical wash and washing procedure (for up to 31 days) as described in the study by Thompson et al. (1976). It is reported that volunteers were instructed not to use products containing triclosan one month prior to and during the study. In Caucasian volunteers, total triclosan plasma concentrations reached a maximum range of 740 to 1030 ng/mL on days 12 to 15. In Negroid volunteers, the study was interrupted on day 18 by one day without scrubbing. In 3 Negroid volunteers steady state plasma levels were reached by day 15 and the maximum observed total triclosan plasma concentrations ranged from 554 to 690 ng/mL. In contrast, in the remaining 3 Negroid volunteers (that included the participants of the previous study) steady state total triclosan plasma concentrations were not reached when scrubbing was stopped on day 24. In these 3 volunteers maximum plasma concentrations of total triclosan ranged from 3400 to 4080 ng/mL. Mean plasma concentrations of free triclosan were less than 3 ng/mL in the volunteers who did not obtain steady state levels, and were 6 and 10 ng/mL by day 19 in the remaining Negroid and Caucasian volunteers respectively.

Beiswanger and Tuohy (1990) compared triclosan blood levels in Caucasian, Negroid and Oriental volunteers following repeated use of consumer products containing triclosan. Thirty-three Caucasian, 28 Negroid and 23 Oriental volunteers completed this 13-wk study using a soap bar containing 0.75% triclosan and a deodorant containing 0.39% triclosan at least once daily along with a dentifrice containing 0.28% triclosan at least twice daily. Triclosan concentrations were determined in plasma by GLC/ED detection analysis. Due to concerns of non-compliance with regards to use of soap and deodorant in Oriental volunteers the results for this racial group are not presented here. In Caucasians total triclosan levels increased from a mean baseline (i.e. pre-study) value of 2.6 ng/mL to 36.7, 32.1 and 25.2 ng/mL on wk 3, 6 and 13 respectively. Comparable values were seen in Negroid volunteers (2.2, 34.3, 33.6 and 28.5 ng/mL respectively).

In a further study in Negroid volunteers (Wagner and Le Sher, 1977), 5 subjects aged 36 to 45 years old (sex not reported) completed a study washing and showering (twice on day 1 and three times thereafter) with soap bars containing 1% triclosan for up to 45 days. Triclosan concentration was determined in blood samples by GC/EC detection analysis. It is reported that volunteers were instructed not to use triclosan related products a month prior to the study and were supplied

with control soap, shampoo and deodorant. Volunteers used on average 11.6 to 27.4 g soap per day. No consistent relationship was seen between the amount of soap used and plasma levels of total triclosan. Plasma levels of free triclosan were less than 10 ng/mL during the treatment period. Levels of conjugated triclosan reached steady state levels in 3 volunteers after about 12 days (and ranged from 148 to 2580 ng/mL) while levels continued to rise in 2 volunteers for more than 30 days (maximum levels of 632 and 1054 ng/mL).

In a well reported 20-day hand washing study to evaluate the steady state toxicokinetics of triclosan (Ciba Specialty Chemicals Corporation, 2002), 7 male and 6 female healthy volunteers (aged from 18 to 62 yrs old) washed their hands 6 times a day (i.e. every 2 hours) for 15 seconds with on average, approximately 3.5 g/liquid hand wash containing approximately 1.0% triclosan. Volunteers did not use a triclosan containing toothpaste and were asked to refrain from using triclosan-containing products during the duration of the study. Additionally, prior to the study baseline levels of free and total triclosan in plasma were determined using HPLC and daughter mass spectra generated by fragmentation of a parent ion. The level of detection for free and total triclosan was 1 ng/mL and 5 ng/mL respectively. It is reported that only 1 baseline value of free triclosan (3.6 ng/mL) was above the detection limit while 7 of the volunteers had values above the detection limit for total triclosan (maximum value of 27.9 ng/mL). Triclosan was present in the plasma predominantly in the conjugated form. The maximum free and total triclosan levels seen during the experiment were 31 and 229 ng/mL in males and 70 and 158 ng/mL in females respectively on day 20, while the mean value for total triclosan was 96 ng/mL in males and 44 ng/mL in females. The time to steady state levels was estimated to be approximately 1 wk. Although throughout this study the mean total levels of triclosan were significantly higher in males than in females there was considerable inter-individual variability with corresponding large standard deviations for mean values. Consequently, the difference in mean total triclosan levels is not considered indicative of a sex difference but due to random biological variation in the small study population.

A 21-day hand washing study was conducted in 9 males and 9 females to compare the absorption of triclosan following use of a hand wash containing 0.25% or 1% triclosan (Ciba-Geigy Corporation, 1973a). Blood samples were analysed by GC/EC detection. In this briefly reported study, a dose dependent increase in mean plasma levels of an unspecified conjugate were observed 10 and 21 days after washing (28 and 68 ng/ml with 0.25% triclosan respectively, and 87 and 94 ng/ml with 1% triclosan). Additionally, levels were determined in 3 males and 3 females who had used the 1% hand wash 7 days after cessation. Mean plasma levels (16 ng/ml) were observed to be close to the limit of detection (10 ng/ml).

Absorption was also seen in a 14-day hand washing study in 4 volunteers (3 males and 1 female) who washed their hands with a surgical scrub detergent containing 0.75% triclosan twice a day (Ciba-Geigy Corporation, 1972a). Volunteers had no contact with triclosan prior to the study, and analysis of the blood using GC prior to study initiation detected no triclosan. Triclosan was detected in all volunteers after two washes, and maximum levels were reached in all volunteers after 8 washes (8.3 to 18.0 ppb).

A study analysed triclosan in blood and urine samples during and following use of an antiperspirant spray containing 0.1% triclosan for 4 wks (Hong et al., 1976). However, as the dose applied was simply determined by weight difference of cans

before and after use of the product there is very limited confidence in the derived absorption values, and hence this study is not discussed further in this report.

In a briefly reported full body bathing study (Ciba-Geigy Corporation, 1972a), 2 volunteers (sex not reported) bathed daily for 75 days in a bath to which was added a product (not further defined) containing 0.75% triclosan. It is reported that the dose was 75 mg triclosan/bath. The study also included a single control volunteer. Blood samples were collected throughout the study and triclosan levels determined by GC/EC analysis. Triclosan was detected in plasma prior to the study initiation in one volunteer (5.8 ppb) and the control (8.0 ppb). Levels in the control remained generally steady throughout the study. In volunteers exposed to triclosan an increase in plasma levels was seen immediately (from the earliest sampling time of 2 h after the first bath). Plasma triclosan levels ranged from 11.2 to 19.5 ppb and 6.3 to 10.6 ppb in the 2 volunteers throughout the study.

A study is available that investigated triclosan deposition in skin and factors influencing it (Black et al., 1975). The backs of male volunteers, 1 per treatment, received a single application, or 6 applications in three days, of 0.25 mL of a conventional soap or non-soap detergent suspension each containing 0.08% (w/v) ³H-labelled triclosan for 2 min. Pairs of full depth skin biopsies taken from 10 min and up to 4 days after a single wash and 2 wks after the sixth wash were analysed by autoradiography. Although data is presented in the study summary it is unclear which treatment it relates to. However, following a single application with the two soap suspensions, it is reported that very low levels of radioactivity were detected in the stratum corneum, epidermis and dermis, and no silver grains were seen in the follicles or sebaceous glands. Additionally, it is reported that the differences between soap vehicles and single versus repeated washes were small. Furthermore, it is stated that while the pattern of localisation in human skin was similar to that in the guinea-pig skin (except none were seen in the pilosebaceous system), the amount of radioactivity present in human skin was lower.

Summary

In human studies the only estimation of oral absorption of triclosan comes from excretion of total triclosan (i.e. free triclosan and its conjugates) in the urine up to 5 days after topical application of products/formulations containing up to 3% triclosan. Data from robust studies indicate absorption to be generally at least 3% to 7%, though at least 14% was seen in one volunteers for a 12 h exposure, while occlusive dressing can significantly increase absorption. Limited data from full depth skin biopsy reports suggest that the rate of dermal absorption of triclosan may be less in humans compared to animals (i.e. guinea-pigs).

Oral

In a study using ¹⁴C-triclosan (Stierlin, 1972b), a male volunteer aged 30 yrs ingested a gelatine capsule containing 200.5 mg radio-labelled triclosan (equivalent to 2.4 mg/kg bw) and oral absorption as determined by liquid scintillation counting of urine collected over 72 h was 87.4%.

In a further study using ¹⁴C-labelled triclosan (Ciba-Geigy Limited, 1976c), blood samples were drawn immediately prior to ingestion of a gelatine capsule containing 204 mg radio-labelled triclosan (equivalent to 2.6 mg/kg bw) by a healthy 43 year old male volunteer, then 30 min and 1, 2, 4, 8, 24 and 72 h after ingestion. Peak

concentrations of total radioactivity in blood and plasma were reached 4 h after administration. Within 6 days, 57.1% of the radiolabel was excreted in the urine.

Four healthy children aged 9 to 12 yrs old (sex not reported) received a single dose of 30 mL of 0.01% triclosan aqueous solution that contained 3mg triclosan and blood samples collected up to 72 h after administration (Concordia Research Laboratories Inc., 1997a). Plasma concentrations of triclosan were determined by GC/EC analysis. Non-triclosan personal care products were used prior to and during the study. Maximum concentrations seen from the earliest sampling time of 12 h post-administration ranged from 82.3 to 175.2 ng/mL.

In a study completed in 9 children aged 8 to 12 yrs old (sex not reported) using the same dose levels and methodology as described above (Colgate-Palmolive Company, 1997a), triclosan was detected in the blood of some individuals from the earliest sampling time of 10 min post administration, and in all children after 15 min. Peak plasma concentrations of triclosan ranged from 271 to 808 ng/mL and the mean time to reach peak concentrations was 1.8 h. Additionally, the area under the concentration time curve (AUC) over 24 h was 4571 ng/h/mL. No information on the avoidance of personal care products containing triclosan is provided for this study.

Eight healthy volunteers (4 males and 4 females) aged 18 yrs and over received a single dose of 100 mL of a 0.01% triclosan aqueous solution that contained 10 mg triclosan and blood samples collected up to 72 h after administration (Concordia Research Laboratories, 1997b). Plasma concentrations of triclosan were determined by gas chromatography using electron capture analysis, and non-triclosan personal care products were used prior to and during the study. Peak plasma concentrations of triclosan ranged from 494 to 1325 ng/mL, and the mean time to reach peak concentration was 1.6 h.

Data is available from a combined human tolerance and toxicokinetic study (Lucker et al., 1990). Although the study was conducted in 20 healthy male volunteers it is not clear how many volunteers the pharmacokinetic data is based upon. Volunteers received a single gelatine capsule containing 1 mg triclosan and calcium carbonate with blood samples collected prior to administration and up to 72 h after administration. The study also determined steady state blood levels in volunteers receiving a gelatine capsule containing 15 mg triclosan and calcium carbonate daily for 30 days. Plasma concentrations of free triclosan and its glucuronide and sulfate conjugates were determined by GC/EC analysis. Volunteers were instructed to avoid using cosmetics containing triclosan 2 wks prior to, and throughout, the study.

Only 'traces' of free triclosan were detected in the plasma following single and repeated administration. The mean maximum concentration of total triclosan (i.e. free triclosan and its conjugates) following single administration was 20.3 ng/mL and the mean time to reach the peak concentration was 5.0 h. Corresponding steady state values were 845.6 ng/mL and 4.0 h. It is reported that 91% of the administered 1 mg triclosan was excreted in the urine over 96 h. During the steady state phase it was determined that the percentage of administered dose excreted in the urine over a 24 h period was approximately 80% to 85%.

A repeat dose study was conducted to determine when the steady state blood level of triclosan occurred in 9 healthy male volunteers administered 2 mg triclosan twice daily in an aqueous solution for 21 days (Colgate-Palmolive Company,

1989). Blood levels of free triclosan and its glucuronide and sulfate conjugates were determined 7, 14 and 21 days after the initial dose and urinary levels of such over 24-hour periods. Free triclosan was only detected in the blood in 1 volunteer on day 14 only (detection limit 10 ng/ml). The mean maximum blood concentration of total triclosan was calculated to be 191.2 ng/ml, reached on day 16. In comparison, total triclosan excreted in the urine was 71% of the daily dose on day 7 and 41% by day 21.

Absorption data are also available from studies that investigated the toxicokinetics of triclosan following ingestion of triclosan containing products.

The toxicokinetics of triclosan were investigated in 21 adult volunteers (sex not reported) following both single and repeated brushing of teeth with 1.25 g dentifrice containing 0.3% triclosan (i.e. 3.75 mg triclosan) with the dental slurry then being ingested (Colgate-Palmolive Company, 1997b).

For the single exposure, triclosan concentrations were determined in the plasma over 72 h post brushing/ingestion. Prior to brushing, triclosan was detected in plasma in two individuals (13 and 22 ng/mL). Increased levels of triclosan were not detected in the plasma 5 min after brushing, but were detected in 14 volunteers after 15 min and in all volunteers by 30 min. The maximum triclosan concentration seen in plasma was 338 ng/mL. The mean peak plasma concentration, the mean time to reach it, the mean absorption rate constant (estimated using a one-compartment model with first-order absorption) were 243 ng/mL, 4.0 h and 0.68 h^{-1} respectively.

For the repeated exposure, volunteers brushed their teeth and then ingested the 'slurry' three times daily for 12 days. The maximum triclosan concentration seen in plasma was 794 ng/mL. The mean AUC values for 0 to 24 h was 8833 ng/mL, and once corrected for the number of doses ($n = 3$) administered during a 24 h dosing period was 2844 ng/mL. This value was similar to the AUC value estimated after a single exposure (i.e. from 0 to infinity) suggesting linear disposition after repeated brushing.

A further study is available in which 8 healthy volunteers (4 males and 4 females) aged 18 yrs and over brushed with 2 g toothpaste containing 6 mg triclosan and then ingested the dental slurry (Concordia Research Laboratories, 1997b). Blood samples were taken up to 72 h after ingestion and triclosan plasma concentrations determined by GC/EC analysis. Volunteers used non-triclosan personal care products prior to and during the study. Peak plasma concentrations of triclosan ranged from 260 to 939 ng/mL and the mean time to reach peak concentrations was 3.0 h.

A study is available that compared plasma triclosan concentration in 6 healthy volunteers (3 per sex) who expelled dental slurry to 8 volunteers (4 per sex) who swallowed the dental slurry (BIBRA International, 1997). Both sets of data are reported in the 'Other data' subsection (see section 17.1.3).

Summary

In human studies the only estimation of absorption of triclosan comes from excretion of total triclosan (i.e. free triclosan and its conjugates) in the urine up to 6 days after administration. Data from a number of studies indicates absorption to be at least 41% to 97% in humans.

17.1.3 Other data

A study is available in the rat that investigated absorption following intravaginal administration (Siddiqui and Buttar, 1979). Anaesthetised Wistar rats were administered 5 mg/kg bw ¹⁴C-triclosan in corn oil, a neck collar fitted to prevent possible oral ingestion of the test material and immediately transferred to metabolic cages. Five females were sacrificed at predetermined times up and including 24 h after administration of triclosan, and radioactivity measured in blood, urine, faeces and a number of tissues by liquid scintillation counter. Approximately, 26% and 12% of the applied dose remained in the vagina after 4 and 24 h respectively. Radioactivity in the blood was seen to peak between 2 and 4 h and declined rapidly up to 6 h and more slowly thereafter. Absorption over 24 h as determined by radioactivity in urine and faeces combined, was 39.9%.

A number of experiments are available that investigated gingival absorption following topical mouthrinse application in beagle dogs (1 male, 1 female) that did/did not have plaque removed prior to initiation (Lin et al., 1994). Anaesthetised dogs were administered 2 to 5 mL of a mouthrinse containing 0.03% triclosan in applicator trays that enclosed one half of the upper jaw for 15 min a day for 7 consecutive days. Free triclosan and its conjugates were measured in blood and urine by gas chromatography up to 12 h post dosing. No free triclosan was detected in plasma in any experiment (limit of detection 10 ng/mL). Assuming that plasma is 4% of body weight then the peak total triclosan plasma levels seen 6 to 8 h after application were equivalent to 0.7% to 2.7% of the applied dose. Mean total plasma concentrations were not statistically different between animals with or without teeth cleaned of plaque. Absorption, as determined by daily urinary excretion of total triclosan, ranged from 1% to 4% of the applied dose.

A number of studies are available, often briefly reported, using personal care products containing triclosan that investigated the buccal absorption of triclosan in humans.

A repeat dose study was conducted to compare when steady state blood level of triclosan occurred in 9 healthy male volunteers brushing twice daily for 21 days with a dentifrice containing 0.2% triclosan against 9 healthy male volunteers administration 2 mg triclosan by the oral route twice daily for 21 days (Colgate-Palmolive Company, 1989). The triclosan solution simulated the maximum absorption of triclosan possible from the dentifrice. Free triclosan was not detected in the blood at anytime in volunteers brushing and instructed not to swallow the dentifrice. The mean maximum concentration of total triclosan in these volunteers was calculated to be 26.7 ng/ml, which was reached on day 12. Only 5% to 10% of the daily dose was excreted in the urine. Compared to that observed in volunteers administered the triclosan solution, under normal conditions of dentifrice usage the amount of triclosan absorbed is 9% to 14% of the amount that would be absorbed and excreted if an equivalent dosage of triclosan was ingested.

A study is available comparing the plasma triclosan concentration in 6 healthy volunteers (3 per sex) who expelled dental slurry against 8 volunteers (4 per sex) who swallowed the dental slurry (BIBRA International, 1997). Prior to study commencement it was ensured that toiletries used by volunteers were triclosan free. Volunteers (aged 18 to 51 years old) brushed their teeth with toothpaste containing 0.3% triclosan for 1 minute 4 times daily for 14 consecutive days. Triclosan concentrations were determined prior to and throughout the experiment, though no

information is provided on triclosan analysis. No significant sex difference was observed in this study, though the mean maximum plasma triclosan concentration was lower in subjects who expelled the dental slurry (132 ng/mL males, 159 ng/mL females) compared to those that ingested (951 ng/mL males, 805 ng/mL females) as was the mean AUC (32509 and 37202 h x ng/mL in males and females respectively, compared to 244117 h x ng/mL in males and 193595 h x ng/mL in females).

A study was conducted to determine the buccal absorption of triclosan from a mouthrinse containing 0.03% triclosan (Lin, 2000). Nine male volunteers rinsed twice daily with the mouthrinse for 21 days. It was estimated that 2% to 4% of the daily triclosan dose (9.0 mg) was absorbed, though the absence of information on how triclosan was analysed in the plasma limits the significance that can be attached to these findings. Other briefly reported studies by Lin are available. In one study (Lin, 1988), blood samples from 10 volunteers (sex not reported) were analysed by gas chromatography prior to and after brushing with a dentifrice containing 0.6% triclosan for 13 days. Absorption was seen as indicated by the presence of triclosan conjugates but not free triclosan in all volunteers (mean total triclosan of 25 ng/mL) on day 13.

Thirty-five Caucasian, 26 Negroid and 22 Orientals volunteers completed a 13-wk study using a dentifrice containing 0.28% triclosan at least twice daily (Beiswanger and Tuohy, 1990). Total triclosan levels in the plasma, as determined by GLC/ED analysis, increased from a pre-study value of 1.0 ng/mL to 21.6, 22.7 and 18.2 ng/mL on week 3, 6 and 13 respectively in Caucasians. Corresponding values were 0.6, 25.7, 23.0 and 24.2 ng/mL respectively in Negroid volunteers and 0.6, 20.2, 20.5 and 14.4 ng/mL respectively in Oriental volunteers.

Although two studies are available that determined triclosan levels in the blood following brushing with a toothpaste containing triclosan (Lin 1989; Safford, 1991), these studies have methodology limitations and/or an absence of information on detection of analysis. As these limitations restrict the significance that can be attached to the findings they are not discussed further here. Additionally, a study that investigated the oral retention of triclosan in plaque is not discussed here, as it provides no data on absorption (Gilbert, 1987).

In vitro

A study investigated in vitro dermal absorption in human and rat skin tissue using a diffuse cell system (Moss et al., 2000). In these experiments ³H-labelled triclosan radioactivity was measured by HPLC. Human breast or abdominal skin and dorsal rat skin were exposed to 7 µl of 64.5 mM ³H-triclosan in ethanol-water (9:1) for up to 24 h. Absorption over 24 h as determined by radioactivity in the receptor fluid was 6.3% and 23% of the applied dose in human and rat skin respectively. Furthermore, in the human and rat tissue samples 24% and 18.2% of the administered dose remained bound in the epidermis and dermis respectively (with an additional 22% and 25% in the stratum corneum respectively). The steady-state flux of radioactivity into the receptor fluid was 12.5 µmol triclosan/cm²/h in human skin over 24 h and 87.8 µmol triclosan/cm²/h in rat skin from 7 to 24 h. The results of this in vitro study indicate that penetration of triclosan through rat skin was approximately 4 times faster than through human skin.

A series of studies are available that determined the in vitro dermal absorption of a number of formulations all containing 0.2% w/w ¹⁴C-labelled triclosan in human skin using a diffusion cell system. The formulations tested and the exposure period prior to rinse-off from the skin surface was 10 min for a soap solution (Ciba Specialty Chemicals, 1998d), 30 min for a dishwashing liquid (Ciba Specialty Chemicals, 1998b), 24 h for a water/oil emulsion (Ciba Specialty Chemicals, 1998a) and 24 h for a deodorant (Ciba Specialty Chemicals, 1998c).

The recovery of the applied dose for all these formulations ranged from 84% to 95%. Absorption over 24 h as determined by radioactivity in the receptor fluid was 2.3%, 2.3%, 3.9% and 0.85% for the soap solution, dishwashing liquid, w/o emulsion and deodorant respectively. Corresponding rates of steady-state flux of radioactivity into the receptor fluid were approximately 0.001 $\mu\text{mol}/\text{cm}^2/\text{h}$ between 2 and 6 h post exposure, 0.01 $\mu\text{mol}/\text{cm}^2/\text{h}$ between 2 and 6 h, 0.008 $\mu\text{mol}/\text{cm}^2/\text{h}$ between 8 and 24 h and 0.002 $\mu\text{mol}/\text{cm}^2/\text{h}$ between 8 and 24 h. These studies clearly indicate that formulation affects absorption of triclosan.

Summary

The data indicate rapid absorption of triclosan across mucous membranes, though evidence is available that indicates absorption is significantly less than observed following ingestion. In humans, normal use of toothpaste containing 0.2% triclosan resulted in absorption of 9% to 14% of the amount that would be absorbed if an equivalent dosage of triclosan were ingested. In vitro dermal data indicates that formulation affects absorption of triclosan and supports the in vivo evidence that the rate of dermal absorption of triclosan is less in humans compared to animals (i.e. rats).

17.2 Distribution

17.2.1 Animal studies

Rat

In an experiment by Hong et al. (1976), 72 h after topical application of 400 mg/kg bw ¹⁴C-labelled triclosan in 5% soap solutions to 2 male rats (strain not reported) 4.41% and 2.16% of the administered radio-label was detected in the carcass (dried and filtrate combined) and intestine respectively with only trace amounts (0.48% to less than 0.01%) in the blood, liver, kidney, lungs, brain, intestine, heart and testes. Similarly, radioactivity (2.72%) was detected in the carcass and blood (0.02%) of female rats (strain and number not reported) 24 h after topical application of 100 μL of 64.5 mM of ³H-labelled triclosan in ethanol/water (9:1 v/v) (Moss et al., 2000).

Distribution of radioactivity was determined in groups of 3 male RA rats from 2 h up to 8 h after oral administration of 5 mg/kg bw mg bw ³H-labelled triclosan (Stierlin, 1972a). High levels of radioactivity were detected in the gastrointestinal contents and faeces. Maximum levels of radioactivity detected 2 to 4 h after administration equated to 2.79%, 13.85%, 7.24%, 3.66% and 0.54% of the applied dose in the blood, carcass, stomach, liver, and kidneys respectively. Levels in all other organs/tissues were 0.24% to less than 0.01% (i.e. heart, muscle, brain, bone marrow, testes, adrenal, spleen and thyroid). In this experiment, approximately 90% of the dose was detected in faeces 8 h after dosing. This data together with the

observed relatively slow decline in blood radioactivity levels observed in a further experiment by Stierlin (1972a) in rats¹⁰ is indicative of enterohepatic circulation. This is supported by the author's statement that after intra-duodenal or oral administration of 5 mg/kg bw of triclosan to rats, an average of 65% of the dose was detected in the bile within 7 to 10 h (data for this experiment not provided).

Seventy-two hours after oral administration of 5 mg/kg bw ¹⁴C-labelled triclosan to 2 male Sprague-Dawley rats (Lin and Smith, 1990), mean radioactivity in the carcass and liver accounted for 0.80% and 0.09% of the administered dose respectively. In a number of other organs (e.g. brain, heart, kidney, lung etc) the mean dose detected ranged from 0.034% to less than 0.001%. Blood was obtained from these animals up to 72 h after dosing, and the observance of 2 peak plasma concentrations for the glucuronide and sulphate conjugates within 6 h of dosing suggests enterohepatic recirculation. Furthermore in the same study, 2 peak plasma concentrations were also observed within 6 h of dosing in male Sprague Dawley rats administered 5 mg/kg bw unlabelled triclosan.

A study is available that investigated enterohepatic circulation (Ciba-Geigy Limited, 1975a). Initially, 4 male RA 25 outbreed SPF rats with biliary-fistula received 5mg/kg ¹⁴C-labelled triclosan by iv injection. Over 6 h, the mean radioactivity detected in the bile and urine was equivalent to 72.9% and 0.5% of the applied dose respectively. A further 2.0% and 0.6% was detected in the intestine and stomach 6 h after administration respectively. Pooled bile from these animals was then administered intraduodenally to a further 4 male RA 25 outbreed SPF rats with biliary-fistula (0.3 ml for which the amount of ¹⁴C-label was determined). Over 6 h, the mean radioactivity detected in the bile and urine was 38.8% and 0.1% of the applied label, with a further 51.0% and 0.4% detected in the intestine and stomach 6 h after administration. The amount of radioactivity detected in the bile and urine corresponds to 28.4% of the original iv dose. Thus, this study provides good evidence that triclosan undergoes significant enterohepatic circulation in the rat.

Additionally, in 2 male Colworth-Wistar rats whose bile ducts were cannulated and bile collected in 30 min aliquots following oral administration of 5 mg/kg bw ³H-labelled triclosan (Black et al., 1975), 55% of the dose was collected over 4.5 h.

In an experiment by Hong et al. (1976), 72 h after oral administration of 50 mg/kg bw ¹⁴C-labelled triclosan to 4 male rats (strain not reported) 5.56% of the administered radio-label was detected in the carcass (dried and filtrate combined) with only trace amounts (i.e. less than 0.08%) in the blood, liver, kidney, lungs, brain and heart. In the same study (Hong et al., 1976), lower levels of radioactivity were seen in the carcass and organs of rats 96 h after administration of the same dose.

Distribution of radioactivity was determined in groups of 4 male RA rats following a single or 14 consecutive daily oral doses of 5 or 30 mg/kg bw ¹⁴C-labelled triclosan (Ciba-Geigy Limited, 1977b). For the brain, radioactivity was determined in specific regions. Twenty-four hours after administration of a single dose of 5 mg/kg bw higher radioactivity levels (0.25 to 0.55 µg/g) could be found in the blood, plasma, lung, pituitary gland, sciatic nerve, optic nerve, liver and kidney in

¹⁰ Mean blood concentrations of total radioactivity in 4 rats 0.5, 1, 2, 4, 8 and 24 h after oral administration of 5mg/kg bw ³H-triclosan was 4.0, 3.1, 2.3, 2.0, 3.2 and 1.3 µg/mL respectively.

single dose group. Lower levels were detected in other organs (0.01 to 0.16 µg/g). Twenty-four hours after the last repeat dose of 5 mg/kg bw radioactivity in the blood, plasma, pituitary gland, sciatic nerve, thyroid gland and kidneys was approximately 50% to 110% greater compared to those observed for a single dose. Levels in all other organs were comparable and/or at very low levels.

Similar distribution patterns were seen in animals 24 h after receiving a single or repeated oral dose of 30 mg/kg bw, though generally higher levels of radioactivity were detected in all organs than seen with 5 mg/kg bw (1.79 to 6.46 µg/g in blood, plasma, lung, pituitary gland, sciatic nerve, liver and kidney following repeated dosing). Overall, 30 mg/kg bw repeated administration did not result in an accumulation of radioactivity in organs, though the values determined in blood and organs with 30 mg/kg bw did not increase proportionally to that after 5 mg/kg bw, but were approximately 20% to 50% higher than the theoretical values extrapolated from the low dose.

A number of experiments are reported in a well-conducted study by van Dijk (1996). Ninety-six hours after oral administration of 2 or 200 mg/kg bw ¹⁴C-labelled triclosan to groups of 5 male BRL-HAN Wistar rats the mean radioactivity detected in the liver and kidneys combined and residual carcass at both dose levels was less than 0.05% and 0.2% to 0.3% of the applied dose respectively. In a further experiment by van Dijk (1996) using the same concentrations, radioactivity was detected in the liver and kidneys of groups of 4 male BRL-HAN Wistar rats sacrificed over 96 h following a single (gavage) dose and up to 96 h after administration of ¹⁴C-labelled triclosan in the diet on day 14 following 13 days of unlabelled triclosan feed. Additionally, plasma AUC levels were greater than AUC's in the liver and kidney of these animals suggesting that triclosan and/or its metabolites do not accumulate in these organs.

In a carcinogenicity study (Parkes, 1986), groups of 3 to 20 Sprague-Dawley rats were sacrificed 13, 26, 52, 78 and 104 wks after administration of triclosan in the diet at dose levels equivalent to 0, 12, 40 or 127 mg/kg bw/day in males and 0, 17, 56 or 190 mg/kg bw/day in females, and levels of triclosan and its conjugates determined in the blood, liver and kidney. Overall, levels of triclosan and its conjugates combined in the blood, liver and kidney were proportional to the feeding level.

Groups of 5 female Wistar rats were sacrificed up to 24 h after intravaginal administration of 5 mg/kg bw ¹⁴C-triclosan and triclosan levels determined in the liver, kidneys, skeletal muscle, peritoneal fat and brain (Siddiqui and Buttar, 1979). Maximum levels of triclosan were seen in the liver, kidney, skeletal muscle and peritoneal fat 4 h after administration (2.01, 2.34, 0.37 and 0.52 µg/g respectively) and for the brain 2 h after administration (0.14 µg/g).

Mice

Groups of 3 male ddY mice were sacrificed 6, 12 and 18 h after a topical application of 1.6 mg ³H-labelled triclosan in ethanol/olive oil (Kanetoshi et al., 1992). Radioactivity levels in tissues reached maximum or constant levels 12 to 18 h post application. Maximum levels were 402, 13.4, 10.0, 7.5, 6.6, 4.3, 1.8, 1.3, 1.1 and 0.5 µg/g in the gall bladder, liver, fat, lung, blood, kidneys, heart, testes, spleen and brain respectively. Compared to an oral study using the same dose and strain of mice (see Kanetoshi et al., 1988b below), the maximum radioactivity in tissues in

this dermal study ranged from 14% to 67% of the maximum values following oral administration (e.g. 36% and 67% in the gall bladder and fat respectively).

In a study that primarily investigated distribution (Kanetoshi et al., 1988b), groups of 3 male ddY mice were administered 1.6 mg ³H-labelled triclosan by gavage and sacrificed up to 96 h later. Whole body autoradiography was also undertaken on those animals sacrificed at 6 and 24 h. Whole body autoradiography at 6 h showed the highest radioactivity in the intestine due to unabsorbed tritiated compound, which had been transferred to the rectum. Radioactivity was also high in the gall bladder with lower but significant radioactivity in the liver, heart, lung, kidneys and hypodermic fat. No radioactivity was seen in the brain or testes. At 24 h the radioactivity decreased in each tissue except the gall bladder where it remained high. Furthermore, distinct radioactivity was seen in the small intestine. These results suggest enterohepatic circulation of triclosan. Additionally, it was seen that radioactivity peaked in blood and organs 3 to 6 h after administration of ³H-labelled triclosan. Maximum levels of triclosan were 1130, 83.0, 44.8, 43.0, 19.6, 15.0, 13.1, 8.6, 8.2 and 1.9 µg/g in the gall bladder, liver, blood, lung, kidneys, fat, heart, testes, spleen, and brain respectively.

Groups of 6 male and 6 female Swiss (Howes et al., 1989a) and C-57 (Howes et al., 1989b) mice were administered 188 and approximately 200 mg/kg bw ¹⁴C-labelled triclosan by gavage respectively, and a single animal of each sex and strain was sacrificed 0.5, 1, 2, 4, 8 and 24 h post dosing and whole body autoradiography undertaken. In Swiss mice it is reported that the stomach and gastrointestinal tract in all animals contained the highest level of radioactivity. Radioactivity appeared in well-perfused organs (e.g. liver, kidney) within 30 min of dosing. At times when radioactivity was clearly highest in the body (2 to 4 h), several tissues were prominent and included: adrenals, bone marrow, skin, surfaces of the eye and contents of the orbit, heart, lung, pituitary, testes, thyroid, tongue, trachea (associated with the cartilaginous rings), uterus, cervix and vagina. At later times radioactivity was seen in the gall bladder and bile duct and the evidence of radioactivity in the lower gastro-intestinal tract at 24 h is suggestive of enterohepatic circulation. No radioactivity was seen in the central nervous system, skeletal muscle, bone, thymus, spleen, eye, lymph nodes or salivary gland. The same distribution pattern of radioactivity and evidence suggesting enterohepatic circulation was seen in C-57 mice.

Groups of 15 male and 15 female Crl: CD-1 mice received a single gavage dose of 2 or 200 mg/kg bw ¹⁴C-labelled triclosan or the same radiolabelled dose in the diet on day 14 following 13 days of unlabelled triclosan feed at the same dose level (van Dijk, 1995). Ninety-six hours after administration of the radiolabel by either dosing schedule the mean radioactivity detected in the liver ranged from less than 0.05% to 0.1% of the applied dose and was less than 0.05% in the kidney, bile, and other organs/tissues (excluding intestinal tract) in animals at both dose levels. For the residual carcass, the mean radioactivity level was 1.4% of the applied dose in males receiving 200 mg/kg ¹⁴C-labelled triclosan on day 14 and ranged from 0.1 to 0.3% in all other groups. Additionally in another experiment by van Dijk using groups of 23 male Crl: CD-1 mice (1995), the observance of similar kidney and plasma levels of radioactivity compared to 2- to 3-fold higher levels in the liver after single as well as repeated oral administration of 2 or 200 mg/kg ¹⁴C-labelled triclosan suggests possible retention of triclosan and/or its metabolites in mouse liver.

Hamster

Groups of 6 male and 6 female Syrian hamsters were administered approximately 130 mg/kg bw ¹⁴C-labelled triclosan by gavage and a single animal of each sex was sacrificed 0.5, 1, 2, 4, 8 and 24 h post dosing and whole body autoradiography undertaken (Howes and Moule, 1989). It is reported that the stomach and gastrointestinal tract in all animals contained the highest level of radioactivity. Radioactivity appeared in well-perfused organs (e.g. liver, kidney) within 30 min of dosing. At times when radioactivity was clearly highest in the body (2 to 4 h), several tissues were prominent and included: adrenals, bone marrow, skin, surfaces of the eye and contents of the orbit, heart, lung, pituitary, testes, thyroid, tongue, trachea (associated with the cartilaginous rings), uterus, cervix and vagina. At later times radioactivity was seen in the gall bladder and bile duct and the evidence of radioactivity in the lower gastro-intestinal tract at 24 h is suggestive of enterohepatic circulation. No radioactivity was seen in the central nervous system, skeletal muscle, bone, thymus, spleen, eye, lymph nodes or salivary gland.

Groups of 5 male and 5 female Syrian golden hamsters received a single gavage dose of 2 or 200 mg/kg bw ¹⁴C-labelled triclosan or the same radiolabelled dose in the diet on day 14 following 13 days of unlabelled triclosan feed at the same dose level (van Dijk, 1994). One hundred and sixty-eight hours after administration of the radiolabel by either dosing schedule the mean radioactivity detected in the liver, kidney and other organs/tissues (excluding intestinal tract) all ranged from less than 0.05% to 0.1% of the applied dose in animals at both dose levels. For the blood and carcass, the mean radioactivity level in the groups ranged from 0.1% to 0.8% and 0.3% to 1.1%, while radioactivity in the bile was less than 0.05% of the applied dose in all groups. Additionally in this study, and in contrast to the finding in mice (van Dijk, 1995), plasma levels of radioactivity determined in groups of up to 16 male Syrian hamsters were over 2 times higher than seen in the liver after a single as well as repeated oral administration of 2 or 200 mg/kg bw ¹⁴C-labelled triclosan, and provide no evidence that retention of triclosan and/or its metabolites occurs in hamster liver.

Guinea-pig

A series of experiments are available by Black et al. (1975) that employed 5 male Dunkin-Hartley guinea-pigs per group per sacrifice time. In the experiment that examined the most tissues, radioactivity was detected in the blood, depot fat, liver, kidney, brain and testes immediately after topical application of 0.5 mL of a superfatted soap containing 1% ³H-labelled triclosan for 2 min of lathering then wash. Levels in the brain and testes decreased thereafter (from 2.2 to 1.7 ppb and 11.0 to 6.3 ppb respectively at 48 h), while levels in the blood, depot fat, liver and kidney were seen to increase at 48 h (6.3, 15.7, 18.5 and 16.2 ppb respectively) then decrease thereafter. Repeated application of the same dose applied twice daily for a total of 9 applications resulted in higher levels in the tissues examined immediately after the last dose (19, 28, 62 and 70 ppb in blood, depot fat, liver and kidney respectively, the only tissues examined).

Dog

While studies are available that clearly show absorption of triclosan after dermal (Hong et al., 1976) and oral (Stierlin, 1972a; Ciba-Geigy Limited, 1977b; Parkes,

1978b) administration, no investigation of the distribution of triclosan was conducted in these studies.

Monkey

In a 90-day study (Parkes, 1979), 2 male and 3 female infant Rhesus monkeys were bathed daily for 5 min with 15 mL of a soap solution containing 0.1% triclosan (i.e. 1 mg/mL), killed 1 to 5 days after the treatment period and levels of total triclosan (i.e. triclosan and conjugated triclosan combined) determined in organs and tissues (Parkes, 1979). Excluding the treatment area, highest concentrations were present in the kidney (0.1 to 0.9 ppm), liver (less than 0.1 to 0.5 ppm) and lung (0.2 to 1.3 ppm). No triclosan and its conjugates or trace levels only were found in brain, bone marrow, eye, skeletal muscle, thymus for all animals, and ovary in females.

While studies are available that clearly show absorption of triclosan after oral administration, such as by Caudal et al. (1975), Ciba-Geigy Limited (1976b; 1977b) and Parkes (1978b), no investigation of the distribution of triclosan was conducted.

17.2.2 Human studies

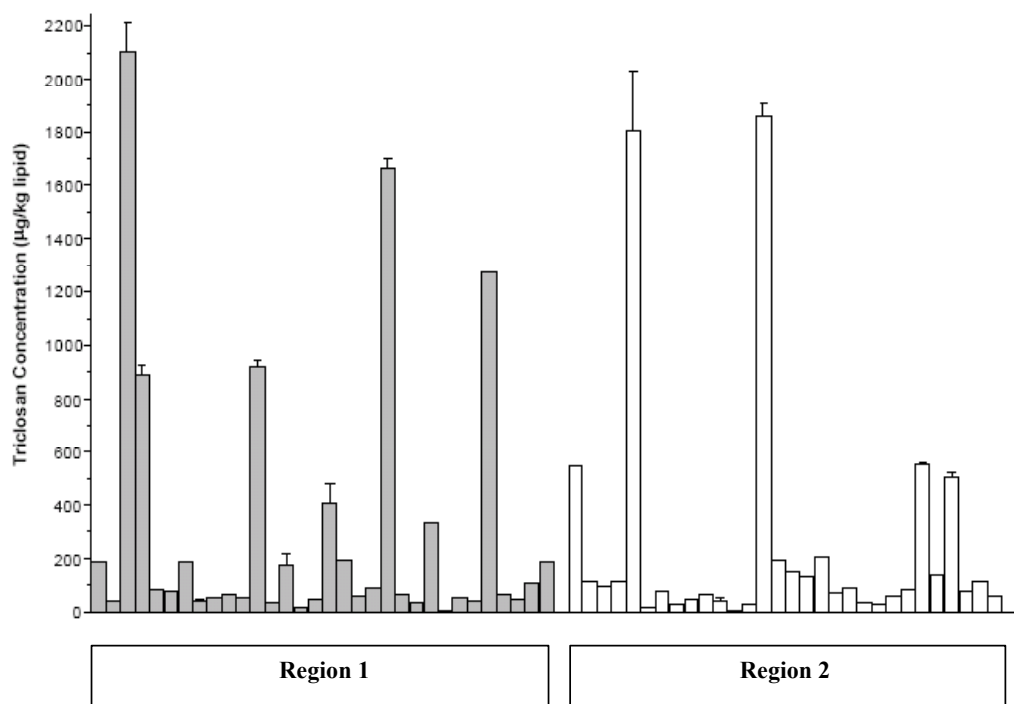
While many studies are available that clearly show absorption of triclosan following oral and dermal administration (see subsection 17.1.2), only limited data on distribution is available.

Five randomly selected samples of human breast milk from a mothers milk centre in Stockholm Sweden were analysed by GC/mass spectrometry (MS) for triclosan (Adolfsson-Erici et al., 2002). In this briefly reported study, triclosan was detected in 3 samples (60, 130 and 300 µg/kg lipid weight). The remaining 2 samples and a sample of cow's milk contained triclosan at levels less than 20 µg/kg lipid weight (the limit of detection).

Similarly, a total of 62 human milk samples were obtained from two US milk banks (approximately half the samples from each), the mothers milk bank in San Jose, California and the mothers milk bank in Austin, Texas and analysed by GC/MS for triclosan (Plautz, 2005). The analytical method had a quantification limit of 5 ng/g lipid. Triclosan ranged from 6 µg/kg lipid to approximately 2200 µg/kg lipid (stated to be equivalent to approximately 0.2 to 55 µg/kg milk) with a similar range of concentrations seen between the two sources of milk samples (see Figure 17.1). Additionally, 15 samples were analysed in duplicate and similar results obtained (indicated by error bars in Figure 17.1)

In a study commissioned by NICNAS the National Research Centre for Environmental Toxicology at Queensland University determined triclosan levels in 141 breast samples from 12 regions throughout Australia that were collected 2 to 8 wks post partum from primipara mothers aged 16 to 45 years. Samples were analysed by GC/MS, and triclosan levels (form not distinguished) were seen to range from less than 0.019 ng/g milk (the limit of quantification) to 19 ng/g milk (equivalent to 19 µg/kg milk). In comparison, levels in two samples of cow's milk were both determined to be 0.24 ng/g milk (equivalent to 0.24 µg/kg milk). A comprehensive summary of this NICNAS commissioned study is provided in Appendix E.

Figure 17.1: Triclosan in human milk samples



Very recently, human breast and blood samples taken twice from 36 mothers in a childcare centre in Stockholm, Sweden, were analysed by GC/MS/electron capture negative ionisation for triclosan (Allmyr et al., 2006). Monitoring of the mothers personal care products for triclosan was also undertaken. Nine mothers used personal care products labelled as containing triclosan. Twenty-six mothers were denoted as controls, based on the lack of labelling of triclosan in their personal care products. One mother was excluded from the analysis as there was uncertainty concerning her exposure to personal care products containing triclosan.

Triclosan in plasma was seen to range from 0.40 – 38 (mean 16) ng/g and 0.49 – 38 (mean 6.7) ng/g for the two sampling times in triclosan exposed mothers. Values in controls were 0.018 – 4.1 (0.072) ng/g and 0.010 – 19 (0.067) ng/g. Levels in breast milk ranged from 0.32 – 0.95 (mean 0.54) ng/g and 0.022 – 0.84 (mean 0.33) ng/g in triclosan exposed mother and <0.018 (the limit of quantification) – 0.35 (mean 0.019) ng/g and <0.018 – 0.33 (mean <0.018) ng/g in controls.

The data from this study indicate mean triclosan concentrations in the plasma are significantly higher than in the milk for both triclosan exposed and control mothers. The higher concentrations in the plasma and milk of triclosan-exposed mothers compared to controls suggest that personal care products containing triclosan are a major source of systemic exposure. The presence of triclosan in the whole study population indicates, however, that there are sources of exposure other than personal care products.

No binding of the radioactive material to the cellular constituents of the blood occurred following ingestion of a gelatine capsule containing 204 mg ¹⁴C-labelled triclosan (equivalent to 2.6 mg/kg bw) by a healthy male volunteer (Ciba-Geigy Limited, 1976c).

17.2.3 Other data

In vitro

The plasma protein binding of 3.2, 6.4 and 16 µg/mL ¹⁴C-labelled triclosan was determined in human, rat and hamster blood by an equilibrium dialysis method in vitro (Sagelsdorff and Busner, 1995). Equilibrium was reached for all samples and concentrations after 4 to 5 h, and 98.4% to 99.2%, 98.1% to 98.7% and 98.7% to 99.0% of the radioactivity was bound (non-covalent binding) to human, mouse and hamster plasma proteins respectively. There was no marked difference between species, and the ratio of bound to unbound fraction was constant over the tested concentrations indicating no saturation of binding up to 16 µg/mL ¹⁴C-labelled triclosan. A further in vitro study using human blood and the same methodology is also available (Wagner, 1973). At concentrations up to 7.9 µg/mL ¹⁴C-labelled triclosan 99.8% of the radioactivity was bound to serum proteins, with the data indicating no saturation of binding. Additionally, a further experiment by Wagner (1973) indicates that in plasma the majority of ¹⁴C-labelled triclosan binds to albumin.

Summary

The available data in rodents indicate that following dermal or oral administration of radio-labelled triclosan, radioactivity is widely distributed to organs and tissues. Overall, highest levels were generally seen in well-perfused and excretory organs such as liver, lung, kidney, gastrointestinal tract and gall bladder. There is evidence that suggests that the liver is a specific target organ in mice, with elevated levels seen in this organ compared to in the plasma and kidney, and that retention of triclosan and/or its metabolites may occur in the liver. Investigations in rats provide evidence of enterohepatic circulation. Although not specifically investigated in mice and hamsters limited evidence is available for enterohepatic circulation in these species. The only study available in monkey provides limited evidence of a wide distribution of triclosan and/or its metabolites following dermal exposure. While the observance of triclosan in breast milk samples indicates the potential for wide spread distribution in humans following absorption.

17.3 Metabolism

17.3.1 Animal studies

Rat

Following dermal application of 100 µL of 64.5 mM of ³H-labelled triclosan to groups of 3 female rats (strain not reported) recovery of radioactivity in the urine over 24 h was 0.88% of the applied dose, and the urinary radioactivity comprised approximately 50% triclosan, 40% triclosan glucuronide and 10% triclosan sulphate as determined by HPLC (Moss et al., 2000). In contrast in the faeces, 5 and 3.5% of the applied dose was identified as triclosan glucuronide and triclosan respectively, while triclosan sulphate was not detected.

The effect of anaesthesia (ether or nembutol) on triclosan levels in blood was investigated in groups of 5 rats (strain and sex not reported) 3 h after topical application of 200 mg/kg ¹⁴C-labelled triclosan (Hong et al., 1976). Parent compound was detected in blood from all animals. However, a statistically

significant decrease in triclosan levels was seen when nembutol (but not ether) was used as anaesthesia compared to no anaesthesia. Thus, it appears that the choice of anaesthesia can influence the metabolism of triclosan and, therefore, the authors recommend that anaesthesia not be used when blood samples are taken from rats.

Van Dijk (1996) investigated the conjugating capacity of the liver. The livers from groups of 4 male BRL-HAN Wistar rats sacrificed 0.5, 1, 2 or 4 h after a single gavage dose of 2 or 200 mg/kg bw ¹⁴C-labelled triclosan, or the same radiolabelled dose in the diet on day 14 following 13 days of unlabelled triclosan feed at the same dose level, were pooled and thin-layer chromatography (TLC) analysis undertaken to determine the amount of triclosan. The amounts of triclosan observed was 91.1% and 75.6% along with 5.2% and 21.7% triclosan conjugates and/or metabolites following administration of 2 and 200 mg/kg bw respectively. Corresponding values following repeated administration of 2 and 200 mg/kg bw were 87.2% and 66.1% and 8.6% and 30.8% respectively. Thus, liver extracts showed higher percentages of conjugated triclosan and/or metabolites at the top dose level as compared to the percentages at the low dose level, indicating a higher conjugating /metabolising capacity at 200 mg/kg bw. Similarly, further experiments by van Dijk (1996) in the same sex and strain of rat showed lower levels of triclosan compared to conjugated triclosan and/or metabolites following a single dose of 2 (3.7% and 9.3% respectively) or 200 mg/kg bw (1.7% and 10.3%) ¹⁴C-labelled triclosan.

In a study investigating the metabolic profile of triclosan (Tulp et al., 1979), male Wistar rats (number not reported) received a single gavage dose of 500 mg/kg bw triclosan and metabolites identified by TLC/MS in urine and faeces collected for 7 days after dosing as well as liver and fat samples obtained on day 7. Unchanged triclosan was detected in the urine, faeces, liver and fat. The main route of metabolism was by aromatic hydroxylation of the ortho- and meta- positions of the ether bond of the benzene ring. Hydroxylated metabolites were detected in urine (five) and faeces (three) but not in liver or fat. In the faeces triclosan and its metabolites were mostly unconjugated, while in the urine both triclosan and its metabolites appear partly as conjugates. A minor route of metabolism was by scission of the ether bond producing 2,4-dichlorophenol and 4-chlorocatechol, and both these metabolites were detected in urine, 2,4-dichlorophenol in faeces and neither metabolite in liver or fat samples. This study also investigated the potential for metabolic formation of chlorodibenzo-*p*-dioxins or chlorodibenzofurans and found no evidence of either.

Triclosan levels in plasma were below the limit of detection (50 ppb) from 30 min (earliest sampling time) to 72 h after oral administration of 5 mg/kg bw ¹⁴C-labelled triclosan to 2 male Sprague-Dawley rats (Lin and Smith, 1990). The radioactivity in the plasma was determined to be triclosan glucuronide and triclosan sulphate whose levels were approximately equal within 6 h of dosing. Thereafter, levels of the sulphate conjugate were approximately 2-times greater than the glucuronide. Similar results were seen when the same dose of unlabelled triclosan in aqueous solution or slurry of toothpaste in water was gavaged to male Sprague-Dawley rats (Lin and Smith, 1990). In these studies with unlabelled triclosan it was seen that over 72 h 0.09% to 0.13%, 0.05% to 0.12% and 0.07% to 0.21% of the applied dose was detected in the urine as triclosan, triclosan glucuronide and triclosan sulphate respectively. Corresponding values in the faeces were 47.3% to 53.6%, 5.6% to 5.0% and 3.1% to 5.0% respectively.

Similarly, up to 24 h after oral administration of 5 mg/kg bw ¹⁴C-labelled triclosan less than 1% of the radioactivity detected in the plasma was identified as triclosan (Ciba-Geigy Limited, 1977b).

Radioactivity detected in the urine of male rats up to 96 h after oral administration of 50 mg/kg bw ¹⁴C-labelled triclosan was mainly in the form of triclosan conjugates (Hong et al., 1976).

Data on levels of triclosan and its conjugates in blood, liver and kidney are available from a carcinogenicity study in male and female Sprague-Dawley rats that received triclosan in the diet up to 127 and 190 mg/kg bw/day in males and females respectively (Parkes, 1986). In both sexes, the main form seen in the liver was triclosan (21.7 to 50.1 µg/g) followed by sulphate conjugate (8.8 to 19.5 µg/g) and then glucuronide conjugate (5.3 to 10.8 µg/g). In contrast, very little triclosan was seen in the blood and kidney and the sulphate conjugate was more predominant than the glucuronide conjugate in both sexes (33.8 to 85.7 µg/g in the blood, and 16.5 and 20.5 µg/g in the blood, and 26.2 to 51.3 µg/g and 19.4 to 27.8 µg/g in the kidney, respectively).

The metabolites in bile collected over 10 h from 5 male RA rats following oral administration of 5 mg/kg bw ³H-labelled triclosan was determined by TLC (Stierlin, 1972a). Thirty percent of the radioactivity was determined to be triclosan, 40% as glucuronide, and the remaining 30% as 2 or 3 unconjugated (unidentified) metabolites. In a further study (Black et al., 1975), bile collected over 4.5 h from 2 male Colworth-Wistar rats, whose bile ducts were cannulated and had received 5 mg/kg bw ³H-labelled triclosan by gavage, essentially contained triclosan glucuronide. Similarly, the radioactivity in the urine and faeces in this study was present as the glucuronide with very little present as triclosan.

Mice

Metabolites were determined in the plasma, and in the urine, liver and kidney, in groups of 15 and 24 male Crl: CD-1 mice respectively, 4 h after a single gavage dose of 2 or 200 mg/kg bw ¹⁴C-labelled triclosan or the same radiolabelled dose in the diet on day 14 following 13 days of unlabelled triclosan feed at the same dose level (van Dijk, 1995).

In the plasma, the majority of radioactivity recovered was as the sulphate conjugate in all groups (73% to 90%) except low dose males receiving a single dose. Excluding this group, it was seen that no triclosan was detected though low levels of glucuronide conjugate were present (5% to 21%). In the liver, triclosan (24% to 65%) and the sulphate conjugate (34% to 76%) were detected in all groups. Glucuronide conjugate was not detected. Similarly in the kidney, triclosan was detected in all groups (44% to 67%) along with the sulphate conjugate (24% to 51%) while no glucuronide conjugate was detected. Varied results were seen in the urine.

For the single low dose group, no glucuronide conjugate was detected in the urine with only 19% and 2% of the radioactivity recovered determined to be triclosan and the sulphate conjugate respectively. For the low dose repeat group, triclosan, glucuronide conjugate and sulphate conjugate were all detected in the urine (38, 4 and 3% of the recovered radioactivity respectively). No sulphate conjugate was detected in single and repeat high dose animals, though the predominant metabolite varied between the two groups (65% triclosan and 23% glucuronide conjugate for

the single dose group with corresponding values of 30% and 63% for the repeat dose group respectively).

Additionally, low levels of four unidentified non-triclosan conjugates were detected in the plasma, liver and kidney. In the plasma low amounts of radioactivity represented non-triclosan conjugates (0.4% to 6.0% of the administered radioactivity) while in liver and kidney negligible and low amounts (less than 0.5% to 2.9%) were detected. In urine, four unidentified non-triclosan conjugates and two unidentified metabolites were detected that accounted for 11% to 15% and 2% to 4% of the administered radioactivity in low and high dose groups respectively. This indicates that the phase I metabolism of triclosan in male Crl: CD-1 mice is reduced at the high dose group compared to the low.

Overall, this well conducted study provides evidence that the sulphate conjugate produced in the liver transported via the plasma to the kidney undergoes re-conjugation in the kidney to the glucuronide before being eliminated into the urine.

A further experiment by van Dijk (1995) using 15 male and 15 female Crl: CD-1 and the same dose levels and dosing regime determined metabolites in faeces collected over 72 h from administration of ¹⁴C-labelled triclosan. Of the radioactivity recovered, triclosan was found predominantly (45% to 61% of the administered radioactivity) with low levels of the glucuronide conjugate (1% to 7%) detected in females that received a single low dose and males and females that received a single high dose. No sulphate conjugate was detected in any group.

Male and female Swiss (Howes et al., 1989a) and C-57 (Howes et al., 1989b) mice were administered 188 and approximately 200 mg/kg bw ¹⁴C-labelled triclosan by gavage respectively, a single animal of each sex sacrificed at set-time points up to 24 h post dosing, and metabolites determined in the urine and faeces by TLC. In C-57 mice, approximately 40% of the radioactivity obtained in urine over 24 h was conjugated with little triclosan detected. In contrast, triclosan was mainly found in the faeces. Similar findings were observed in Swiss mice.

Hamster

Metabolites were determined in the plasma, and in the urine, liver and kidney, in groups of 5 and 16 male Syrian golden hamsters respectively, 1 to 2 h after a single gavage dose of 2 or 200 mg/kg bw ¹⁴C-labelled triclosan or the same radiolabelled dose in the diet on day 14 following 13 days of unlabelled triclosan feed at the same dose level (van Dijk, 1994).

In plasma, the majority of the radioactivity recovered was as the glucuronide conjugate in all groups (24% to 56%) except high dose males receiving a single dose. Excluding this group, lower levels of the sulphate conjugate were detected (7% to 28%) while no triclosan was detected in any group. In the liver, the predominant form of radioactivity in all groups was as triclosan (55% to 73% of the recovered radioactivity) with lower levels of the sulphate conjugate detected (8% to 38%). The glucuronide conjugate was detected in single dose animals (2% to 8%) but not repeat dose. In the kidney, the predominant form of radioactivity was as the glucuronide conjugate (46% to 60%) with triclosan also detected in all dose groups (29% to 37%). Low levels of the sulphate conjugate were detected in all groups (3% to 7%) except the high dose repeat group. For all groups, the majority of radioactivity recovered in urine was as the glucuronide conjugate (56% to 82%). Triclosan was also detected in all groups (1% to 7%) while none of the

radioactivity in urine was as the sulphate conjugate. Comparison of the metabolism patterns at the low and high dose levels in the plasma, liver and kidney following administration of 2 or 200 mg/kg bw ¹⁴C-labelled triclosan, indicates that the conjugating capacity to form triclosan sulphate in the liver of male Syrian golden hamsters was specifically enhanced at the high (single and repeated) dose.

Additionally, low levels of four unidentified non-triclosan conjugates and a metabolite were detected in the plasma, liver and kidney. For the low dose groups the majority of the recovered radioactivity in the plasma was as these non-triclosan conjugates (60% to 65%) while much lower levels were seen in the liver (17% to 19%) and kidney (15% to 21%). In the high dose groups, the levels of these non-triclosan conjugates in the plasma, liver and kidney were seen to decrease (5% to 15%, 1% to 2% and 3% to 10% respectively). Similarly in the urine lower levels of these non-triclosan conjugates were seen in high dose groups compared to low dose groups. Thus, these results indicate less extensive phase I metabolism of triclosan at the high dose as compared to the low dose.

In this well conducted study, overall, the presence of sulphate conjugate in the liver and plasma and its absence in the kidney and urine, where triclosan was mainly detected as the glucuronide conjugate, suggest that re-conjugation occurs in the kidney to the glucuronide before it is eliminated into the urine.

A further experiment by van Dijk (1994) using 5 male and 5 female Syrian golden hamsters and the same dose levels and dosing regime determined metabolites in faeces collected over 96 h from administration of ¹⁴C-labelled triclosan. Of the radioactivity recovered, triclosan was found predominantly in all groups (6.9% to 21.1% of the administered radioactivity) with low levels of the glucuronide conjugate also detected (0.2% to 5.1%). No sulphate conjugate was detected in any group.

Dog

Only small amounts of triclosan were detected in the blood (132 ppb) from a single beagle dog (sex not reported) that received daily topical application of 200 mg/kg bw triclosan in water for up to 4 months (Hong et al., 1976). In contrast, considerable amounts of triclosan conjugates were seen in the urine and bile (approximately 250 000 and 609 000 ppb respectively).

TLC analysis indicated that less than 1% of the radioactivity in the blood was as triclosan 3 h after oral administration of 5 mg/kg ¹⁴C-labelled triclosan to 2 male beagle dogs (Ciba-Geigy Limited, 1976b). Eighty-nine percent of the radioactivity was as triclosan sulphate and 7% as the triclosan glucuronide. Similar results were seen 6 h after dosing. In a further study in which 5 mg/kg bw ¹⁴C-labelled triclosan was administered by gelatine capsule to 2 male beagle dogs (Ciba-Geigy Limited, 1977b), approximately one third and 35% of the radioactivity present in urine and faeces collected over 144 h following dosing was as triclosan respectively.

In urine collected over 120 h following oral administration of 5 mg/kg bw ¹⁴C-labelled triclosan to 2 male beagle dogs (Stierlin et al., 1972a), TLC analysis indicated that 30% of the radioactivity detected was as triclosan and 20% to 40% as glucuronides. Of the radioactivity in the faeces, 60% was as triclosan with only 'a small percentage' as glucuronides.

In a study investigating buccal absorption of triclosan in beagle dogs (1 per sex) following application of 2 to 5 mL of a mouthrinse containing 0.03% triclosan (Lin et al., 1994), sulphate conjugate was determined to be the major metabolite in plasma and urine. No triclosan was detected in the plasma though a small amount was detected in the urine. No difference was seen between the sexes.

Monkey

Two 3-day old Rhesus monkeys (sex not reported) were washed with a soap solution containing 1 mg/mL triclosan and blood samples taken up to 24 h later (Parkes, 1978a). No triclosan was detected. Glucuronide conjugate levels were seen to decrease from the earliest sampling time of 1 h and sulphate conjugate levels to increase.

In a 90-day study (Parkes, 1979), 5 male and 5 female infant Rhesus monkeys bathed daily for 5 min with 15 mL of a soap solution containing 0.1% triclosan (i.e. 1 mg/mL) and levels of triclosan and its conjugates determined in blood taken on day 1 or 2 and then at 15 day intervals. No triclosan was detected. In the first two days levels of the glucuronide and sulphate conjugate were comparable, but the sulphate then increased as the glucuronide decreased. On day 90, 80% to 90% of the triclosan detected was as the sulphate conjugate. In urine collected over the treatment period, some triclosan was detected, though the majority was present as the glucuronide conjugate. In contrast, essentially all the triclosan detected in the faeces was unconjugated.

TLC analysis indicated that none of the radioactivity in the blood was as triclosan 8 and 12 h after oral administration of 5 mg/kg ¹⁴C-labelled triclosan to 2 male baboons (Ciba-Geigy Limited, 1976b). At 8 h, 24% and 33% of the radioactivity was as triclosan glucuronide and triclosan sulphate respectively. Though by 12 h, 11% was the glucuronide and 44% the sulphate. In urine collected 72 h following dosing, 6% of the radioactivity was as triclosan and 75% as the glucuronide. Similar findings were seen in a further experiment when 2 male baboons ingested a gelatine capsule containing 5 mg/kg bw ¹⁴C-labelled triclosan (Ciba-Geigy Limited, 1977b). Additionally in this experiment, 69% of the radioactivity detected in the faeces was as triclosan.

One female and three male rhesus monkeys received an oral dose of 5 mg/kg bw triclosan and triclosan and its conjugates determined in blood, urine and faeces up to 5 days after dosing (Parkes, 1978b). Essentially all the triclosan in the blood existed in conjugated form. Initially the glucuronide predominated but after 3 to 5 h the sulphate predominated. Similarly in a 1-year chronic study (Caudal et al., 1975), blood samples taken from male baboons that received daily doses of triclosan up to 300 mg/kg bw indicated nearly all the triclosan present existed in conjugated form.

17.3.2 Human studies

In a 20-day hand washing study in which 7 male and 6 female healthy volunteers (aged from 18 to 62 years old) washed their hands 6 times a day (i.e. every 2 h) for 15 seconds with on average approximately 3.5 g/liquid hand wash containing approximately 1.0% triclosan, triclosan was present in the plasma predominantly in the (undetermined) conjugated form (Ciba Specialty Chemicals Corporation, 2002).

Triclosan conjugates were detected in the plasma of 5 Negroid volunteers aged 36 to 45 year old (sex not reported) during the 45 days that they washed and showered (twice on day 1 and three times thereafter) with soap bars containing 1% triclosan (Wagner and Le Sher, 1977). The plasma samples from subjects with lower plateau levels of conjugated triclosan (less than 400 ng/mL) contained primarily glucuronide conjugate, and plasma samples from those subjects with higher plateau levels (greater than 400 ng/mL) contained primarily sulphate conjugates. In these subjects, all triclosan in the urine was reported as the glucuronide conjugate while faecal samples contained mainly free triclosan with low amounts of conjugates.

In urine collected over 48 h after topical application of 150 mg triclosan in a cream to 6 healthy male volunteers (Caudal et al., 1974), the mean percentage of the dose administered identified as triclosan and triclosan glucuronide was 3.90 and 0.01 respectively. In a further study in which triclosan was administered in a cream (Stierlin, 1972b), the radioactivity in urine collected over 72 h from application of 3% ³H- or ¹⁴C-labelled triclosan was predominantly as triclosan glucuronide in both female subjects.

Thirty-three Caucasian, 28 Negroid and 23 Oriental volunteers used a soap bar containing 0.75% triclosan and a deodorant containing 0.28% triclosan at least once daily, along with a dentifrice containing 0.28% triclosan at least twice daily, for 13 wks (Beiswanger and Tuohy, 1990). While there are concerns of non-compliance with regards to use of soap and deodorant in Oriental volunteers, no difference was seen in the pattern of metabolism: triclosan glucuronide was seen to be the predominant metabolite in plasma in Caucasians, Negroids and Orientals throughout the study with very low levels of free triclosan seen in comparison. Inefficiencies in the analytical procedures used prevented a reliable quantitation of triclosan sulphate levels.

A healthy male volunteer ingested a gelatine capsule containing 204 mg ¹⁴C-labelled triclosan (equivalent to 2.6 mg/kg bw) and blood samples were taken 30 min and 1, 2, 4, 8, 24 and 72 h later (Ciba-Geigy Limited, 1976c). In the plasma, triclosan accounted for less than 1% of total radioactivity at all sample times, compared to 33% to 50% of triclosan glucuronide while a further unidentified conjugate was also identified at levels slightly less than triclosan glucuronide. In urine collected over 72 h following dosing approximately 1% of the total radioactivity was as triclosan with nearly all the remaining radioactivity identified as triclosan glucuronide.

In a similar study in which a male volunteer ingested a gelatine capsule containing 200.5 mg ¹⁴C-labelled triclosan (equivalent to 2.4 mg/kg bw) almost all of the radioactivity detected in urine collected over 72 h was reported as triclosan glucuronide while 30% to 40% of the radioactivity in the faeces was as triclosan (Stierlin et al., 1972b).

Data is available from a combined human tolerance and toxicokinetic oral study (Lucker et al., 1990), though it is not clear how many volunteers the pharmacokinetic data is based upon. The study had a single dose phase where volunteers received a single gelatine capsule containing 1 mg triclosan and calcium carbonate and a repeat dose phase when volunteers received 15 mg triclosan and calcium carbonate daily for 30 days so steady state blood levels were obtained.

Only 'traces' of triclosan were detected in the plasma following single and repeated administration. Of the total amount of triclosan detected in the plasma the main

metabolite was glucuronide conjugate (97%) with low amounts of sulphate conjugate also detected after a single dose (4%), however during steady state the amount of sulphate conjugate (53%) increased to levels greater than that of the glucuronide conjugate (37%). Following a single dose less than 1% of the given dose was as triclosan in the urine with the glucuronide conjugate the main metabolite (82% of the given dose) with low amounts of the sulphate conjugate also present (8%). Comparable values were seen following repeated dose administration. For faeces, data is only presented for repeated dose administration, and in contrast to that seen in the urine triclosan was mainly detected (6% of the dose administered) with lower and comparable levels of glucuronide and triclosan conjugate (approximately 3% each).

The AUC for the glucuronide conjugate did not change during the study. In contrast, the AUC increased significantly for the sulphate conjugate but no increase was seen in the elimination of sulphate conjugate in urine. Therefore, the data suggest that triclosan sulphate was converted to triclosan glucuronide in the kidney before elimination.

In 9 healthy male volunteers who ingested 2 mg triclosan twice daily in an aqueous solution for 21 days, triclosan was only detected in the blood of 1 volunteer at one sample time (Colgate-Palmolive Company, 1989). In contrast the glucuronide and sulphate conjugates were detected in all volunteers at all sampling times (maximum mean levels of 72 and 100 ng/mL respectively).

No triclosan but conjugated triclosan, mainly present as the glucuronide, was detected in the plasma of groups of 10 volunteers (sex not reported) who all used toothpaste containing 0.215% triclosan and toiletry products (soap, talc and antiperspirant) that contained triclosan or were triclosan free for 56 days (BIBRA International, 1988). Inter-subject variation prevented a meaningful comparison of the data between the two groups.

In a study investigating buccal absorption of triclosan (Lin, 1988), no triclosan but triclosan glucuronide and triclosan sulphate (mean of 23 and 2 ng/mL respectively) were detected in blood samples from 10 volunteers (sex not reported) after brushing with a dentifrice containing 0.6% triclosan for 13 days.

In further studies that investigated buccal absorption, no triclosan was detected in the plasma of 9 male volunteers during and after twice-daily use of a mouthrinse containing 0.03% triclosan for 21 days (Lin, 2000). Triclosan glucuronide and triclosan sulphate were detected in the plasma from the first sampling time. The same metabolism pattern was also seen in a 12-wk study where participants brushed their teeth twice daily with toothpaste containing 0.2% triclosan (Lin, 1989), and in 9 male volunteers that brushed twice daily for 21 days with a dentifrice containing 0.2% triclosan (Colgate-Palmolive Company, 1989).

In a study in 35 Caucasian, 26 Negroid and 22 Mongoloid (Oriental) volunteers who used a dentifrice containing 0.28% triclosan at least twice daily for 13 wks (Beiswanger and Tuohy, 1990), triclosan glucuronide was seen to be the predominant metabolite in plasma in Caucasians, Negroids and Orientals throughout the study with very low levels of free triclosan in comparison. Inefficiencies in the analytical procedures used prevented a reliable quantitation of triclosan sulphate levels.

In an in vitro study triclosan was shown to be sulfonated and glucuronidated in human liver cytosol and microsomes, respectively (Wang et al., 2004). Additionally, this study indicated that triclosan inhibited the sulphonation and glucuronidation of phenolic xenobiotics, such as 3-hydroxybenzo[a]pyrene (3-OH-BaP), in human liver in vitro. Furthermore, in the presence of varying degrees of concentrations of triclosan the inhibition of 3-OH-BaP sulfonation was non-competitive, whereas that of glucuronidation was competitive.

Summary

Triclosan was primarily metabolised to glucuronide and sulphate conjugates in rodents, dogs, monkeys and humans, though there is also evidence for small amounts of other unidentified metabolites. No difference in metabolic pattern was seen between Caucasian, Negroid and Oriental volunteers. Studies in rodents indicate the liver has a high conjugating capacity for triclosan, while in vivo and in vitro data in humans and rodents demonstrate that triclosan is also metabolised to glucuronide and sulphate conjugates in the skin. Following oral or dermal absorption triclosan was rapidly removed from the blood in humans and animals. The data indicate extensive first pass metabolism following absorption from the gastrointestinal tract. The extent to which the primary metabolites triclosan glucuronide and triclosan sulphate are formed, and the ratio of each, varies with the type of dosing (i.e. single versus repeat) and the species. In humans, with increasing levels of triclosan and its metabolites in the plasma there is an increase in circulating sulphate conjugates which can reach levels greater than the glucuronide. In the faeces of rodents, primates and humans triclosan is mainly excreted unchanged, while in urine the main metabolite is triclosan glucuronide. There is evidence in humans and rodents of re-conjugation in the kidney to the glucuronide before elimination into the urine.

17.4 Elimination and excretion

17.4.1 Animal studies

Rat

Twenty-four hours after dermal application of 100 μ L of 64.5 mM of 3 H-labelled triclosan to groups of 3 female rats (strain not reported), 7.72% of the administered dose remained in the carcass with a further 4.31% and 36.33% in the skin and the stratum corneum respectively (Moss et al., 2000). Over 24 h the primary route of excretion was through the faeces (11.84% of the applied dose) with urine being a minor route (0.88%).

Seventy-two hours after dermal application of 400 mg/kg bw 14 C-labelled triclosan to two male rats (strain not reported) 12.7% of the administered dose remained in tissues (including skin), organs and carcass (Hong et al., 1976). Over 72 h the primary route of excretion was through the faeces (14.7% of the applied dose) with urine being a minor route of exposure (0.5%).

A number of experiments are available comparing the toxicokinetics of triclosan following dermal application in a solution or cream (Ciba-Geigy Limited, 1976a). Over 96 h following application of 0.61 mg/kg bw 3 H-labelled triclosan in ethanol to 4 male SIV-50 rats the major route of excretion was the faeces (65.7% of the applied dose) with the urine being a minor route (3.2%). The same was seen over

96 h following application of 5mg/kg bw ¹⁴C-labelled triclosan in acetone to 2 male SIV-50 rats (88.9% and 2.8% respectively), and over 48 h when 1 male Wistar rat received 5mg/kg bw ³H-labelled triclosan in a cream (21.9% and 1.2%) and 4 female SIV-50 females received 37 mg/kg bw ³H-labelled triclosan in vaseline (32.2% and 10.6%).

Over 96 h following topical application of 0.2 mL ethanol containing 162 µg ³H-labelled triclosan to 4 female Colworth-Wistar rats (Black and Howes, 1975) twice as much of the applied dose was excreted through faeces (3.1 dpm x 10⁻⁸ tritium) compared to urine (1.5 dpm x 10⁻⁸ tritium). In the same study (Black and Howes, 1975), the faeces was also seen to be the primary route of excretion over 48 h following topical application of shampoos containing 0.05% to 2.0% of ³H-labelled triclosan to groups of 3 to 12 female Colworth-Wistar rats.

A number of oral experiments are reported in a well-conducted study by van Dijk (1996). Ninety-six hours after oral administration of 2 or 200 mg/kg bw ¹⁴C-labelled triclosan to groups of 5 male BRL-HAN Wistar rats a mean of 0.4% and 0.3% of the administered dose remained in the intestinal tract (with contents), liver, kidney and residual carcass combined respectively. Over 96 h the primary route of excretion was through the faeces (mean of 81.2% and 82.2% of the applied dose respectively) with urine being a minor route (11.2% and 12.2%).¹¹

In a further experiment by van Dijk using the same dose levels (1996), groups of 4 male BRL-HAN Wistar rats received ¹⁴C-labelled triclosan as a single gavage dose on day 1 or in the diet on day 14 following 13 days of unlabelled triclosan feed. Overall, for single administration, the elimination of radioactivity from the plasma from 1 to 72 h followed first order kinetics with a half-life of 12.6 h. Similarly for the high dose, elimination of radioactivity from the plasma from 4 to 72 h followed first order kinetics with a half-life of 10.0 h. The half-life of triclosan in the liver following single administration of the low and high dose was 9.8 and 11.0 h respectively, with corresponding half-life values of 12.0 and 13.0 h for the kidney. For the repeated dose schedule for both low and high dose treatment half-lives in the plasma, liver and kidney were found to be similar to those following single treatment.

Groups of 2 to 3 male Sprague-Dawley rats were administered 5 mg/kg bw unlabelled triclosan in aqueous solution or a slurry of toothpaste in water or 5mg/kg bw ¹⁴C-labelled triclosan in aqueous solution (Lin and Smith, 1990). Following administration of ¹⁴C-triclosan the elimination half-life for total radioactivity from the plasma was determined to be 14.7 to 15.2 h, with values of 5.9 to 7.3 h and 9.1 to 11.4 h for triclosan glucuronide and triclosan sulphate respectively. For the unlabelled triclosan solution the half-life for triclosan, triclosan glucuronide and triclosan sulphate were 11.5, 9.1 and 9.7 h respectively (with corresponding values of 65, 10.5 and 13.8 h following administration of the toothpaste slurry). Seventy-two hours after oral administration of 5 mg/kg bw unlabelled or labelled triclosan 1.1% to 2.8% of the administered dose remained in tissues, organs and carcass. Over 72 h the primary route of excretion was through the faeces (57.3% to 83.7% of the administered dose) with urine being a minor route (0.2% to 5.9%).

¹¹ A further 2.4 and 3.5 % of the applied radioactivity was detected in cage washings from animals receiving 2 or 200 mg/kg bw/day ¹⁴C-labelled triclosan respectively.

Seventy-two hours after oral administration of 50 mg/kg bw ¹⁴C-labelled triclosan to 4 male rats (strain not reported) 6.0% of the administered dose remained in tissues, organs and carcass (Hong et al., 1976). The primary route of excretion was through the faeces (79.4% of the administered dose over 72 h) with urine being a minor route (4.4%), while no radioactivity was detected in expired air. Using the same dose level and methodology (Hong et al., 1976) comparable levels of the administered dose were seen in the urine and faeces over 96 h following administration, however, the amount of the administered dose remaining in tissues, organs and carcass had decreased substantially (1.6%).

In groups of 2 male Wistar rats gavaged with 5 mg/kg bw ³H-labelled triclosan, the mean concentration of the dose that remained 2 h after administration in tissues, organs (excluding gastro-intestinal contents) and carcass was 32.4%, and had diminished to 13.4% and 3.7% after 6 and 8 h, respectively (Stierlin, 1972a). In the same study using the same dose level and 3 male Wistar rats 91.3% and 3.0% of the administered dose was excreted in the faeces and urine respectively over 72 h. Additionally, the faeces was the primary route of excretion over 168 h in 4 male and 4 female SIV-50 rats administered 0.38 mg/kg bw ³H-labelled triclosan (Stierlin, 1972a).

Over 24 h following intravaginal administration of 5 mg/kg bw ¹⁴C-labelled triclosan to 5 female Wistar rats (Siddiqui and Buttar, 1979), twice as much of the applied dose was excreted through faeces (26.1%) compared to urine (13.8%).

Mice

In a well conducted study by van Dijk (1995), groups of 15 male and 15 female Crl: CD-1 mice received a single gavage dose of 2 or 200 mg/kg bw ¹⁴C-labelled triclosan or the same radiolabelled dose in the diet on day 14 following 13 days of unlabelled triclosan feed at the same dose level. Ninety-six hours after administration of a single low dose a mean of 0.2% and 0.3% of the administered dose remained in the plasma, bile, intestinal tract (with contents), liver, kidney, other organs/tissues and residual carcass combined in males and females respectively. The corresponding value in males and females receiving a single high dose was 0.2% and 0.3% respectively. Ninety-six hours after day 14 for the repeated dose schedule, the values were 0.4% and 0.3% in low dose males and females respectively and 1.6% and 0.3% in high dose males and females respectively. Over 96 h the primary route of excretion was through the faeces (65.6% to 78.4% in single dose animals and 50.1% to 76.2% in repeated dose animals) with urine being a minor route (12.3% to 29.5% in single dose animals and 17.2% to 38.9% in repeated dose animals). Taking into account the radioactivity in the faeces, urine and cage wash (2.1% to 4.8% of the applied radioactivity was detected in cage washings from animals receiving 2 or 200 mg/kg bw/day triclosan by single or repeated dose), elimination was virtually complete by 96 h. Additionally, the elimination half-life of radioactivity in plasma determined in groups of 36 males and 35 females following a single dose of 2 or 200 mg/kg bw ¹⁴C-labelled triclosan was seen to be similar in both sexes (9.1 to 11.8 h in males and 8.9 to 9.9 h in females).

Excretion of radioactivity was determined over 24 h following oral administration of 188 and approximately 200 mg/kg bw ¹⁴C-labelled triclosan to Swiss (Howes et al., 1989a) and C-57 (Howes et al., 1989b) mice respectively. Both these studies indicated that the biliary route was the major route of excretion and is likely to

have resulted in a half-life of triclosan that was determined to be approximately 8 h in both strains of mouse. In Swiss mice 43.8% and 27.9% of the applied dose was excreted in urine in a single male and female respectively (which includes a value of 5.1% in the male and 3.6% in the female from radioactivity in cage rinsings and spital debris that the authors assumed to have been contaminated with urine), with corresponding values of 46.8% and 25.2% in the faeces. In C-57 mice 25.9% and 40.2% of the applied dose was excreted in the urine in a single male and female respectively (which includes a value of 9.3% in the male and 12.2% in the female from radioactivity in cage rinsings and spital debris that the authors assumed to have been contaminated with urine), with corresponding values of 37.3% and 42.6% in the faeces. Though reduced excretion rates were seen between the sexes in these studies the conflicting results in the two strains of mice together with the small number of animals used means no reliable conclusions can be made on these observed reduced rates.

Over 96 h following oral administration of 1.6 mg ³H-labelled triclosan to 3 male ddY mice 78% of the administered dose was excreted (Kanetoshi et al., 1988b), with approximately twice as much of the administered dose (i.e. about 50%) seen in the faeces than the urine.

Hamster

A well conducted study by van Dijk (1994) is available in groups of up to 5 male and 5 female Syrian golden hamsters that used the same methodology and dose levels as used for determining absorption in male and male female mice (van Dijk, 1995).

One hundred and sixty-eight hours after administration of a single low dose a mean of 2.4% and 0.6% of the administered dose remained in the blood, bile, intestinal tract (with contents), liver, kidney, other organs/tissues and residual carcass combined in males and females respectively. The corresponding value in males and females receiving a single high dose was 1.2% and 0.6% respectively. One hundred and sixty-eight hours after day 14 for the repeated dose schedule, the values were 1.7% and 0.6% in low dose males and females, respectively and 0.6% in both high dose males and females. Over 168 h the primary route of excretion was through the urine (60.4% to 80.0% in single dose animals and 63.7% to 70.0% in repeated dose animals) with faeces being a minor route (12.9% to 28.9% in single dose animals and 25.2% to 35.0% in repeated dose animals)¹². In this study the elimination half lives of radioactivity in the plasma determined following a single dose of 2 or 200 mg/kg bw ¹⁴C-labelled triclosan to groups of 12 male and 12 female Syrian hamsters was seen to be similar in both sexes (29.1 to 32.0 h in males and 24.5 to 27.0 h in females).

Over 24 h following oral administration of approximately 130 mg/kg bw ¹⁴C-labelled triclosan to Syrian hamsters (Howes and Moule, 1989), 66.0% and 75.0% of the applied dose was excreted in the urine in a single male and female respectively (which include a value of 19.0% in the male and 14.1% in the female from radioactivity in cage rinsings that the authors assumed to have been contaminated with urine), while the faeces was a minor route of excretion (0.3% and 0.1% in the male and female respectively).

¹² A further 2.4% to 7.5% of the applied radioactivity was detected in cage washings from animals receiving 2 or 200 mg/kg bw/day triclosan by single or repeated dose.

Guinea-pig

Over 48 h following a single topical application (2 min lathering then wash) of a super-fatted soap containing 0.08% ³H-labelled triclosan to 5 male Dunkin-Hartley guinea-pigs (Black et al., 1975) the primary route of excretion of the radiolabel was through the urine (10.9 µg) with the faeces seen as a minor route (0.2 µg). The same was also observed for a repeated schedule in which animals were washed twice per day for 4 days (67.1 µg in urine over 96 h compared to 6.8 µg in faeces).

Rabbit

Over 72 h following dermal application of 6, 8.6 or 10.7 mg/kg bw ³H-labelled triclosan in different vehicles to groups of 3 male blue Vienna rabbits 47.3% to 49.7% of the administered dose was excreted in the urine (Ciba-Geigy Limited, 1976a). Therefore, the urine is a significant route of excretion, and was seen to be the major route in a study that determined the dose excreted in the urine (52.0%) and faeces (34.9%) in 1 female silver fawn rabbit over 72 h following dermal application of 0.42 mg/kg bw ¹⁴C-labelled triclosan in hexane (Ciba-Geigy Limited, 1976a). In the same study using 1 or 2 male blue Vienna rabbits the primary route of excretion was also seen to be the urine (26.7% to 48.6%) over 72 h following topical application of 0.3 or 3 mg/kg bw ³H-labelled triclosan in cream (with less than 1% to 1.4% seen in the faeces). The same was also seen in female silver fawn rabbits following a single or repeated wash with a soap solution containing 0.1% ¹⁴C-labelled triclosan (Ciba-Geigy Limited, 1976a).

Over 72 h following oral administration of 5 or 50 mg/kg bw ³H-labelled triclosan to groups of 3 male rabbits the primary route of excretion was through the urine (60.4 to 74.1 of the administered dose) with faeces being a minor route (15.5% to 22.4%) (Stierlin, 1972a).

Dog

Over 120 h following oral administration of 5 mg/kg bw ¹⁴C-labelled triclosan to 2 male beagle dogs the primary route of excretion was through the faeces (69.8% to 71.4% of the administered dose) with urine being a minor route (8.3% to 8.8%) (Stierlin, 1972a). Additionally, excretion in the faeces was still occurring 96 to 120 h after administration (2.1% in each animal), though no radioactivity was detected in the urine during this time.

Over 144 h following oral administration of approximately 5 mg/kg bw ¹⁴C-labelled triclosan to 2 male beagle dogs the primary route of excretion was through the faeces (76.7% to 59.9% of the administered dose) with urine being a minor route (10.2% to 14.2%) (Ciba-Geigy Limited, 1977b). Furthermore, the elimination rate is relatively slow as 2.0% to 4.0% of the dose was still detected in the urine and faeces combined, 96 to 144 h after ingestion of triclosan.

Monkey

During a 90-day repeat dermal study in which 5 male and 5 female infant Rhesus monkeys were bathed daily for 5 min with 15 mL of a soap solution containing 0.1% triclosan, total triclosan levels (i.e. triclosan and its conjugates combined) ranged from 0.3 to 4.8 ppm in the urine and less than 0.1 to 10.5 ppm in the faeces (Parkes, 1979). Only trace levels were detected in the urine and faeces during the 30-day recovery period after cessation of treatment.

Over 120 h following oral administration of 5 mg/kg bw triclosan to 3 male and 1 female rhesus monkeys, the primary route of excretion in 2 males and the female was urine with faeces being a minor route (46.5% to 60.8% of the administered dose in urine compared to 26.0% to 38.5% in faeces), while comparable levels of the administered dose were seen in the urine (43.2%) and faeces (46.8%) in the remaining animal (Parkes, 1978b).

Over 144 h following oral administration of approximately 5 mg/kg bw ¹⁴C-labelled triclosan to 2 male baboons the primary route of excretion was the urine (53.1% to 60.3% of the administered dose) with faeces being a minor route (20.2% to 30.1%) (Ciba-Geigy Limited, 1977b). It was seen that small amounts of the administered dose were still being excreted 96 to 144 h after ingestion of triclosan (0.3% to 0.4% in urine and faeces combined).

In a 1-year oral study in which groups of 2 male and 2 female baboons were administered 30, 100 or 300 mg/kg bw/day triclosan (Caudal et al., 1975), 1 week after cessation of treatment no triclosan could be detected in the plasma while conjugated triclosan was present up to the last sampling time of 4 wks after cessation of treatment (mean of 3785, 9230 and 7030 ng/mL in animals that received 30, 100 and 300 mg/kg bw/day respectively).

17.4.2 Human studies

In two briefly reported studies that measured triclosan and its glucuronide in urine only, 48 h following topical application of 150 mg triclosan to 6 volunteers 2.5% to 6.5% of the dose was excreted (Caudal et al., 1974), and 5 days following topical application of a soap containing ¹⁴C-labelled triclosan 5.8% to 15.0% of the dose was excreted (Maibach, 1969).

One month apart, 4 healthy male volunteers received a 12 h topical application of 1.0 mL of a patient skin prep containing 0.5% triclosan (i.e. 5 mg triclosan) to intact skin, abraded skin and skin initially covered with an occlusive dressing for the first 2 h (Thompson et al., 1975b). For non-occlusive sites 6% to 14% of the applied dose was detected in the urine over 72 h post application, while in contrast the value observed following occlusion was 40% to 58%.

Six healthy male volunteers washed their hands and forearms twice consecutively with 5mL per wash of a skin cleanser containing 0.5% triclosan (i.e. total dose of 50 mg triclosan) for a total of 5 min (Thompson et al., 1976). An additional group of 6 male volunteers repeated this procedure three times daily for 7 consecutive days with a final wash on day 8. For the single exposure, the mean elimination half-life of triclosan and its conjugates from the plasma was determined to be 0.6 to 1.6 days while 2.2% to 6.6% of the applied dose was excreted in the urine over 96 h following topical application. Within the repeat dose group the initial and final half-life was determined to be 0.7 to 1.3 days and 1.4 to 2.1 days in 4 Caucasians respectively, with corresponding values in 2 Negroid volunteers of 11.2 to 15.7 days and 11.3 to 15.6 days¹³.

The two Negroid volunteers from the above study had also participated in a further multiple scrub study (Thompson, 1975). This study was conducted in 5 and 6

¹³ Thompson (1975) indicates that the half-lives reported by Thompson et al. (1976) are for final values, and reports the initial half-life values for the six male volunteers and two Negroid volunteers that are provided in the above summary.

Caucasian and Negroid volunteers respectively (sex not reported), and used the same surgical wash for up to 31 days as in the study by Thompson et al. (1976). Initial and final mean elimination half-lives are reported, which for Caucasian volunteers was determined to be 0.4 to 1.0 days and 6.3 to 13.0 days respectively. Half-life information for the Negroid volunteers was only available from an interim report that stated in 2 volunteers the determined initial and final values were 1.0 to 1.5 days and 6.2 to 11.0 days respectively. While in 3 Negroid volunteers corresponding values were 13.1 to 28.0 days and 9.6 to 15.5 days respectively. It appears that the results for 1 Negroid volunteer were omitted as the volunteer stopped using the surgical wash on day 19.

In a 20-day hand washing study in 7 males and 6 females the average half-life for triclosan and its conjugates in plasma was calculated to be 37 and 27 h in males and females respectively (Ciba Specialty Chemicals Corporation, 2002). The difference in half-lives is not considered indicative of a sex difference but due to random biological variation observed in the small study population.

Over 72 h following ingestion of a gelatine capsule containing 200.5 mg ¹⁴C-triclosan (equivalent to 2.4 mg/kg bw) by a 30-year old male volunteer (Stierlin, 1972b), 87.4% and 11.0% of the administered dose were recovered in the urine and faeces respectively. Over 144 h following ingestion of a gelatine capsule containing 204 mg ¹⁴C-labelled triclosan (equivalent to 2.6 mg/kg bw) by a 43-year old male volunteer (Ciba-Geigy Limited, 1976c), 57.1% and 14.9% of the administered dose was recovered in the urine and faeces respectively.

In 9 healthy male volunteers administered a 2 mg oral dose of triclosan twice daily in an aqueous solution for 21 days the total triclosan (i.e. triclosan, triclosan glucuronide and triclosan sulphate) excreted in the urine was 71% of the daily dose on day 7 and 41% by day 21 (Colgate-Palmolive Company, 1989). In the same study, 10% and 5% of the daily dose was excreted on days 7 and 21 respectively in 9 healthy male volunteers brushing twice daily with a dentifrice (and expelling the slurry) containing 0.2% triclosan.

Data is available from a combined human tolerance and toxicokinetic study (Lucker et al., 1990). Although the study was conducted in 20 healthy male volunteers it is not clear on how many volunteers the pharmacokinetic data is based upon. The study had a single dose phase where volunteers received a single gelatine capsule containing 1 mg triclosan and calcium carbonate and a repeat dose phase when volunteers received 15 mg triclosan and calcium carbonate daily for 30 days so steady state blood levels were obtained. The mean elimination half-life of total triclosan (triclosan and its conjugates) was determined to be 28.5 h for a single dose and 22.8 h during the saturation phase. Additionally, during the saturation phase approximately 80% to 85% of the administered dose was excreted in the urine over a 24 h period while over 6 days approximately 8% was excreted in the faeces.

In 4 healthy children aged 9 to 12 years (sex not reported) who received a single oral dose of 30 mL of 0.01% triclosan aqueous solution that contained 3 mg triclosan the mean half-life of triclosan was calculated to be 12.7 h (Concordia Research Laboratories Inc., 1997a). In a further study using an oral dose of 3 mg triclosan the mean elimination half-life was determined to be 16.2 h in 9 children aged 8 to 12 years (sex not reported) that completed the study (Colgate-Palmolive Company, 1997a).

In a 2-phase study (Concordia Research Laboratories, 1997b), 8 healthy volunteers (4 males and 4 females) aged 18 yrs and over initially received a single oral dose of 10 mg triclosan and a week later brushed with toothpaste containing 6 mg triclosan then ingested the dental slurry. The mean elimination half-life of triclosan in the plasma was determined to be 19.9 and 20.0 h following ingestion of triclosan in solution and in dental slurry respectively. Furthermore, for 21 adult volunteers (sex not reported) who brushed with toothpaste containing 3.75 mg triclosan then ingested the dental slurry; the mean elimination half-life of triclosan in the plasma was determined to be 14.6 h (Colgate Palmolive Company, 1997b).

Triclosan was detected as an interfering contaminant in urine samples from athletes tested by the Australian Sports Drug Testing Laboratory in 1998 (data provided by Australian Government Analytical Laboratories, personnel communication). Of 147 samples tested 134 contained detectable amounts of triclosan (the limit of detection was 3 ng/mL), ranging from 3 ng/mL to 580 ng/mL. Though the method for determining triclosan levels in this study was not validated for the analyte.

Urine samples (2517) collected from US general population (age 6 years and older) for the National Health and Nutrition Examination Survey (from 2003 – 2004) were analysed for total triclosan concentration (free plus conjugated). Triclosan was detected in about three quarters of urine samples analysed (geometric mean = 13.0 µg/L and 95th percentile = 459.0 µg/L). Concentrations differed by age and socio-economic status but not by race/ethnicity and sex. The concentrations of triclosan appeared to be highest during the third decade of life and among people with the highest household income (Clafat et al., 2007).

The presence of triclosan in human breast milk samples in studies conducted by Adolfsson-Erici et al. (2002), Plautz (2005), the National Research Centre for Environmental Toxicology at Queensland University for NICNAS (See Appendix E) and Allmyr et al. (2006), indicate that this is a potential route of maternal elimination and exposure of breastfeeding infants to triclosan.

Triclosan was detected in maternal and cord blood samples received from the Academic Hospital of Groningen, The Netherlands (Peters, 2005). This study determined only the triclosan level and not its metabolite methyl-triclosan. Approximately half of the samples analysed (16 out of 39 maternal blood and 8 out of 17 cord blood samples) contained triclosan above the detection limit of 0.1 ng/g serum. Triclosan levels in cord blood samples were higher than in maternal blood samples and the concentrations ranged from 0.1 to 1.3 ng/g serum in maternal blood and 0.5 to 5.0 ng/g serum in cord blood.

Summary

Following oral administration of triclosan the half-life elimination from the plasma ranged from approximately 10 to 15 h in rats, 8 to 12 h in mice, 25 to 32 h in hamsters and for humans 13 to 16 h in children and 15 to 29 h in adults. Furthermore, in hamsters, rabbits, primates and humans the primary route of excretion is via the urine with the faeces a lesser route of excretion. In humans up to 87% of the administered dose was excreted in the urine and elimination was relatively rapid. In contrast, excretion via the faeces was the primary route following oral administration to rats, mice and dogs. Following dermal application of triclosan the final elimination half-life from the plasma ranged from approximately 34 to 312 h in Caucasians and from 149 to 374 h in Negroid volunteers indicating that elimination rates for triclosan vary widely between

humans, and provide limited evidence of an ethnic difference. The available dermal data indicates the primary route of excretion is the faeces in the rat and the urine in the rabbit. For primates, overall, neither faecal nor urinary excretion appears to be strongly favoured over the other following dermal or oral exposure. Enterohepatic circulation has been demonstrated in rats, with limited evidence for such in mice and hamsters. Data in humans indicate that triclosan and/or its metabolites can be excreted in milk.

The major route of excretion is via the urine with the faeces being of secondary importance in humans, hamsters, rabbits and primates following oral exposure, whilst the reverse was seen in rats, mice and dogs. The available dermal data, in rats and rabbits, indicates the same predominant routes of excretion. In humans up to 87% of the administered dose was excreted in the urine and elimination was relatively rapid; the majority of the dose was excreted by 72 h post dose. Though a significant difference was observed in the rate of elimination between some Negroid volunteers compared to Caucasians, there are no data available to explain why this difference was observed. However, the human oral and dermal data provide no evidence of a bioaccumulation potential. Likewise, the tissue distribution data in rats and hamsters following single and repeated dosing provides no evidence of bioaccumulation in these species, though there is limited evidence in mice that retention of triclosan and/or its metabolites may occur in the liver.

The observance of triclosan and/or its metabolites in human breast milk indicates potential excretion in breast milk. However, the data do not allow a reliable quantitative determination to be made on the potential dose excreted by this route following exposure to triclosan. Though the first pass metabolism and relatively rapid elimination of triclosan suggest that the potential for transfer to the foetus and bioaccumulation may be limited.

There are no data on the toxicokinetics of triclosan following inhalation exposure. However, the observation of clinical signs of toxicity such as muscle spasms seen in a repeat dose inhalation study in the rat indicates that absorption via the inhalation route can occur, but the data do not allow a quantitative estimation of absorption to be made. Furthermore, because first pass metabolism would not take place following exposure by this route, bioavailability of triclosan is likely to be substantially greater than is associated with the oral route, or the dermal route where metabolism of triclosan to its conjugates has been demonstrated in the skin.

18. Effects on Laboratory Animals and Other Test Systems

18.1 Acute toxicity

18.1.1 Oral

In a well-reported gavage study (Wnorowski, 1994a), 5 male and female Sprague-Dawley rats received 5000 mg/kg bw triclosan in 2.5% suspension of carboxymethylcellulose in distilled water and observed for 14 days. One female died on day 3. Lethargy, abdominal distension, diarrhea, piloerection, hunched posture, ocular discharge and/or irregular respiration were seen in all animals. These clinical signs were absent in most survivors by day 7. At necropsy, discolouration of the lungs and gastro-intestinal tract along with injection of the blood vessels of the gastro-intestinal tract was seen in the animal that died. No treatment related changes were seen in animals that survived to 14 days. In this study the median lethal dose (LD50) was greater than 5000 mg/kg bw triclosan.

The acute toxicity of triclosan, in either an emulsifiable solution or corn oil, was investigated in rats, mice or dogs (Lyman and Furia, 1969). Groups of 4 to 5 animals of both sexes received 2500 or 5000 mg/kg bw triclosan. In mice and rats, no signs of toxicity were reported at 2500 mg/kg bw and the LD50 was determined to be 4530 mg/kg bw in both species. In dogs, vomiting was seen up to 11 h after dosing at 2500 mg/kg bw and above. No deaths were seen at either dose level, thus, the LD50 in dogs was greater than 5000 mg/kg bw.

In further briefly reported experiments by the same authors (Lyman and Furia, 1969), an LD50 value greater than 5000 mg/kg bw triclosan was obtained in rats. Animals were seen to lie down on their stomach and slight 'numbness' reported in animals from the lowest dose administered of 100 mg/kg bw. In another experiment, groups of 5 male and 5 female rats were administered 2000 to 6800 mg/kg bw triclosan. The LD50 was determined to be 4400 mg/kg bw and 3700 mg/kg bw in males and females respectively. Although clinical signs of toxicity were reported it is not clear at what dose level they were seen. However, no gross pathological changes were seen in animals that died or were sacrificed 14 days after dosing.

In an old and briefly reported study (Litchfield and Wilcoxon, 1949), the effect of vehicle on the LD50 value of triclosan was investigated. Groups of 4 rats per sex were administered 3500 to 5500 mg/kg bw triclosan in water or 100 to 5500 mg/kg bw triclosan in corn oil. LD50 values for triclosan for both sexes combined were 4000 mg/kg bw and 1700 mg/kg bw in water and corn oil respectively.

In a very briefly reported study (Pieckacz, 1978), groups of 10 female Wistar rats were administered 2000 - 8500 mg/kg bw triclosan in oil (type not specified). The LD50 was 4000 mg/kg bw. No further details reported.

In a study investigating the acute toxicity of triclosan, groups of 4-6 male Wistar rats received a single dose of 625 to 2500 mg/kg bw in gum tragacanth (Chow et al., 1977). A control group was also included (number not reported). Blood was

taken to measure parameters of hepatotoxicity 24 h after treatment, and animals sacrificed at preselected times up to 72 h and kidney cortical slices prepared to determine nephrotoxicity. At 2500 mg/kg bw 20% of the animals died. No effect was seen on plasma activities of glutamic-oxaloacetic transaminase and glutamic-pyruvic transaminase, which are generally accepted as indicators of liver injury. In kidney cortical slices 24 h after treatment, triclosan produced a dose related, and statistically significant, inhibition of *p*-aminohippurate (PAH) at 625 mg/kg bw and above but had no effect on *N*-methylnicotinamide. At 2500 mg/kg bw PAH accumulation had recovered to approximately control values by 72 h post treatment. In contrast, in vitro investigations in the same study indicated triclosan decreased both PAH and *N*-methylnicotinamide accumulation in kidney cortical slices.

18.1.2 Dermal

In a poorly reported study in New Zealand rabbits (Lyman and Furia, 1969), the LD50 of triclosan, administered in a 'slurry' or propylene glycol was reported to be equal to or greater than 9300 mg/kg bw.

18.1.3 Inhalation

In a well-reported inhalation study (Duchosal and Thevenaz, 1990), 5 male and 5 female Wistar rats were exposed, nose only, to 0.15 mg/L of an aerosol of triclosan for 4 h. Forty-four percent of particles had a particle size equal or less than 3 µm, and the exposure concentration used was the highest attainable by the investigators with the test system used. No deaths or clinical signs of toxicity were seen during or up to 14 days after exposure. At necropsy, the lungs were incompletely collapsed in 1 female. In this study the median lethal concentration (LC50) was greater than 0.15 mg/L. However, considering the very low dose tested in this study, it is not possible to use this value to make a conclusion about the acute inhalation toxicity of triclosan.

Limited data are available from a 21-day repeat dose inhalation toxicity study in rats (Ciba Geigy Limited, 1974 – see sub-section 18.4). In this study nine RAI rats per sex/dose group were exposed nose only on day 1 to an aerosol of 0, 0.05, 0.23 or 1.30 mg triclosan /L of air in 10% ethanol. The control group received 10% ethanol. Concentrations were reduced to 0.12 or 0.30 mg/L in the top two exposure groups from day 2 due to deaths seen at 1.30 mg/L. At this highest dose, two females died on day 1, and four males and five females died on day 2. Deaths occurred before the second exposure (Personal communication, Colgate-Palmolive Pty Ltd., 2008). There were no deaths in the control group, or the other test dose groups. Considering that >50% deaths occurred after a single exposure (2 h) at 1.3 mg/L, the LC50 for triclosan is determined to be <1.3 mg/L (or <1300 mg/m³).

18.1.4 Intravenous

A poorly reported study is available in both male and female rats (Lyman and Furia, 1969) and mice (Walther, 1968). Animals were administered triclosan in triethylene glycol and water (1:2) and the LD50 was reported to be 29 mg/kg bw in the rat and 19 mg/kg bw in the mouse.

18.2 Irritation and corrosivity

18.2.1 Skin

In a briefly reported study (Sachsse and Ullmann, 1975), 3 Russian rabbits per sex received an un-stated volume and concentration of triclosan for 24 h under occlusive dressing to intact or abraded skin. Skin reactions were scored at 24 and 72 h post application. For intact skin, mean irritation scores for erythema and oedema were 2.5/4.0 and 1.5/4.0 at 24 h and 1.3/4.0 and 0.7/4.0 at 72 h, respectively. The overall primary irritation index (i.e. erythema and oedema combined) for intact skin was 3.0/8.0 indicating a moderate skin irritation potential. Responses with abraded skin were comparable or slightly more severe than those seen with intact skin.

In a range-finding study to determine the maximum sub-irritant concentration for a phototoxicity test (Thomann and Maurer, 1978), 10 Pirbright white guinea-pigs per group were topically administered 0.1 mL of 0.1, 0.5, 1.0 or 5.0% triclosan in DAcA 433¹⁴: saline (4:1). Erythema was observed 24 h post application in 4/10 animals that received 5% triclosan. No skin reactions were seen at 48 h, or for the lower concentrations tested at any time-point.

In a study investigating the irritant potential of triclosan in various vehicles (Shanghai Municipal Prevention Medical Institution, 2002a), groups of 4 New Zealand White rabbits were administered 0.5 ml of various concentrations of triclosan in olive oil, tween-80, tween 80-emulsion, 83% propylene glycol solution, olive oil/60% propylene glycol, 70% ethanol or 0.5% sodium lauryl sulphonate solution, under occlusive dressing for 4 h. Skin reactions were scored 1, 24 and 48 h after removal of the test material.

No skin reactions were seen with triclosan up to the top concentration tested of 20%, 50% and 50% in olive oil, tween-80 and tween-80 emulsion respectively. In contrast, erythema (grade 1 or 2) was seen with 20% and 50% triclosan in 83% propylene glycol solution, 20%, 30% and 60% triclosan in olive oil/60% propylene glycol, 20% triclosan in 70% ethanol and 4%, 5%, 10% and 20% triclosan in 0.5% sodium lauryl sulphonate solution. Oedema (grade 1) was also seen in a single animal at 48 h for 20% triclosan in 70% ethanol and 60% triclosan in olive oil/60% propylene glycol.

In a non-standard study (Baert et al., 1996), 0.3% triclosan in an alumina hydrate and glycerol/sorbital paste was applied once daily to the cheek pouch of Syrian golden hamsters for 4 days. The histological structure of the mucosa was examined on day 5, and observed to be similar to that of control animals.

The phototoxic potential of 1% triclosan in 80% DAcA 433 was investigated in 20 Pirbright white guinea-pigs per group using both UV and filtered light (Thomann and Maurer, 1978). Animals were irradiated with UV light for 5 min or filtered light for 15 min and skin reaction measured (including skin thickness) 4, 24 and 48 h later. No phototoxicity activity was seen for triclosan with either irradiation source. Similarly, in a poorly reported study (Urbach, 1973), no evidence of phototoxicity was observed for triclosan in Skh:hairless-1 mice or Hanford Labco miniature swine. However, the minimal details reported limits the significance that can be attached to the results of this study.

¹⁴ DAcA 433: 40 % dimethylacetamide, 30 % acetone and 30 % ethanol.

18.2.2 Eye

In a well-reported study (Ullmann, 1980), 3 New Zealand White rabbits per sex received a single instillation of 0.1 g of triclosan into the eye. Eyes were examined 1, 2, 3, 4 and 7 days after instillation. The mean eye irritation scores are provided in Table 18.1.

Table 18.1 - Mean eye irritation scores (n = 6)

	Mean eye irritation scores (Draize)				
	Day 1	Day 2	Day 3	Day 4	Day 7
Cornea	3	2.5	1.5	1.0	1.0
Iris	0.67	0.67	0.33	0.33	0.33
Conjunctiva:					
Redness	2.33	1.83	1.67	0.67	0.5
Chemosis	2.17	1.50	0.83	0.83	0.33
Discharge	2.33	2.0	1.33	1.17	0.67

The mean corneal opacity score on day 1 indicates that the chemical is a severe eye irritant. However, the mean scores from day 3 onwards (Table 18.1) show that triclosan is not likely to cause serious eye damage. Maximum primary irritation scores of 15.0/80, 3.3/10 and 13.7/20 were calculated for the cornea, iris and conjunctival effects, respectively, 1-day post-instillation. The primary irritation index determined over 72 h post instillation (i.e. readings taken at 24, 48 and 72 h) was 24.9/110 indicating a slight irritation potential, though irritation was still evident at the end of the study on day 7 post instillation (mean primary irritation scores of 5.0/80 in the cornea, 1.7/10 in the iris and 3.0/20 in the conjunctiva indicating minimal irritation).

In a series of experiments Lyman and Furia (1969) investigated the eye irritation potential of triclosan. In the first experiment 200 mg of 1%, 2%, 5%, 10% or 20% triclosan in gum arabic was instilled into the eyes of 2 rabbits and observations taken 10, 30 60 and 120 min and 24 h later. After 2 h, 1% to 5% triclosan caused slight to distinct erythema and slight oedema of the conjunctiva. No irritation was seen at 24 h with these concentrations. Eye irritation was seen at 24 h with 10% triclosan and above. With 20% triclosan, pronounced erythema and slight oedema of the conjunctiva were still apparent at 24 h. However, the results of this study are not conclusive as the observation period was only up to 24 h.

In the second experiment an unreported volume of triclosan (described only as the 'active ingredient') was instilled into the eyes of 6 rabbits and observations taken 24, 48 and 72 h later. The mean primary irritation index over 24 to 72 h was calculated as 86.8/110, indicating the chemical as a severe eye irritant.

A further two experiments were conducted by Lyman and Furia (1969). In these experiments rabbit eyes were rinsed 2 or 4 seconds after instillation of triclosan. These experiments provide no useful data in determining the eye irritation potential of triclosan as the exposure periods were too short.

In summary, triclosan is considered an eye irritant, but there is no conclusive evidence that the chemical causes serious eye damage.

18.3 Sensitisation

In a well-reported Buehler study (Wnorowski, 1994b), 30 Hartley guinea-pigs were employed in both the treated and control groups. At induction occluded patches were applied for 6 h 3 times per wk for 3 wk. Initially 25% triclosan in propylene glycol was used for inductions 1 and 2, but was then reduced to 10% for inductions 3 and 4 due to signs of irritation, and was further reduced to 2% for inductions 5 to 9. At challenge, 12 days after induction, 5% triclosan in propylene glycol was applied under occlusive dressing for 6 h and skin reactions evaluated 24 and 48 h post application. Weak non-confluent (very faint) erythema (score 0.5) was seen in 6/10 test animals at 24 h post challenge, 5/10 animals after 48 h, and in 2/5 control animals at 48 h only. More severe skin reactions (score 1 to 3) were seen in all 10 positive control animals, along with very faint erythema in 3/5 positive controls. Overall, the results of this study do not indicate a skin sensitisation potential.

In a briefly reported Buehler study (Toxicological Resources, 1974), a 10% solution of a soap bar containing 1% triclosan was applied topically at induction under occlusive patches for 5 h, three times a wk for 3 wk, to a test group of 5 Hartley guinea-pigs. The study included a control group of 6 animals. Challenge was conducted 14 to 21 days after the last induction application. Irritation was observed after the 'first few induction' applications. No 'significant' oedema or erythema was reported in treated or control animals at challenge.

In a modified Maximisation test (Maurer et al., 1979), 0.1% triclosan in propylene glycol was injected intradermally at induction, 3 times a wk for 3 wk to a test group of 20 Pirbright white guinea-pigs. The study included a control group of 20 animals. A first challenge was conducted 14 days after the last induction dose, with animals receiving an intradermal injection of 0.1% triclosan in propylene glycol. A second challenge was conducted 14 days after the initial challenge, with animals receiving a 0.1% triclosan (in soft white petrolatum) in propylene glycol under occlusive dressing for 24 h. Skin reactions were evaluated 24 h after the first and second challenge. Skin reactions, whose intensity were not reported, were seen in 4/20 test and 4/19 control animals for the first challenge, and 3/20 test and 1/19 control animal for the second challenge. The briefly reported results of this study do not indicate a significant skin sensitisation potential.

In a 'split adjuvant' test that employed 20 test and 20 control Hartley guinea-pigs (Lachapelle and Tennstedt, 1979), occluded patches containing 10% triclosan in petrolatum were applied on days 0, 2 and 7 at induction along with an intradermal injection of Freund's complete adjuvant on day 4. At challenge on day 22, 3% triclosan under occluded patch was applied for 24 h and skin reactions assessed 24 and 48 h post challenge. Slight erythema was observed in 7/20 test animals at induction. At challenge, a skin reaction was seen in 1/20 test animals that faded progressively between reading times. No skin reactions were seen in control animals at induction or challenge. The results of this study do not indicate a skin sensitisation potential.

In a series of poorly reported experiments in guinea-pigs (Lyman and Furia, 1969), no skin sensitisation was reported in two studies that used intradermal administration of triclosan, a Buehler study, and a study that applied triclosan topically to the ear, nipple and back. However, the limited experimental details and reporting of results means no reliable conclusions can be drawn from the data and, hence, these studies are not discussed further.

No data are available on the respiratory sensitisation potential of triclosan.

18.4 Repeat dose toxicity

18.4.1 Inhalation

In the only repeat dose inhalation study available (Ciba Geigy Limited, 1974), nine RAI rats per sex per group were exposed nose-only to an aerosol of 0, 0.05, 0.23 or 1.30 mg/L triclosan in 10% ethanol for 2 h on day 1, and 0, 0.05, 0.12 and 0.30 mg/L triclosan in 10% ethanol for 2 h/day 5 days/wk on exposure days 2 to 15 respectively (21-day study). The control group received 10% ethanol. Surviving animals were sacrificed at the end of the exposure duration, except for 4 animals per sex per group exposed to 0, 0.12 or 0.23 mg/L triclosan that were sacrificed after a 17 day recovery period. All animals underwent a comprehensive autopsy.

Concentrations were reduced on day 2 in the top two exposure groups due to deaths seen in 2 females at the initial (top) concentration of 1.30 mg/L. In the highest dose group, 4 males and 5 females died on day 2. Deaths occurred after one day (2 h) of exposure (Personal communication, Colgate-Palmolive Pty. Ltd., 2008). A further male died on day 18 in the highest dose group. There were no deaths in the control group or in other test dose groups. Severe clinical signs of toxicity, such as muscle spasms, were observed during the first week of treatment in the top exposure group. Conjunctivitis was seen in animals at 0.30 mg/L throughout the treatment period. In rats that died acute purulent inflammation with focal ulceration of mucous membranes in the nasal cavity and trachea was seen, along with haemorrhage and severe acute congestion and oedema in the lung. Slight focal inflammation in mucous membranes was seen in 2 of the 6 surviving animals exposed to 0.30 mg/L triclosan, along with changes in haematology parameters associated with inflammatory changes in the respiratory tract. Clinical chemistry changes were also seen in both sexes at this exposure concentration. At 0.12 mg/L a slight decrease in body weight gain (6%) and increase in alkaline phosphatase levels (24%) was seen in males only, along with slight decreases in feed consumption in both sexes. Slight inflammatory changes were also seen in the nasal cavity of 1 male and in the trachea of 1 female. No treatment related changes (including histopathology findings) were seen at 0.05 mg/L triclosan and in the control group. There were no significant differences between animals in the recovery group and controls. The presence of ethanol is not considered to have contributed to the mortalities and histopathological effects seen in the animals received doses above 0.05 mg triclosan/L and therefore, not considered to have contributed to an additive or synergistic effect. The no-observed adverse-effect concentration (NOAEC) was determined to be 0.05 mg/L in this study with inflammation of the nasal tract or trachea observed in both sexes at 0.12 mg/L.

18.4.2 Oral

Studies are available in the mouse, rat, hamster rabbit, dog and baboon. The data indicate that the mouse is the most sensitive species to the systemic toxicity of triclosan.

Mice

A dietary study was conducted primarily in male mice to investigate biochemical and structural effects of triclosan on the liver and their reversibility (Molitor et al.,

1992). Groups of 9 male CD-1 mice received triclosan at a dose equivalent to 0, 18, 54, 258 or 951 mg/kg bw/day for 14 days, or 0 or 951 mg/kg bw/day for 14 days followed by a 28 day recovery period. Additionally, groups of 3 female CD-1 mice received triclosan at a dose equivalent to 0, 20, 271 or 1106 mg/kg bw/day for 14 days. Electron microscopy examination of the liver was undertaken on 3 males from all groups and 3 females from the control and top dose group only. Traditional light microscopy was not undertaken.

Hunched back and posture were observed in all animals receiving 951 mg/kg bw/day or greater. At sacrifice, a statistically significant decrease in body weight gain was seen in males receiving 951 mg/kg bw/day (15%) and in the recovery group (8%) at the top dose. No statistically significant decrease in body weight was seen in females at the top dose, or in feed consumption in either sex.

In males, a dose-related and statistically significant increase in relative liver weight was seen in males receiving 54 mg/kg bw/day triclosan and above for 14 days (56%, 137% and 171%) compared to controls. An associated and statistically significant increase was also seen in microsomal protein at 18 mg/kg bw/day and above (25%, 25%, 41%, and 58% at 18, 54, 258 and 951 mg/kg bw/day respectively) and cytochrome P-450 content at 54 mg/kg bw/day and above (68%, 234% and 338% at 54, 258 and 951 mg/kg bw/day respectively). Increases in enzyme activities that were statistically significant and dose related compared to controls were seen for lauric acid 11-hydroxylation (48% to 342%), lauric acid 12-hydroxylation (199% to 733%), ethoxyresorufin O-de-ethylase (83% to 402%) and pentoxyresorufin O-depentylase (332% to 2288%) at 18 mg/kg bw/day and above, and peroxisomal fatty acid β -oxidation (63% to 239%) and glutathione S transferase (59% to 161%) at 54 mg/kg bw/day and above. Additionally, a statistically significant though not dose related increase was seen in total testosterone hydroxylation activity at 18 mg/kg bw/day and above (57% to 519%). Immunoblot analysis using anti-rat antibodies to P450 isoenzymes showed a dose related, but not statistically significant, increase in microsomal cytochrome P-450 CYP3A and CYP4A protein compared to controls at 18 mg/kg bw day and above (167% to 742% and 52% to 680% respectively) and decrease in microsomal cytochrome P-450 CYP1A protein at 54 mg/kg bw/day and above (44% to 61%).

In males, electron microscopy showed changes to hepatocyte organelles. A marginal to moderate proliferation of smooth endoplasmic reticulum in a 'few' cells was seen at 18 mg/kg bw/day and above, and at 54 mg/kg bw/day and above reduced and disorganised rough endoplasmic reticulum, a moderate to 'striking' proliferation and increase in size of peroxisomes, and lipid vacuoles in hepatocyte nuclei. In the recovery group, with the exception of some liver enzyme parameters, all these observed changes in treated males were essentially comparable to control values.

In females, compared to controls, a dose-related and statistically significant increase in relative liver weight was seen at 271 and 1106 mg/kg bw/day (177% and 221% respectively). Unlike the males no significant increase was seen in microsomal protein in females, though a statistically significant reduction in cytosolic protein was seen at 1106 mg/kg bw/day (13%). A statistically significant increase in pentoxyresorufin O-depentylase was seen at 20 mg/kg bw/day and above (169%, 880% and 1484% at 20, 271 and 1106 mg/kg bw/day respectively), and peroxisomal fatty acid β -oxidation activity at 271 mg/kg bw/day and above (316% and 249% respectively). Immunoblot analysis showed a dose related

increase in microsomal cytochrome P-450 CYP3A and CYP4A protein at 20 mg/kg bw/day and above (440% to 5751% and 141% to 752% respectively). This was not statistically significant. Though a decrease was seen in microsomal cytochrome P-450 CYP1A protein at 20 mg/kg bw/day and above (30% to 52%) this decrease was not dose related. All the structural changes seen in males were also seen in females at 1106 mg/kg bw/day, the only treatment related dose level for which electron microscopy examination was undertaken.

The biochemical and structural changes seen in both sexes in this study are suggestive of a peroxisome proliferation activity in the liver. At the lowest doses of 18 and 20 mg/kg bw/day in males and females respectively, the only changes seen were a statistically significant increase in a number of liver enzymes and non-significant increases in microsomal cytochrome P-450 content in the presence of minimal ultramorphological observations in a few cells detectable with electron microscopy. These minimal changes are not considered of sufficient biological significance to constitute a lowest-observed-adverse-effect level (LOAEL). Consequently, a no-observed-adverse-effect level (NOAEL) of 18 mg/kg bw/day in males and 20 mg/kg bw/day in females is identified based on histopathological changes in a significant number of liver cells, together with biochemical changes in males and females at 54 and 271 mg/kg bw/day respectively.

In a well-conducted 28-day study (Ciba-Geigy Limited, 1987), 5 MAGf mice per sex per group were administered triclosan in the diet that was equivalent to 0, 6.5 or 136 mg/kg bw/day in males and 0, 8.3 or 169 mg/kg bw/day in females. The study also included a 14-day recovery group of 5 animals per sex receiving the top dose.

No deaths, clinical signs of toxicity, effect on body weight gain, food or water consumption, or urinalysis were seen. Effects were seen in the liver at the top dose in both sexes. These consisted of an increase in relative organ weight (66% to 76%), microscopic changes such as hypertrophy and cell necrosis of hepatocytes along with clinical chemistry changes reflective of liver damage, slight decreases in red blood cell parameters (generally less than 10%) and increases in platelets. Furthermore, electron microscopy of the liver revealed hypertrophy of the smooth endoplasmic reticulum and increase in the number of peroxisome in hepatocytes. The only effect seen at the low dose was a slight but statistically significant decrease in phosphate levels in females (14%) that was reversible. At the end of the recovery period, no reversibility was seen in elevated urea and creatine plasma levels at the top dose, while only a partial return was seen in alanine aminotransferase in both sexes and aspartate aminotransferase activity in males.

The only effect seen at the low dose was a reversible decrease in one biochemical parameter in one sex. In the absence of any other findings, the NOAEL is considered to be 6.5 and 8.3 mg/kg bw/day in males and females respectively based on effects on the liver and associated changes in haematology and clinical chemistry parameters.

In a well-conducted 13-wk study (Trutter, 1993), 15 CD-1 mice per sex per group were administered triclosan in the diet at a dose equivalent to 0, 25, 75, 200, 350, 750 or 900 mg/kg bw/day. The study also included an interim sacrifice group of mice administered triclosan in the diet at 0 (20 per sex), 25, 350 or 900 mg/kg bw/day (10 per sex per group) for 7 wk. Furthermore, livers from 5 to 7 animals per sex per group receiving 0, 25, 350 or 900 mg/kg bw/day for 7 wk or 0, 25, 75,

200, 350 or 900 mg/kg bw/day for 13 wk also underwent immunochemical staining to determine whether cell proliferation was induced (Eldridge, 1993).

In the terminal sacrifice group (13 wk) no treatment related deaths were seen. Hunched posture, hypoactivity and pale body colour was seen in both sexes at 900 mg/kg bw/day. At 750 mg/kg bw/day hunched posture and hypoactivity were seen in a single male and female animal. Compared to controls, a statistically significant decrease in body weight gain was seen at terminal sacrifice in females at 900 mg/kg bw/day (8%) with an associated decrease seen in feed consumption (16%). Feed consumption was also decreased at 750 mg/kg bw/day (11%). No significant effect was seen on body weight gain and feed consumption in males. A statistically significant and generally dose related decrease in erythrocytes, haemoglobin and haematocrit was seen in males at 25 mg/kg bw/day and above (8% to 30%, 8% to 32% and 8% to 29% respectively), and in females a decrease in erythrocytes and haemoglobin that was dose-related (9% to 25% and 11% to 27% respectively). Additionally, statistically significant, and dose-related, increases were seen in alanine aminotransferase and aspartate aminotransferase in one or both sexes at 350 mg/kg bw/day or higher. Furthermore, statistically significant but not dose related decreases were seen in total cholesterol in both sexes (ranging from 72% to 94%), globulin in males (11% to 32%) and an increase in alkaline phosphatase in females (58% to 148%) at 25 mg/kg bw/day and above, along with an increase in alkaline phosphatase (188% to 337%) in males at 350 mg/kg bw/day and above. At necropsy, a number of treatment related effects were seen whose incidence and/or severity increased with dose.

For the liver, a dose related increase was seen in absolute and relative weight in both sexes at 25 mg/kg bw/day (6% and 2% respectively in males and 7% and 9% respectively in females) that was statistically significant from 75 mg/kg bw/day compared to controls (ranging from 23% to 205%). Additionally, dose-related centrilobular hepatocellular hypertrophy, vacuolisation and Kupffer cell/macrophage pigment accumulation was seen in males from 75 mg/kg bw and in females from 200 mg/kg bw. Hepatocyte pigment accumulation was seen from 200 mg/kg bw/day in both sexes, and bile pigment accumulation, inflammation and necrosis in males from 200 mg/kg bw and in females from 350 mg/kg bw. The incidence and/or severity of necrosis was generally greater in males than females, with necrosis observed in a single male at 75 mg/kg bw/day. Furthermore, compared to controls, a statistically significant and dose related increase in cell proliferation was seen in males at 200 mg/kg bw/day and above (3.5- to 15-fold increase) and in females at 350 mg/kg bw/day and above (6.1- to 7.1-fold increase).

For the kidney, a statistically significant decrease in absolute and relative weight was seen in males at 350 mg/kg bw/day and above (ranging from 11% to 19%) and relative kidney weight only in females at 900 mg/kg bw/day (13%). An increase in chronic inflammation of the kidney was also seen in females at 350 mg/kg bw/day and above.

Statistically significant changes, absolute and relative, were seen in further organs from 750 mg/kg bw/day including a decrease in uterus weight in females (ranging from 38% to 45%). Histopathological changes seen in the uterus at 200 mg/kg bw/day and above, along with the cervix and mammary gland at 350 and 750 mg/kg bw/day and above respectively were attributed to delayed onset of maturity rather than a direct toxic effect of triclosan. An increase was seen in cystic hyperplasia of the glandular stomach in males at 200 mg/kg bw/day and above and

in females at 350 mg/kg bw/day and above. Minimal hypertrophy of the zona fasciculata in the adrenal cortex was also observed in males at 200 mg/kg bw/day and above. Increased extramedullary hematopoiesis was seen in the spleens of both sexes at 750 and 900 mg/kg bw/day with marginal increases also seen in males at 200 and 350 mg/kg bw/day.

All animals in the interim groups survived to the scheduled 7-wk sacrifice. Hunched posture, and hypoactivity was seen in a single female at 900 mg/kg bw/day. A statistically significant decrease in body weight gain was seen in males at 900 mg/kg bw/day (9%). As in the main study, statistically significant decreases were seen in haematological parameters: at 350 mg/kg bw/day and above in both sexes (ranging from 8% – 18%) with a marginal decrease in haemoglobin (6%) in females only at 25 mg/kg bw/day. An increase in the corrected white blood cell count (200%) was seen in females only at 900 mg/kg bw/day. A statistically significant decrease in total cholesterol was also seen in males only at 25 mg/kg bw/day (54%). Additionally, statistically significant changes often dose-related were seen in a number of clinical chemistry parameters at 350 mg/kg bw/day and above. A statistically significant and dose related increases in absolute and relative liver weight was seen in both sexes at 350 mg/kg bw/day and above (89% and greater) along with necrosis and increased cell proliferation (3.2- to 8.0-fold increase). In contrast to findings for animals sacrificed at 13 wk, hepatocellular hypertrophy was seen in males and females from 25 mg/kg bw/day. Overall, the findings in the interim group support those seen in the main 13-wk study.

In this study, histopathological changes to the liver have been seen in males at 75 mg/kg bw/day and above and in females at 200 mg/kg bw/day and above. However, trends in non-histological findings have been observed at lower dose levels including the lowest dose level administered. Consequently, overall, it is considered that a NOAEL cannot be identified in animals from this 13-wk study, and a LOAEL of 25 mg/kg bw/day is identified based upon the dose-related trends in several haematology parameters, significant increase in relative liver weight and a statistically significant depression in total cholesterol.

Rat

A study was conducted primarily to investigate biochemical and structural effects of triclosan on the liver and their reversibility (Molitor and Persohn, 1993). Groups of 5 male Sprague Dawley rats received triclosan in the diet at a dose equivalent to 0, 23, 108 or 518 mg/kg bw/day for 14 days, 0 or 463 mg/kg bw/day for 14 days followed by a 28 day recovery period, or 409 mg/kg bw/day for 42 days, after which animals were sacrificed. Electron microscopy examination of the liver was undertaken for 3 animals in the control and top dose group sacrificed after 14 days and for all groups sacrificed after 42 days. Traditional light microscopy was not undertaken.

No clinical signs of toxicity were seen at any dose level. No statistically significant change in body weight gain or feed consumption was seen following administration of triclosan. Compared to controls, a statistically significant increase in relative liver weight and cytochrome P-450 was seen in animals that received 518 mg/kg bw/day for 14 days (53% and 127% respectively) and 409 mg/kg bw/day for 42 days (19% and 180%), along with an increase in microsomal protein (24%) in animals administered 409 mg/kg bw/day for 42 days (24%), while a decrease in cytosolic protein was seen in animals that received 518 mg/kg bw/day

for 14 days (19%) and 409 mg/kg bw/day for 42 days (18%). A statistically significant change was seen in a number of other enzyme activities.

A statistically significant decrease in ethoxyresorufin O-de-ethylase was seen in animals that received 23, 108 and 518 mg/kg bw/day for 14 days (56%, 50% and 52% respectively), though this decrease was not dose related and no statistically significant change was seen in animals receiving 409 mg/kg bw/day for 42 days. Similarly, though an increase was seen in specific testosterone hydroxylation activity in animals that received 108 mg/kg bw/day and greater for 14 days, and 409 mg/kg bw/day for 42 days, no statistically significant change was seen in total activity. A statistically significant increase in pentoxyresorufin O-depentylase activity in rats that received 108 and 518 mg/kg bw/day for 14 days (189% and 1043% respectively) and 409 mg/kg bw/day for 42 days (550%), along with an increase in glutathione S transferase and lauric acid 12-hydroxylation in animals that received 518 mg/kg bw/day for 14 days (65% and 181% respectively) and 409 mg/kg bw/day for 42 days (59% and 164%). No increase in peroxisomal β -oxidation was seen in triclosan treated animals.

Immunoblot analysis using rat antibodies to P450 enzymes showed a dose related, but not statistically significant, increase in microsomal cytochrome P-450 CYP1A, CYP2B, CYP3A and CYP4A protein in animals receiving 108 mg/kg bw/day and above for 14 days compared to controls (of 125%, 550%, 31%, and 16% and greater respectively). An increase in these proteins was also seen in animals receiving 409 mg/kg bw/day for 42 days (306%, 2492%, 206% and 72% respectively). Electron microscopy showed a moderate to striking proliferation of smooth endoplasmic reticulum membranes in rats receiving 518 mg/kg bw/day for 14 days and 409 mg/kg bw/day for 42 days. An increase in cytoplasmic lipid vacuoles was also seen in these animals, while after 42 days treatment many mitochondria had dilated intra-mitochondrial cristae that sometimes contained helically arranged fibrils. With the exception of some liver enzyme parameters, all these observed changes were absent in the recovery group.

The statistically significant decrease in ethoxyresorufin O-de-ethylase seen in animals receiving 23 mg/kg bw/day for 14 days is not considered biologically significant as the decrease was not dose related and the change was not seen in animals receiving 409 mg/kg bw/day for 42 days. Statistically significant increases in more than one enzyme activity was seen in animals receiving 108 mg/kg bw/day and greater for 14 days though no histological examination of the liver was undertaken at this dose level or lower. Histological changes to the liver were seen in those animals examined by electron microscopy: rats receiving 518 mg/kg bw/day for 14 days and 409 mg/kg bw/day for 42 days. Consequently, it is considered that the absence of histopathological examination at 23 and 108 mg/kg bw/day is a methodology limitation of this study that prevents identification of a robust NOAEL. Though in contrast to the findings of a similar study in mice (Molitor et al., 1992) the biochemical and morphological findings in rats were not suggestive of a peroxisome proliferation activity, with the study authors stating that the biochemical changes induced by triclosan were comparable to a barbiturate-type inducer.

A study was conducted to investigate the potential for triclosan to induce cell proliferation in the liver as measured by immunohistochemical staining for replicative DNA synthesis (Persohn and Molitor, 1993). Groups of 3 to 5 male Sprague Dawley rats received triclosan in the diet at a dose equivalent to 0 or 6000

ppm for 2, 4, 7, 14 or 42 days or 0, 300 or 1500 ppm for 14 or 42 days. An additional group of 5 animals received 6000 ppm triclosan in the diet for 14 days followed by a 28-day recovery period.

No deaths or clinical signs of toxicity were observed in any dose group. Compared to controls, a slight decrease in body weight was generally seen on day 1 and 2 of dosing, and an associated marked decrease in feed consumption was also generally seen on days 1 to 3 at 6000 ppm. However, while feed consumption was increased thereafter, a reduction in body weight gain (10%) that did not achieve statistical significance was seen at 6000 ppm following 42 days of treatment. A statistically significant increase in absolute (53%) and relative (52%) liver weight and decrease in the total number of hepatocyte nuclei (29%) and labelling index (52%) was seen on day 14 at the top dose. Following 42 days treatment a statistically significant increase in relative liver weight only (19%) and decreases in the total number of hepatocyte nuclei (22%) was seen at the top dose. Compared to controls, a statistically significant decrease in body weight (13%) and absolute liver weight (17%) were still evident in the 6000 ppm recovery group. No treatment related effects were seen at doses up to and including 1500 ppm.

Therefore, triclosan did not induce replicative DNA synthesis in hepatocytes, and the results of this study indicate hypertrophy of the liver occurring from day 14 at 6000 ppm (equivalent to 518 mg/kg bw/day) with a NOAEL of 1500 ppm (equivalent to 108 mg/kg bw/day) identified for effects on the liver.

In a neurotoxicity study (Ciba-Geigy Limited, 1973b), 5 to 10 rats per sex per dose received 0, 100, 300, 1000 or 2000 mg/kg bw/day triclosan by gavage 5 days per wk for 2 wk. At the top dose 17/20 animals died and, compared to controls, decreased body weight gain was seen in survivors. Slight polyuria, polydipsia and ataxia were seen in all rats at 300 mg/kg bw/day. Severity increased with dose, with decreased muscular tension and slight tympany also seen at 1000 mg/kg bw/day and above. Additional clinical signs of toxicity such as cachexia and slow and spastic respiration were seen at 2000 mg/kg bw/day. Brain weights between treated and control animals were similar and neurohistological analysis of the brain and sciatic nerve showed no treatment related effects. Therefore, a NOAEL of 100 mg/kg bw/day was determined in this 2-week study based on clinical signs of toxicity.

In a poorly reported 4 wk gavage study (Lyman and Furia, 1969), 5 rats per sex per dose received 0, 50, 100, 200, 500 or 1000 mg/kg bw/day triclosan 6 times per wk. Two animals died at the top dose. It was stated that no difference was seen between controls and triclosan treated animals in blood and urine parameters (though the parameters investigated were not reported). No significant difference was seen in body weight gain between treated groups. Thus, the NOAEL is 500 mg/kg bw/day in this poorly reported 4-wk study that investigated a limited number of parameters.

In a 13-week study (Litton Bionetics Inc., 1983), 25 Sprague Dawley rats per sex per dose were administered triclosan in the diet at a dose equivalent to 0, 65, 203 or 433 mg/kg bw/day in males and 0, 82, 259 or 555 mg/kg bw /day in females. Ten of these animals per sex per dose underwent interim sacrifice on day 45.

No treatment related deaths or clinical signs of toxicity were seen. At the end of the study a slight decrease in body weight gain was seen in both sexes (8%) at the top dose, with a gradual decrease in food consumption observed through the dosing

regime. No effect was seen on water consumption. A slight but statistically significant decrease outside the normal count range was seen in erythrocytes (6%), haemoglobin (7%) and haematocrit (7%) in females at the top dose. A statistically significant decrease in erythrocytes in males from the mid dose was reported to be within normal count ranges. A statistically significant and dose-related decrease in cholesterol (19% to 35%) and triglycerides (54% to 70%) was seen in males from the low and mid dose group respectively, along with an increase in creatine (17%) in females at the top dose. Statistically significant changes were seen in other clinical chemistry parameters in males at the top dose only, in the absence of a dose response. At urinalysis a marked increase was reported in the presence of ketones in males at the top dose (over 50% of animals compared to 21% in controls). Also at the top dose, a statistically significant increase in relative liver weight was seen in males (32%) and females (13%).

At necropsy, mild centrilobular cytomegaly of the liver was seen in 14 and 15 males and 10 and 13 females in the mid and top dose groups respectively, along with minimal to mild fatty metamorphosis in 2 and 6 males but no females. Mild centrilobular cytomegaly was also seen in a single male in the low dose group. A statistically significant and dose related decrease in relative spleen weight (11% to 12%) and increase in relative kidney weight (12% to 17%) was seen at the mid dose and above in males and females respectively. These changes were seen in the absence of histopathological changes. The interim sacrifices also showed effects on the liver in both sexes at the mid dose and above.

Though a statistically significant decrease in cholesterol was seen in the low dose group, this was in males only and was seen in the absence of any other finding excluding mild centrilobular cytomegaly in a single animal. Consequently, a NOAEL of 65 and 82 mg/kg bw/day is determined in this study for males and females respectively based on histopathological changes in the liver in a significant number of animals.

In a well-conducted carcinogenicity bioassay in Sprague Dawley rats (Ciba-Geigy Corporation, 1986), 60 rats per sex per group were administered triclosan in the diet for 2 years at doses equivalent to approximately 0, 12, 40 and 127 mg/kg bw/day in males and 0, 17, 56 and 190 mg/kg bw/day in females. The study also included additional interim sacrifice groups receiving the same dose levels that were sacrificed at 13, 26 and 78 wk along with 1 year. The results of the 1 year interim sacrifice group of 20 control and 10 test animals per sex receiving the same dose levels are reported below. It also included an additional 10 animals per sex receiving a dose level equivalent to 247 mg/kg bw/day in males and 422 mg/kg bw/day in females for 1 year. The group size for the other interim sacrifice groups was 5 animals per sex per dose and only histopathological findings for these groups are presented below.

In animals sacrificed at 13 week, centrilobular hepatocyte hypertrophy and hepatocytic "inclusions" were seen in the livers of male rats at 127 mg/kg bw/day (in 5/5 and 4/5 males respectively, absent in controls). Hypertrophied hepatocytes contained fine-grained or flocculent eosinophilic cytoplasm. Hyaline-staining inclusions, that were usually ring-shaped or spherical, were present in the cytoplasm of some of these enlarged hepatocytes. These changes in the liver were absent in triclosan treated females at 13 wk and in both sexes at 26 wk.

In interim animals sacrificed at 1 year, no significant difference in survival or clinical signs of toxicity was observed between triclosan treated and control animals throughout the study. Compared to controls, a statistically significant reduction in body weight gain was seen in males at 247 mg/kg bw/day (10%) and in females at 190 (6%) and 422 mg/kg bw/day (23%) treated for 1 year. Compared to controls, slight but statistically significant changes were seen in a number of haematology and biochemical parameters. However, only those that were dose related are reported below.

In males, a statistically significant decrease in mean corpuscular volume was seen at 127 mg/kg bw/day and above (2% to 3% respectively), a decrease in serum aspartic aminotransferase (21% to 23%) at 40 mg/kg bw/day and above, and a decrease in blood urea nitrogen (16%), total bilirubin (58%) and increase in the albumin to globulin ratio (14%) at 247 mg/kg bw/day. In females, a statistically significant increase in mean corpuscular haematocrit concentration (2% to 5%) was seen at 17 mg/kg bw/day and above, a decrease in total bilirubin (37% to 40%) at 190 mg/kg bw/day and above, and a decrease in haematocrit (5%), mean corpuscular volume (5%) and triglycerides (67%) at 422 mg/kg bw/day. No statistically significant changes were seen in urinalysis parameters in either sex.

Compared to controls, no statistically significant changes were seen in absolute and relative organ weights. At histopathology, a statistically significant increase in centrilobular hepatocyte hypertrophy and hepatocytic “inclusions” were seen in the livers of male rats at 247 mg/kg bw/day (in 20% and 60% animals, respectively; absent in controls). These changes to the liver were not seen in males at 127 mg/kg bw/day or in females up to and including 422 mg/kg bw/day.

In animals sacrificed at 78 week, although centrilobular hepatocyte hypertrophy was seen in the livers of male rats (in 2/5 animals) at 127 mg/kg bw/day, it did not reach statistical significance and was seen in the absence of hepatocyte inclusions. These changes in the liver were absent in the control groups and triclosan treated females.

In animals treated up to 2 years, no significant difference in survival or clinical signs of toxicity was observed between triclosan treated and control animals throughout the study. In contrast to interim sacrifice animals, no statistically significant difference in body weight gain was seen in females. However, a trend was apparent from wk 52 to wk 88 for females receiving 190 mg/kg bw/day (6% and 8% decrease respectively) though at the end of the 2 year dosing period no reduction was seen in body weight gain. No significant reduction was seen in body weight gain in males, though feed consumption was generally significantly greater than controls for most of the dosing period in animals in the top dose group. A number of treatment related changes were seen in haematology, biochemical and urinalysis parameters. However, only those that were dose related are reported below.

In males, a statistically significant decrease in mean corpuscular volume (6% to 7%) and increase in mean corpuscular haemoglobin concentration (5% to 6%) was seen at 40 mg/kg bw/day and above, along with an increase in clotting time (55%) and decreases in % of monocytes (25%) at 127 mg/kg bw/day (55%). Non-segmented neutrophils were also seen at 127 mg/kg bw/day but were absent in control animals. Additionally, changes in erythrocyte morphology such as polychromasia, hypochromia, poikilocytosis, anisocytosis and/or targeting were

seen in 7% and 17% males at 40 and 127 mg/kg bw/day respectively, but were absent in control animals. In contrast to findings in interim sacrifice males no statistically significant changes were seen in biochemical or urinalysis parameters at terminal sacrifice. In females, a statistically significant decrease was seen in white blood cells at 190 mg/kg bw/day (33%) compared to controls, along with a decrease in blood urea nitrogen (38%) and urine specific gravity (38%).

Compared to controls, the only dose-related and statistically significant change in absolute and relative organ weight was an increase in ovaries of terminal females at 190 mg/kg bw/day (75% and 69% respectively). These organ weight changes occurred in the absence of histological changes. Furthermore, no statistically significant treatment related histopathological changes were seen in any other organs in males or females of the top dose group.

Overall, the data from the interim 1 year and terminal sacrifice animals show changes in haematology and/or biochemical parameters occurring from 40 and 56 mg/kg bw/day in males and females respectively, though these changes were seen in the absence of histopathological findings. Histopathological changes were only seen in the liver of males. These changes were seen at 127 mg/kg bw/day after 13 and 78 wk treatment and at 247 mg/kg bw/day after 1 year of treatment. However, the incidence was only statistically significant after 13 wk and 1 year of treatment, while these changes to the liver were not seen in males treated with up to 127 mg/kg bw/day for 26 wk and 2 year. Although histopathological changes to the liver were not consistently seen at 127 mg/kg bw/day they were absent in controls at all time points. Consequently, the NOAEL is determined to be 40 mg/kg bw/day in males and 56 mg/kg bw/day in females based on mild clinical chemistry and/or haematology changes, together with histopathological changes to the liver in males and a trend for reduction in body weight gain in females.

Hamster

A dietary study was conducted primarily in hamsters to investigate biochemical and structural effects of triclosan on the liver and their reversibility (Thomas, 1994). Five Syrian hamsters per sex per dose were administered triclosan in the diet for 14 days at a dose equivalent to 0, 50, 310 and 799 in males and 0, 46, 314 and 959 mg/kg bw/day in females. An additional group of 5 animals per sex received 0 mg/kg bw/day triclosan in the diet, with 5 males receiving 653 mg/kg bw/day and 5 females 826 mg/kg bw/day, for 14 days followed by a 28-day recovery period. Electron microscopy examination of the liver was undertaken in 3 animals per sex from each treatment group. Traditional light microscopy was not undertaken. Furthermore, as a comparison to known inducers of metabolising enzymes groups of 5 males received a daily ip injection of 80 mg/kg bw phenobarbital sodium in saline, 25 mg/kg bw 3-methylcholanthrene in corn oil or 100 mg/kg bw pregnenolone-16 α -carbonitrile in coil oil for 4 days, or were daily gavaged with 250 mg/kg bw nafenopin for 14 days, and biochemical investigation and electron microscopy of the liver undertaken as for triclosan treated animals.

No clinical signs of toxicity were seen in any test group. A reduction in body weight was seen in males and females at the top dose (reported to be 11% and 10% of the initial body weight respectively), with a statistically significant reduction in body weight gain seen in females at the mid dose (15%) compared to controls. Over the treatment period a statistically significant decrease in feed consumption was seen in males (31%) and females (14%) at the top dose. At necropsy,

macroscopic examination showed spots or patches of white pigmentation on the kidney in all animals in the top dose group and 1 female in the mid dose group. A statistically significant increase in relative liver weight was seen in males (15%) and females (12%) at the top dose, though electron microscopy of liver sections revealed no treatment related changes to hepatocyte organelles.

In the liver, compared to controls, a statistically significant increase was seen in both sexes for microsomal total protein content (21% to 25%) at the top dose, and a dose related increase in microsomal P-450 content (33% to 72%) in both sexes at the mid dose and above. A statistically significant and dose-related increase was seen in ethoxyresorufin (58% to 199%), and pentoxyresorufin O-de-alkylase (95% to 329%) activity in mid and high dose animals. At the top dose a statistically significant increase in lauric acid 11-hydroxylation (58% to 59%), lauric acid 12-hydroxylation (6% to 140%) and glucuronosyltransferase activity with morphine (49% to 66%) was seen in both sexes along with a decrease in peroxisomal cytosolic glutathione S-transferase activity (49% to 66%). A statistically significant and dose related increase in androstenedione was seen at the mid dose and above in males (52% to 92%), though no effect was seen on testosterone hydroxylation. Although statistically significant increases were seen in a few other liver parameters at the mid or high dose, they were only observed in one sex, while no effect was observed on peroxisomal palmitoyl-CoA β -oxidation and glucuronosyltransferase activity in 1-naphthol, or bilirubin levels in either sex. Immunoblot analysis using anti-rat antibodies to P450 isoenzymes revealed a moderate increase in microsomal cytochrome P-450 CYP4A protein in males at the mid (60%) and high dose (144%) compared to controls, and a dose related decrease in microsomal cytochrome P-450 CYP3A proteins in females in the low, mid and high dose groups (38%, 60% and 85% respectively).

In the recovery group, body weight and enzyme activity were essentially comparable to control values, while a slight though statistically significant increase was still apparent in relative liver weight in males (7%). No white pigmentation was observed in the kidney at necropsy. In males, overcompensation of cytochrome P-450 CYP4A induction was seen (43% decrease) with the reverse apparent in females for cytochrome P-450 CYP3A (51% increase).

In this study, compared to the known inducers of metabolising enzymes, the biochemical changes induced by triclosan were most comparable to a barbiturate-type inducer. Though triclosan induced increases in levels of cytochrome P-450 CYP4A protein activity and lauric acid 12-hydroxylase activity, and decreased cytosolic glutathione S-transferase activity that were also seen with the peroxisome proliferator nafenopin, in contrast to nafenopin (and findings in mice in a study by Molitor et al., 1992), no effect was seen on peroxisomes in the liver. A NOAEL of 46 mg/kg bw/day in females and 50 mg/kg bw/day in males is identified in this study for decreased body weight gain and pigmentation of the kidney in females and biochemical changes to the liver in both sexes.

In a 13 wk study (Schmid et al., 1994), 15 to 20 Syrian golden hamsters per sex per dose were administered triclosan in the diet at a dose equivalent to 0, 77, 199, 356, 755 or 901 mg/kg bw/day in males and 0, 75, 196, 352, 748 or 893 mg/kg bw/day in females. A further 10 animals per sex receiving approximately 0, 75, 350 and 900 mg/kg bw/day were sacrificed at wk 7.

No treatment related deaths or clinical signs of toxicity were seen. A dose-related statistically significant decrease in body weight gain was seen in males (8% to 10%) and females (10% to 23%) at 755 and 748 mg/kg bw/day and above respectively. Feed consumption was reduced in females at 748 mg/kg bw/day (12%) and above, and in both sexes at the top dose (10% and greater). A dose related increase was also seen in water consumption at 199 and 196 mg/kg bw/day and above in males and females respectively (that compared to controls reached 167% in males and 110% in females at the top dose). Slight dose related increases in coagulation times were seen at 755 and 748 mg/kg bw/day and above in males and females respectively (3% to 44%). At urinalysis, a statistically significant dose related increase in polyuria (92% to 262%) was seen at 356 and 352 mg/kg bw/day and above in males and females respectively. A slight to moderate increased incidence of blood in urine, that was statistically significant, was seen at 199 and 196 mg/kg bw/day and above in males and females respectively, along with statistically significant decreases in urine specific gravity (2% to 3%) and osmolality (31% to 65%). Though blood was seen in the urine of 5 males only at 77 mg/kg bw/day, and was not seen in control animals, it did not reach statistical significance. A statistically significant increase in the incidence of changes in erythrocyte morphology was seen, along with an increase in indices indicating microcytic anaemia in animals at the top dose. Additionally, clinical chemistry changes seen at 755 and 748 mg/kg bw/day and above in males and females respectively were indicative of disturbances to liver and renal function.

At necropsy, a statistically significant increase in relative liver (21% to 36%) and brain weight (14% to 38%) was seen at 748 and 755 mg/kg bw/day and above in males and females respectively along with various other organ weights in only one sex. However, these increased organ weights were seen in the absence of histopathological changes. In contrast, statistically significant increases in relative kidney weight (36% to 43%) in both sexes at the top dose were seen in the presence of significant increases in the incidence and severity of tubular casts, basophilia and dilation compared to controls. A slight increase in the incidence and/or severity of these histopathological changes in the kidney was seen at 356 mg/kg bw/day and above in males and 352 mg/kg bw/day and above in females, the incidence and severity of which were seen to increase with dose. Additionally, diffuse proliferation of the pelvic urothelium was absent in controls but seen in 1 male, 2 animals per sex, and 3 males and 1 female at 352 mg/kg bw/day, 748 - 755 mg/kg bw/day and the top dose group respectively. Statistically significant increases in relative spleen weight in both sexes at the top dose (21% to 22%) were seen in the presence of minimal to slight haemopoiesis in all females and 14/15 males. In controls, minimal haemopoiesis was seen in only 2 females. Histopathological changes were also seen in the stomach. Compared to controls, a significant increase in the incidence and severity of erosion to the stomach was seen at 755 and 748 mg/kg bw/day and above in males and females respectively. At the interim sacrifice, histopathological changes to the kidneys were seen in all animals at the top dose.

In addition to histopathological examination of the kidneys from animals sacrificed at wk 7 and 13 in the above study by Schmid et al. (1994) immunochemical staining was also undertaken to determine whether cell proliferation was induced (Persohn, 1994). Additionally, cell proliferation was also determined in liver samples from control and top dose animals only. Testicular tissue served as a positive control in these investigations.

In the kidney, cell proliferation data was only presented for 0, 199 (for 13-wk only), 356 and 901 mg/kg bw/day in males and 0, 196 (for 13 wk only), 352 and 893 mg/kg bw/day in females. A statistically significant increase in cell proliferation was seen in kidney tubular epithelium at 13 wk in males at 356 (mean labelling index (LI) 2.04) and 901 mg/kg bw/day (LI 4.32) compared to controls (LI 0.43), and in females at the top dose (LI 2.81 compared to 0.32 in controls). Statistically significant, increases were also seen in males and females at 356 and 352 mg/kg bw/day and above respectively at the earlier sacrifice time of 7 wk. Compared to controls, no increase in cell proliferation was seen in the liver of males and females receiving up to 901 and 893 mg/kg bw/day respectively, while prominent staining (i.e. cell proliferation) of spermatogonia confirmed the suitability of the methodology used. Therefore, in this 13-wk study, the histopathological changes reported in the kidney of males at 356 mg/kg bw/day and above by Schmid et al. (1994) were also seen in the presence of statistically significant increases in cell proliferation that are regarded as a compensatory response to cell damage. In contrast, while histopathological changes were reported in the kidney of females at 352 mg/kg bw/day and above by Schmid et al. (1994) a statistically significant increase in cell proliferation in this organ was only seen in females at 893 mg/kg bw/day (though a mean labelling index was not determined for females receiving 748 mg/kg bw/day).

In this 13-wk study reported by Schmid et al. (1994) and Persohn (1994) histopathological changes to the kidney were seen at 356 and 352 mg/kg bw/day and above in males and females respectively. Furthermore, blood was seen in the urine of males and females that reached statistical significance at 199 and 196 mg/kg bw/day and above respectively together with decreases in urine specific gravity and osmolality. Though blood in the urine was seen in some males at 77 mg/kg bw/day it did not reach statistical significance, was seen in the absence of any other treatment related effect, and was not observed in females at 75 mg/kg bw/day. Consequently, the NOAEL for this study is considered to be 77 and 75 mg/kg bw/day in males and females respectively for significant effects on urinalysis parameters together with blood in the urine in both sexes.

In a well-conducted carcinogenicity bioassay in Syrian hamsters (Huntingdon Life Sciences Ltd., 1999), 60 hamsters per sex per group were administered triclosan in the diet at doses that equated to 0, 0, 12.5, 75, or 250 mg/kg bw/day for 90 to 95 wk. The study also included an additional 52 wk interim group of 10 animals per sex receiving the same dose levels. For statistical analysis both control groups were combined.

Compared to controls, a rapid increase in the incidence of deaths was seen after 80 weeks of treatment in male hamsters receiving 250 mg/kg bw/day. At 250 mg/kg bw/day a gradual deterioration was seen in the general clinical condition of male hamsters during the latter period, with lethargy, hunched posture, pallor, thin appearance and unsteady gait observed. Compared to controls a statistically significant decrease was seen in body weight gain in males receiving 250 mg/kg bw/day (48% at the end of wk 90 and 72% at the end of wk 95). A slight, though statistically significant, decrease was seen in feed consumption in females at 250 mg/kg bw/day (3%). Water intake varied throughout the study, but was generally slightly increased in animals at 250 mg/kg bw/day compared to controls. A number of treatment related changes seen in haematology, biochemical and urinalysis parameters are summarised below.

A slight, though statistically significant, decrease in packed cell volume was seen in both interim (2%) and terminal (13%) females at 250 mg/kg bw/day. A statistically significant decrease in haemoglobin (2%), red blood cell count (10%) and mean corpuscular volume (3%), were seen in these terminal females at 250 mg/kg bw/day compared to controls, and in terminal males a slight, though statistically significant, decrease was seen in mean corpuscular haemoglobin concentration at 75 (2%) and 250 mg/kg bw/day (4%) along with an increase in mean corpuscular volume (2% and 5% respectively). In terminal males and females at 250 mg/kg bw/day a statistically significant increase was seen in total white cell count (28% and 31% respectively). Although a slight but statistically significant reduction in prothrombin time was seen in males at 12.5 mg/kg bw/day and above the reduction was not dose related (2% to 5%), while in females a slight though statistically significant and dose related reduction was seen in a different clotting parameter, activated partial prothrombin time, at 12.5 mg/kg bw/day and above (9%, 10% and 11%). A statistically significant increase in blood urea nitrogen values was seen in both sexes at 250 mg/kg bw/day that increased with the treatment period in females (26% and 4% at the interim and terminal sacrifices respectively) but were 'static' in males (30% and 29%). A statistically significant increase in urinary volume and decrease in specific gravity was consistently seen throughout the study in males (72% and 1% respectively at terminal sacrifice) and females (91% and 1%) at 250 mg/kg bw/day. Additionally in both sexes at 250 mg/kg bw/day, a statistically significant decrease in protein values and urinary pH was often seen up to terminal sacrifice along with a slight increase in the incidence of haem pigments and erythrocytes in the urine at the week 13 to 78 investigations. No other observed changes in parameters were considered treatment related.

Although at 250 mg/kg bw/day a slight reduction was seen in some absolute organ weights at terminal sacrifices, the observed changes were not consistent between sexes and were seen in the absence of histological change. At histopathology, effects were seen on the kidney at 250 mg/kg bw/day in both sexes at the interim and terminal sacrifice. At terminal sacrifice a statistically significant increase in the incidence of nephropathy was seen in both males (93% of animals) and females (83%) at 250 mg/kg bw/day compared to controls (66% and 33% respectively). Additionally in males at 250 mg/kg bw/day and compared to controls, a statistically significant increase in the incidence of abnormal spermatogenic cells (33% animals vs 4% controls animals), absence of spermatozoa (20% vs 9%) and reduced number of spermatozoa (33% vs 6%) were seen in the epididymides, along with an increased incidence of partial depletion of one or more generation of germ cells in the testes (67% vs 20%). Additionally in males, focal and multifocal atypical hyperplasia in the fundic region of the stomach was seen at 250 mg/kg bw/day (8% and 18% animals respectively), which was absent in control animals. Similarly, a statistically significant increase in the incidence of distended gastric glands of the stomach, sometimes containing debris, was seen in top dose females (28%) compared to controls (3%). Where data is available, the severity of these changes was greater at the top dose than in controls. Observed changes at all other triclosan treated dose levels were not dose related nor statistically significantly different compared to controls, or were of a similar incidence to that observed in control animals.

Therefore, at 12.5 mg/kg bw/day the only effect seen that was dose related was a slight though statistically significant decrease in activated prothrombin time in females only. Similarly, at 75 mg/kg bw/day a slight though statistically significant

and dose related decrease was seen in mean corpuscular haemoglobin concentration, along with increase in mean corpuscular volume, in males only. Systemic toxicity was clearly evident in both sexes at 250 mg/kg bw/day, with statistically significant changes seen in a number of haematology, clinical chemistry and urinalysis parameters along with nephrotoxicity and histopathological changes to the stomach. Therefore, the finding of changes in 1 or 2 haematology parameters in a single sex at 12.5 and 75 mg/kg bw/day in the absence of histopathological changes are not considered to provide reliable evidence of systemic toxicity based on the weight of evidence and, thus, the NOAEL is considered to be 75 mg/kg bw/day in both sexes in this study.

Rabbit

In a 90-day dietary study (Leuschner, 1970a), 6 New Zealand White rabbits per sex per dose were administered triclosan at doses equivalent to 0, 12.5, 25, 62.5 or 125 mg/kg bw/day. Haematology, clinical chemistry and urinalysis parameters along with organ weight and histological examination were only undertaken in control and top dose animals. No deaths, clinical signs of toxicity, effect on body weight gain, food or water consumption, were seen. Compared to controls, no treatment related changes were seen in any of the parameters investigated in animals at the top dose. Consequently, the NOAEL is determined to be 125 mg/kg bw/day in this 90-day study.

In a 90-day gavage study that investigated a limited number of parameters (Paterson, 1969), 3 rabbits per sex were administered 0, 3, 30 or 150 mg/kg bw/day triclosan daily. One male at 30 mg/kg bw/day that had consistently lost weight and died on day 17 was replaced. A male and female died at 30 mg/kg bw/day along with 1 male and 2 females at 150 mg/kg bw/day. No clinical signs of toxicity or treatment related effects on body weight gain, haematology, clinical chemical or urinalysis parameters were seen. At necropsy, macroscopic examination revealed pulmonary infection in 3 animals at 30 and 150 mg/kg bw/day. Microscopy revealed oedema and necrosis in the lung of 1 male and 1 female at 30 mg/kg bw/day. Lung oedema was also seen in 2 males, and 1 female in the presence of necrosis, at 150 mg/kg bw/day. An increase in relative kidney (approx. 40%) and lung (approx 135%) weight was also seen at 150 mg/kg bw/day. No other treatment related effects were seen at necropsy. However, the small number of animals used and incidence of pulmonary infection means the data is not reliable for determining the dose-response relationship for triclosan.

Dog

In a 90-day study (Leuschner et al., 1970b), 4 Beagle dogs per sex per group were administered triclosan in the diet at a dose equivalent to 0, 5, 12.5 or 25 mg/kg bw/day. No deaths, effect on body weight gain, food or water consumption were seen. Pasty to thin faeces were observed occasionally in all dose groups and consequently is not considered treatment related. Compared to controls, no treatment related effects were seen in haematology, clinical chemistry or urinalysis parameters at the top dose, the only dose level tested. No treatment related histological findings or effects on organ weight were seen at any dose level and, thus, the NOAEL is determined to be 25 mg/kg bw/day in this 90-day study.

In a briefly reported 91-day study (Paterson, 1967), 3 Beagle dogs per sex per group were administered daily gelatine capsules containing 0, 25, 50, 100 or 200

mg/kg bw/day triclosan. Limited haematology, clinical biochemistry and urinalysis investigations were undertaken together with a limited histopathological examination.

Two animals per sex died at 200 mg/kg bw/day, 2 males at 100 mg/kg bw/day and 1 female at 25 mg/kg bw/day. Diarrhoea was seen in animals at 25 mg/kg bw/day and above, and the severity and frequency increased with dose. Emesis was also seen in some animals at 25 mg/kg bw/day and above. Body weight changes were not determined. Haematology and clinical chemistry assessment revealed a number of 'abnormal' values in individual animals at 25 mg/kg bw/day and above suggestive of liver dysfunction, as were urinalysis findings of bile salts and polymorphonuclear leucocytes in the urine at 25 mg/kg bw/day and above.

Statistically significant and dose related changes in combined male and female relative organ weight were only seen in the pancreas (35% to 50%), kidneys (38% to 44%) and adrenals (12% to 29%) at 100 mg/kg bw/day and above. However, histopathological changes were only seen in one of these organs, the kidney. At necropsy, focal interstitial nephritis being seen in 1 female at 100 mg/kg bw/day and 1 male and 1 female at 200 mg/kg bw/day. Additionally, 'unusual' Kupfer cell activation, bile retention and/or necrosis was seen in the liver of 1 female, 2 males, and 2 animals of each sex at 25, 100 or 200 mg/kg bw/day respectively. In addition, pathological fat was seen in the liver of 1 or more male and female animals at 25 mg/kg bw/day and above. Severe liver damage was associated with bone marrow hyperplasia, and was seen in 1 female, 1 animal per sex, 2 animals per sex, and 2 females at 25, 50, 100 and 200 mg/kg bw/day respectively. All these histopathological changes were absent in control animals. Thus, in contrast to the findings in the 90-day dietary study in Beagle dogs by Leuschner et al. (1970b), a NOAEL could not be identified in this study where triclosan was administered by gelatine capsule. The LOAEL of 25 mg/kg bw/day was based on clinical signs of toxicity, liver damage and enhanced haemopoietic activity.

Baboon

The repeat dose toxicity of triclosan was investigated in male and female baboons (*Papio cynocephalus* and *anubis*). In this study animals received triclosan daily in gelatine capsules for either 4 or 13 weeks (Noel et al., 1969). A total of 1, 1, 1, 3 and 1 animals per sex received 0, 1, 10, 30 or 100 mg/kg bw/day triclosan for 4 wk respectively, and a total of 3 animals per sex received 0 or 3 mg/kg bw/day triclosan for 13 wk.

No deaths, effect on body weight gain, food or water consumption were seen in animals dosed for either 4 or 13 wk. The only clinical signs of toxicity observed were agitation, anger and aggression in the female receiving 100 mg/kg bw/day for 4 weeks. No treatment related effects were seen on haematology, clinical chemistry or urinalysis parameters, or organ weights in animals for either dosing period.

At the autopsy of animals administered triclosan for 4 wk, dark nodules were seen in the large intestine wall in some animals at 10 mg/kg bw/day and above that were suggestive of a parasitic infection, while evidence of chronic interstitial pneumonitis was seen in all animals including controls. For animals administered triclosan for 13 weeks, histopathological findings of parasitic infection to the gastrointestinal tract and chronic interstitial pneumonitis were similar between control and treated animals. Overall, the results in baboons do not indicate systemic

toxicity following administration of 100 mg/kg bw/day triclosan for up to 13 wk. However, the small number of animals per dose and incidence of pulmonary infection limits the significance that can be attached to the data, and it is not considered reliable for determining the dose-response relationship for triclosan.

In a one-year study (Ciba-Geigy Limited, 1975b), triclosan was administered in gelatine capsules to 7 baboons (*Papio* spp) per sex per group at dose levels of 0, 30, 100 or 300 mg/kg bw/day. Two animals per sex per group were sacrificed after 6 months, and 3 animals per sex per group at the end of the dosing period, with remaining animals retained without treatment for a 28-day recovery period.

No deaths were seen. Diarrhoea was reported in all animals at 100 mg/kg/day from the 181-270 day treatment period and in all animals at 300 mg/kg/day from the first 90 days of treatment. The incidence was dose related, and diarrhoea was also seen in a single female at 30 mg/kg bw/day on one instance during the first 90 days of treatment. At the end of the 1 year dosing period, a decrease in body weight gain was seen in males at 100 (10%) and 300 mg/kg bw/day (10%) that was not statistically significant. No effect was seen on food consumption. At 1 year study termination, slight, but statistically significant, decreases in one or more red cell parameter (<10%) seen in both sexes combined at 300 mg/kg bw/day that were stated to be within the control range, as were slight decreases in serum potassium levels (13%). A statistically significant decrease was also seen in glutamic oxaloacetic transaminase (14%) and alkaline phosphatase (30%) for both sexes combined at 300 mg/kg bw/day at 1 year study termination. No effect was seen on urinalysis parameters. Statistically significant increases were reported in mean relative kidney and liver weight at 300 mg/kg bw/day and in mean absolute brain weight from 30 mg/kg bw/day in the absence of treatment related histopathological changes in these or any other organ after 1 year. No treatment related effects were seen in animals at the end of the 28-day recovery period.

Therefore, in this study systemic toxicity was seen in all animals at 100 mg/kg bw/day and above, with the only effects seen at 30 mg/kg bw/day a single instance of diarrhoea within the first 90 days of treatment in 1 animal, along with an increase in absolute mean brain weight in the absence of histopathological changes. Consequently, the NOAEL for this study is considered to be 30 mg/kg bw/day in both sexes, based on clinical signs of toxicity consistently seen in a number of animals.

The US EPA (2008) used the NOAEL of 30 mg/kg bw/d in baboons for acute and chronic dietary exposure risk assessment to establish an acute and chronic reference dose value (similar to ARfD and ADI respectively, in Australia) of 0.30 mg/kg bw/d for triclosan, with an uncertainty factor of 100 for inter- and intra-species variation.

18.4.3 Dermal

Lyman and Furia investigated the toxicity of triclosan in a series of poorly reported experiments (Lyman and Furia, 1969). It is stated (data not provided) that there was no evidence of local toxicity or systemic toxicity in rats following daily 3 h topical application of 0.4 ml of 5% triclosan for 5 days or 0.4 ml of 2.5% or 5% triclosan 5 times per week for 4 wk. Similarly, no systemic toxicity was reported for rabbits receiving daily application of a soap powder paste containing 15% triclosan for 23.5 h per day for 3 days. Overall, the limited reporting of

experimental details and results mean no reliable conclusions can be drawn from the data and, hence, these studies are not discussed further.

Burns investigated the toxicity of triclosan in two 14-day studies in CD-1 mice (Burns, 1996; 1997a) and a 14-day study in the Crl:CDBR rat (Burns, 1997b). In these three studies, groups of 10 animals per sex per group received a daily topical application of 0 (untreated control), 0 (acetone or propylene glycol vehicle control), 0.3, 0.6, 1.5, 3.0 or 6.0 mg/day triclosan. The default body weight values in Table 18.2 have been applied to convert mg/animal/day to mg/kg bw/day. In mice (Burns, 1996; 1997a), daily triclosan intakes were estimated to be 0, 0, 10, 20, 50, 100 and 200 mg/kg bw/day in males and 0, 0, 12, 24, 60, 120 and 240 mg/kg bw/day in females, and in rats 0, 0, 1.5, 3.0, 7.5, 15 and 30 mg/kg bw/day in males and 0, 0, 1.7, 3.4, 8.6, 17.1 and 34.3 mg/kg bw/day in females (Burns, 1997b).

Table 18.2 - Default body weight values for dose calculations

Species	Sex	Body weight (kg)
Rat	M	0.5
(lifetime studies)	F	0.35
Rat	M	0.2
(other studies)	F	0.175
Mouse	M	0.03
	F	0.025

These values are taken from Gold et al. (1984).

M: male, F: female.

No treatment related deaths, effect on body weight gain or water consumption were seen in any study. Contrasting results were seen on food consumption in the two mice studies: at the top dose a decrease was seen in one study and increase in the other. Dose related irritation was seen at the application site in both species.

In mice, signs of irritation, such as erythema, oedema, fissuring, eschar, alopecia, thickening or discolouration of skin was seen in males and females at 50 and 60 mg/kg bw/day and above, with microscopic changes to the skin (acanthosis and hyperkeratosis) also seen at the application site. Furthermore, at 100 mg/kg bw/day and above ulceration and inflammation were seen at the application site. In the mouse studies centrilobular hypertrophy of the liver was seen at 50 mg/kg bw/day and above. Additionally, liver necrosis was seen in both sexes in both studies at 100 mg/kg bw/day and above. However, in one study (Burns 1997a) the incidence was not dose related in males (maximum incidence of two males at 100 mg/kg bw/day) while necrosis was also seen in a single male and female receiving the vehicle only. Necrosis was also seen in three females receiving vehicle only in the other study (Burns 1996) (maximum incidence of 5 males and 5 females at 200 and 240 mg/kg bw/day respectively). The necrosis had an irregular non-zonal pattern. Consequently, overall, the irregular non-zonal pattern of the observed liver necrosis and its presence in control animals cast doubt on it being treatment related.

In rats, erythema, eschar or scaling were reported at the application site in animals at 15 mg/kg bw/day and above. Eschar formation was also seen in a single female at 8.6 mg/kg bw/day. These macroscopic changes corresponded with histopathological changes seen in the skin at necropsy. In contrast to mice, no histopathological changes were seen in the liver of rats.

In these 14-day studies, a NOAEL of 20 and 24 mg/kg bw/day is identified in male and female mice respectively for both local irritant effects and systemic toxicity (i.e. liver hypertrophy). In contrast, the data in rats indicate a NOAEL for local irritant effects of 7.5 and 3.4 mg/kg bw/day in males and females respectively, with no systemic toxicity seen up to the top dose of 30 mg/kg bw/day in males and 34.3 mg/kg bw/day in females.

Ninety day dermal studies are available in the rat (Trimmer, 1994), dog (Dorner, 1973) and monkey (Hazelton Laboratories, 1979).

In the 90-day rat study (Trimmer, 1994), groups of 10 Sprague Dawley rats per sex per group received a daily (occlusive) topical application of 0, 10, 40 or 80 mg/kg bw/day triclosan in propylene glycol for “at least 6 h”. The study also included a 28-day recovery group of 10 animals per sex that received 80 mg/kg bw/day. No treatment related effect was seen on mortality, clinical signs of toxicity, body weight gain, food or water consumption, haematology, clinical chemistry or organ weight. Dermal erythema and/or oedema were seen at 10 mg/kg bw/day and above, and severity was seen to increase with dose. Additionally, at necropsy, hyperplasia, hyperkeratosis, inflammation and focal necrosis were seen at the application site. With the exception of 1 animal, dermal findings were observed to return to normal in the recovery group.

At necropsy, observations of coagulative necrosis of the liver, focal cortical tubular degeneration of the kidney and microscopic changes to the bladder in a small number of animals in the absence of a dose response are not considered treatment related. Occult blood was seen in the urine of 3 to 4 males per group at 40 mg/kg bw/day and above, including the recovery group, and 2 females in the 40 mg/kg bw/day and recovery group. This finding was seen in the absence of other significant clinical chemistry or haematological changes or treatment related histopathological changes. Furthermore, the severity and incidence of occult blood in the urine increased during the recovery period in males and females. Thus, while the significance of this finding is unknown, it is not considered to provide reliable evidence of systemic toxicity based on the weight of evidence, and a NOAEL of 80 mg/kg bw/day is identified for such. For local irritant effects a NOAEL could not be identified, and thus the LOAEL was 10 mg/kg bw/day. The US EPA (2008) identified the NOAEL as 40 mg/kg bw/d based on increased occult blood in urine at 80 mg/kg bw/d.

In a briefly reported 90-day study (Dorner, 1973), groups of 4 Beagle dogs per sex received daily topical applications of 0, 2, 20 or 200 mg/kg bw/day triclosan in cornstarch for an unspecified time period. No treatment related effect was seen on mortality, clinical signs of toxicity, body weight gain, food or water consumption, haematology, clinical chemistry, organ weight or histopathology. Dose related dermal irritation was reported at the application site. No further details are available. The limited information provided, such as exposure duration, means that this study is not considered reliable for determining the dose-response relationship for triclosan.

In a further briefly reported 90-day study (Hazelton Laboratories, 1979), no treatment related effects were seen in newborn Rhesus monkeys that received a daily topical application to the trunk of 0 or 15 mg triclosan in soap solution that was lathered for 5 min and ‘later’ washed. However, as the dose cannot be reliably

determined in mg/kg bw/day this single dose study is of negligible value and is not discussed further.

18.5 Genotoxicity

18.5.1 In vitro

Studies in bacteria

In an Ames test using direct plate incorporation (Arni and Muller, 1978a), *Salmonella typhimurium* strains TA92, TA100, TA1535 and TA1537 were exposed to triclosan at concentrations up to 7.29 µg/mL in the presence and absence of metabolic activation (liver S9). Cytotoxicity was observed in all strains at 7.29 µg/mL with S9 and at 0.09 µg/mL and above without S9. No increase in the number of revertants was seen in any of the tested cultures. Controls gave results that confirmed the validity of the test, and the negative results were confirmed in a second independent experiment.

A negative result was obtained in a further direct plate incorporation Ames test that exposed *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 to triclosan at concentrations up to 5.0 µg/plate with S9, and 0.167 µg/plate without S9 (Pharmakon USA, 1993a). Dose selection was determined from the results of a range finding study. In the main study, cytotoxicity was observed with and without S9, controls gave results that confirmed the validity of the test, and negative results were confirmed in further independent experiments.

In an Ames test with pre-incubation (Jones and Wilson, 1988), *S. typhimurium* strains TA98, TA100, TA1535 and TA1537 were exposed to triclosan at concentrations up to 1.5 µg/plate with and without S9. Doses were selected from a range finding study. Cytotoxicity was observed at 1.5 µg/plate in all strains with S9 and most strains without S9. No increase in the number of revertants was seen in any of the tested cultures. The result was confirmed in a second independent experiment, and controls gave results that confirmed the validity of the test.

Data is available from two briefly reported studies that tested a large number of cosmetic ingredients including triclosan in the Ames test. In a briefly reported study for which only the abstract and tables were translated from Japanese (Morita et al., 1981), a negative result was obtained in *S. typhimurium* strains TA98 and TA100 tested up to 1 µg triclosan/plate with and without S9. Cytotoxicity was seen in both strains at the top concentration without S9 while controls gave results that confirmed the validity of the test. Similarly in the other study (Gocke et al., 1981), a negative result was reported in *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 with and without S9. No further details available.

In a further Ames test for which only the abstract and tables were translated from Japanese (Onodera et al., 1995), a negative result was obtained in *S. typhimurium* strains TA98 and TA100 tested from 1 to 1000 µg triclosan/plate with and without S9. Cytotoxicity was observed without S9 in both strains from 1 µg/plate and from 10 or 50 µg triclosan/plate with S9. The result was confirmed in a second independent experiment, and controls gave results that confirmed the validity of the test.

A negative result was obtained with triclosan in a host-mediated bacterial reverse mutation assay with *S. typhimurium* strains TA98, TA100, TA1535 and TA1537

(Arni and Muller, 1979). However, the absence of a positive control limits the significance that can be attached to this negative finding.

In a briefly reported reverse mutation assay for which only the abstract and tables were translated from Japanese (Morita et al., 1981), a weak positive result was reported for triclosan in *Bacillus subtilis* with and without S9 at 5 mg triclosan/disk. The observance of a weak positive response at this very high dose level is not considered to provide reliable evidence of a significant in vitro mutagenic activity.

Studies in fungi

In a gene mutation and mitotic recombination assay (Arni and Muller, 1978b), *Saccharomyces cerevisiae* was exposed to triclosan at concentrations up to 0.2 mg/mL without S9. Colony growth was completely inhibited at 0.2 mg/mL. An increase in recombinants was seen at 0.03 and 0.04 mg/mL in the absence of cytotoxicity. However, the increase was not dose-related and no significant increase was seen at 0.05 mg/mL in the absence of cytotoxicity. Controls gave results that confirmed the validity of the test. Overall, this study in a single replicate in the absence of a dose-response is not considered to provide robust evidence of a significant in vitro mutagenic potential.

Similarly, although a positive result was reported in a gene mutation and mitotic recombination assay in *S. cerevisiae* without S9 at 0.2 mg/mL triclosan (Fahrig, 1978a), the use of only one concentration and replicate, along with the absence of a positive control, means no reliable conclusions can be drawn from the data on the mutagenic potential of triclosan.

Studies in mammalian cells

In a well-conducted chromosome aberration study (CCR Cytotest Cell Research, 1990), Chinese hamster V79 cells were exposed to triclosan for 4 h with and without S9 at concentrations up to 3 µg/mL, and harvested from 7 to 28 h. A statistically significant increase in the incidence of chromosome aberrations was seen at 3.0 µg/mL at 18 and 28 h without S9, and at 18 hours with S9, in the absence of cytotoxicity.

In contrast, in a chromosome aberration test that exposed Chinese hamster ovary cells (CHO) to triclosan at concentrations up to 1 µg/mL without S9 and 38 µg/mL with S9, no increase in the frequency of chromosomal aberrations was seen under any treatment condition. Treatment was for 24 h in the absence of S9; and for 6 h in the presence of S9 with 18 h recovery prior to harvest (Brooker et al., 1988). However, while dose selection was determined from the results of a range finding study and positive controls produced clear increases in chromosome aberrations, the negative result was not confirmed by conducting a second independent experiment.

In a gene mutation test (Henderson et al., 1988a), mouse lymphoma L5178Y cells (tk locus) were exposed to triclosan at concentrations up to 20 µg/mL without S9 and 15 µg/mL with S9, for 3 h. Significant increases in mutation frequency were seen with and without S9 only at concentrations that were cytotoxic (i.e. the cell survival rate was less than 10%). The positive controls gave clear increases in mutation frequency. This study concluded that triclosan did not demonstrate mutagenic potential in this in vitro test system.

In a further gene mutation test, conducted without S9 only (Strasser and Muller, 1978), no increase in mutation frequency was seen in mouse lymphoma L5178Y cells exposed to 15.8 µg/mL triclosan for 18 hours and 28.9 µg/mL for 4 h. Test concentrations produced a 20% cell survival rate. It is not reported whether a positive control was included.

A negative result was obtained with triclosan in a host-mediated point mutation assay with mouse lymphoma cells (Strasser and Muller, 1978). However, the absence of a positive control limits the significance that can be attached to this negative finding.

In two well-conducted unscheduled DNA synthesis (UDS) assays triclosan did not induce UDS in male Fischer F344 rat hepatocytes at concentrations up to 80 µg/mL (Riach, 1988) and 250 µg/mL (Pharmakon USA, 1993b) in the presence of severe cytotoxicity. In both studies the positive control produced clear increases in UDS.

18.5.2 Studies in *Drosophila*

In a *Drosophila melanogaster* sex-linked recessive lethal assay (Magnusson, 1979), male flies (wild type Karsnas) were fed a 1% sugar solution containing 100 or 1000 ppm triclosan for 24 h, or 1000 ppm triclosan in a corn oil solution mixed in corn agar substrate for 7 days. Males were then mated with females (Muller-5). Females were replaced every 3 days to make a total of 3 broods. No mutagenic effect was observed. However, as no toxic effect was seen with any dose there is a concern that dose levels were not maximised. Furthermore, a positive control was not included.

A negative result was also reported in a briefly reported *D. melanogaster* sex-linked recessive lethal assay that used Berlin K (wild type) and Basc strains (Gocke et al., 1981). In this study, a single dose level of 2.5 mM triclosan in 5% sucrose was used that was stated to be close to the LD50, and 3 successive broods obtained.

However, for an insect system such as these there is too little comparative data with mammalian cells and the relevance of findings to the mammalian in vivo system is uncertain (Aardema et al., 1998).

18.5.3 In vivo

Studies in somatic cells

In a bone marrow chromosome aberration test (CCR Cytotest Cell Research, 1991), 5 Wistar rats per sex per dose per sampling time received a single oral dose of 0 or 4000 mg/kg bw triclosan that was determined to be the maximum tolerated dose from a dose-ranging study. Bone marrow was sampled at 6, 24 and 48 h post dosing and 50 metaphases examined per animal. No increase in the incidence of chromosomal aberrations was seen for triclosan. Similarly, a negative result was obtained in an oral bone marrow chromosome aberration test in Chinese hamsters (Muller and Strasser, 1973). In this study, 4 females per group were gavaged with up to 600 mg/kg bw/day triclosan daily for 2 days. Bone marrow was sampled 2 h after the last dose and 100 metaphase cells analysed per animal. No information on toxicity was reported. In both these studies the positive control gave a clear increase in the frequency of chromosome aberrations.

In a micronucleus assay (Henderson et al., 1988b), 5 Swiss mice per sex per dose per sampling time received a single oral dose of 0 or 5000 mg/kg bw triclosan and bone marrow was sampled 24, 48 and 72 h later and 1000 polychromatic erythrocytes examined per animal. Compared to controls, a small but statistically significant decrease in the mean ratio of polychromatic to normochromatic erythrocytes (P/N ratio) was seen for triclosan treated groups at 24 and 48 h. No increase in the incidence of micronuclei was seen following triclosan treatment, while the positive control gave a clear increase in the frequency of micronuclei. Similarly, a negative result was obtained in a further oral micronucleus assay (Langauer and Muller, 1974). In this study, 3 Chinese hamsters per sex per group received up to 600 mg/kg bw triclosan by gavage for 2 consecutive days, bone marrow sampled 24 h after the last dose and 1000 PCEs examined per animals. No information on toxicity was reported. The positive control gave a clear increase in the frequency of micronuclei.

A negative result was obtained in an intraperitoneal (ip) mouse micronucleus assay (Gocke et al., 1981). In this briefly reported study, 2 NMRI mice per sex per dose received 0, 579 or 869 mg/kg bw triclosan at 0 and 24 h, bone marrow sampled 6 h later and 1000 PCEs scored per animal. It was reported that two of the four animals died at the top dose. No further details are available.

A bone marrow chromosome aberration test (Strasser and Muller, 1979) and micronucleus assay (Langauer and Muller, 1978) is available in Chinese hamsters that used an extended exposure period. Both oral studies used 6 animals per sex per dose, tested up to 600 mg/kg bw/day triclosan 3 times a wk for 12 wk. For each animal examined, 100 metaphases were scored in the chromosome aberration study and 1000 bone marrow cells in the micronuclei study. Deaths were seen at 600 mg/kg bw/day in the chromosome aberration study and at 300 mg/kg bw/day and above in the micronucleus assay. A negative result was obtained in both studies. However, the analysis of cells from only 2 or 3 animals per sex per group, and the absence of a positive control, means that the negative result from these non-standard studies (i.e. extended dosing duration) cannot be regarded as completely reliable.

In a mouse spot test C57BL/6JHan (a/a) females were mated with T (a/a, b/b, c^{ch}p/c^{ch}p, s/s) males (Fahrig, 1978b), and pregnant females administered a single intraperitoneal (ip) injection of 50 mg/kg bw/day triclosan between days 7 to 11 of gestation. Light-grey, grey, and brown spots were seen in 1, 3, and 4 offspring respectively, from a total of 332 offspring. These spots were not seen in 245 consecutive, or 1160 pooled, controls. Overall frequency of spots was 0.1% in controls vs 2.4% in treated animals. A positive control was included but the results were not reported. Consequently, overall, the use of only one dose level, and absence of information on toxicity and results with the positive control means that no reliable conclusions can be drawn from the data on the mutagenic potential of triclosan.

In contrast, triclosan was not mutagenic in an ip mouse spot test in which C57BL/E (a/a) females were mated with T (a/a, b/b, c^{ch}p/c^{ch}p, dse/dse, s/s) males, and pregnant females administered 0, 1, 2, 4, 8, or 25 mg/kg bw triclosan on day 9 or 10 of gestation (Russell and Montgomery, 1980). Deaths were seen in dams at 25 mg/kg bw along with reductions in litter size and postnatal survival. However, the use of 60% v/v methanol as a vehicle and its unknown contribution towards the

observed toxicity limits the significance that can be attached to this negative finding.

Studies in germ cells

In a rodent dominant lethal assay (Fritz, 1971), 12 male NMRI mice per group received a single oral dose of 0, 750 or 1500 mg/kg bw triclosan and were mated with 3 or 4 untreated females every week for 8 wk. Slight convulsions were seen in males at 1500 mg/kg bw triclosan. No difference was seen between control and treated animals in the number of implantations and dominant lethal findings. However, the absence of a positive control and low number of pregnant females per mating interval (i.e. 17 to 33) means that this negative result cannot be regarded as completely reliable.

Data are available from two oral chromosome aberration studies in spermatogonia. In these studies 8 male NMRI mice per group received 0, 189, 378, 756 or 1512 mg/kg bw/day triclosan either daily for 5 days and killed 24 h after the last dose (Hool et al., 1978) or were administered triclosan on days 0, 2, 3, 5 and 9 and killed 3 days after the last dose (Hool et al., 1979). Clastogenic effects were evaluated in 100 metaphases from each of 6 animals per group in each study. Deaths occurred in both studies for animals that received 1512 mg/kg bw/day triclosan. No increase in the incidence of chromosome aberrations was seen in either study. However, the absence of a positive control in either study limits the significance that can be attached to these negative findings.

18.6 Carcinogenicity

In a well-conducted carcinogenicity bioassay in Sprague-Dawley rats (Ciba-Geigy Corporation, 1986), 60 rats per sex per group were administered triclosan in the diet at 0, 300, 1000 or 3000 ppm for 2 years. Doses were equivalent to approximately 0, 12, 40 and 127 mg/kg bw/day in males and 0, 17, 56 and 190 mg/kg bw/day in females. The study also included additional interim sacrifice groups. The results of interim sacrifices at 1 year of 20 control animals per sex and 10 animals per sex receiving the above doses of triclosan plus an additional dose level equivalent to 247 mg/kg bw/day in males and 422 mg/kg bw/day in females are also reported below. All animals were subject to a thorough gross and microscopic examination either at death or at the end of the dosing period.

No significant difference in survival were observed between triclosan treated and control animals throughout the study for animals treated up to 2 years. In males 20/60, 18/60, 26/60 and 20/60 animals survived until the end of the 2 year dosing period in the control, low, mid and high dose groups respectively. Corresponding survival rates among females were 19/60, 16/60, 21/60 and 17/60. A statistically significant reduction in body weight gain was seen in males at 247 mg/kg bw/day (10%) and in females at 422 (23%) and 190 mg/kg bw/day (6%) treated for 1 year. However, at the end of the 2 year dosing period no significant difference was seen in body weight gain between treated and control animals. No clinical signs of toxicity were seen in animals treated up to 2 years. Further non-tumour toxicological findings are reported in the repeat dose toxicity sub-section. In this study, no treatment related tumours were observed in male and female rats administered up to 127 and 190 mg/kg bw/day triclosan respectively for 2 years, or in males and females administered 247 and 422 mg/kg bw/day for 1 year.

In a well conducted carcinogenicity bioassay in Syrian hamsters (Huntingdon Life Sciences Ltd., 1999), 60 hamsters per sex per group were administered triclosan in the diet at doses that equated to 0, 0, 12.5, 75, or 250 mg/kg bw/day for 90 to 95 wk. The study also included additional interim sacrifice groups. The results of interim sacrifices at 52 wk of 10 animals per sex receiving the above dose levels are also presented below. All animals were subject to a thorough gross and microscopic examination either at death or at the end of the dosing period.

Compared to controls, a rapid increase in the incidence of deaths was seen after 80 wk of treatment in male hamsters receiving 250 mg/kg bw/day. From wk 81-95 a total of 72, 68, 64, 51 and 134 animals died at 0, 0, 12.5, 75 and 250 mg/kg bw/day respectively. Compared to controls (combined) a statistically significant decrease was seen in body weight gain in males receiving 250 mg/kg bw/day: 48% at the end of wk 90 and 72% at the end of wk 95. A slight, though statistically significant, decrease was seen in feed consumption in females at 250 mg/kg bw/day (3%). A gradual deterioration in the general clinical condition of male hamsters was seen during the latter period, with lethargy, hunched posture, pallor, thin appearance and unsteady gait observed. Further non-tumour toxicological findings are reported in the repeat dose toxicity sub-section. In this study, no treatment related tumours were observed in male and female hamsters administered up to 250 mg/kg bw/day triclosan for 90 to 95 wk.

18.7 Fertility

The effect of triclosan on fertility was evaluated in an extensive dietary two-generation study in Crl:CD (SD) Br rats (Morseth, 1988). The F0 generation consisted of 25 rats per sex per group administered triclosan in the diet at dose levels corresponding to 0, 17, 56 and 176 mg/kg bw/day in males and 0, 23, 73 and 229 mg/kg bw/day in females, during a pre-mating period of at least 10 wk and a mating period of up to 3 wk. Females were also administered the test material throughout gestation and lactation. F0 males and F0 females were sacrificed after the delivery and weaning of F1 pups respectively. Thirty male and female F1 generation offspring from each group were retained after weaning for assessment of their reproductive capacity. F1 animals were administered triclosan in the diet for the same pre-mating and mating period. Again females received triclosan during gestation and lactation, and male and female parental animals were sacrificed as for F0 parental animals. For all F0 and all F1 reared animals, clinical observations, body weight and feed consumption data were collected regularly throughout the study. After sacrifice, all F0 and F1 parental animals were subject to a thorough macroscopic examination and reproductive organs removed for histopathological examination if required. Pups were subject to limited gross macroscopic examination only.

No treatment related deaths and clinical signs of toxicity were seen in F0 and F1 parental animals. Additionally, no treatment related effect on body weight gain or feed consumption was seen in F0 parental animals. Compared to controls, a statistically significant decrease in mean body weight gain of 11%, 14% and 16% was seen over gestation at 23, 73 and 229 mg/kg bw/day respectively. However, compared to controls, a statistically significant decrease in mean body weight was only seen on day 20 at 23 (7%) and 73 (6%) mg/kg bw/day. In contrast, a statistically significant decrease in mean body weight was seen on day 0 (12%), 7 (12%), 14 (11%) and 20 (13%) at the top dose. A statistically significant reduction

in feed consumption of 10% was also seen in dams during the first 7 days of gestation at 229 mg/kg bw/day. No treatment related effect was seen on oestrous cycling, pregnancy rate and gestation length in F0 and F1 dams. At histopathology the most common finding in F0 and F1 parental animals was dilated renal pelvis. Although this finding was absent in controls for the F0 generation and seen in 1 F0 male at both 56 and 176 mg/kg bw/day and in 1, 1 and 3 F0 females at 23, 73 and 229 mg/kg bw/day respectively, it was found in both control and treated F1 parental animals with no treatment related response pattern evident.

In F1 pups, postnatal survival from day 0 to day 4 was slightly reduced at the top dose (82% survival) compared to the other groups (90%, 94% and 96% in the control, low and mid dose groups respectively). Survival from postnatal day 4 onwards was similar in all dose groups. Additionally at the top dose, a statistically significant decrease in body weight gain was seen in male and female F1 pups on postnatal day 14 (12% and 15% respectively) and 21 (10% and 12%), and at necropsy dilated renal pelvises were seen in 7, 4, 9 and 14 F1 pups in control, mid, low and high dose groups respectively. During the growth and development phase statistically significant decreases in mean body weight gains were seen in both sexes from wk 0 to 12. Decreases were greater than 10% in females for each wk and wk 0 to 4 only in males. No significant difference was seen between controls and treated animals for food consumption.

In F2 pups although a slight decrease in postnatal survival was seen at the top dose from day 0 to 4 (87%, 97%, 90% and 84% survival in the control, low, mid and top dose groups respectively), and from day 4 to 21 (93%, 99%, 99% and 86% respectively) the incidence decreased with time. At the top dose a statistically significant but slight (less than 10%) decrease in mean body weights was also seen in both sexes compared to controls. No treatment related changes were seen on feed consumption or at necropsy of F2 pups. In F2 animals maintained up to postnatal day 91 no treatment related effects were seen on body weight gain, feed consumption or at necropsy.

No effect was seen on fertility up to and including the top dose. Overall, there was some evidence of systemic toxicity in parental animals in this two-generation study, with reductions in body weight gain of 10% or greater seen in F1 males and females at the top dose of 176 and 229 mg/kg bw day respectively during the growth and development stage. Though a decrease was seen in body weight gain during gestation in F1 dams at 23 mg/kg bw/day and above, the decrease was only statistically significant on day 20 of gestation, was not dose related and was less than 10% at 23 and 73 mg/kg bw/day. Consequently, these changes seen at gestation are considered likely to reflect a 'carry over' from the growth phase rather than a specific effect on gestation and, thus, the changes seen at 23 and 73 mg/kg bw/day alone are not considered to provide robust evidence of systemic toxicity. Therefore, the NOAEL for reproductive toxicity is 176 and 229 mg/kg bw/day in males and females respectively with corresponding NOAEL values for systemic toxicity of 56 and 73 mg/kg bw/day.

Additionally, data are available from repeat dose studies of 90 days and longer that examined reproductive organs (see sub-section 18.4). These are an oral 90-day and carcinogenicity study in both the rat (Litton Biotechnics Inc., 1983; Ciba-Geigy Corporation, 1986) and hamster (Schmid et al., 1994; Huntingdon Life Sciences Ltd., 1999) along with 90-day oral studies in the mouse (Trutter, 1993), rabbit (Paterson, 1969; Leuschner et al., 1970a), dog (Paterson, 1967; Leuschner et al.,

1970b) and baboon (Noel et al., 1969). An oral 1 year study is also available in the baboon (Ciba-Geigy Limited, 1975b) as well as a 90-day dermal study in the rat (Trimmer, 1994) and Rhesus monkey (Hazelton Labs Inc., 1979).

In the carcinogenicity study in the hamster (Huntingdon Life Sciences Ltd., 1999), effects were clearly seen on spermatogenesis at 250 mg/kg bw/day. However, these effects in males were seen in the presence of an increased incidence of deaths, deterioration in the general clinical condition and reduction in body weight gain in excess of 40%. Thus, the effects on spermatogenesis are considered a secondary non-specific consequence of marked systemic toxicity. No other treatment related effect on the reproductive organs was seen in the other 90-day or longer repeat dose studies.

18.8 Developmental toxicity

Rat

In a dose range-finding study (Biodynamics Inc., 1992a), groups of 5 mated female Sprague-Dawley rats were gavaged with 0, 5, 10, 25, 50 or 75 mg/kg bw/day triclosan in 1% carboxymethylcellulose in a 20% glycerine in water suspension on days 6 to 15 of gestation. Animals were sacrificed on day 20 of gestation and foetuses examined for gross morphological abnormalities. No deaths or clinical signs of toxicity were seen. Although compared to controls mean dam body weight gain was reduced at 75 mg/kg bw/day over the dosing period (30%), this decrease was due to a slight reduction in body weight in a single animal. Excluding the aforementioned dam, no treatment related effect was seen on feed consumption. No treatment related gross histopathological changes were seen in dams at necropsy. No effect was seen on the number of implantation sites per litter, resorption rate or number of live foetuses, though compared to controls a reduction in mean foetal body weight was seen at 75 mg/kg bw/day (15%) that was outside the historical control range. No treatment related gross alterations were observed in foetuses. From the results of this study, dose levels in the range 0 to 150 mg/kg bw/day triclosan were used in the main study.

In the main study (Biodynamics Inc., 1992b), groups of 24 or 25 mated Sprague-Dawley rats were gavaged with 0, 15, 50 or 150 mg/kg bw/day triclosan in 1% carboxymethylcellulose in a 20% glycerine in water suspension on days 6 to 15 of gestation. Animals were sacrificed on day 20 and foetuses subject to gross examination and limited visceral and skeletal examination. No treatment related deaths, clinical signs of toxicity, effect on body weight gain or gross histological changes were seen in dams. Compared to controls, a slight but statistically significant reduction in feed consumption was seen at 150 mg/kg bw /day (8%) over days 6 to 11 of gestation. No effect was seen on the number of implantations, resorptions, live foetuses or foetal body weight. No treatment related visceral changes or skeletal malformations were seen. Although, compared to controls, slight increased incidences in foetuses with one or more variations in retarded ossification were seen in triclosan treated groups (91.2%, 92.4%, 92.9% and 95.3% at 0, 15, 50 and 150 mg/kg bw/day respectively) the incidences did not differ statistically. Furthermore, though several variations seen at 150 mg/kg bw/day involving the cranium, vertebrae, sternum, metacarpals and pelvic girdle were outside the historical control range for foetal and litter incidence a dose response was not evident for these findings. Therefore, at the top dose of 150 mg/kg bw/day

the decrease in food consumption is only suggestive of a maternal toxic effect, while the limited evidence of retarded ossification at the same dose are also only suggestive at most of a minor skeletal effect. Consequently, triclosan was not a developmental toxicant in the rat in this study, and the NOAEL for both developmental and maternal toxicity is 50 mg/kg bw/day.

A study is available in Colworth Wistar rats where dose levels were determined from an unreported preliminary study that stated 300 mg/kg bw/day was the highest tolerable dose (Denning et al., 1992). In the main study, groups of 30 mated females were gavaged with 30, 100 or 300 mg/kg bw/day triclosan in corn oil on days 6 to 15 of gestation. A group of 60 control animals received vehicle only. On day 21 of gestation 25 triclosan treated animals per group and 50 control animals were sacrificed. Remaining animals were allowed to deliver and rear the pups until day 21 and external postnatal development features such as eye and pinnae opening and incisor teeth eruption recorded. Foetuses and pups were subject to routine external, visceral and skeletal examination. Slight diarrhoea, generally in the first few days of treatment, was seen in 1/30 and 21/30 dams at 100 and 300 mg/kg bw/day respectively. Compared to controls, a statistically significant reduction in body weight gain of 28% and 9%, and 15% and 10% for feed consumption, was seen at 300 mg/kg bw/day from treatment days 6 to 10 and 10 to 15 respectively. No treatment related effects were seen in foetuses or pups.

Therefore, in this study that included a postnatal phase, triclosan did not exhibit developmental toxicity up to 300 mg/kg bw/day a dose level that produced evidence of maternal toxicity as shown by a 28% decrease in body weight gain from gestation day 6 to 10. Consequently, the NOAEL for developmental toxicity is 300 mg/kg bw/day and the NOAEL for maternal toxicity is 100 mg/kg bw/day.

In a briefly reported study translated from Japanese (Kawashima, 1987), groups of 20 mated female Wistar rats were gavaged with 0, 100, 200 or 400 mg/kg bw/day triclosan in olive oil on days 7 to 17 of gestation. Animals were sacrificed on day 20 and subject to external, visceral and skeletal examination (it is not reported what visceral and skeletal parameters were investigated). No deaths were seen. Piloerection, incontinence and diarrhoea were observed in 9/20 dams at 400 mg/kg bw/day, though the duration of these clinical signs of toxicity is not reported. No effect was seen on body weight gain. Feed consumption data was presented in graphical form, and although an accurate quantitative estimate cannot be made a significant reduction in feed consumption is apparent at 400 mg/kg bw/day compared to controls. No significant effect was seen on implantation rate or the number of live foetuses, though a statistically significant increase was seen in the incidence of foetal deaths at 400 mg/kg bw/day (7.05% dead implants) compared to controls (1.59%). No treatment related effect was seen on foetal body weight or visceral and skeletal morphology. Therefore, the only effect seen in foetuses was an increase in dead implants at 400 mg/kg bw/day that was seen in the presence of maternal toxicity (clinical signs of toxicity and decreased feed consumption). However, due to the lack of methodology details and limited reporting of results it is considered that no reliable conclusions can be drawn from this study on the potential developmental toxicity of triclosan.

In a briefly reported study translated from Polish (Piekacz, 1978), groups of only 10 mated female Wistar rats were gavaged with proportions of the determined LD50 in this strain of rat that equated to 0, 4, 8, 16, 40 or 80 mg/kg bw/day triclosan in oil (type not specified) on days 6 to 15 of gestation. Animals were

sacrificed on day 21 of gestation and foetuses subject to gross examination and limited visceral and skeletal examination. No effect on maternal body weight gain was seen, the only parameter measured in dams. No treatment related effect were seen in the fetal parameters investigated: number of foetuses and number of live/dead foetuses; foetal body weight; placental weight; foetal length; resorptions; skeletal parameters (sternum skull and ribs); and palate development. However, as the study employed a small number of animals per dose and investigated a limited number of maternal and developmental parameters, only limited significance can be attached to the negative finding.

Data on postnatal effects are available from the dietary 2-generation study in Crl:CD (SD) Br rats (see sub-section 18.7 for a more comprehensive study summary). In this study (Morseth, 1988), 25 rats per sex per group were administered triclosan in the diet at dose levels corresponding to 0, 23, 73 and 229 mg/kg bw/day in females throughout their mating period and up to day 21 post partum (i.e. the end of weaning).

In F1 pups, though postnatal survival was slightly reduced from day 0 to day 4 at the top dose compared to the other groups, it was similar in all dose groups from day 4 onwards. While in F2 pups at the top dose, though a slight decrease was seen in postnatal survival from day 0 the incidence decreased with time. Similarly at the top dose, although a statistically significant decrease in body weight gain was seen in male and female F1 pups on postnatal day 14 and 21 the reduction in body weight gain diminished with time, and no such decrease was seen in either sex from postnatal days 0 to 7. While in F2 male and female pups at the top dose, though statistically significant the decrease seen in mean body weight gain was slight (i.e. less than 10%). Although a slight increase was seen in dilated renal pelvises in F1 pups at the top dose it was not dose-related, and was not observed in F2 pups. Therefore, the results from this two-generation study do not provided robust evidence that triclosan is a post-natal developmental toxicant.

Mice

In a dose finding study (Argus Research Laboratories Inc., 1992a), groups of 8 mated Crl:CD-1 (ICR)BR mice were administered triclosan in the diet at a dose equivalent to 0, 4.8, 9.4, 17.1, 39.0, 71.6 or 127.8 mg/kg bw/day on days 6 to 15 of gestation. Animals were sacrificed on day 18 of gestation and the foetuses were examined for gross morphological abnormalities. No deaths or clinical signs of toxicity were seen. Compared to controls, body weight gain was decreased at the later stages of the dosing period at 127.8 mg/kg bw/day (14% from day 12 to 16), with a decrease seen in terminal body weight at day 18 (9%). Feed consumption was also reduced during the dosing period at 127.8 mg/kg bw/day (14%). No treatment related gross histopathological changes were seen in dams at necropsy, though an increase was seen in absolute and relative liver weight at 71.6 (11% to 13% respectively) and 127.8 mg/kg bw (23% to 25% respectively). Compared to controls, a statistically significant decrease in foetal body weight was seen at 39.0 (6%), 71.6 (11%) and 127.8 mg/kg bw/day (6%). Additionally at 127.8 mg/kg bw/day an increase was seen in the total resorptions (1.8% versus 0.8% in controls, with both early and late resorptions increased) and the % of resorbed conceptuses per litter (15.0% vs 7.4%) that were outside the historical control range (0.5% to 1.5% and 4.1% to 11.2% respectively). The number of dams with resorptions was also increased at 127.8 mg/kg bw/day (87.5% vs 42.8%). No treatment related

gross alterations were observed in foetuses. From the results of this study, dose levels in the range 0 to 350 mg/kg bw/day triclosan were used in the main study.

In the main study (Argus Research Laboratories Inc., 1992b), groups of 25 mated CrI:CD-1 (ICR)BR mice were administered triclosan in the diet at a dose equivalent to 0, 10, 25, 75 or 350 mg/kg bw/day on days 6 to 15 of gestation. Animals were sacrificed on day 18 and the foetuses were subjected to routine external, visceral and skeletal examination. No treatment related deaths or clinical signs of toxicity were seen. Compared to controls, a statistically significant increase in body weight gain was seen on days 8 to 9 of gestation (30%) at 350 mg/kg bw/day, along with a slight increase in terminal body weight (6%), in the absence of effects on feed consumption. At necropsy a statistically significant increase in absolute and relative liver weight was seen at 75 (7% to 17%) and 350 mg/kg bw/day (43% to 53%) compared to controls. Furthermore, a statistically significant increase in animals with tan areas in the liver was seen at 350 mg/kg bw/day (14 of 25 animals). It was also present in a single animal at 75 mg/kg bw/day. This finding was not seen in control animals.

Slight, but statistically significant increases in foetal body weight were seen in males at 75 mg/kg bw/day (4%) and in males (8%) and females (6%) at 350 mg/kg bw/day. A statistically significant increased foetal incidence of irregular ossification of the interfrontale section of the skull was seen at 75 (16.8% vs 6.2% in controls) and 350 mg/kg bw/day (15.2%), but was within the historical control range¹⁵ (3.6% to 25.2%). Similarly, the statistically significant increase in litter incidence for this finding at 350 mg/kg bw/day (54.5% vs 27.3%) was also within the historical control range (18.8% to 63.6%). Compared to controls, a statistically significant reduction in the foetal incidence of ossified forelimb phalanges was seen at 350 mg/kg bw/day (10.72% vs 11.68%) that was just outside the historical control range (10.77% to 11.67%). No other treatment related effects were seen.

Therefore, the observance of an increased incidence in resorptions in the dose finding study is not considered robust evidence of a developmental effect, as it was not reproducible in the well-conducted main study at greater dose levels. Additionally, decreases in foetal body weight from 75 mg/kg bw/day in the main study were slight (4% to 8%) and not considered biologically significant. Similarly, skeletal findings, with the exception of delays in fore paw ossification at 350 mg/kg bw/day, were within historical control ranges. In dams, liver toxicity (tan livers) was seen in 1 animal at 75 mg/kg bw/day and a significant number at 350 mg/kg bw/day. Consequently, the minimal finding in the main study of a delay in ossification of forelimb phalanges in foetuses at 350 mg/kg bw/day is considered to be a secondary non-specific consequence of maternal (liver) toxicity that was seen in a significant number of animals. Thus, the NOAEL for both developmental and maternal toxicity is 75 mg/kg bw/day.

Rabbit

In a dose range-finding study (Biodynamics Inc., 1992c), groups of 5 mated New Zealand White rabbits were gavaged with 0, 5, 25, 50 or 75 mg/kg bw/day triclosan in 1% carboxymethylcellulose in a 20% glycerine in water suspension on days 6 to 18 of gestation. Animals were sacrificed on day 30 of gestation and the foetuses

¹⁵ For fetal skeletal effects the historical control data came from 4 studies, 1 of which was oral the others i.v. with a total of 584 foetuses examined from 84 litters.

were examined for gross morphological abnormalities only. No treatment related deaths or clinical signs of toxicity were seen, though slight maternal body weight losses were seen often throughout the dosing period at 75 mg/kg bw/day, as were decreases in feed consumption. Red foci were observed in the lungs of animals in the control and treated groups. Although a slight increased incidence was seen in these red foci at 50 and 75 mg/kg bw/day there was no dose response and, thus, this finding is of questionable biological significance. No foetal effects were seen up to and including 75 mg/kg bw/day. From the results of this study, dose levels in the range of 0 to 150 mg/kg bw/day triclosan were used in the main study.

In the main study (Biodynamics Inc., 1992d), groups of 18 or 19 mated New Zealand White rabbits were gavaged with 0, 15, 50 or 150 mg/kg bw/day triclosan in 1% carboxymethylcellulose in a 20% glycerine in water suspension on days 6 to 18 of gestation. Animals were sacrificed on day 30 and the foetuses were subjected to routine external, visceral and skeletal examination. No treatment related deaths or clinical signs of toxicity were seen. Compared to controls, slight but statistically significant losses in mean body weight were seen on days 14 (7.3%) and 16 (7.9%) of gestation at 150 mg/kg bw/day, and over the day 16 – 19 gestation period a statistically significant decrease was seen in mean maternal body weight gain (65%). Statistically significant decreases in feed consumption were also seen during the dosing period (up to 41.4% on day 15). No treatment related effects were seen at necropsy. Pregnancy rates were not affected by treatment with triclosan, nor were the sex ratio or mean foetal body weight per litter. Although a slight decrease was seen in the number of implantation sites per litter and number of live foetuses per litter, along with a decrease in % resorptions per litter, at 150 mg/kg bw/day, these changes were not statistically significant and were within historical control ranges. At 0, 15, 50 and 150 mg/kg bw/day an increased incidence of additional subclavian arteries was seen for fetal (3.5%, 4.8%, 3.1% and 9.7% respectively) and litter incidence (25.0%, 33.3%, 26.7% and 31.3% respectively) that was outside the historical control range (1 foetus out of a total of 2176 from 256 litters). However, as the increased incidence in foetuses was not dose related, was not statistically significant at 150 mg/kg bw/day, and the litter incidence was comparable to controls, it is considered a chance finding and not treatment related. No treatment related skeletal findings were observed. Consequently, it is considered that no developmental effects were seen in this study up to 150 mg/kg bw/day in the presence of marked maternal toxicity as indicated by slight losses in body weight during the dosing period. Thus, the NOAEL for developmental toxicity is 150 mg/kg bw/day and the NOAEL for maternal toxicity is 50 mg/kg bw/day.

Hamster

A non-standard study is available in Syrian hamsters translated from Polish (Piekacz, 1978). However, in this briefly reported study the basis for doses administered at 1/50, 1/100, 1/250, 1/500 and 1/1000 of the LD50 for that strain of hamster, or what these dose levels equate to in mg/kg bw/day, is not clear. Additionally, although a decrease was seen in the number of foetuses at the top dose along with an increased incidence in resorptions, the dams were reported to be dying at this dose (no further information provided). Overall, the limited information on the dose administered and the reported severe maternal toxicity mean no reliable conclusions can be drawn from this study and, consequently, it is not discussed further.

18.9 Other data

18.9.1 Antimicrobial resistance – 2002 EU review

Recent scientific papers investigating the possible impact of the use of triclosan on the development of antimicrobial resistance resulted in the European Commission (EC) Scientific Steering Committee (SSC) to consider the following questions.

- Is the use of triclosan in cosmetic products safe, taking into account the risk of resistance development by certain micro-organisms?
- Is it necessary in the safety assessment to take into consideration the fact that triclosan is used in other consumer products?

The SSC installed a working group of experts to undertake a review of the data and provide a scientific report that would allow the SSC to address the above questions (see EC Health & Consumer Protection Directorate-General, (2002b) for a comprehensive summary of the working group). The opinion of the SSC is presented below (see EC Health & Consumer Protection Directorate-General (2002a) for a comprehensive opinion of the SSC).

The SSC considered that “triclosan is a useful and effective biocide which has been safely used for many years across a broad range of dental, medical, cosmetic and household products and is increasingly finding a use in clinically important applications.

At high (*biocidal*) concentrations, triclosan is very effective and unlikely to produce a major problem of anti-microbial resistance. However, at sub-biocidal and bacteriostatic, concentrations, triclosan is capable of penetrating bacteria and initiating changes related to important mechanisms of antimicrobial resistance including possibly transferable mechanisms of resistance, though the scientific evidence for transferability has been disputed. Sound scientific laboratory evidence exists for the development of triclosan related mechanisms for antimicrobial resistance, but the evidence as to whether these mechanisms are shared by other antimicrobial agents or whether they are transferable to micro-organisms other than those used in the laboratory is limited and contradictory. No evidence of such resistance has been seen so far in clinical isolates, and there is no epidemiological evidence to suggest a problem in clinical practice. There are, however, very few targeted studies of resistance to triclosan in relevant clinical or wider environments. Although, the stability and persistence of triclosan resistance has not been widely studied, the limited information available points to it being stable over a three to ten year period.”

The SSC therefore concluded “there is no convincing evidence that triclosan poses a risk to humans or to the environment by inducing or transmitting antibacterial resistance under current conditions of use.”

In addition to further recommendations by the SSC that information be sought on a number of specific technical/use issues, the SSC also recommended, that “the broader issue of the relationship between the use of biocides and the development of clinically relevant antimicrobial resistance be kept under continuous review.”

Since the EU review of 2002 a number of studies have been identified in published scientific journals investigating antimicrobial resistance to triclosan. A summary

of these studies together with an updated assessment of antimicrobial resistance to triclosan, are presented below.

18.9.2 Antimicrobial resistance – studies since the 2002 EU review

Recent laboratory studies of resistance and cross-resistance

Fan et al. (2002) identified elevated resistance to triclosan (minimum inhibitory concentration [MIC] >0.25 µg/ml) in seven of 31 clinical isolates of *Staphylococcus aureus* (MIC 0.016 µg/mL in 24 sensitive isolates). The resistant isolates were all enoyl-ACP reductase (EAR) over-producers (3-5 times that of sensitive isolates). In those EAR overproducing strains with MIC 1-2 µg/mL for triclosan, a mutation in EAR was also detected: a phenylalanine residue at position 204 in the wild type protein replaced by a cysteine. An isolate with intermediate resistance to triclosan (MIC 0.25 µg/mL) showed overproduction of EAR but no mutation in the enzyme. The F204C mutation gave rise to an EAR that was unable to bind triclosan to form the inhibited ternary complex EAR-triclosan-NAD⁺. Thus, mutation of EAR and overproduction of the enzyme were synergistic in giving rise to elevated resistance to triclosan in *S aureus* from clinical environments.

Brenwald and Fraise (2003) used clinical multi (methicillin) resistant *S aureus* (MRSA) isolates to select (under triclosan pressure in the laboratory) two triclosan resistant mutants, and compared these with four naturally occurring triclosan resistant MRSA variants. One mutant and one natural isolate had amino acid changes in EAR. The others were concluded to have resistance due to other genetic changes.

Chuanchuen et al. (2003) examined a highly resistant (MIC >1000 µg/mL) laboratory strain (PAO1) of *Pseudomonas aeruginosa* and a series of its mutants over-expressing, or deleted for, genes encoding multidrug efflux pumps. Deletion of certain pumps brought about reduction of triclosan resistance (MIC 16-128 µg/mL). In other deletants, triclosan resistance remained >1000 µg/mL, indicating that the deleted genes encoded multidrug efflux pumps not relevant to triclosan efflux. The authors report that multiple efflux pumps have been described in *Ps aeruginosa*, some of which use triclosan (or other biocides and antibiotics) as a substrate, and some of which are silent until appropriate substrates are presented, thus presenting a complex picture of cross resistance and its expression in this bacterium. Consequently, it is considered that the (intrinsic) resistance seen in the sensitised deletants is likely to be due to either cell envelope impermeability or resistant isoforms of EAR in *Ps aeruginosa*.

In contrast, Champlin et al. (2005) found that the same highly resistant standard PAO1 strain of *Ps aeruginosa* could be sensitised by mutational alteration of the cell envelope (MIC >256 µg/mL in wild type PAO1 decreased to 64 µg/mL in mutant). Moreover, permeabilisation of the cell envelope by treatment of cells with three independently acting chemical agents (polymyxin, compound 48/80, and ethylenediaminetetraacetate (EDTA)) (which have been used previously by the authors to sensitise gram negative bacteria to antibiotics) brought about nearly complete inhibition of growth in the presence of 2 µg/mL of triclosan with polymyxin and compound 48/80, and about 50% inhibition in the case of EDTA. The results of other experiments aimed at deciding the relative importance of multidrug efflux and outer envelope permeabilisation were not conclusive.

Nevertheless, comparison of this study, which concluded that outer envelope permeability is the determinant of triclosan resistance in *Ps aeruginosa* PAO1, with that of Chuanchuen et al. (2003), which concluded that multidrug efflux pumps are the basis of triclosan resistance, indicates at least three mechanisms of resistance to triclosan in *Ps aeruginosa*.

Champlin et al. (2005) also found that *Pseudomonas multocida* is sensitive to triclosan (MIC 0.13 µg/mL), illustrating the difficulty of drawing general conclusions about triclosan resistance in pseudomonads.

Escalada et al. (2005) found that triclosan inhibited fatty acid synthesis in wild type sensitive *Escherichia coli* (MIC 0.1 µg/mL), in a mutant triclosan resistant *E coli* (MIC >1000 µg/mL) and in intrinsically resistant *Ps aeruginosa* (which is assumed to be MIC >1000 µg/mL as quantitative information on resistance is not provided, nor is the genotype specified). However, complete inhibition of fatty acid synthesis (and bacteriostasis) occurred at 1 and 40 µg/mL triclosan for the wild type *E coli* and the two triclosan resistant types, respectively. No comment is made by the authors concerning the wide divergence seen between the measured MICs in the two triclosan resistant types and, the much lower concentrations observed for complete inhibition of fatty acid synthesis and associated bacteriostasis.

Walsh et al. (2003) tested five biocides against four triclosan resistant variants of *E coli* previously selected in the laboratory (MICs greater than 250 µg/mL compared with 0.1 µg/mL for common parent). These triclosan resistant variants were only marginally more resistant (one dilution doubling) to the biocides eugenol and C10-16 alkyldimethyl N-oxides, while resistance was unchanged towards the other three biocides (thymol, didecyldimethylammonium chloride and trichlorocarbanalide) or was lower towards the didecyldimethylammonium chloride in two of the triclosan resistant mutants.

Braoudaki & Hilton (2004a) examined the effect of laboratory selection of triclosan resistance in *E. coli* strains K12 (a standard genetic strain), and O55 and O157 (clinical serotypes, with strain O157 known to carry additional genetic material compared to strain K12, and with evidence of spontaneous mutation rates much greater than strain K12¹⁶). Triclosan resistant mutants selected after several (strains K12 and O55) or a single (strain O157) passage through triclosan showed increases of MIC from 1 µg/mL or less to 1024 µg/mL or greater. Triclosan resistant strain K12 showed cross-resistance to chloramphenicol, while strain O55 showed cross-resistance to trimethoprim. By comparison, strain O157 showed cross-resistance to chloramphenicol, trimethoprim, tetracycline, amoxicillin, benzalkonium chloride and chlorhexidine. This suggests a multiresistance efflux pump over-expressed in strain O157 as a result of triclosan exposure. Possible mechanisms for the single cross resistances in the other two strains were not proposed. The results suggest that there may be considerable variation in clonal response in clinical populations exposed to triclosan.

Braoudaki & Hilton (2004b) extended this study to compare *E. coli* O157 with three serotypes of *Salmonella enterica* (Enteritidis, Typhimurium and Virchow). The multiple cross-resistance to antibiotics and biocides in laboratory selected triclosan resistant strain O157 was confirmed. Resistant *S enterica* serotypes were selected on benzalkonium chloride, chlorhexidine or erythromycin, then tested for

¹⁶ LeClerc et al. (1996). High mutation frequencies among *Escherichia coli* 157:H7. *Science*, 274, p1208 – 1211.

cross-resistance to a panel of antibiotics and biocides. No cross-resistance was seen when serovars Enteridis and Typhimurium were selected on benzalkonium chloride. Cross-resistance was seen when serovars Enteridis and Typhimurium were selected on erythromycin: to chloramphenicol for Enteridis and to chlorhexidine for Typhimurium. Serovar Virchow showed cross-resistance to a range of antibiotics and biocides when selected on benzalkonium chloride, chlorhexidine or erythromycin. However, this study is incomplete in a number of respects, for example, the failure to select resistant variants on triclosan and compare them with strain O157, which means that this study has little relevance in regard to triclosan usage.

Braoudaki & Hilton (2005) then sought to identify the mechanisms of resistance in the same *S enterica* serovars adapted to growth in the presence of erythromycin, benzalkonium chloride, and triclosan, by measuring characteristics of the outer membrane of the cells (lipopolysaccharide, cell surface charge, and hydrophobicity), together with an inner membrane function (efflux pump activity). On the basis of restored sensitivity to the antimicrobial agents in the presence of an inhibitor and an uncoupler of membrane transport systems (thus 'switching off' the efflux pump), the authors concluded that more than one type of efflux system was functioning in each resistance isolate, and that this, plus increased hydrophobicity of the cell surface, contributed to resistance of the three *S enterica* serovars examined.

Randall et al. (2004) also examined serovars of *S enterica*, and isogenic antibiotic multiresistant variants of these. Prior exposure to triclosan led to higher rates of mutation to ampicillin and cyclohexane (a biocide) resistance. Prior exposure to a crude phenolic farm disinfectant led to increased mutation rate to the antibiotics ampicillin, ciproflaxacin, and tetracycline, as well as cyclohexane. Overall, molecular analyses of genetic changes offered little insight into mechanisms of resistance.

McBain et al. (2004) exposed ten representative species of oral bacteria to escalating sub-lethal concentrations of triclosan, to select triclosan resistant variants. They included *E.coli* strain K12 as a control showing selectable triclosan resistance as a well-characterised trait. The triclosan resistant variant of the control *E. coli* K12 yielded a 400-fold increase in resistance to triclosan, without change in resistance to chlorhexidine, minocycline, or tetracycline. Minor increases (approximately two-fold) were seen in resistance to triclosan in *Prevotella nigrescens* and in two species of viridans streptococci. Mean changes in resistance (MICs and minimal bacterial concentrations [MBCs]) of the bacteria to chlorhexidine, minocycline, or tetracycline did not exceed two-fold (i.e. one dilution step), except for a transient five-fold increase in the MBC for *Streptococcus sanguis*. Before exposure to triclosan the oral bacteria were not highly sensitive to triclosan, with the exception of *Neisseria subflava* (MIC and MBC 0.1 µg/mL, similar to *E. coli*); seven of the species lay in the range 3-8 µg/mL MIC and MBC, and two species had MICs and MBCs of 16-21 µg/mL.

In a further laboratory-based study on triclosan resistance, Sanchez et al. (2005) investigated the multidrug resistance pump SmeDEF in the opportunistic environmental bacterial pathogen *Stenotrophomonas maltophilia*. SmeDEF is implicated in both intrinsic and acquired antibiotic resistance in this organism. The study sought to determine whether triclosan might select mutants that overproduce SmeDEF. Five out of 12 triclosan resistant mutants did overproduce SmeDEF,

making them less susceptible to three (tetracycline, chloramphenicol and ciprofloxacin) of a panel of four antibiotics tested. In the case of tobramycin, SmeDEF overproducing variants were usually more sensitive to the antibiotic (one exception in the six variants tested). The authors speculate that multidrug pump over-producers may not be as physiologically fit as their sensitive cohorts.

Analyses of bacteria from clinical or natural settings

Because studies in this category are relevant to the practical use of triclosan, they are presented in greater detail than the laboratory studies (above).

Schmid and Kaplan (2004) examined nearly 200 independent, non-consecutive clinical isolates of *S aureus* and *S epidermidis* collected during 2001 and 2002 throughout the US to determine whether triclosan resistance might be rising among MRSA as a consequence of the use of triclosan in hospitals to control MRSA outbreaks. Laboratory strains (not resistance selected) of staphylococci are normally very sensitive to triclosan (MIC <0.2 µg/mL). Examination of 50 isolates of MRSA and 50 of multi (methicillin) sensitive *S aureus* (MSSA) showed that the distribution of triclosan resistance across these was nearly identical, with a small tail of more resistant types (MIC 2-4 µg/mL) slightly skewing the MRSA upwards, such that the 50th percentile of MICs (MIC50) was the same in both groups (0.12 µg/mL) with the MIC90 (90th percentile) unchanged at 0.12 µg/mL for MSSA isolates, but skewed to 0.25 µg/mL for MRSA. Though no statistical tests of the differences were made, it is doubtful that the MRSA population is significantly different from the MSSA. Since MRSA have high level resistance to varying numbers and types of antibiotics and biocides, this result suggests that the selection factors leading to multiple antibiotic resistance in *S aureus* (i.e. in the evolution of MRSA from MSSA) are not selecting triclosan resistance, nor it seems is triclosan (assumed to be in the clinical environments from which these MRSA are isolated) selecting for significant resistance within the MRSA group.

Among the *S epidermidis* subsets: multi (methicillin) resistant *S epidermidis* [MRSE] 47 isolates and multi (methicillin) sensitive *S epidermidis* [MSSE] 49 isolates, the MIC50 for triclosan was again 0.12 µg/mL, but the distribution of resistance was clearly bimodal, with a small sub-group (larger in the MRSE) with MICs at 4-8 µg/mL, and the MIC90 figures rising to 8 µg/mL for MRSE and 1 µg/mL for MSSE.

The significance of this study lies in the low level of resistance to triclosan among the MRSA, a group that should have had abundant opportunity to respond to environmental biocides such as triclosan, and secondly, the slightly more resistant tail in both MRSE and MSSE. No data are presented to indicate the mechanism(s) by which resistance in these outlier groups is mediated, and whether it is likely to be amplifiable and transferable.

Sullivan et al. (2003) studied the effects on the major oral microbiota of toothpaste containing triclosan among nine subjects over 14 days. Teeth were brushed with toothpaste containing 0.3% triclosan twice daily. Saliva samples for culturing the oral microflora were collected on days 0 and 14. Bacterial sampling at these times revealed no change to populations of aerobic bacteria (and the yeast *Candida*) or anaerobic bacteria, apart from a small (5.5%) but statistically significant decline in the number of lactobacilli. Notable was the small numbers of bacterial cells in

saliva for each of the 14 microbial groups or species enumerated (ranging from 2.4 – 7.6 cfu/mL).

Triclosan concentrations in saliva immediately after tooth brushing were 3.6 µg/mL, declining with a half-life of <2 min to 0.2 µg/mL at the final sampling time 15 min later. This study had as its focus the viridans streptococci, since this group has been implicated as the infectious agents in endocarditis resulting from transient bacteraemias from invasive dental procedures including even tooth brushing. Resistance to four antibiotics (benzylpenicillin, gentamycin, erythromycin, tetracycline) was measured. There were no statistically significant differences in susceptibility to the panel of antibiotics between days 0 and 14. All three subtypes of viridans streptococci tested were intrinsically resistant to triclosan, with MIC50's of 32-128 µg/mL.

Though a non-triclosan toothpaste control is not essential in this sort of longitudinal study, such a control group would have been useful in terms of the quantitation of microbiota cell numbers in saliva, and to have revealed to what extent biocide and antibiotic resistant markers are present in the oral microbiota in the absence of triclosan selection pressure.

The significance of this study by Sullivan and colleagues is that it represents one of the few in which triclosan concentration is measured in a natural environment, and representative bacterial groups are enumerated to permit quantitative effects of triclosan to be assessed or predicted. It also shows that the concentration of triclosan in the aqueous phase of a normal biological environment, released from a highly concentrated source, may decline very rapidly. The possible causes of such decline are not considered, but are of considerable interest. Furthermore, the measured environmental concentration of triclosan immediately after toothbrushing (3.6 µg/mL) is lower than the resistance levels determined in the majority of bacteria by McBain et al. (2004), albeit at the laboratory level.

Lambert (2004) considered whether antibiotic resistance is prerequisite for the emergence of bacteria resistant to biocides. Resistance data (eight biocides, including triclosan, and 14 antibiotics) were collected for a set of 87 isolates of MRSA, 169 MSSA, and 111 *Pseudomonas aeruginosa*, all taken either in 1989 or in 2000. The results were subjected to statistical analysis to compare isolates taken a decade apart within the three groups, and between the two subsets of staphylococci.

Among the staphylococci, both MRSA and MSSA, small but statistically significant increases were seen over the decade in resistance to six of the eight biocides tested (the exceptions were two bleach formulations to which there was high resistance throughout). Thus, antibiotic multiresistance is not correlated with biocide resistance. Of the ten antibiotics tested against the staphylococci, five showed no significant change in either group (MRSA or MSSA), while of the other antibiotics, three (ciprofloxacin, erythromycin, and gentamycin) showed small but statistically significant increases in resistance in the MSSA, and three (clindamycin, gentamycin, and vancomycin) showed statistically significant decreases in the MRSA. Thus, although biocide resistance increased slightly among the MRSA over the decade represented by the isolates, antibiotic resistance did not, and even decreased in some cases. Among the MSSA the small increases in biocide resistance were accompanied by similar small increases in resistance to some antibiotics but not to all.

Among the isolates of *Ps aeruginosa*, there was an increase in resistance (MIC_{mean}) to one biocide (benzethonium chloride) and to one antibiotic (ciprofloxacin). However, there was a significant decrease in resistance to five biocides, and to three antibiotics. There was no significant change in susceptibility to two other biocides (including triclosan) and to three other antibiotics. Thus, overall, it was observed that over the decade selection for resistance to both the biocides and the antibiotics tested decreased among the isolates of *Ps aeruginosa*.

Lambert therefore concluded that increased biocide resistance is not correlated with increased antibiotic resistance in clinical isolates of *S aureus* and *Ps aeruginosa*, and hence continued use of biocides in hospital hygiene is justified.

In an extensive study of 224 Upper Manhattan households, Aiello et al. (2005) tested the effect of biocides (triclosan, a quarternary ammonium compound, and bleach) present in domestic cleaning products (soaps and detergents) on antimicrobial resistance over a period of one year. Around 40% of persons using plain soaps and detergents (no biocide) carried one or more bacteria with resistance to a biocide or antibiotic on their hands at the beginning of the year, while 43% of those in the biocide-user group carried such bacteria. At year's end, the carriage rate was 41% and 50% in non-user and biocide-user groups respectively. The rise in both groups was not statistically significant.

In a parallel analysis (Aiello et al., 2004) a more detailed characterisation of resistance to triclosan and antibiotics was undertaken in 628 isolates of staphylococci and gram-negative bacteria taken from the study participants. Of six gram-negative bacterial species and four staphylococcal species examined, only four showed significant differences in the proportion of isolates with altered triclosan or antibiotic resistance at the end of the study: *Acinetobacter iwoffii* (higher triclosan resistance); *Klebsiella pneumoniae* (lower triclosan resistance); *S aureus* (lower triclosan resistance) and *Enterobacter cloacae* (lower antibiotic resistance). Thus, over the ten bacterial groups examined there was generally either no significant change in triclosan or antibiotic resistance, or resistance declined, with the single exception mentioned of triclosan resistance in *Acinetobacter iwoffii*.

Isolates of the four staphylococcal species studied for triclosan resistance again showed the bimodal distribution of susceptibility described above for *S aureus* and *S epidermidis* by Schmid and Kaplan (2004), with one group clustered at a MIC of 0.06 µg/mL (sensitive) and the second at 2 µg/mL (resistant).

Overall, while certain trends or tendencies in the data of Aiello et al. (2004, 2005) were perceived, statistical analysis indicated that the use of biocides in domestic cleaning products did not bring about an increase in bacterial triclosan resistance, nor resistance to antibiotics over the year in the homes examined. One tendency perceived was that the general level of triclosan resistance was trending up, regardless of whether triclosan was used in the home.

Similar conclusions to those of Aiello et al. (2004, 2005) were reached in two earlier and differently configured studies by McBain et al. (2003) and Cole et al. (2003).

McBain et al. (2003) exposed sink-drain microbial microcosms in a single UK house to pulsed (10 min) or long-term (6 months) commercial dishwashing detergent containing triclosan. Biofilm microcosms in the drains harboured very large stable populations of bacteria (approximately 10¹⁰ cells/g biofilm)

representing at least 27 species. Triclosan exposure decreased the population diversity but not its size. Many species were already triclosan resistant, though whether this was because of prior exposure to triclosan, or due to cross-resistance to other biocides used, was not examined. Clones of some of these expanded in size in response to triclosan. Triclosan did not affect bacterial community profiles of susceptibility to the biocides or antibiotics tested. Evidence was seen of triclosan biodegradation by bacteria isolated from sink drain biofilms.

Cole et al. (2003) investigated cross resistance between antibiotics and biocides in a cross section of significant gram negative and gram positive target bacteria isolated from kitchens, bathrooms, soil, and persons, in 30 households (USA and UK) which used commercial products containing biocides and 30 households which did not. While antibiotic resistance was common (e.g. in 74% and 73% of coagulase-negative staphylococci (i.e. not *S aureus*) from non-user and biocide-user homes respectively, and 76% and 78% respectively of enterobacteria), consistent antibiotic and biocide cross resistance to the panel of antimicrobials tested against bacteria from user and non-user homes was not seen. However, increased prevalence of potential pathogens was detected in non-user homes.

Physiological fitness of bacteria resistant to biocides and antibiotics

There are two immediate possibilities for the failure to detect an unequivocal correlation or connection between biocide usage and antibiotic resistance in environmental studies, and vice versa, when such a phenomenon is readily demonstrable in the laboratory. First, resistant mutants may arise more readily under laboratory conditions, implying higher mutation rates. Second, resistant variants arise at comparable rates in the natural environment but fail to thrive and are out-competed under these conditions. The latter implies differences in 'physiological fitness' between parent and mutant cells.

Sanchez et al. (2002) and Alonso et al. (2004) have attempted to investigate the issue of fitness, focusing specifically on multi-drug efflux pumps (which underlie multiple antibiotic and biocide resistance, including resistance to triclosan) in *Ps aeruginosa* and *St maltophilia*. As noted earlier, mutants that overproduce or up-regulate these pumps may become multiply cross resistant to antibiotics and biocides. These pumps are also believed to remove metabolites from inside cells, or take up inhibitory substances (other than added xenochemicals) from the external environment. Consequently, overproduction or up regulation of such efflux pumps might result in over-secreting/uptaking cells, which might not compete well with non-mutant parental cells not exhibiting such deviation from normal secretion/uptake patterns.

In laboratory experiments by Sanchez et al. (2002) it was observed that two *Ps aeruginosa* multi-drug resistant mutants showed decreased survival in water suspensions of cells or on dry surfaces (i.e. conditions of nutrient limitation) compared with their common parent. Additionally, they also produced lesser amounts of phenazines and proteases (indicating impaired secretion functions), and expressed lower virulence in a nematode (*Caenorhabditis elegans*) model system.

Using a more direct approach, Alonso et al. (2004) competed a parental strain of *St maltophilia* against its multi-drug resistant mutant that overproduces the SmeDEF efflux pump. In broth cultures (without antimicrobials) cycled 12 times through logarithmic growth (nutrient abundance) and stationary phase (nutrient paucity),

the wild type parent progressively outgrew the mutant such that there was fewer than one mutant cell per 100 000 parent cells (from initial equal numbers of each) at the end (day 12) of the experiment. Metabolic profiling indicated substantial differences between parent and mutant in their capacities to utilise specific nutrients to support growth. Additionally, in a slime mould (*Dictyostelium discoideum*) model assay system, the mutant was less virulent than the wild type parent.

19. Effects on Human Health

19.1 Skin irritation

In a human patch test (Shanghai Municipal Prevention Medical Institution, 2002b) 25 male and 25 female healthy volunteers had five patch chambers attached to their back for 24 h containing 2%, 4%, 10% or 20% triclosan in 0.5% sodium lauryl sulphonate (SLS) solution, or 0.5% SLS solution alone. Sites of application were examined and skin reaction evaluated 30 minutes and 24 and 48 h after patch removal. Thirty min after patch removal skin reactions were seen in 2/50 (both grade 1), 8/50 (5 grade 1, 2 grade 2 and 1 grade 3) and 12/50 (6 grade 1, 4 grade 2 and 2 grade 3) volunteers at 4%, 10% and 20% triclosan respectively. The incidence and severity of the skin reaction decreased with subsequent readings. At 24 h irritation was seen in 1/50, 5/50 and 10/50 volunteers at 4%, 10% and 20% triclosan respectively, and by 48 h irritation was only seen in 3/50 and 5/50 volunteers at 10% and 20% triclosan respectively.

In a further human patch test, 6 female and 4 male healthy volunteers had a patch chamber attached to their forearm for 24 h containing 0.3% triclosan (Barkvoll and Rolla, 1994). No skin reactions were observed when the test sites were viewed 10 minutes and 4 h post-treatment.

For the induction phase of a modified human maximisation test (Lachapelle and Tennstedt, 1979), 20 volunteers received a 24 h topical application of 5% aqueous SLS (occlusive dressing) to the forearm then a 24 h topical application of 20% triclosan (occlusive dressing) to the same site on days 1, 3, 5, 7 and 11. It is reported that skin reactions were seen in 17/20 volunteers during the later stages of induction, with ulceration seen in a few cases (no further details reported).

In a poorly reported repeated patch study (Colgate Palmolive Co., 1972), no skin irritation was seen in 106 females following ten 48 h applications of triclosan (concentration not reported) to the back, twice a week for 5 wk.

In two poorly reported experiments (Lyman and Furia, 1969), skin reactions were seen in 2 out of 50 volunteers following application of 0.5% triclosan in 1% soap (no further details available), while no conclusions could be drawn from a study investigating the irritant potential of triclosan due to the probable masking effect of the vehicle used (up to 2.5% ivory soap).

Studies are available that have investigated (directly or indirectly) the skin irritation potential of consumer products containing triclosan (Terrizzi et al., 1999; Skaare et al., 1997a; Bendig, 1990). However, the co-exposure to other chemical ingredients in the consumer product (whose concentration are not reported) means that these studies provide no reliable data to determine the skin irritation potential of triclosan and, hence, are not discussed further. Similarly, summaries of studies that investigated the influence of mouth rinses or toothpaste containing triclosan on oral mucosa are not presented here (Skaare et al., 1996; 1997b).

Studies are also available that investigated the potential for triclosan-induced phototoxic skin reactions.

In a briefly reported study (Urbach, 1973) no evidence of phototoxicity was reported in 5 volunteers following application of 0.1% triclosan to the back for 1 h then irradiation of the site with 1 of 4 light sources and readings taken 24 and 48 h post exposure. Similarly, no phototoxic reaction was seen in 10 healthy male volunteers following application of 2.5% triclosan in petrolatum for 1 h, to normal and Scotch Tape stripped skin, then irradiation of the site with UV light and readings taken 4-6 and 24 h later (Kligman, 1969).

In two poorly reported experiments (Lyman and Furia, 1969), no phototoxic skin reactions were seen in 10 volunteers following application of 10% triclosan in petroleum jelly to the shoulder blade for 24 h then irradiation of the site with UV light, or in a test with 25 volunteers (no further details provided). In a further poorly reported study (Colgate Palmolive Co., 1972), 104 females received a soap containing triclosan (concentration not reported) to the back and the site then irradiated with UV light, while another site received test material only. Skin reactions were recorded 24 and 48 h later. No phototoxic skin reactions were observed.

19.2 Sensitisation

19.2.1 Skin sensitisation

Numerous studies are available investigating the skin sensitisation potential of triclosan, many of which are briefly reported.

Volunteer studies

A modified human maximisation test was conducted in 20 adult volunteers (Lachapelle and Tennstedt, 1979). The induction phase consisted of a 24 h topical application of 5% aqueous SLS (occlusive dressing) to the forearm then a 24 h topical application of 20% triclosan in petrolatum (occlusive dressing) to the same site on days 1, 3, 5, 7 and 11. On day 25 challenge patches were applied to the back containing 5%, 2%, 1% and 0% triclosan in petrolatum and readings taken 48 and 96 h later. Skin reactions were seen in 17/20 volunteers during the later stages of induction, with ulceration seen in a few cases (no further details reported). No skin reactions were seen at challenge.

In a further study (Marzuli and Maibach, 1973; 1974), 61, 58 and 25 adult volunteers over a three and a half wk induction phase received (usually) 10 applications of 5%, 20% or 20% triclosan in petrolatum to the same site on the upper arm (occlusive dressing) for 48 to 72 h, respectively, and were then challenged 2-weeks later with 5%, 1% and 1% triclosan in petrolatum for 72 h respectively. Challenge concentrations were stated to be non-irritant. No skin reactions were seen at challenge in any group. However, the limited methodology details presented, such as justification for induction concentrations and non-reporting of findings at induction, limits the significance that can be attached to this negative finding.

No evidence of skin sensitisation has been observed in a number of poorly reported studies: in 10 volunteers who received 25% triclosan in vaseline in a study reported to be conducted to the maximisation procedure (Lyman and Furia, 1969); in 106 females who received 10 applications of a soap containing triclosan (concentration not reported), twice a wk for 5 wk, and were challenged 14 days later (Colgate

Palmolive Co., 1972); and in 100 volunteers in a repeat patch test and 50 volunteers in a prophetic patch test (DeSalva et al., 1989). However, the minimal methodology details available limits the significance that can be attached to these findings. Similarly, in a briefly reported study (Oshima et al., 1991), no positive patch tests were seen in 31 males in a dental school with no history of allergy who were tested with 40 dental components including triclosan.

Studies in patients

A total of 627 patients with suspected contact dermatitis were patch tested with 13 preservatives in Holland over a 4-month period and no positive reactions were seen with 2% triclosan (De Groot et al., 1986). A similar investigation was undertaken in Switzerland where 2295 patients with suspected contact dermatitis were patch tested with 13 preservatives over a 12-month period (Perrenoud et al., 1994). Positive reactions to 2% triclosan were reported in 0.8% of patients.

Data are available from 24 dermatology clinics in Germany that over a 5 year period conducted patch tests with preservatives, antimicrobials and industrial biocides on patients with suspected contact dermatitis (Schnuch et al., 1998). Of 11406 patients patch tested with 2% triclosan positive reactions were seen in 0.3% patients and responses deemed questionable or irritative in nature in 0.5% patients. While in a Scandinavian multi-centre study (Wennersten et al., 1984), a single case (0.1%) of contact dermatitis was seen with 2% triclosan in 745 patients with suspected photodermatitis.

Studies are also available in patients with cosmetic related skin reactions. In a multi-centre study in America from 1977 to 1983 a total of 713 patients with cosmetic related contact dermatitis were patch tested with a number of substances (Adams and Maibach, 1985). Positive reactions to triclosan (concentration not reported) were observed in a single patient (0.1%). Of 179 patients with suspected cosmetic allergy and patch tested with a series of 16 fragrances and 9 preservatives only 2 patients (1.1%) gave a positive reaction to 2% triclosan (De Groot et al., 1985). A poorly reported study is available investigating cosmetic intolerance in 5202 patients (Broeckx et al., 1987). In this study patients were patch tested with a number of test series. Positive reactions were seen in 7 patients (0.1%) to triclosan (concentration not reported), of which 1 patient had a 'pure allergy' (without irritation) to cosmetics only, as did a further 155 patients who did not give a positive reaction to triclosan.

In a poorly reported American study of eczema patients (Mitchell et al., 1982), positive reactions to 2% triclosan were seen in 1% of 699 patients tested between 1978 – 1979 and 2% of 585 patients tested between 1979 – 1980. Similarly in a Finnish study (Hannuksela et al., 1976), a positive reaction to 1% triclosan was only seen in 1 of 1796 eczema patients (0.06%).

In a study that investigated cutting fluid dermatitis (Grattan et al., 1989), 174 patients were patch tested with a standard series and a cutting fluid series that contained triclosan. Results were provided in minimal detail, and only for the commonest allergens. No results were presented for triclosan. Additionally, in a study of occupational skin disease in the metal industry no positive patch tests were obtained with triclosan in 252 metal workers (Goh and Yuen, 1994).

No positive reactions to 2% triclosan were seen in 9 patients with chronic actinic dermatitis patch tested with a standard series (Lim et al., 1998).

Case reports

Between 1982 and 1998, 3 out of 102 patients (2.9%) at a dermatology clinic gave a positive response to 2% triclosan (Steinkjer and Braathen, 1998). All three had dermatitis of the hands and/or face, and though two patients had used a steroid-antibiotic cream that contained 3% triclosan a positive reaction to the cream was only seen in one patient who was atopic. The third patient had not used the cream and no triclosan source could be identified. In another dermatology clinic, 2 of 291 patients (0.7%) gave a positive response to 2% triclosan over a 2-year period (Roed-Petersen et al., 1975). Of these two patients, a man with dermatitis of both feet gave a positive patch test to a foot-powder he had used, and when patch tested with the foot-powder ingredients only gave a positive reaction to triclosan. The other patient, an atopic female, who had dermatitis of the armpit, had used a deodorant stick that contained triclosan. In a further dermatology clinic, 2 of 1100 patients (0.2%) gave a positive response to 2% triclosan (Wahlberg, 1976). Both patients were atopic and had come into contact with a soap and/or deodorant that contained triclosan. In the same study no reactions were seen in 432 and 470 patients patch tested with 0.5% and 1.0% triclosan respectively.

A woman with no history of eczema developed acute dermatitis of the axillae, groin, neck and face following use of a deodorant spray containing triclosan (Hindson, 1975). Following testing to the standard patch test series a positive reaction was seen to 2% triclosan in addition to the deodorant spray. A positive patch test to 2% triclosan was also seen in a nurse who had dermatitis of the hands and used a hand wash containing triclosan both at work and home (Wong and Beck, 2001). Furthermore, one woman developed eczematous lesions of the hands and feet, another vesicular lesions of the right arm and a man red scaly patches on the face, following use of an antimicrobial-antimycotic cream containing a high concentration of triclosan (3%) (Veronesi et al., 1986). They were all tested with a standard antimicrobial series. A positive patch test was seen with 2% triclosan in all three cases.

19.2.2 Photo-sensitisation

Following a negative skin sensitisation test in 106 females a photo-sensitisation test was conducted in 104 of these females two weeks later (Colgate Palmolive Co., 1972). In this poorly reported study, a soap containing triclosan (concentration not reported) was applied to the back and the site irradiated with UV light, with another site receiving test material only. Females were challenged 1 week later by the same procedure, and skin reactions recorded 24 and 48 h post challenge. A minimal skin reaction was seen at the irradiated site in one individual, which was no longer apparent at the 48-h reading. Since the subject stated she had experienced itching at the site, it was proposed that the skin reaction was provoked by scratching.

In a poorly reported study (Lyman and Furia, 1969), no photoallergic reactions were reported in 25 volunteers or 45 'subjects' tested with 0.5% triclosan in 1% soap. Similarly, in three briefly reported studies, no positive photoallergic reactions were seen in 102 patients, photo-patch tested with 2% triclosan (Steinkjer and Braathen, 1998), four groups of healthy volunteers, 42 – 60 per group, photo-patch tested with up to 20% and 5% triclosan at induction and challenge respectively (Marzulli and Maibach, 1973), and 25 healthy male volunteers tested with 10% triclosan in petrolatum at induction and challenge (Kligman, 1969).

No positive reactions to 2% triclosan were seen in 9 patients with chronic actinic dermatitis tested with a photo-patch series (Lim et al., 1998).

In a 3 year study of 108 patients with a suspected photodermatitis tested with a photo-patch series, a single positive reaction (0.9% of patients) was seen to 2% triclosan (Trevisis et al., 1994). In a Scandinavian study of 745 patients with suspected photodermatitis tested with a photo-patch series, positive reactions were seen in two patients (0.3%) to 2% triclosan (Wennersten et al., 1984).

In a study investigating cross-photosensitisation (Durbize et al., 2003), 18 patients with photocontact dermatitis to ketoprofen were patch and photopatch tested with a photodermatology standard series that contained triclosan. Two positive photopatch tests (11.1%) and 1 positive patch test (5.6%) were seen with triclosan. The authors suggest that photosensitivity to ketoprofen can lead to hyper-photosusceptibility to other different non-benzophenone-related compounds in some individuals.

19.3 Repeat dose toxicity

In a combined human tolerance and pharmacokinetics study (Lucker et al., 1990), 20 healthy male volunteers ingested a gelatine capsule containing 0 mg triclosan on days 1 – 2, 1 mg on day 3, a dose of 5, 9, 12, 15, 18, 21, 24, 27 and 30 mg on days 7 – 15 respectively (the tolerance phase of the study) and 15 mg on days 16 – 52. Volunteers were asked to avoid cosmetics containing triclosan during the trial, and consumption of alcohol and xanthine-containing beverages (e.g. coffee, tea, cola) were forbidden. Pre- and follow up checks comprised of physical examination, vital signs (blood pressure and heart rate), ECG, lung function, urinalysis, clinical chemistry and haematology analysis, neurology examination, and pupillometry. Fourteen of the 20 volunteers completed the study. Although slight changes (often with the placebo dose) were seen in some parameters, particularly clinical chemistry parameters, the authors reported that such changes were not unusual in their experience (i.e. chance findings) and were not biologically significant and, concluded that triclosan was well tolerated in this study. However, due to the variation in the dose administered during the trial the study is of limited value in identifying a robust NOAEL and, consequently, the results are not presented here in detail.

A study primarily investigating free and conjugated triclosan concentrations in volunteers receiving soap, talc, antiperspirant and toothpaste with or without triclosan for 56 days, also measured clinical chemistry and haematology parameters (BIBRA International, 1988). Although no treatment related effects were observed on clinical chemistry or haematology parameters the total dose of triclosan administered cannot be determined. Consequently, there is insufficient information available in this study to determine a reliable NOAEL. Furthermore, the co-exposure to other chemical ingredients in the consumer product, whose concentration are not reported and biological significance cannot be determined, this study provides no reliable data to profile the systemic toxicity of triclosan.

Additional studies are available that investigated urinalysis, clinical chemistry and/or haematological parameters following use of personal care products containing triclosan (Colgate Palmolive Co., 1989; Barnes, 1991; Safford, 1991; Fishman, 1993; Lin, 1994; BIBRA, 1997). However, while no treatment related

effects were seen in these parameters, they are of limited value for the reasons stated above and, hence, are not discussed further.

20. Regulatory Classification Based on Hazard

20.1 Occupational

This section discusses the classification of the health effects of triclosan according to the NOHSC *Approved Criteria for Classifying Hazardous Substances* (the Approved Criteria) (NOHSC, 2004) or, in the case of physicochemical hazards, the *Australian Code for the Transport of Dangerous Goods by Road and Rail* (ADG Code) (FORS, 1998). The Approved Criteria are cited in the NOHSC *National Model Regulations for the Control of Workplace Hazardous Substances* (NOHSC, 1994c) and provide the mandatory criteria for determining whether a workplace chemical is hazardous or not.

Where adequate human data were unavailable, the classification for health hazards has been based on experimental studies (animal and in vitro tests). In extrapolating results from experimental studies to humans, consideration was given to relevant issues such as quality of data, weight of evidence, metabolic and mode of action/mechanistic profiles, inter- and intra-species variability and relevance of exposure levels.

Classification of triclosan in accordance with the OECD *Globally Harmonized System of Classification and Labelling of Chemicals* can be found in Appendix F.

Triclosan was listed in the Office of the Australian Safety & Compensation Council's (ASCC) *List of Designated Hazardous Substances*, contained in the Hazardous Substances Information System (HSIS), with the risk phrase, Toxic by inhalation (R23) (prior to July 2008) (<http://www.ascc.gov.au/applications/hsis/>).

20.1.1 Physicochemical hazards

Triclosan is a fine white crystalline powder with a melting point of 54°C – 57.3°C. Triclosan did not undergo autoignition at temperatures up to and including 350°C nor is there any evidence in the literature of any explosive properties or significant inflammable properties.

Under extreme conditions such as high alkalinity at high temperature and pressure, triclosan can be converted to chlorinated dibenzo-*p*-dioxines (Fiege et al., 2000).

Classification: Triclosan does not meet the ADG Code (FORS 1998) for classification as a dangerous good on the basis of physicochemical hazards.

20.1.2 Health hazards

Acute toxicity

Only animal data are available. In a well-reported oral study conducted in 1994, 1/5 female and 0/5 male Sprague Dawley rats administered 5000 mg/kg died. Thus, the LD50 is greater than 5000 mg/kg. Although rat oral LD50 values of 1700, 4000 and 4530 mg/kg were reported for both sexes combined along with values of 3700 and 4400 mg/kg in females and males respectively, these are from briefly reported

studies conducted in 1949 and 1969 and not considered as reliable. Similarly, a very briefly reported study from 1978 reports an oral LD50 value of 4000 mg/kg in female Wistar rats. The study conducted in 1969 also reported an oral LD50 value of 4530 mg/kg in mice (both sexes combined) while no deaths were seen in dogs administered up to and including 5000 mg/kg.

In the only dermal study available, which is poorly reported, the LD50 value in New Zealand rabbits was 9300 mg/kg or greater depending on the vehicle used.

In a 4 h aerosol inhalation study, the LC50 value in Wistar rats was greater than 0.15 mg/L, which was the highest technically achievable rat respirable concentration. Due to the very low dose tested, it is not possible to derive a definitive LC50 value for classification of triclosan using this study. However, in a 21-day repeat dose inhalation (aerosol) study, 44% of males and 78% of females died after a single 2 h nose only exposure to 1300 mg triclosan/m³ air in 10% ethanol (i.e. prior to second exposure on day 2), indicating that LC50 for triclosan in both sexes combined is <1300 mg/m³ (equivalent to <1.3 mg/L). There were no deaths or histopathology findings in the control group that received 10% ethanol only. Therefore, the presence of ethanol is not considered to have contributed to the deaths or resulted in an additive or synergistic effect (Approved Criteria: NOHSC, 2004).

OECD Test Guidelines for acute inhalation toxicity testing state that the period of exposure should be 4 h. Similarly, LC50 ranges in the Approved Criteria for classification as an acute inhalation toxicant are for 4 h exposure periods. Applying Haber's rule (i.e. concentration x time = constant), it is estimated that 44% of males, 78% of females and 61% of both sexes combined would die following a single 4 h exposure to 0.65 mg/L. Thus, the 4-h concentration causing 50% mortality in males would be >0.65 mg/L, while the 4 h concentration causing death in 50% of females (and 50% in both sexes combined) would be <0.65 mg/L.

The LC50 (aerosol) ranges for classification with 'Harmful by inhalation (R20)', Toxic by inhalation (R23) and 'Very toxic by inhalation (R26)' are >1 mg/L/4h and ≤5 mg/L/4h, >0.25 mg/L/4h and ≤1 mg/L/4h, and ≤0.25 mg/L/4h respectively. It is considered, that the values derived from applying Haber's rule suggests that the triclosan (aerosol) 4 h LC50 concentration is likely to be >0.65 mg/L and <1 mg/L in males and >0.25 mg/L and <0.65 mg/L in females (and both sexes combined). Thus, classification with 'Toxic by inhalation (R23)' and not 'Very toxic by inhalation (R26)' is considered appropriate.

Classification: Based on the available animal data triclosan does not meet the Approved Criteria (NOHSC, 2004) for classification as a hazardous substance for acute oral and dermal toxicity. Triclosan meets the Approved Criteria for classifying as 'Toxic by inhalation (R23)'.

Irritation and corrosive effects

A number of skin irritation studies are available in human volunteers, though most are poorly reported. In the most detailed study available, 50 volunteers received patches containing 2%, 4%, 10% and 20% triclosan in 0.5% sodium lauryl sulphate for 24 h. Twenty-four and 48 h after patch removal skin irritation was seen in 1 or more volunteers receiving 4%, 10% or 20% triclosan. Similarly, skin irritation has been seen in a number of animal studies in rabbits and guinea-pigs. Depending on the vehicle, irritation has been observed in animals receiving 0.5 ml of 4% triclosan

and greater for 4 h. In studies investigating phototoxicity no evidence of phototoxic skin reactions were seen in human volunteers and guinea-pigs following application of up to 10% and 1% triclosan respectively.

Although skin irritation has been seen in both human and animal studies, quantitative data on the intensity of the observed skin irritation is often absent. However, qualitatively, irritation has been observed with triclosan at very low concentrations (i.e. from 4%) in both humans and animals. Therefore, overall, the data indicate that triclosan possesses a significant skin irritation potential, and it is expected that significant inflammation of the skin would be observed with much higher concentrations.

Only animal data are available for eye irritation. In the most recent and well reported study conducted in 1980, the mean eye irritation scores seen over 72 h following instillation of 0.1 g triclosan into the rabbit eye warrant classification of triclosan as an eye irritant (Table 18.1). Mean score for corneal opacity after 24 h was 3, indicating serious eye damage, but the mean scores for cornea opacity after 48 and 72 h were 2.5 and 1.5, respectively. Mean score for chemosis was 2.17 after 24 h, for triclosan to be classified as an eye irritant. Ocular lesions were seen at the end of the observation period, however mean scores of 1 for cornea opacity, 0.33 for iris lesion, 0.5 for redness of the conjunctivae and 0.33 for chemosis on day 7 are too low to expect that triclosan may cause serious eye damage. The end of the observation period was however 7 days instead of 21 as recommended in OECD Test Guideline 405. Consequently, conflicting and extreme results have been seen in this study for classification. Furthermore, while eye irritation was reported in rabbits in the remaining studies they are relatively old, having been conducted in 1969, and are less well reported with methodology limitations: 10% triclosan and above resulted in 'eye irritation' at 24 h post instillation at the end of the observation period, and an unreported volume and concentration of triclosan resulted in an irritation index of 86.8/110 over 72 h.

Overall it is considered that the data indicate that triclosan does possess a significant eye irritation potential. In the most recent study slight ocular irritation was still present when the study was ended on day 7 instead of 21. However, classification as an eye irritant with risk phrase R36 – 'Irritating to eyes' and not R41 – 'Risk of serious damage to eyes' is considered appropriate.

In the only available 21-day repeat dose inhalation toxicity study, >50% rats received the highest dose (1300 mg triclosan/m³ air with 10% ethanol on day 1 and 301 mg triclosan/m³ air with 10% ethanol from day 2) showed acute purulent inflammation with focal ulceration of the mucous membrane in the nasal cavity and in the trachea. Similar effects were seen in some rats of the mid dose group (227 mg/m³ on day 1 and 115 mg/m³ from day 2). No histopathological changes were seen in the control group that received ethanol only. Therefore, the presence of ethanol is not considered to have contributed to an additive or synergistic effect (Approved Criteria: NOHSC, 2004). Considering these effects on the respiratory system, triclosan is considered to be a respiratory irritant.

Classification: Based on the human and/or animal data triclosan meets the Approved Criteria (NOHSC, 2004) for classification as irritating to the eyes (R36), respiratory system (R37) and skin (R38).

Sensitising effects

Numerous studies are available investigating the skin sensitisation potential of triclosan though many are briefly reported. In volunteers, no skin reactions were seen at challenge in a modified human maximisation test, a study conducted to the maximisation procedure, and human repeat insult patch tests. In studies in 2295, 11406, 745, 713, 179, 5202, 699 and 1796 patients with suspected contact dermatitis or eczema, positive reactions to 2% triclosan were seen in 0.8, 0.3, 0.1, 0.1, 1.1, 0.1, 1.0, and 0.06 % patients respectively. Additionally, no positive reactions were seen in 627 patients with suspected contact dermatitis, 174 patients with cutting fluid dermatitis, 252 patients from the metal industry with occupational skin disease and 9 patients with chronic actinic dermatitis. Therefore, while there is the potential for widespread consumer exposure to triclosan due to its use in a large number of personal care products, only a small number of case studies are available in humans who are not atopic and have demonstrated positive reactions to such products and triclosan a product ingredient. Thus, the human data indicate that at most triclosan possesses a very weak skin sensitisation potential.

Similarly in a guinea-pig modified Maximisation test, the skin reactions of an unspecified intensity seen in 4/20 test and 4/19 control animals at the first challenge and 3/20 test and 1/19 control animals at the second challenge do not indicate a significant skin sensitisation potential. Whereas results in guinea-pigs from 2 Buehler studies, a 'split adjuvant' test and a number of briefly reported studies, often non-standard, did not indicate a skin sensitisation potential.

Furthermore, in photo-patch studies in 108 and 745 patients with suspected photodermatitis positive reactions to triclosan were only seen in 0.9% and 0.3% patients respectively. In contrast, no positive reactions to triclosan were seen in a number of studies in volunteers or patients with group sizes of up to 104.

Classification: Based on the available human and animal data triclosan does not meet the Approved Criteria (NOHSC, 2004) for classification as a skin sensitiser.

Effects from repeated or prolonged exposure

Although human data are available, they provide no reliable information to identify a robust NOAEL or profile the systemic toxicity of triclosan. However, animal data are available for the oral, dermal and inhalation routes of exposure. A large number of oral studies are available with NOAELs identified in the rat, mouse, hamster, dog and baboon.

In oral studies, a NOAEL could not be identified in the mouse. A LOAEL of 25 mg/kg bw/day was identified from a 13-wk study based on dose-related trends in several haematology parameters, a significant increase in relative liver weight and a statistically significant depression in total cholesterol in both sexes. In the rat, a NOAEL of 40 and 56 mg/kg bw day was identified from a 2 year carcinogenicity study based on mild clinical changes and hepatocyte hypertrophy and hepatocytic 'inclusion' in males and mild clinical changes and a trend for reduced body weight gain in females respectively. While in the hamster, a NOAEL of 75 mg/kg bw/day was identified in both sexes in a 90 to 95 wk study based on nephrotoxicity, histopathological changes to the stomach and clinical changes at 250 mg/kg bw/day. However, while the collective data indicate that the mouse is the most sensitive species, there is evidence that (unlike the rat and hamster) it is sensitive to peroxisome proliferator type effects that are not considered a risk to human health.

In other species, no effects were seen in a 90-day rabbit study up to and including the top dose of 125 mg/kg bw/day, and a NOAEL of 100 mg/kg bw/day was identified in a baboon 1 year study based on clinical signs of toxicity. While in beagle dogs extreme conflicting results were seen at the top dose of 25 mg/kg bw/day in two studies of approximately 90 days duration, though the small group sizes (3 to 4 animals per sex per group) employed in both studies prevent identification of a robust NOAEL in this species.

In dermal studies local irritant effects were clearly seen in test animals. However, while no reliable evidence of systemic toxicity was seen in the rat up to the top dose of 80 mg/kg bw/day in a 90-day study, a NOAEL of 20 - 24 mg/kg bw/day was identified based on histological changes to the liver (hypertrophy) in a 14-day mouse study at 50 - 60 mg/kg bw/day and greater.

In the only inhalation study available, an NOAEC of 0.05 mg/L was identified in the rat based on inflammation of the nasal tract and changes in clinical chemistry parameters following exposure to an aerosol of 0.12 – 0.23 mg/L and greater, 2 h/day 5 days/wk for 3 wk.

Therefore, overall, the data from rodent studies indicates that the principal effect following ingestion and topical application of triclosan are hepatic effects. However, the hepatic effects seen, generally hepatocyte hypertrophy, are not considered to be toxicologically significant to warrant classification. Similarly, the irritation and clinical chemistry changes seen in the only inhalation study are not indicative of serious damage to health that warrants classification.

Classification: Based on the available animal data triclosan does not meet the Approved Criteria (NOHSC, 2004) for classification as causing serious damage to health by prolonged exposure through inhalation, ingestion or dermal contact.

Genotoxicity

Only in vitro studies and animal data are available. In vitro, negative results were seen in a number of studies in bacteria with (+S9) and without (-S9) metabolic activation up to cytotoxic concentrations. Although a single positive result is available it is from a briefly reported study and was seen only at a very high dose level. Similarly, although positive results were seen in two studies in fungi limitations in the methodology prevent any reliable conclusions on the mutagenic potential of triclosan. In mammalian cells in vitro conflicting results have been observed. In chromosome aberration and gene mutation studies both a negative and positive result have been reported (+/-S9). The significant increase in mutation frequency was only seen at cytotoxic concentrations. Negative results were also seen in two UDS assays. Thus, there are a substantial number of in vitro studies available for triclosan with very limited evidence of a genotoxic potential (i.e. a single robust chromosome aberration study).

In somatic cells in vivo, negative results were seen in the available 3 bone marrow chromosome aberration studies and 4 micronucleus studies. Both a positive and negative result is available in the mouse spot test, though limitations in the methodology prevent any reliable conclusions being drawn from either study. Although there are limitations in the methodology of the available germ cell studies, only negative results were seen in the dominant lethal study and 2 chromosome aberration studies in spermatogonia. Thus, there are a number of

studies available in somatic and germ cells and no reliable evidence of a genotoxic potential.

Classification: Based on the available in vitro and animal data triclosan does not meet the Approved Criteria (NOHSC, 2004) for classification as a mutagen.

Carcinogenicity

Only animal data are available. A well-conducted oral carcinogenicity study is available in both the rat and hamster. In the rat, no treatment related tumours were observed in males and females administered up to 127 and 190 mg/kg bw/day triclosan in the diet respectively for 2 years. There are concerns that dose levels may not have been maximised in the rat study. At the top dose only mild clinical changes were seen in both sexes along with histopathological changes to the liver in males that were inconsistently seen in animals sacrificed throughout the course of the study, and a trend for reduced body weight gain in females that was less than 10% at study termination.

Similarly, no treatment related tumours were seen in male and female hamsters administered up to 250 mg/kg bw/day triclosan in the diet for up to 95 weeks. Though in contrast to the rat study, dose levels were clearly maximised in the hamster study with clear signs of toxicity seen at the top dose that included nephrotoxicity and histopathological changes to the stomach in both sexes. Additional signs of toxicity seen in males only at this dose included a statistically significant decrease in body weight gain of 48% and greater from week 90. Therefore, the bioassay in both the rat and hamster provide no evidence of a carcinogenic potential.

Classification: Based on the available animal data triclosan does not meet the Approved Criteria (NOHSC, 2004) for classification as a carcinogen.

Reproductive effects

Fertility

Only animal data are available. In the only fertility study available, no effects on fertility were seen in a well conducted dietary two-generation study in the rat up to the top dose level of 176 and 229 mg/kg bw/day in males and females respectively. Furthermore, there was some evidence of systemic toxicity in parental animals at the top dose, with reductions in body weight gain of 10% or greater seen in F1 males only and females during the growth and development stage.

Additionally, a number of chronic oral repeat dose studies are available in rodents, rabbits, dogs and baboons that examined reproductive organs, including a carcinogenicity study in the rat and hamster. In the carcinogenicity study in hamsters, although adverse effects were seen on spermatogenesis at 250 mg/kg bw/day, they were seen in the presence of marked systemic toxicity in males (including a reduction in body weight gain in excess of 40%) and are thus considered a secondary non-specific consequence of such. No other treatment related effect on reproductive organs was seen in the remaining oral studies or a 90-day repeat dermal study in the rat and Rhesus monkey. Therefore, these repeat dose studies also provide no evidence that triclosan may have a direct adverse effect on fertility.

Classification: Based on the available animal data triclosan does not meet the Approved Criteria (NOHSC, 2004) for classification as a reprotoxicant.

Developmental

Only animal data are available using the oral route of exposure. In a rat study, the minor finding of an increased incidence in retarded ossification at 150 mg/kg bw/day did not obtain statistical significance and was a secondary non-specific consequence of maternal toxicity. In a further robust study in the rat, no effect on development was seen up to and including 300 mg/kg bw/day, a dose that produced marked maternal toxicity. Additionally in the rat, no robust evidence of a postnatal development effect was seen in studies that assessed such including a two-generation study. In other species, no effects on development were seen in the rabbit up to 150 mg/kg bw/day, a dose that produced marked maternal toxicity. While in the mouse, the observed reductions in male and female foetal body weight of just 8% and less are not considered biologically significant. Additionally in this study, the minimal treatment related finding at 350 mg/kg bw/day of a reduction in ossified forelimb phalanges that was just outside the historical control range is considered to be a secondary non-specific consequence of maternal (liver) toxicity. Thus, the data from these numerous robust studies provide no evidence that triclosan has a direct effect on development.

Classification: Based on the available animal data triclosan does not meet the Approved Criteria (NOHSC, 2004) for classification as a developmental toxicant.

Effects during lactation

Triclosan has been detected in human breast milk samples. However, the toxicokinetic data in humans provide no evidence of a bioaccumulation potential following oral or dermal exposure. Furthermore, triclosan is not present at potentially toxic levels in human breast milk samples as the maximum concentration detected (which was from a US study) was 55 µg/kg milk. This represents a daily intake of 8.79 µg/kg bw/day in 1 month old babies if the mean milk intake is taken as 751 g/day and body weight is 4.7 kg (see sub-section 8.14.1, Table 8.71). In the most appropriate test available a well-conducted two-generation study in the rat the results did not indicate the presence of an adverse effect on the offspring due to the transfer in milk: no significant effect was seen during weaning at the top dose whose incidence/magnitude was maintained or increased through weaning in both F1 and F2 pups. Thus, taking the NOAEL of 229 mg/kg bw/day (the top dose) the maximum concentration detected in human breast milk represents a margin of safety of 26052. However, even if a conservative approach is adopted by taking a NOAEL of 73 mg/kg bw/day based on the minimal changes observed in pups that are not considered to provide robust evidence of an effect during lactation, then the margin of safety is still 8305.

Consequently, although no cross-fostering study is available in experimental animals investigating effects during lactation, the available data in humans and animals provide no evidence that triclosan may have the potential to cause harm to breastfed babies.

Classification: Based on the available data triclosan does not meet the Approved Criteria (NOHSC, 2004) for classification for lactational effects.

20.2 Public

20.2.1 Scheduling in SUSDP

The National Drugs and Poisons Schedule Committee (NDPSC) is a statutory committee established under the *Therapeutic Goods Act 1989* (as amended) and the *Therapeutic Goods Regulations 1990* (as amended). The NDPSC classifies drugs and poisons into Schedules (the Standard for the Uniform Scheduling of Drugs and Poisons) for inclusion in the relevant legislation of the States and Territories. The Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP) also includes model provisions about containers and labels, a list of products recommended to be exempt from those provisions, and recommendations about other controls on drugs and poisons. The NDPSC Regulations are available online at:

<http://scaleplus.law.gov.au/html/pastereg/0/25/top.htm>.

According to the Guidelines for National Drugs and Poisons Schedule Committee (NDPSC), triclosan should be included in the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP), based on its acute toxicity profile.

Triclosan has the following toxicity profile:

Acute oral toxicity:	LD50 >5000 mg/kg bw in the rat
Acute dermal toxicity:	LD50 \geq 9300 mg/kg bw in the rabbit
Acute inhalation toxicity:	LC50 <1300 mg/m ³ in the rat with 2 h exposure
Skin irritation:	Moderate
Eye irritation:	Severe after 24 h, but slight from 48 h. Minor effects seen until day 7
Skin sensitization:	Very weak skin sensitisation potential
Respiratory tract irritation:	Irritant

Repeat dose toxicity of triclosan: Triclosan shows a low hazard for repeated use, with a NOAEL of 40 mg/kg bw/day and 56 mg/kg bw/day identified in a 2 year carcinogenicity study in the rat for mild clinical changes and hepatocyte hypertrophy and hepatocytic 'inclusion' in males and mild clinical changes and a trend for reduced body weight gain in females respectively. These observed effects which were not seen in each sex, are not considered to be irreversible.

SUSDP Schedule

The inhalation toxicity (LC50 <1300 mg/m³ based on 2 h exposure) and irritation effects of triclosan are consistent with the NDPSC criteria for scheduling. Therefore, the NDPSC may wish to consider inclusion of triclosan in the SUSDP, with appropriate cut-offs and/or exemptions for consumer products.

The major source of exposure of the community to triclosan comes from cosmetics and personal care products with about 15 tonnes per year being used in these products. Consequently it is also recommended that NDPSC consider establishing a protective cut-off.

The EU cut-off value for cosmetic and personal care products is provided below as being protective to health and promotes international harmonisation:

*Triclosan (as a preservative) for cosmetic use:
0.3% or less in all cosmetic preparations*

The community can also be exposed to triclosan used in cleaning products. Currently the level of exposure from this source is relatively low with less than 1 tonne/year being used in industrial cleaning products that may also be available to the general public through retail outlets. NICNAS will monitor the use of triclosan in cleaning products and consider the need for a cut-off value(s) for these products. Based on the information gathered further recommendations may be made to the NDPSC.

21. Effects on Organisms in the Environment

21.1 Wildlife

There has been little field-based environmental monitoring of the effects of triclosan on organisms in their natural environment.

No information was available on the potential effects of triclosan exposure to reptiles (e.g. snakes, lizards, and tortoise), Australian native birds or other Australian native terrestrial wildlife species (e.g. mammals, birds). No freshwater or marine mammal (e.g. platypus, dolphin) toxicity data were available.

21.1.1 Mammals

The kinetics, metabolism and toxicity of triclosan to laboratory (eutherian) mammals (e.g. rats, mice, rabbits) are presented in Sections 17 and 18, respectively. With a level of caution, this information may be extrapolated to wildlife species of a broadly similar taxonomic class.

21.1.2 Birds

Only oral toxicity data were available for birds. No subchronic or chronic oral avian studies were available. Acute oral toxicity data were available for only two North American bird species. The results, summarised in Table 21.1, indicate low oral toxicity to birds under the laboratory conditions tested.

Acute dose studies

Bio-Life Associates Ltd (1993a) conducted a 14-day acute oral toxicity test in mallard ducks (*Anas platyrhynchos*) using the method of US EPA (1989a, 71-1) with good laboratory practice (GLP). Both range-finding and definitive tests were performed. Three groups of mallards (randomly assigned, 19 weeks old, 10 per group and 5 per sex) were exposed to triclosan (99.7% purity) given as a single oral dose via 4 gelatin capsules on day 1 and monitored from day 1 to 14 for signs of toxicity. Birds were weighed on days 0, 1, 3, 7, and 14. Group feed consumption was monitored daily (and expressed as the average mass of food/water consumed per bird). Water and food were provided *ad libitum*. Nominal doses administered to each group were equivalent to 0, 681, 1470 and 2150 mg/kg body weight (bw).

Four arbitrarily assigned mallards (2 male, 2 female) from the control and each treatment group were subjected to gross pathological examinations. No mortality, clinical signs or pathological abnormalities were evident in the control group or at doses up to 2150 mg/kg bw. There were no significant differences in body weights or feed consumption between the control and treatment groups. Control birds weighing 1055 g (SD \pm 126) consumed 75-91 g/bird/day. Mallards treated with triclosan consumed between 89-113 g/bird/day. The no-observed-effect level (NOEL) was 2150 mg/kg bw, and the median lethal dose (LD50) is greater than 2150 mg/kg bw (Bio-Life Associates Ltd, 1993a).

Bio-Life Associates Ltd (1993b) conducted a 14-day acute oral toxicity test in bobwhite quail (*Colinus virginianus*) using the method of US EPA (1989a, 71-1) with GLP. Both range-finding (7 d) and definitive tests were performed.

Seven groups of quails (randomly assigned, 21 weeks old, 10 per dose and 5 per sex) were exposed to triclosan (99.7% purity) given as a single oral dose via gelatin capsules on day 1 and monitored from day 1 to 14 for signs of toxicity. Birds were weighed on days 0, 1, 3, 7, and 14. Group feed consumption was monitored on days 3 or 4, 7 and 14 (and expressed as the average mass of food/water consumed per bird). Water and food were provided *ad libitum*. Dose administered during the range finding tests were equivalent to 464, 681, 1000, 1470 and 2150 mg/kg bw. Doses administered to each group in the definitive tests were equivalent to 0, 147, 316, 464, 681, 1000 and 1470 mg/kg bw (nominal).

In the range-finding test, one female from the 1470 mg/kg bw group and one male from the 2150 mg/kg bw group were experiencing tremors, while a male from the 1000 mg/kg bw group was inactive. Mortality was evident at all doses. Diarrhoea (green-coloured and chalky) was noted during the range-finding test.

During the definitive tests, mortality was evident in groups treated with doses of 316 mg/kg bw (1), 681 mg/kg bw (5), 1000 mg/kg bw (4) and 1470 mg/kg bw (10). Using the simplified method of Litchfield and Wilcoxon (1949), a 14-day LC50 of 862 mg/kg bw (95% CI 635-1170) was calculated for both sexes combined. No mortalities occurred at doses of 147 and 464 mg/kg bw. Clinical signs of toxicity were noted during the tests at all doses (e.g. diarrhoea, discoloured excreta, lethargy, wing-beat convulsions); however, complete remission of all clinical signs was achieved in survivors by day 9. Compared to controls, body weights were significantly lower in groups dosed with ≥ 681 mg/kg bw, and reduced feed consumption was noted in birds treated at ≥ 316 mg/kg bw. In addition to a random selection of 24 survivors, four arbitrarily assigned quail (2 male, 2 female) from the control and each treatment group were subjected to gross pathological examinations, and most birds examined had, in particular, liver discoloration abnormalities (i.e. ≥ 147 mg/kg bw). Since a small amount of diarrhoea was noted under the pen of birds fed 147 mg/kg bw, a NOEL could not be achieved in this test.

Repeat dose studies

Data from one repeat dose study was available. Bio-Life Associates Ltd (1993c) conducted a repeat dose 8-day acute oral toxicity test in bobwhite quail using the method of US EPA (1989a; 71-2 in conjunction with the method of US EPA 1985c) with GLP. Five groups of quail (randomly assigned, 13 days old, 10 per group, indeterminate sex) were exposed to triclosan (99.7% purity) fed in the diet for 5 days followed by a recovery period of 3 days where birds were offered untreated diets.

Diets included 0, 312, 625, 1250, 2500 and 5000 ppm (nominal) or 0, 331, 564, 1173, 2492 and 5469 ppm (measured, HPLC). Dietary doses (measured) were calculated to approximate 0, 45-49, 76-86, 159-179, 346-379 and 566-864 mg/kg bw (lower and upper range for day 5 and 8). Treatment diets were formulated using the following procedures. Triclosan, in an amount equivalent to 65 g, was added to 195 g acetone and mixed into 7935 g of standard laboratory diet to form a standard premix. The standard premix was blended for 15 minutes. An additional 5000 g of

stock diet was then mixed (15 mins) into the standard premix, forming a test diet equivalent to 5000 ppm. The 2500 ppm diet was prepared by mixing equal quantities (6500 g) of stock diet and 5000 ppm test diet. Each dilution series was developed in a similar manner. The vehicle control consisted of 195 g of acetone blended in 13000 g of stock diet. The stability of the triclosan in the dietary treatments was assessed by sampling each treatment diet at days 1 and 5 and analysis using HPLC (methanol extraction), with no significant losses reported. Birds were weighed on days 0, 5 and 8. Group feed consumption was monitored daily (grams of food/water eaten ÷ no. birds). Water was provided *ad libitum*.

Four arbitrarily assigned quail from the control and each treatment group were subjected to gross pathological examinations. Gaseous intestines were evident in two birds fed the 5000 ppm diet. No other abnormal gross pathological findings were recorded in 24 arbitrarily selected survivors. One mortality was recorded in the 2500 ppm diet group and 4 in the 5000 ppm diet group. Compared to controls, the average body weight in the 5000 ppm group was depressed on test days 5 and 8. Reduced feed consumption was also noted in the 5000 ppm group. The 8 d NOEL was determined to be 1250 ppm (nominal, equivalent to 179 mg/kg bw measured) and the 8 d LC50 was >5000 ppm (nominal, equivalent to >864 mg/kg bw measured).

Table 21.1 - Oral toxicity data for birds.

Species	Conditions	Endpoint	Result	Reference
Mallard <i>Anas platyrhynchos</i>	14 d Single oral dose (gelatin capsules)	LD50	>2150 mg/kg bw ^a	Bio-Life Associates Ltd (1993a)
		NOEL	2150 mg/kg bw ^a	
Bobwhite quail <i>Colinus virginianus</i>	14 d Single oral dose (gelatin capsules)	LD50	862 mg/kg bw ^a	Bio-Life Associates Ltd (1993b)
		NOEL	<147 mg/kg bw ^a	
	8 d 5 day repeat dose in diet	LC50	>5000 ppm ^a	Bio-Life Associates Ltd (1993c)
		LD50	>864 mg/kg bw ^b	
		NOEC	1250 ppm ^a	
		NOEL	179 mg/kg bw ^b	

a. Nominal concentration. b. Measured concentration.

21.2 Terrestrial invertebrates

Invertebrate toxicity data are limited to one study with earthworms. RCC (1990b) investigated the survival of adult earthworms (*Eisenia foetida foetida*; body weights 201-287 mg) exposed to triclosan in artificial soil substrate at various nominal test concentrations (64, 128, 256, 513, 1026 mg/kg dry weight basis) using OECD TG 207 Section 2: Earthworm, Acute Toxicity Test under GLP. Worms were acclimated to the soil substrate for 24 h prior to testing.

The artificial soil consisted of sphagnum moss (10%), clay/clay-loam (21%) and sand (<0.2 mm; 69%). During mixing, 165 mL of bi-distilled water containing the suspended test article and acetone at the desired concentration were added drop-wise. By this procedure, the soil moisture content of the artificial soil was adjusted to 38.4%. At day 14, the soil moisture varied between vessels from ~30%-60%, this is not expected to affect the validity of the test.

The test article (triclosan; 10.0 g) was dissolved in 50 mL acetone. From this stock solution, a series of dilutions in acetone (dilution factor of 1+1) were made. The preparations were made immediately prior to the application. Soil pH was 7.4 at day 1 and 7.8-7.9 at day 14.

Five concentrations and a control (with acetone) were tested. Therefore, 2775 µL of the respective dilutions were added to the artificial soil. In addition, 165 mL of bi-distilled water was added to each test vessel. The final concentration of acetone in the soil (dry weight basis) was 0.51%. For the acetone control, 2775 µL of acetone was added to the soil. The test was performed with 4 replicates of each concentration (10 worms/vessel).

Worms were placed on the surface of the soil in the vessels. Mortality and toxicity symptoms (reaction of worms to mechanical stimulus) were assessed on days 7 and 14 after application by emptying the content of each vessel onto a stainless steel plate and the living worms counted and replaced back into the test vessels. The body weights of 10 worms of each batch of surviving worms were recorded at days 1 and 14.

The quality of the worms used was assessed by determining the LC50 (Logit analysis) of a toxic control (2-chloroacetamide; 25, 50 and 100 mg/kg soil). The 7 d and 14 d LC50 values for the toxic control were 55.6 and 75.2 mg/kg soil, respectively. Based on previous experience, these results are within acceptable ranges.

No mortality or abnormal symptoms were observed in the control or at the highest test concentration and an LC50 of >1026 mg/kg (dry weight) was derived (NOEC 1026 mg/kg dry wt). After 14 days of exposure, the mortality of treated animals up to a concentration of 1026 mg/kg was between 2.5%-7.5%, which is in the acceptable range of 10% for the control recommended by the OECD test guideline. Body weights at day 0 and 14 were not significantly different from controls and no abnormal symptoms were detected in live worms. It should be noted that these results are based on nominal concentrations and that in the 21-day phytotoxicity study significant loss of triclosan was noted (see below).

21.3 Terrestrial plants

Soil tests

Phytotoxicity data from two soil test studies show significant loss of triclosan from test vessels and the results should be considered with caution due to the initially rapid loss and inability to accurately quantify the exposure concentrations. In both tests, it is likely that the phytotoxicity of triclosan is underestimated. No comment was provided in either of the tests as to the fate of the lost triclosan.

Springborn Laboratories (1992) investigated the phytotoxicity of triclosan on seedling growth of six plant species (monocotyledons: corn, ryegrass, wheat; dicotyledons: cucumber, soybean, tomato) grown in sand based on the protocol for conduct of a seedling growth toxicity test (US FDA, 1990), and GLP. Of the species tested, ryegrass and wheat are standard OECD test species. Effects on morphology, survival, shoot length, shoot weight and root weight were assessed after 21 days exposure. Shoot lengths were measured on days 0, 1, 3, 5, 7, 14 and 21 to establish growth rate curves. Morphological abnormalities (wilt, necrosis,

chlorosis, foliar lesions, and leaf blotch) were monitored daily for each plant. Roots and shoots samples were dried at 70°C for several days and weighed (± 0.1 g).

Nominal (and initial mean measured) soil test concentrations included 10 (11), 30 (33), 100 (96), 300 (280) and 1000 (930) $\mu\text{g } ^{14}\text{C}$ -triclosan/kg sand with enough radiolabelled test material added to achieve a concentration of approximately 2000 disintegrations per minute (dpm)/gram of soil. Unlabelled triclosan was also used. Solvent (acetone) control and controls were also tested. A stock solution of radiolabelled test material was prepared by diluting triclosan (23.59 μg) to volume with acetone in a 50 mL volumetric flask. Samples of stock solution were collected for analysis (mean measured concentration 472 $\mu\text{g/mL}$).

To prepare each nominal test concentration of 1000 and 300 $\mu\text{g/kg}$, unlabelled test material (0.0461 g and 0.0114 g, respectively) and ^{14}C radiolabelled stock solution (7.440 mL and 7.425 mL, respectively) were diluted with acetone to volume in separate 200 mL volumetric flasks. These solutions were prepared with an additional 10% of test material based on pilot testing results. To this, 8.12 mL of radiolabelled stock solution (472 $\mu\text{g/mL}$) was added, and brought to volume with acetone. This solution was prepared with an additional 20% of test material. The 30 $\mu\text{g/kg}$ and 10 $\mu\text{g/kg}$ treatments were prepared by diluting the appropriate amounts of radiolabelled stock solution (3.45 mL and 1.15 mL, respectively) to volume with acetone in separate 200 mL volumetric flasks. These solutions were also prepared with an additional 20% of test material. To prepare each control, solvent control and treatment, each 45 kg batch of sand was divided into three 15 kg aliquots. To each of the aliquots, one third (66 mL) of the appropriate stock solution was added. Each volumetric flask used to deliver the solution was then rinsed with 25 mL of acetone and the rinse was added to the third sand aliquot. The solvent control received 5 mL of acetone per kg of sand and then the 25 mL acetone rinse, equivalent to the amount of acetone received per treatment level. Each sand aliquot (except control) was mixed for 10 minutes and then the three aliquots were combined within a fibreglass container and mixed twice daily for two days to allow the acetone to evaporate.

Prior to, and at the completion of testing, sand samples were collected for analytical testing. At day 21, triclosan concentrations in treatment soils were 3.4, 21, 34, 136 and 290 $\mu\text{g/kg}$ soil, with recoveries ranging from 29%-70% of the initial test concentration. Each replicate consisted of a 13 cm tall pot containing ~ 1.5 kg of washed, 20-40 mesh quartz sand as support medium. The organic matter content of the sand was 0.14% and pH 7.5. Each pot was placed on a saucer and nutrient solution was added to the saucer on a daily basis. Lighting was provided daily for 16 h and the tests were conducted at 20°C to 30°C with $>60\%$ humidity.

The test results presented in Table 21.2 indicate that triclosan has the potential to affect terrestrial plants. The lowest NOEC and LOEC values based on initial test concentrations were 96 and 280 $\mu\text{g/kg}$, respectively, for cucumber growth. The mode of phytotoxic action was not described. No stimulatory effects of triclosan were noted for any species.

During the 21-day seedling tests by Springborn Laboratories (1992), algae grew on the surfaces of sand substrates in a few of the test vessels. The authors suggested that the algae species might have been *Chlamydomonas*, *Protosiphon* and *Chlorella*. While their presence is unlikely to have affected the phytotoxicity tests, it is noteworthy that the algae were able to grow on the test media from about day 15 onwards. However, the test concentrations of triclosan in the soil media between

days 15-21 were much less than the initial concentrations (i.e. 3.4-21 μg triclosan/kg soil).

Table 21.2. Phytotoxicity data for plant seedlings

Species	Media	Endpoint	Parameter	Result		TW
				($\mu\text{g}/\text{kg}$)*	($\mu\text{g}/\text{kg}$)**	AVE
Corn	Sand	LOEC	No effect	>930	>290	>610
		NOEC		930		
Cucumber	Sand	LOEC	Shoot length	280	45	162
		NOEC		96	34	65
Ryegrass	Sand	LOEC	Root weight	930	290	610
		NOEC		280	45	162
Soybean	Sand	LOEC	No effect	>930	>290	>610
		NOEC		930	290	610
Tomato	Sand	LOEC	Root & shoot weight	930	290	610
		NOEC		280	45	162
Wheat	Sand	LOEC	Shoot weight	930	290	610
		NOEC		280	45	162

Sources: Springborn Laboratories (1992). * Day 0 mean measured test concentration (dry weight). ** Day 21 mean measured test concentration (dry weight). TW AVE = time-weighted mean concentration ($\mu\text{g}/\text{kg}$).

A further 28-day test using cucumber was conducted by ABC Laboratories Inc. (1997b) using the method of US FDA (1990). The test was conducted similarly to that described above by Springborn Laboratories (1992). Test soil consisted of sieved Kansas sandy loam (1.6% OM, 73% sand, 15% silt, 12% clay, CEC 8.8, pH 5.4, bulk density 1.19). Phytotoxicity to cucumber (measured as visual phytotoxicity ratings, percent emergence, shoot length, dried shoot weight, dried root weight) under these conditions at day 28 was not evident. Although no effects were evident with an initial exposure concentration of 1000 $\mu\text{g}/\text{kg}$ soil, the final test concentrations at day 28 were ~20% (191 $\mu\text{g}/\text{kg}$ remaining) of the initial test concentration, and ~60% (392 $\mu\text{g}/\text{kg}$) of the initial test triclosan concentrations had been lost from the test vessels by day 14. No explanation for these losses was provided. By using the initial test concentrations to calculate the phytotoxicity test values, effect levels to cucumber are probably underestimated in this test. The time-weighted mean concentration in the highest treatment was 446 $\mu\text{g}/\text{kg}$ (measured days, 0, 14, 21, and 28), which is greater than determined by Springborn Laboratories (1992). The organic matter content of this test soil was higher than used by Springborn Laboratories (1992), which may have reduced the bioavailability of the triclosan to the plants tested.

Topical tests

In a 2-year study, Mmbaga and Sauve (2004) indirectly investigated the phytotoxicity of topically applied triclosan to the plant species flowering dogwood

(*Cornus florida*), and in general found no phytotoxic effects due to triclosan at the application rates used. The study was primarily conducted to assess the fungicidal properties of various products containing triclosan to powdery mildew. Products used in the study included Palmolive® Original Dish Soap, Equate® Antibacterial Liquid Hand Soap and Ajax® Antibacterial Dish Soap, each containing 0.2% triclosan (2 mg/mL) and other proprietary constituents. In addition to these biorational products, conventional fungicides and a blank (water) control were also tested. The treatments were applied to plants in a randomised block design at a rate of 18.3 mL/L (36.6 mg triclosan/L) until leaf run-off occurred and when powdery mildew symptoms were first observed on the plants. Applications were made weekly or semi-monthly using an 8002 flat fan nozzle and CO₂-pressurised backpack sprayer (275 kPa). Applications were made on two occasions (2000 and 2001). Phytotoxic effects were monitored by analysis of plant growth by stem diameter (calliper) and height, and most treatments improved growth relative to the control, which was heavily infested with powdery mildew. The exception was Palmolive®, which was phytotoxic (reduced stem diameter, margin and tip necrosis); however, each product tested had equivalent concentrations of triclosan and the adverse effect is unlikely to be due to triclosan. Currently, no soap products containing triclosan are registered for use as fungicides in agricultural situations.

21.4 Aquatic organisms

The environmental effects of triclosan on aquatic organisms have been reviewed by Hansen and Kallqvist (2001), Orvos et al. (2002), Reiss et al. (2002) and Samsøe-Petersen et al. (Danish Environmental Protection Agency, 2003b). The majority of the aquatic toxicity data available are for freshwater species.

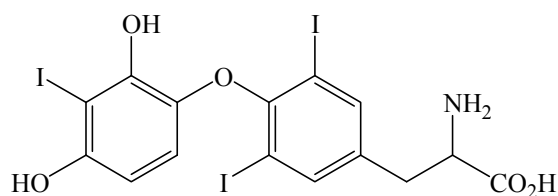
21.4.1 Amphibians

Fort (2008) has investigated the effect of the anti-bacterial agent, triclosan (Ingrasan® DP 300) on anuran metamorphosis using prometamorphic *Xenopus laevis*. An amphibian metamorphosis assay was performed. Nieuwkoop and Faber stage 51 (NF stage 51) *X. laevis* were exposed to four concentrations of triclosan (0.6, 1.5, 7.2, and 32.3 µg/L) for 21 days. The endpoints investigated were survival, hind limb length, body length, (whole body and snout to vent length [SVL]), developmental stage, wet weight and thyroid histology. Whole thyroid tissue and plasma samples were collected for endogenous thyroid hormone (thyroxine [T4]) analysis, and tail fin tissue biopsy samples were collected during the exposure to measure effects on TH receptor beta (TRβ) expression. Modest increases in TRβ expression in tail fin biopsies were observed from exposure day 21 in larvae exposed to 1.5 and 7.2 µg/L triclosan, but not at 0.6 or 32.3 µg/L triclosan treatments. A reduction in larval growth at exposure d 21 in 1.5 µg/L treatment was noted. However, no significant differences in developmental stages between the laboratory control and the triclosan treatments were observed. In addition, no effects on thyroid histology were detected. Finally, no changes in either thyroid gland or serum T4 levels were found. Based on these results, triclosan was determined to not interfere with metamorphosis at the test concentrations studied. Based on the range of endpoints used in this study, the No Observed Effect Concentration (NOEC) was 32.3 µg/L triclosan. These results are in contrast to the results reported by Veldhoen et al. (2006) (discussed below), which indicated a response to triclosan on the metamorphosis from tadpoles to frogs for the North

American bullfrog, *Rana catesbeiana*. The levels tested in the Veldhoen study are well below the levels tested in this study.

Veldhoen et al. (2006) investigated the effects of exposure to environmentally relevant concentrations (0.03-3.0 µg/L) of triclosan to tadpoles of the North American bullfrog, *Rana catesbeiana*. The study was designed to examine whether triclosan induces changes in the thyroid hormone-mediated process of metamorphosis and alters the expression profile of thyroid hormone receptor (TR) α and β , basic transcription element binding protein (BTEB) and proliferating cell nuclear antigen (PCNA) gene transcripts.

Pre-metamorphic tadpoles were immersed in the triclosan concentrations and injected with 1×10^{-11} mol/g body weight 3,3',5-triiodothyronine (T_3) or vehicle control (Sodium hydroxide solution). Morphometric measurements and steady-state mRNA levels obtained by quantitative polymerase chain reaction were determined. mRNA abundance was also examined in *Xenopus laevis* XTC-2 cells treated with triclosan and/or 10 nM T_3 .



3,3',5-triiodothyronine (T_3)

Tadpoles pre-treated with triclosan concentrations as low as 0.15 ± 0.03 µg/L for 4 days showed increased hind limb development and a decrease in total body weight following T_3 administration. Triclosan exposure also resulted in decreased T_3 -mediated TR β mRNA expression in the tadpole tail fin and increased levels of PCNA transcript in the brain within 48 h of T_3 treatment, whereas TR α and BTEB were unaffected. Triclosan alone altered thyroid hormone receptor α transcript levels in the brain of pre-metamorphic tadpoles and induced a transient weight loss. In XTC-2 cells, exposure to T_3 plus nominal concentrations of triclosan as low as 0.03 µg/L for 24 h resulted in altered thyroid hormone receptor mRNA expression. Therefore, exposure to low levels of triclosan disrupts thyroid hormone-associated gene expression and can alter the rate of thyroid hormone-mediated postembryonic anuran development. If the data are interpreted as an acceleration of metamorphosis, then the animals could be smaller than usual metamorphs, which has the potential to result in reduced survivability.

Direct lethal and sublethal effects of triclosan (Irgasan) and interactive effects of triclosan and acetaminophen (an analgesic organic contaminant also found in wastewater) on tadpoles of the northern leopard frog *Rana pipiens* have been investigated by Fraker and Smith (2004). Eggs were incubated and tadpoles introduced to the experimental conditions when free swimming and able to feed (Gosner Stage 26; mean mass 0.018 g wet wt). Test aquaria consisted of 1.2 L clear plastic containers holding 1 L of aged tap water and test substance(s). Fifteen tadpoles were tested per test concentration (3 replicates of 5 tadpoles). Tadpoles were fed every 5 days during the 24-day exposure period. Test solution triclosan concentrations (0.23, 2.3, 23 and 230 µg/L) were prepared by serial dilution of a stock solution prepared by direct addition of a measured quantity of triclosan to

aged tap water. Test solutions were renewed weekly. A control (aged tap water only) was also tested; however, any effect of impurities potentially in the dilution water was not evaluated in the test. Test solution concentrations were not chemically analysed and are reported as nominal concentrations.

Observations of tadpole mortality and sublethal effects (activity level, startle response) were made daily. Changes in activity level and startle response were used as an indicator of the potential for reduction in fitness. Activity level by tadpoles was scored either as the proportion of tadpoles that were inactive or active, where active was determined as movement through the water or feeding when observed. Inactivity was defined as lying stationary on the bottom of the test aquaria or floating in the water column with no body movement. After activity scoring, aquaria were tapped firmly and the proportion of tadpoles reacting to the stimulus scored (e.g. no reaction, darting away, jerky movement). Tadpoles were weighed after day 24 and initial and final mean masses were compared among treatments and controls.

Experimental conditions including test methodology, temperature, photoperiod, dissolved oxygen levels, pH and observations of test solution (e.g. clarity, colour, test substance precipitation) were not reported and consequently the potential influence of these parameters on the test results cannot be evaluated.

Very limited test data were presented, and only graphically, and although survivorship was investigated LC50 and NOEC values were not calculated or reported. No significant effect on survival was evident except when exposed to 230 µg/L where mortality rate was ~60%-65%, and the chronic NOEC (survival) was 23 µg/L. A 24 d (chronic) LC50 of between 23-230 µg/L was estimated from the data available.

Statistically significant differences of test results were identified using separate two-way ANOVA and post hoc Fisher's PLSD tests. Startle response by tadpoles exposed to 230 µg triclosan/L was significantly lower than those of the control group. Tadpole activity was significantly less than the control in all triclosan exposure concentrations (i.e. NOEC <0.23 µg/L) and tadpoles in the 23 µg/L group were significantly heavier than other groups tested; however, the absence of dose-response relationships for these endpoints casts doubt on their utility and accuracy. The mechanism for the toxicity of triclosan to tadpoles is not known.

Acetaminophen (up to 1000 µg/L) had no direct effect on tadpole activity level, startle response, survival or growth (biomass) after 24 days exposure, and there was no interaction of acetaminophen on the effects of triclosan in *Rana pipiens*.

The authors indicated that in another study (Fraker and Smith, unpublished, cited in Fraker and Smith, 2004), acetaminophen and triclosan interacted by lowering activity level but not startle response in the frog species *Xenopus laevis*. However, triclosan (230 µg/L) had no effect on *X. laevis* survival but body weight was reduced when compared to the control.

The authors suggested that changes in activity level or startle response may potentially be ecologically relevant by indicating a reduction in fitness of tadpoles by affecting their foraging efficiency, predator avoidance ability and potentially their reproductive success; however, definitive conclusions regarding these sublethal effects cannot be made as they were not assessed further in this study.

The effects of triclosan on production of plasma vitellogenin (VTG) and testosterone in male South African Clawed Frogs (*Xenopus laevis*) was investigated (Matsumara et al., 2005). Male frogs with a body weight around 50-60 g were maintained in glass tanks under a 16:8 h light:dark photoperiod at around 24°C and acclimatised for 7 days. Exposure was either via the water or intraperitoneal injection. In the water exposure groups, six frogs per treatment were exposed to nominal concentrations of 20, 100 and 200 µg/L triclosan (dissolved in DMSO) in dechlorinated tap water for 14 days. A control group was exposed to the solvent carrier only (DMSO, 100 µL/L) and a positive control group was exposed to a nominal concentration of 1 µg/L of estradiol-17β (E2). The test water was changed every 24 h and blood samples taken at the end of the exposure period.

In the intraperitoneal exposure group, 6 frogs per treatment were injected with 4, 40 and 400 µg/g bw triclosan dissolved in propylene glycol. The control frogs were injected with the solvent carrier only and the positive control group was injected with 20 µg/g E2. After injection, the frogs were transferred to glass tanks containing dechlorinated tap water and maintained for 7 days. Blood samples were taken at the end of the exposure period.

For both exposure systems, each group of frogs was kept in a 30 L glass tank under a 16:8 h light:dark photoperiod at around 24°C and fed 0.3% bw of a commercial diet every day. Plasma VTG levels were measured using enzyme-linked immunosorbent assay (ELISA) in a VTG assay kit specifically for frogs. Plasma testosterone levels were measured by an ELISA previously described in the literature. Hepatic EROD and PROD activities in frog liver microsomes were also measured. All statistical analyses were performed using Stat View J 5.0 with experimental data checked for assumptions of homogeneity of variance across treatments using a Bartlett test. When the assumptions were met, data were analysed by one-way ANOVA followed by Dunnett's multiple comparison test. When homogeneity was not observed, a nonparametric Kruskal-Wallis test was used followed by a Mann-Whitney *U* test with Bonferroni's adjustment. Differences were considered significant at a $p < 0.05$ or $p < 0.01$.

The results in the paper are only presented graphically so the following results provide approximate values only.

In the water exposure test, solvent control frogs had a mean plasma VTG level of around 0.32 µg/mL. Levels in all triclosan treatment groups and the positive control group were less than 60% of these levels at around 0.18 µg/mL. However, this was not deemed statistically significant in the report.

In the intraperitoneal injection group, levels of plasma VTG were around 0.1 µg/mL in the solvent control. Levels in all treatment groups were approximately the same at around 0.04 µg/mL. The treatment levels were therefore all around 60% lower than the solvent group, but these were not deemed statistically significant in the report. Induction of plasma VTG levels in the positive control were observed with much more elevated levels at around 30000 µg/mL.

Testosterone levels were measured in the intraperitoneal injection group only, and levels of plasma testosterone in the solvent control group was around 5 ng/mL. This compared to around 5, 3 and 2.5 ng/L in the 4, 40 and 400 µg/g bw groups respectively, and around 4 ng/mL in the positive control group. While the report notes the lower testosterone levels in the two highest treatment groups compared to the control, this is not deemed statistically significant. All triclosan treatment

groups were lower than that in the solvent control group and frogs in the highest treatment group had lower testosterone levels than the control group. No significant differences in hepatic cytochrome P450 1A and 2B activities were observed among all the treatment groups. Frogs injected with 20 µg/g E2 had significantly higher plasma VTG levels than the control group.

The study found no difference between the EROD and PROD activities among the triclosan treatment groups.

21.4.2 Freshwater fish

Acute toxicity

ABC Laboratories Inc. (1990a) conducted a 96-h acute toxicity test with fathead minnows (*Pimephales promelas*). Fish (10 per treatment, mean wt. 0.040±0.020 g; mean length 15±2 mm) were exposed to a control, a solvent control (dimethylformamide) and test concentrations (nominal) of 56, 100, 180, 320 and 560 µg triclosan/L.

Test concentrations were prepared by adding the appropriate aliquots of working standards containing test substance to the test chambers. The working standards were prepared in DMF, and test concentrations were corrected for sample purity (99.7%). The solvent control received a 1.4 mL aliquot of DMF, which was equivalent to the highest amount used in any test solution. There was no visible difference between the test and control solutions in physical appearance. Dilution water had a hardness of 46 mg/L as CaCO₃, alkalinity of 60 mg/L and pH 7.5.

During the test, the test solutions pH ranged from 7.8-7.9, and the test was conducted at 21°C to 22°C. Dissolved oxygen concentrations were monitored daily, with concentrations ranging from 7.3-8.7 mg/L. The LC50 values (95% CI), calculated using the binomial method, are summarised in Table 21.3. During the tests, sublethal effects (fish on bottom of test vessel, loss of equilibrium, laboured respiration, surfacing, quiescence, erratic swimming) were also noted, mainly at concentrations ≥320 µg/L.

In another study using fathead minnows, Mayer and Ellersieck (1986) reported an 96 h LC50 value for fathead minnow of 360 µg/L (95% CI 290-450), which is similar to that described above. Details of the test procedures, including the pH of the test solutions, were not available.

Orvos et al. (2002) reported a study of the effects of triclosan on bluegill sunfish (*Lepomis macrochirus*). Sunfish (10 per treatment) were exposed to nominal triclosan concentrations of 0 (control), 0 (acetone control) 100, 180, 320, 560 and 1000 µg/L in 15.14 L glass aquaria. Stock solutions were prepared in acetone in soft blended water (hardness 40-48 mg/L as CaCO₃). Fish were observed daily for signs of adverse effects. A 96 h LC50 value of 370 µg/L (95% CI 320-440) for sunfish was calculated based on the nominal concentrations. The pH of the test solution was not reported in Orvos et al. (2002).

In an assessment of environmental aspects of triclosan, the European Chemicals Bureau (ECB, 2004) reported acute ecotoxicity data (summarised in Table 21.3) for three fish species; however, the sources of these data were not referenced and full test reports were not made available for this review. The data are presented but

should be interpreted with caution although they are noted to be of similar order of magnitude to the abovementioned LC50 values.

Toxicity data for freshwater fish are summarised in Table 21.3.

Chronic/reproductive toxicity

The potential of triclosan to act as an endocrine disruptor in fish has been examined because its chemical structure closely resembles known non-steroidal estrogens (e.g. diethylstilbestrol, bisphenol A; Ishibashi et al., 2004; Foran et al., 2000).

Table 21.3 Acute toxicity data for freshwater fish

Species	Conditions	Endpoint	Result (µg/L; 95% CI)	Reference
<i>Acute studies</i>				
Fathead minnow	24 h	LC50	360 (180-560)	ABC Laboratories Inc. (1990a)
<i>Pimephales promelas</i>	96 h	LC50	(N)	
	96 h	NOEC	260 (180-320)	Mayer and Ellersieck (1986)
	Static		(N) 100 (N)	
	24 h	LC50	>500	
	96 h	LC50	360 (290-450)	
Zebra fish <i>Brachydanio rerio</i>	96 h	LC50	540	ECB (2004)*
Rainbow trout <i>Oncorhynchus mykiss</i>	96 h	LC50	350	ECB (2004)*
Golden orfe <i>Leuciscus idus</i>	96 h	LC50	560	ECB (2004)*
Bluegill sunfish <i>Lepomis macrochirus</i>	96 h	LC50	370 (320-440) (N)	Orvos et al. (2002)
Medaka <i>Oryzias latipes</i>	48 h	LC50	352±68	Foran et al. (2000)
	96 h (ELS)	LC50	602 (24 h old larvae) 399 (embryos)	Ishibashi et al. (2004)

Species	Conditions	Endpoint	Result ($\mu\text{g/L}$; 95% CI)	Reference
<i>Chronic studies</i>				
Zebrafish or <i>B. rerio</i>	9 d (ELS)	IC25	160	Tatarazako et al. (2004)
		IC50	220	
Medaka or <i>O. latipes</i>	14 d (ELS)	IC25	290	Ferrari et al. (2002)
		IC50	400	
Zebrafish or <i>B. rerio</i>	10 d (ELS)	NOEC	200	
Rainbow trout <i>O. mykiss</i>	96 d (ELS)	MATC	49.3	ABC Laboratories Inc. (1996)*
	Flow-	LOEC	71.3	
	through	NOEC	34.1	

ELS = early life stage. MATC = maximum acceptable toxicant concentration. * Full test report not provided for review. N = nominal.

Foran et al. (2000) study

In a preliminary study, Japanese medaka (*Oryzias latipes*) were exposed for 14 days beginning 2 days post-hatch to triclosan (nominal concentrations of 1, 10, 100, 500 and 1000 $\mu\text{g/L}$) in ethanol or a solvent control (ethanol) at 25°C. Fish were fed brine shrimp daily during the exposure period, and brine shrimp and tetraamin flakes after the exposure period. After exposure, fish were transferred to 30 L aquaria maintained at 27°C. Data for the highest two treatments were discarded as these were lethal to fish fry within 24 and 72 h, respectively. An acute LC50 of 352 $\mu\text{g/L}$ (SD ± 68) was calculated from data collected on survival.

After 10 weeks, the sex of each fish was determined by visual examination of the sexually dimorphic dorsal fin and anal fin morphology. As well, the length of the dorsal and anal fins was measured. Normally, males have longer and morphologically distinct dorsal fins and longer anal fins than females. Sexually dimorphic fin traits were quantified to look for potential effects of triclosan on the development of secondary sexual characters. The proportion of females in each treatment group was similar for triclosan-exposed animals and solvent-treated controls (ethanol 53%, 1 ppb 58%, 10 ppb 45%, 100 ppb 36%). The 36% of females in the 100 $\mu\text{g/L}$ treatment group was not considered significantly different by the authors from the ethanol control. Similar findings were evident for fin traits. These results do not support the hypothesis that triclosan is potently estrogenic but the authors indicated that among the males, animals treated with 100 $\mu\text{g/L}$ had significantly longer dorsal and anal fins than those treated with 10 $\mu\text{g/L}$, suggesting that triclosan is potentially anti-estrogenic or weakly androgenic. However, as the male fin lengths were not significantly different from the control, a more definitive study would be required to validate this hypothesis.

Ishibashi et al. (2004) study

A more definitive study of the effects of triclosan on the early life stages and reproduction of medaka has been conducted by Ishibashi et al. (2004). Tests were conducted on embryos, fry and adult medaka.

Pairs of sexually mature medaka were maintained and spawned eggs collected. Embryos (<24 h post-fertilisation; 60 per treatment) were exposed for 14 days to

nominal triclosan concentrations of 78, 156, 313, 625, 1250 and 2500 µg/L diluted in dechlorinated tap water. Triclosan was initially dissolved in the auxiliary solvent dimethyl sulfoxide (DMSO). A tap water and a solvent control (0.1% DMSO) were also tested. The eggs in each group were placed in a petri dish containing 30 mL of each test solution and incubated on a 16:8 light:dark photoperiod cycle at 25±1°C. Test solutions were replaced each 24 h. Embryos were observed daily under stereoscopic microscope and dead embryos removed. LC50 values were calculated by probit analysis. Hatchability and time to hatching was calculated using data from all embryos. In addition, fifteen 24 h old larvae from each treatment group were placed in 100 mL of test solution and exposed to the same test conditions, concentrations and controls as the embryos described above for 96 h. Test solutions were not changed during the test (static). Larvae were observed daily and dead larvae removed from test aquaria. The 96 h LC50 values for embryos and 24 h old larvae were 399 and 602 µg/L, respectively. Embryonic development, hatchability and time to hatching were all affected by triclosan treatment. The hatchability of fertilised eggs exposed to triclosan for 14 days was significantly decreased at concentrations ≥313 µg/L when compared to controls. Time to hatching of fertilized eggs was significantly delayed at concentrations ≥313 µg/L (NOEC 156 µg/L nominal). All embryos died within 3 days post-fertilisation in the 1250 and 2500 µg/L treatment groups, and died prior to 10 days fertilisation in the 625 µg/L group.

Five male/female pairs of adult mature medaka (300 mg wet wt., and ~30 mm) were exposed to nominal concentrations of triclosan of 20, 100 and 200 µg/L in 1 L beakers for 21 days at 25±1°C (controls also tested including 100 µL/L DMSO). Triclosan concentrations in test waters were measured weekly using an ion trap mass detector and gas chromatogram. The detection limit was 0.01 µg/L based on a linear calibration line and test blanks. Actual triclosan concentrations in test waters were reported based on an average of 0 h (17.3, 75.2 and 162 µg/L) and 24 h (8.3, 46.3 and 111.7 µg/L) values, with actual average concentrations of 12.8, 60.8 and 136.9 µg/L, respectively. Appreciable losses of triclosan were observed in the test solutions and at 24 h, actual concentration were 48%-69% of the initial concentration and actual average concentrations were ~61%-69% of nominal concentrations. Losses were attributed to bioaccumulation in fish, although this was not measured, surface volatilisation, sorption to particulate matter and adherence to aquaria. Test solutions were changed every 24 h. The test included a 16:8 light:dark photoperiod. Fish were fed during the test. Eggs spawned from each female were collected within a few hours after fertilisation, pooled in a petri dish containing ~5 mL of 10% sea water, and checked for fertilisation and developmental stage. During the 21 days testing period, the number of eggs spawned for each treatment group was counted daily and the ratio of fertilised eggs calculated. Each embryo was maintained in dechlorinated tap water until hatching and the hatchability and time to hatching was calculated. During the last 24 h of triclosan exposure, all the fertilised eggs from each pair in each treatment group were collected, the hatched larvae were maintained for 90 d in dechlorinated tap water and observed for cumulative mortality, total length, body weight and sex ratio with the appearance of secondary sex characteristics.

At the end of the F0 generation exposure, livers and gonads were sampled, and the body weight and the total length of each fish measured. The gonadosomatic (GSI, %) and hepatosomatic (HSI, %) indices were also calculated as the ratio of gonad or liver weight to body weight. Hepatic vitellogenin (VTG) levels in male medaka were measured using enzyme linked immunosorbent assay (ELISA) in a VTG

assay kit specifically for medaka (TransGenic Inc, Japan). Purified medaka VTG (1, 4, 26, 64 and 256 ng/mL) was used as the standard, and VTG in diluted samples was measured in duplicate. Concentrations of VTG were calculated from the linear part of the log-transformed medaka VTG standard curve (detection limit 1 ng/mL). EROD and PROD activities in liver microsomes from female medaka were measured by dealkylation of ethoxyresorufin and pentaoxyresorufin, respectively, and detection of the resulting resorufin by HPLC.

The results indicate the following:

- Exposure to triclosan (≥ 313 $\mu\text{g/L}$ for 14 days) impaired reproduction through effects on embryo development, decreased hatchability and delayed hatching of fertilised eggs.
- The total length of female medaka was found to decrease significantly relative to the controls when exposed to ~ 137 $\mu\text{g/L}$ (actual average; NOEC ~ 61 $\mu\text{g/L}$). The effect was not apparent in males, and body weight was not significantly different in males or females. There were no significant differences in the total number of eggs collected during the triclosan exposure period relative to the controls (fertility $>90\%$).
- The HSI of male medaka exposed to ~ 137 $\mu\text{g/L}$ was significantly higher than the control, and the HSI of female fish exposed to ~ 13 $\mu\text{g/L}$ was significantly higher than the control (NOEC <13 $\mu\text{g/L}$).
- The GSI of male medaka exposed to ~ 61 and ~ 137 $\mu\text{g/L}$ was significantly higher than the control. The GSI of female medaka exposed to ~ 13 and ~ 137 $\mu\text{g/L}$ was significantly higher than the control (NOEC <13 $\mu\text{g/L}$).
- Concentrations of hepatic VTG were significantly higher in males exposed for 21 days to ~ 13 and ~ 61 $\mu\text{g/L}$, but at the highest test concentration of 200 $\mu\text{g/L}$, no significant difference relative to the control was observed (NOEC 13 $\mu\text{g/L}$).
- There were no significant differences in EROD or PROD activity in female medaka after 21 days exposure to triclosan.
- In the F-1 generation, the hatching of embryos in the ~ 13 $\mu\text{g/L}$ treatment showed adverse effects; however, there was no dose-response relationship between hatchability and triclosan treatment levels.
- Triclosan did not affect the cumulative mortality of offspring maintained in clean water for 90 days after hatching, and body weight and total length did not differ significantly from the control.
- The sex ratio of males to females was approximately 1:1 for all groups.

The estrogenic activity of triclosan was also measured by a yeast two-hybrid assay in-vitro both with and without rat liver S9 preparation (described by Shiraishi et al., 2000). Triclosan showed only weak estrogenic activity in the absence of rat S9 treatment. The estrogenic activity of triclosan was enhanced about 2-fold by exposure to S9 metabolic activity.

These results suggest that triclosan and/or its metabolite methyl-triclosan (MTCS) may potentially have weak androgenic and/or anti-estrogenic action that has the potential to induce hepatic VTG in male medaka. VTG is a useful indicator of male

fish for detecting estrogenic contamination in the environment, but is not necessarily an indicator of reproductive impairment. Triclosan did not have any adverse effects on the reproductive abilities of adult male and female medaka (i.e. number of eggs produced, fertility) at the concentrations tested in this study.

Houtman et al. (2004) study

The occurrence of triclosan in the bile of wild-caught fish (male bream *Abramis brama*) from three rivers in The Netherlands has been investigated in 1999 by Houtman et al. (2004). Triclosan in bile was analysed by GC/MS-MS. Bile was evaluated for estrogenic activity using the ER-CALUX method (Legler et al., 2002) and a toxicity identification and evaluation (TIE) method that uses bioassay-directed fractionation of estrogenic compounds was performed. Sample locations included lake Bergumermeer, River Drommel and Amsterdam North Sea Canal, and each represents the receiving water for industrial and STP effluent. Triclosan was detected in samples from the latter two sites; North Sea Canal (14 µg/mL of bile) and River Drommel (80 µg/mL of bile). Triclosan did not show any estrogenic activity at concentrations up to 0.1 mM indicating that this compound is not or is very weakly estrogenic relative to other compounds also detected in the bile during this study (e.g. 17β-estradiol).

Tatarazako et al. (2004) study

Tatarazako et al. (2004) have reported early life stage studies for zebrafish (*Danio rerio*) and medaka (*Oryzias latipes*). Eggs at the blastula stage were collected approximately 4 h after fertilization. They were rinsed to remove faecal matter and were transferred to 50 mL glass flasks containing 40 mL of triclosan solution. Various concentrations of triclosan solution (zebra fish: 0.5, 0.25, 0.125 and 0.0625 mg/L with a control, medaka: 1.25, 0.63, 0.31, 0.156 and 0.0781 mg/L with a control) were prepared in triplicate. Control flasks filled with water that was prepared by charcoal filtration were also used in each test. The test solution was provided with a sufficient amount of oxygen, and adjusted to pH 7.0 ± 0.5 with NaOH or HCl. Water hardness was maintained at 200 mg/L CaCO₃. Water was added to each flask (40 mL) for dilution, and 20 eggs were placed in each flask. During the test period, 80% of water in each flask was replaced every day. Live eggs were counted daily. The eggs were incubated in a climate chamber at 25 ± 1°C and a 16 h light/8 h dark photo period. The fry were not fed during the test period, which was terminated more than 9 days (zebra fish) and 14 days (medaka) after hatching, when all of the fry had died. The end point reported in the study was the inhibition of hatching. The study reports an IC₂₅ of 160 µg/L and an IC₅₀ of 220 µg/L for zebra fish and an IC₂₅ of 290 µg/L and an IC₅₀ of 400 µg/L for medaka.

Ferrari et al. (2002) study

Ferrari et al. (2002) have reported the results of a 10 d early life stage study on Zebrafish (*Danio rerio*) in a poster presented at SETAC Europe 2002. The poster quotes a NOEC of 200 µg/L and indicates that the test was conducted according to ISO 12890 (1999). No further details of the study are available, but similar to the above, this study was also carried out for a shorter time than OECD TG210.

21.4.3 Freshwater invertebrates

Acute studies

ABC Laboratories Inc. (1990b) conducted a 48-h acute toxicity test using freshwater crustaceans *Daphnia magna* exposed to triclosan (compound D1063.01) under static conditions and using a non-standard method (Proctor and Gamble protocol). Range-finding and definitive tests were performed with GLP. Daphnids (neonates; 20 per treatment) were exposed to a control, a solvent control and test concentrations (nominal) of 100, 180, 320, 560 and 1000 µg triclosan/L. Test concentrations and stability of the test material during the tests were not measured analytically. Dilution water had a hardness of 160 mg/L as CaCO₃, alkalinity of 174 mg/L (hard) and pH 8.1, and the test was conducted at 21°C to 22°C. Test water temperature (20°C to 21°C), pH (pH 7.9-8.5) and dissolved oxygen concentrations (8.1-8.5 mg/L) were monitored at 0, 24 and 48 h. Test vessels consisted of 250 mL glass beakers containing 200 mL of testing solution. All vessels were covered with loose fitting petri dish covers during the tests. Lighting was maintained with a 16 h photoperiod and with 30 minutes dawn and dusk transition periods. Daphnids were added to the test solutions within 30 minutes of preparation. Daphnids in all test vessels were monitored daily for mortality and abnormal effects. Test compound (99.7% purity) was added to the solvent DMF and mixed to form a 10 mg/mL primary standard. From this primary standard, a 1.0 mg/L working standard was prepared in hard blended water. The working standard was used to prepare the remaining test concentrations. A solvent control was prepared by placing 0.1 mL of DMF in 1 L hard blended water. All test solutions were clear throughout the duration of the test. The 48 h LC50 (95% CI) was 390 (330-460) µg/L. Effects including mortality, quiescence, and/or daphnids tending to the bottom of the test vessels were observed in test concentrations ≥180 µg/L. Daphnids in the control, solvent control and 100 µg/L test concentration were normal during the duration of the tests.

Orvos et al. (2002) reported on the effects of triclosan to freshwater crustaceans *Ceriodaphnia dubia* in solutions of variable pH (pH 6.8-7.0, 7.4-7.6, 8.0-8.2, 8.2-8.5). The full test report was not provided by the notifier. The test procedure followed the method of US EPA (1985a) under static renewal conditions. Dilution water consisted of aged well water (hardness 174 mg/L as CaCO₃). Test pH was achieved with the addition of H₃PO₄ or NaOH. Results are presented in Table 21.4.

Ferrari et al. (2002) have reported the results of a 48 h studies on *Daphnia magna* and *Ceriodaphnia dubia* in a poster presented at SETAC Europe 2002. The poster quotes an EC50s of 303 and 123 µg/L, respectively. The *Daphnia magna* study was conducted according to AFNOR T90-Acute 301 (1996) while the *Ceriodaphnia dubia* study was conducted according to EPA 600/4_90/027 (1991). No further details of the studies are available, but results are consistent with earlier studies (Table 21.4).

Chronic studies

RCC (1990a) conducted a chronic 21-day aquatic toxicity test (survival and reproduction) with *D. magna* using OECD TG 202 (static renewal) and with GLP. Daphnids were exposed to a control, a solvent control (acetone), and test

concentrations (nominal) of 10, 40, 200, 1000 and 5000 µg triclosan/L. Tests were conducted in duplicate in glass beakers, each containing 200 mL of test solution and 10 daphnids. Twenty daphnids per test concentration were kept in bulk culture until presence of eggs in the brood pouch was observed. Ten daphnids with eggs in the brood pouch were separated and kept individually in beakers containing 50 mL medium and the reproduction rate of each single daphnid was followed up to the end of the test. The remaining daphnids were kept in beakers containing 200 mL of test solution (at least 5 daphnids per beaker) and were observed for mortality rate up to the end of the test. Temperature (19.5°C to 22.4°C), pH (7.8-8.2) and dissolved oxygen (8.0-10.1 mg/L) were monitored daily. Test conductivity and hardness were 606 µ siemens/cm and 14.4-15.6 dh°, respectively.

To prepare the stock solution, an amount of test material (5.0 g) was made up to 10 mL with acetone. Test concentrations were prepared daily by dilution of samples of the stock solution. The concentration of acetone in all test samples was estimated to be 0.01% v/v. Test solutions were replaced on test days 2, 5, 7, 9, 12, 14, 16 and 19. Daphnids were fed a mixture of yeast and algae (*Scenedesmus subspicatus*) during the test. Concentrations of the test article were determined by analytical testing on days 0, 2, 19 and 21 for selected test dilutions using HPLC. When compared to the nominal concentrations, recoveries varied widely. In the 200 µg/L (nominal) solution, the measured concentrations on days 0, 2, 19 and 21 were 152, 126, 97 and 154 µg/L, respectively (average 132 µg/L), with recoveries ranging from 48%-77% of nominal. In the 5000 µg/L (nominal) solution, the measured concentrations on days 0, 2, and 21 d were 1505, 2259-4010 and 4570 µg/L, respectively, with recoveries ranging from 30%-91% of nominal. The stock solution (50 mg/mL nominal) contained 6258 mg/mL. No explanation for the widely variable nominal and analytical results was provided in the test report. Test results were calculated using nominal concentrations, and thus are interpreted with caution.

Mortality in the controls was <5% indicating the test was valid. From day 0-5, no mortality was observed in the three lower test concentrations (10-200 µg/L). At the higher concentrations, a mortality rate of 100% was observed after day 2. On day 21, the mortality rate of the three lower concentrations ranged from 5%-15%. Reproduction of young daphnids started after day 9 of the exposure period. The reproductive rate in the solvent control and control were within acceptable limits. Reproduction was normal in daphnids exposed to nominal concentrations ≤40 µg/L; however, at a nominal concentration of 200 µg/L (estimated time-weighted average of 132 µg/L) significant reproductive inhibition was observed. LOEC and NOEC values were estimated to be 132 µg/L (200 µg/L nominal) and 40 µg/L (nominal), respectively.

Springborn Laboratories Inc (1993) conducted a chronic 7-day toxicity test with freshwater crustaceans (*Ceriodaphnia dubia*) using US EPA (1989b) test method under static renewal conditions. Tests were performed at pH 7 and 8.5. *C. dubia* (neonates) were exposed to a control, a solvent control and nominal ¹⁴C-triclosan test solution concentrations of 6.0, 12, 25, 50 and 100 µg/L (pH 7) and 20, 40, 80, 160 and 320 µg/L (pH 8.5 test). Test concentrations were determined analytically on days 0, 3 and 7 by liquid scintillation counter (LSC). Mean measured concentrations over the 7 day period in the pH 7 test were 6.0, 12, 24, 50 and 108 µg/L and in the pH 8.5 test were 20, 46, 90, 182 and 339 µg/L, with no appreciable loss of test material in either test.

Toxicity tests were conducted in 20 mL glass vials. Each treatment consisted of 10 replicates each containing 15 mL of test solution and one daphnid. The primary stock solution was prepared by quantitatively transferring the test material to a 50 mL volumetric flask with acetone. Test concentrations were prepared by adding the appropriate amount of stock solution with dilution water to 1500 mL. Test vessels were loosely covered with plastic film. Test temperature was $25 \pm 1^\circ\text{C}$. Test solutions were renewed 3 times during the tests. The dilution water total hardness (as CaCO_3) and alkalinity were 170 and 120 mg/L, respectively. The pH of the test solution was adjusted using 2N H_3PO_4 . Dissolved oxygen and pH of the test solutions were monitored daily in one replicate from each control and test concentration. Temperature was measured at solution renewal. The pH in the pH 7 and pH 8.5 tests ranged from 7.0-7.5 and 8.2-8.5 during the tests. Test solutions were observed to be clear and colourless with no undissolved material during the tests.

In the pH 7 test, mean survival ranged from 90% (solvent control and control) to 40% (108 $\mu\text{g/L}$). The LOEC and NOEC values for adult survival were 108 and 50 $\mu\text{g/L}$, respectively. At test termination, the mean number of offspring per female ranged from 12 (6 $\mu\text{g/L}$) to 5 (24 and 108 $\mu\text{g/L}$). Based on reproductive success in comparison to the controls (solvent control and control combined), LOEC and NOEC values of 12 and 6 $\mu\text{g/L}$, respectively were calculated. The maximum acceptable toxicant concentration (MATC) was 8.5 $\mu\text{g/L}$ (no confidence limits reported). In the pH 8.5 test, mean survival ranged from 100% (90 $\mu\text{g/L}$ and control) to 70% (339 $\mu\text{g/L}$). There was no significant difference in mortality of adults between the controls (solvent control and control combined) and the test treatments. Based on adult survival, a NOEC of 339 $\mu\text{g/L}$ was calculated. At test termination, the mean number of offspring per female ranged from 30 (20 $\mu\text{g/L}$) to 9 (339 $\mu\text{g/L}$). Based on reproductive success, LOEC and NOEC values of 339 and 182 $\mu\text{g/L}$, respectively, were calculated. The MATC was 248 $\mu\text{g/L}$ (no confidence limits reported). The results for this test performed at pH 7 and pH 8.5 indicate triclosan has a higher toxicity at the neutral pH where the neutral form of triclosan predominates.

Ferrari et al. (2002) have reported the results of a 7 d study on *Ceriodaphnia dubia* and a 48 h *Brachionus calyciflorus* study in a poster presented at SETAC Europe 2002. The poster quotes an NOECs of 4 and 50 $\mu\text{g/L}$, respectively. The *Ceriodaphnia dubia* study was conducted according to AFNOR T90-376 (2000) and the *Brachionus calyciflorus* study was conducted according to AFNOR T90-377 (2000) using the RotoxkitTM. No further details of the studies are available. The results for *Ceriodaphnia dubia* are within the range of previous studies (Table 21.4).

Tatarazako et al. (2004) have reported the results of a 7 d *Ceriodaphnia dubia* reproduction test. *C. dubia* was cultured and maintained at $25 \pm 1^\circ\text{C}$ under a 16-h light/8-h dark photoperiod. The water used for *C. dubia* culture was commonly marketed as mineral water in Japan. This mixture was used in order to stabilize the water quality of test solutions, such as water hardness. *S. capricornium* culture (0.3 mL; 4×10^4 cells/mL) and 0.3 mL of YCT (a mixture of yeast, Cerophyll, and trout chow used as food for *C. dubia*) were added to each 400-mL culture beaker every day. Survival and reproduction tests on *C. dubia* were continued for 7 days in accordance with the methods proposed by US EPA. The percentage of living adults and the mean number of young produced by a female were calculated. Test

medium with seven concentrations of triclosan (1, 0.5, 0.25, 0.125, 0.0625 and 0.0313 mg/L with a control) were prepared along with the diluents and control vehicle. Dilutions were made with fresh culture water. Ten replicate glass chambers (50 mL), containing one neonate born within 24 h, were used for each test concentration. These chambers were tightly closed with Teflon caps to prevent volatilization of test chemicals. The medium was renewed daily. Water quality was analyzed every day. Water hardness, pH and dissolved oxygen were 110 mg/L CaCO₃, 7.0 to 7.5, and 80% to 99%, respectively. Temperature was maintained at 24 ± 1°C. Testing was continued until 60% of the control animals had completed three broods (usually 6 to 7 days). For a test to be valid, it required more than 80% survival rate of control animals and ~ 15 offspring per female over the 7-day test period, which was met. The study reports an IC₂₅ of 170 µg/L and an IC₅₀ of 220 µg/L.

Toxicity data for aquatic invertebrates are presented in Table 21.4.

Table 21.4 Toxicity data for freshwater invertebrates

Species	Conditions	Endpoint	Result (µg/L)	Reference
<i>Acute studies</i>				
Waterfleas	48 h	24 h EC ₅₀	390 (330-460) (N)	ABC
<i>Daphnia magna</i>	Static	48 h EC ₅₀	550 (480-620) (N)	Laboratories Inc. (1990b)
		48 h NOEC	100 (N)	
<i>Ceriodaphnia dubia</i>	48 h, pH 6.8-7.0	EC ₅₀	~130 [~120]*	Orvos et al. (2002)
	48 h, pH 7.4-7.6	EC ₅₀	~180 [~140]	
	48 h, pH 8.0-8.2	EC ₅₀	~240 [~130]	
	48 h, pH 8.2-8.5	EC ₅₀	~420 [~120]	
<i>D. magna</i>	48 h	EC ₅₀	303	Ferrari et al. (2002)
<i>C. dubia</i>	48 h	EC ₅₀	123	
<i>Chronic studies</i>				
<i>D. magna</i>	21 d	NOEC	132 (M) (200 N)	RCC (1990a)
	Semi-static	(surviv.)	40 (N)	
	pH 8.2-8.6	NOEC	132 (M) (200 N)	
		(reprod.)		
		LOEC		
		(reprod.)		
<i>C. dubia</i>	7 d	MATC	8.5 [7.9]*	Springborn
	Semi-static	LOEC	108	Laboratories
	pH 7.0	(surviv.)	50	(1993)
		NOEC	6 [5.6]	
		(surviv.)	12	
		NOEC		
		(reprod.)		
		LOEC		
		(reprod.)		

Species	Conditions	Endpoint	Result (µg/L)	Reference
	7 d	MATC	248 [71.2]	
	Semi-static	NOEC	339	
	pH 8.5	(surviv.)	182 [51.8]	
		NOEC	339	
		(reprod.)		
		LOEC		
		(reprod.)		
<i>C. dubia</i>	7 d	NOEC	4	Ferrari et al. (2002)
<i>C. dubia</i>	7 d	IC25	170	Tatarazako et al. (2004)
		IC50	220	
<i>Brachionus calyciflorus</i>	48 h	NOEC	50	Ferrari et al. (2002)

N = nominal concentration, M = measured concentration. *[] = estimated un-ionised triclosan concentration (modelled).

Methyl-triclosan

The acute toxicity of methyl-triclosan to *Daphnia magna* was determined in a 48 h static test according to the EU Commission Directive 92/69/EEC, Part C.2 (1992) and the OECD Guideline for Testing of Chemicals, No. 202 (2004) (Bätscher 2006a).

A supersaturated dispersion of the test item with the loading rate of 100 mg/L was continuously stirred at room temperature in the dark over 24 hours. Then, the dispersion was filtered. The undiluted filtrate of the dispersion and dilutions 1:3.2, 1:10, 1:32, 1:100 and 1:320 were used as test media. Additionally, a control was tested in parallel.

The analytically measured test item concentrations in the analyzed test media samples (dilution 1:3.2 and the undiluted filtrate) amounted to 0.056 and 0.18 mg/L at the start of the test. The values found at the end of the test were 96 and 98% of the initially measured values in the dilution 1:3.2 and in the undiluted filtrate, respectively. The reported biological results were based on the (arithmetic) mean measured test item concentrations of 0.055 mg/L (dilution 1:3.2) and 0.18 mg/L (undiluted filtrate).

The 48-hour NOEC (highest concentration tested without toxic effects after the exposure period of 48 h) of methyl-triclosan to *Daphnia magna* were determined to be 0.18 mg/L (the highest test level). The 48 h NOEC might even be higher but concentrations above 0.18 mg/L could not be tested due to the limited solubility of the test item in the test water. The 48 h EC50 and the 48 h EC100 were higher than 0.18 mg/L and, thus, above the solubility limit of the test item in the test water.

21.4.4 Freshwater algae and cyanobacteria

Yang et al. (2008)

Recently, Yang et al. (2008) have reported the toxicity of twelve antibacterial agents (triclosan, triclocarban, roxithromycin, clarithromycin, tylosin, tetracycline, chlortetracycline, ciprofloxacin, norfloxacin, sulfamethoxazole, sulfamethazine, trimethoprim and copper) to *Pseudokirchneriella subcapitata* (formerly

Selenastrum capricornutum). The toxicity tests were conducted according to OECD test guideline 201. The individual and combined toxicity of the antibacterial compounds were investigated. For triclosan, the paper reports an IC₅₀ and NOEC of 0.53 µg/L and 0.20 µg/L, respectively. Triclosan was found to be the most toxic of the compounds. Additive toxicity was observed for mixtures of triclosan with triclocarban, sulfamethazine or chlortetracycline, while mixtures of triclosan and norfloxacin showed antagonistic effects on the toxicity. The endpoint obtained in this study is the most sensitive response reported for algae to triclosan (Table 21.5).

Tatarazako et al. (2004)

Tatarazako et al. (2004) investigated the toxicity of triclosan to *Selenastrum capricornutum* Printz (NIBS-35 strain). Conical flasks (50 mL) covered with silicon caps were used for the culture and assay. They were shaken automatically at 4000 rpm at 24±1°C under illumination at 4000 (±10%) lux. To obtain a preculture, a 0.1 mL aliquot of stock culture was inoculated into a 50-mL flask containing 20 mL of growth medium C, and then incubated for 3 days. An equal amount (0.1 mL) of the precultured alga was added to freshly prepared 20 mL medium C, to obtain algal samples at the same growth phase. After 48 h incubation, 1 to 5 mL of the cultured alga was added to medium C. The final volume was adjusted to 20 mL, which contained 4x10⁴ cells/mL. The flasks containing 20 mL each of test solutions at various triclosan concentrations were prepared for the assay. Triclosan solutions at ten concentrations (40, 20, 10, 5, 2.5, 1.25, 0.63, 0.31 and 0.16 µg/L along with a control) were prepared in triplicate. At the start of the assay, 1 mL of the precultured alga was inoculated into each flask. After 72 h, cell density was measured using Coulter Counter ZM (Coulter Electronics Ltd., Fullerton, CA, U.S.A.). The rate of growth inhibition was calculated by dividing the number of cells in cultures containing triclosan at various concentrations by that in the untreated control culture. The study determined an IC₂₅ of 3.4 µg/L and an IC₅₀ of 4.7 µg/L. These results are summarised in Table 21.5.

Ferrari et al (2002)

Ferrari et al. (2002) have reported the results of a 96 h study on the green algae *Pseudokirchneriella subcapitata* (formerly *Selenastrum capricornutum*) in a poster presented at SETAC Europe 2002. The poster quotes a NOEC of 2.6 µg/L. No further details of the study are available. These results are in the range of results reported for this species in other studies (Table 21.5).

RCC (1995) Study

RCC (1995) investigated the growth inhibition of test substance (¹⁴C-FAT 80'023/R; triclosan; 99% purity) to green algae (*Scenedesmus subspicatus*) over a 72 h test period using OECD TG 201 Algae Growth Inhibition Test. Range-finding and definitive tests were conducted. Algae were exposed to a control, a solvent control (acetone), and nominal (and actual measured concentrations by HPLC) test concentrations of 0.6, 1.3, 2.5, 5 and 10 µg/L (0.5, 1.2, 2.1, 4.5 and 9 µg/L).

Stock solution was prepared by adding an amount of test substance (5.79 MBq ¹⁴C-triclosan) dissolved in 1.0 mL acetone (1.000 mg/L measured by Liquid Scintillation Counting LSC). Test dilutions were prepared in acetone by respective

dilution of the stock solution. To prepare test solution concentrations, an aliquot (100 µL) of each of the stock dilutions were diluted to 1000 mL test medium. To 150 mL of these test solutions, an aliquot of 0.8 mL of the algae pre-culture was added to achieve an initial cell density of 10^4 cells/mL. The acetone control consisted of 100 µL/L test medium containing 10^4 cells/mL. Three 50 mL aliquots of triclosan-treated samples, and five 50 mL aliquots of the acetone-treated samples were incubated for cell counting. The final acetone concentration was 0.01%. Algae were also tested using a reference toxicant, potassium dichromate.

Test vessels comprised 50 mL conical Erlenmeyer flasks covered with glass petri dishes. Algae were incubated under continuous stirring (~500 rpm) at $23\pm 2^\circ\text{C}$ and under continuous illumination (8000 lux). Samples of test material (2 mL) were taken at 24, 48, and 72 h to determine cell number in exactly 0.5 mL by means of a calibrated electronic cell counter. Four definitive tests were performed, with the first three discarded due to significant variation in replicates. Initial test solution pH was 8.0. Cell growth in the control increased by a factor >16 within 3 days and the pH in the three highest tests were within the acceptable criterion (± 1.5 pH units). However, during the test, the pH of the control, acetone control and the lowest test concentration (0.6 µg/L) varied by >1.5 pH units, with pH values of 9.7, 10.3 and 10.1, respectively. The higher pH values are attributed by the author to higher algal growth rates. As the cell growth in the acetone control (use to compare with treatments) was greater than in the control, the variation is not considered significant.

To assess the stability of the test substance over the duration of the test, samples were collected after 24 and 72 h for analysis of radioactivity by LSC and directly by HPLC; however, these values (reported below) were compared to the nominal rather than measured concentrations and a true estimate of triclosan during the tests cannot be determined. Based on LSC analyses, most (87%-96%) radioactivity was partitioned in the organic phase at the completion of the test, with 4.2%-13.5% in the aqueous phase. Based on HPLC analyses of the organic phase only, triclosan was the predominant analyte (99.4%-100%); however, after 72 h, recovery of triclosan from the organic phase ranged between 66%-82.5% of the initial nominal concentrations. By HPLC, 2,4-dichlorophenol (DCP) was measured in the organic phase only, being detected at concentrations between 6.7%-16.3%. An unidentified metabolite was also detected in the organic phase at concentrations between 4.4%-6.9%. The total concentration of 2,4-DCP or other unknown metabolite was not determined. No significant growth inhibition was evident in the lowest test concentration compared to the acetone control. At the next higher test concentrations, inhibition rates were ~85%, 91% and 100%, respectively. Results are presented in Table 21.5.

ABC Laboratories Inc. (1997c) Study

ABC Laboratories Inc. (1997c) also investigated the growth inhibition of ^{14}C -triclosan to green algae (*S. subspicatus*) over a 96 h test period using a non-standard test methodology (ABC Protocol No. TSCA 797.1050: Static Bioassay Procedure for Determining the Acute Toxicity of Chemicals and Substances to Algae *Scenedesmus subspicatus*). Range-finding and definitive tests were conducted, both under static conditions. Algae were exposed to a control, a vehicle control (1.0 mL 10 mM NaOH/L), and nominal test concentrations of 0.5, 1.0, 2.0, 4.0 and 8.0 µg/L. Mean time-weighted measured (LSC) test concentrations were

0.36, 0.69, 1.5, 3.1 and 6.1 $\mu\text{g/L}$ (average of 0, 72 and 96 h measured concentrations), ranging from 69%-78% of the nominal concentration.

Stock solution (1.05 mg/mL) was prepared by adding an amount of test substance in acetonitrile. Approximately 1 mL of stock solution was transferred to a culture tube and the acetonitrile was allowed to evaporate under nitrogen gas. The residue was resuspended in acetone to the initial volume. This solution was used as a qualitative standard for spotting TLC plates and was frozen while stored. Stock solution was prepared by transferring a 0.160 mL aliquot of the repurified ^{14}C -triclosan solution to a culture tube, evaporated to dryness under nitrogen, and the residue was resuspended in 5 mL of a 10 mM NaOH solution. A spiking solution was prepared by addition of a 0.1 mL aliquot of stock solution diluted to 1 mL in a 10 mM NaOH solution. LSC analysis was performed on the stock and spiking solutions, yielding concentration of 8.48 and 0.848 μg triclosan/mL, respectively. A working standard solution (8.0 $\mu\text{g/L}$) was prepared by transferring 1.89 mL of stock solution and 0.11 mL of a 10 mM NaOH solution to a 2 L flask and then diluting to a final volume with algae nutrient medium. The final vehicle concentration in the 8.0 $\mu\text{g/L}$ test solution was 10 μM NaOH (1.0 mL/L of 10 mM NaOH). Test concentrations were prepared by transferring 62.5, 125, 250 and 500 mL samples of the working standard to 1 L flasks into which additional vehicle (10 mM NaOH) volumes of 0.94, 0.88, 0.75 and 0.50 mL were added to the 0.50, 1.0, 2.0 and 4.0 $\mu\text{g/L}$ test concentrations, respectively. Each volumetric flask was then brought to a final test volume with algal nutrient medium to yield the abovementioned nominal test concentrations. A 10 μM NaOH vehicle control was prepared by adding a 1.0 mL aliquot of a 10 mM NaOH solution to algal nutrient medium and diluting with media to 1 L.

All test concentrations were observed to be clear with no visible precipitate following preparation. The pH of the test solutions was monitored at 0, 72 and 96 h. Tests vessels comprised 250 mL Erlenmeyer flasks containing 100 mL of test solution. Algae were incubated under continuous stirring (100 rpm) at $24\pm 2^\circ\text{C}$ and under continuous illumination (4300 lux). Five replicates were tested per control, vehicle control and treatment, and the 1.0 $\mu\text{g/L}$ test concentration was replicated 9 times. Each replicate received 1.0 mL of algal inoculum containing 10^6 cells, resulting in an initial test concentration of $8.2\text{-}8.5\times 10^3$ cells/mL. No reference toxicant test was performed. The initial pH of the controls and test solutions was 7.5-7.8. Cell growth in the controls increased by factors >16 within 3 days and the pH in the three highest tests were within the OECD TG 201 acceptable criterion (± 1.5 pH units). However, during the test, the pH of the control, vehicle control and the lowest two test concentrations (0.36 and 0.69 $\mu\text{g/L}$) varied by >1.5 pH units, with pH values of 9.9, 10.1, 10.2, and 9.9, respectively. No reason for the higher pH values was provided, potentially due to higher algal growth rates. As the cell growth in the vehicle control (use to compare with treatments) was the same as in the control, the variation is not considered significant.

To assess the stability of the test substance over the duration of the test, samples were collected daily and analysed for radioactivity by LSC and results compared to the initial measured radioactivity. The percentage loss of triclosan between 0 and 96 h ranged between 35%-51%. Analytical determination of triclosan metabolites in test solutions was not performed after the tests. No significant growth inhibition was evident in the lowest two test concentrations compared to the vehicle control. At the next higher test concentrations, inhibition rates were $\sim 57\%$, $>99\%$ and

>99% respectively (mean cell count of treatment \div mean cell count of vehicle control \times 100). Results are presented in Table 21.5.

Wildlife International Ltd (1999) study

Wildlife International Ltd (1999) also investigated the growth inhibition of ^{14}C -triclosan to green algae (*S. subspicatus*) over a 96 h test period and the effect of humic acid on ecotoxicity of triclosan. The test methodology followed test guidelines from US EPA (1996a-b) and Title 40 of the US Code of Federal Regulations. A range-finding test was initially conducted. Two definitive tests were conducted concurrently, without and with the addition of humic acid (20 mg/L nominal), under static conditions. Algae were exposed to a control (culture medium), a humic acid control, and seven test concentrations (3 replicates of each). Nominal concentrations in the test without humic acid were 0.47, 0.78, 1.3, 2.2, 3.6, 6.0 and 10 μg triclosan/L. In the test with humic acid, the nominal test concentrations were 0.93, 1.6, 2.6, 4.3, 7.2, 12 and 20 μg triclosan/L.

At test initiation, the inoculum contained $\sim 10^6$ cells/mL and by addition of 1.0 mL to each test vessel, the initial cell density in the test solutions was $\sim 10^4$ cells/mL. Cell densities were monitored daily. A primary stock solution was prepared by dissolving the test substance in culture medium at a concentration of 100 μg triclosan/mL. The control consisted of culture medium only. Several drops of 0.1 N NaOH were added to the stock solution to aid in the solubilisation of the test substance (mixed and sonicated). The stock was pH adjusted with 10% HCl to pH 7.5. A primary working stock solution was prepared by diluting the primary stock with culture medium to a concentration of 1.00 μg triclosan/mL (mixed and sonicated). The primary working stock solution was serially diluted with culture medium (30:50) to prepare 6 additional stock solutions used in the test. To prepare test solutions, 5 mL of each stock was added to a 500 mL flask and the flasks were brought to volume with culture medium. After mixing, 100 mL of test solution was added to each replicate test vessel. To prepare test solutions containing humic acid, ~ 0.01 g of humic acid was added to 500 mL flasks containing 100 mL of culture medium. The test solutions were prepared as described above except that 10 mL of each stock solution was added prior to bring to volume with the culture medium. The humic acid control was prepared by addition of 0.01 g of humic acid to 500 mL of culture medium. Recovery of algae cells post-treatment was also assessed. At 96 h, the recovery phase test solutions were prepared. Treatment groups that were maximally inhibited were diluted with culture medium to concentrations of test substance that theoretically would not inhibit growth. A 0.5 mL aliquot of test solution was removed from each replicate flask and was pooled by treatment group then diluted to 100 mL with culture medium. This provided one flask per treatment for observations of growth recovery. A negative control was prepared for comparison by diluting 0.5 mL of solution from a single negative control to 100 mL with culture medium.

Total organic carbon (TOC) was measured in the negative control and humic acid control at test initiation prior to addition of the algae. Dissolved organic carbon (DOC) was measured in each control and all treatment groups at test initiation and termination. TOC and DOC concentrations in the control were less than the limit of detection (LOD 0.5 mg C/L) and 6.5 mg/L, respectively, indicating that the addition of humic acid did increase the TOC content of the medium. DOC in the medium without humic acid was \leq LOD, while DOC concentrations in the medium

with humic acid ranged from 0.7-1.7 mg/L. Consequently, much of the humic acid added did not dissolve.

Samples of test substance were collected at test initiation and termination from the negative control, humic acid control and all treatments for analysis by GC/ECD. Analytical results for the two highest test concentrations were spurious and were discarded by the authors without explanation of the reason for the spurious results (final concentrations higher than initial); however, this did not affect the calculation of the EC50 values as effects in the three highest treatments were >50% when compared to the control. Nevertheless, the spurious analytical results cast doubt on the accuracy of the analytical testing program and overall study findings.

The pH of the test solutions was monitored at 0 and 72 h. Tests vessels comprised 250 mL Erlenmeyer flasks containing 100 mL of test solution. Algae were incubated under continuous stirring (100 rpm) at 24±2°C and under continuous illumination (4300 lux). No reference toxicant test was performed. Cell counts were made using a hemacytometer and a microscope.

At the completion of the test, cells were examined microscopically for visible atypical cell morphology. Algicidal properties were determined on the basis of cell death. Algistatic properties were determined based on recovery and growth of treated cells during the recovery phase. After 96 h, there were no signs of clumping, flocculation or adherence of the algae to the test flasks in any test vessels examined. In addition, there were no noticeable changes in cell colour or morphology when compared to either of the controls indicating that triclosan is not algicidal at the concentrations and conditions tested. However, cells in treatments without humic acid (2.2, 3.6 and 6.0 µg/L) were enlarged as were cells in the treatments with humic acid (4.3, 7.2, 12 and 20 µg/L). Cells were smaller in the 10 µg/L group treated without humic acid. Algal cells in the treatment group resumed normal growth after 8 days of the recovery phase indicating that triclosan is algistatic.

Cell growth in the controls increased by factors >16 within 3 days and the pH in most of the tests were within the OECD TG 201 acceptable criterion (±1.5 pH units). Initial and final test solution pH values in the treatments with humic acid were 7.6 and 7.6-8.1, respectively. The pH of the negative control and test concentration (0.742 µg/L) in the treatment without humic acid varied by 2.0 and 1.8 pH units, respectively, and the pH values at 0 h and 96 h were 7.5-7.6 and 7.8-9.5, respectively. To assess the stability of the test substance over the duration of the test, analytical testing of samples collected at 0 h and 96 h with the treatments without humic acid indicated that between 17%-38% of the initial test concentration was lost due to unidentified causes. For the treatments with humic acid, the 96 h losses ranged between 29%-43%. No reason for these losses was provided, and no analytical testing for triclosan metabolites in the test solutions was performed. In spite of these losses, test values were calculated using the initial test concentrations rather than the time-weighted averages, which would result in the statistically derived test values underestimating the actual toxicity due to the higher initial test concentrations. No significant growth inhibition was evident in the treatment without humic acid at measured concentrations of 0.514 and 0.742 µg/L when compared to the negative control. The higher three test concentrations inhibited growth by 23%, 88% and 96%, respectively. In the presence of humic acid, cell densities were not significantly different from the negative control at test concentrations of 0.991, 1.55 and 2.38 µg/L when compared to the humic acid

control. The 4.41 and 6.98 µg/L treatments inhibited cell growth by 84% and 89%, respectively. The results, presented in Table 21.5, indicate that humic acid had a moderating effect on triclosan toxicity to green algae under the test conditions.

Wildlife International Ltd (1998) study

Wildlife International Ltd (1998) conducted a 96-h toxicity test using the freshwater cyanobacteria (*Anabaena flos-aquae*) according to US EPA (1996b) test methodology (static conditions), and with GLP. Algae were exposed to a control, negative control (culture medium), and 6 treatment concentrations of triclosan (nominal 0.41, 0.81, 1.6, 3.3, 6.5 and 13 µg triclosan/L).

Primary stock of ¹⁴C-triclosan was prepared by quantitatively transferring the test substance to a 100 mL flask brought to volume with DMF. The primary stock solution was analysed by LSC and estimated to contain 0.1924 mg triclosan/mL. The 13 µg/L nominal test concentration was prepared by adding 68 µL of the primary stock to 1 L freshwater algal medium. Five secondary stocks were prepared by 50% serial dilutions of the primary stock. The remaining test concentrations were prepared by adding 68 µL of the appropriate stock solution to 1 L of freshwater algal medium. The solvent control was prepared by adding 60 µL of DMF only to 1 L of freshwater algal medium. The concentration of DMF in the solvent control and all triclosan treatments was 0.068 mL/L. Inoculum contained ~10⁶ cells/mL, and test vessels initially contained 10⁴ cells/mL. Algal cell density was monitored daily. Test vessels consisted of 250 mL Erlenmeyer flasks containing 100 mL of the test solutions. Vessels were incubated at 24±2°C, continuously stirred (100 rpm) and illuminated (2050-2270 lux). Test solution pH was 7.4 on Day 0 and ranged from 7.6-7.8 at 96 h (acceptable).

To assess the stability of the test substance during the tests, samples of test solutions were collected daily for analysis by LSC and HPLC.

Measured concentrations of triclosan in treatments at day 0 were 0.436, 0.836, 1.76, 3.52, 6.70 and 13.1 µg/L (within 101%-110% of nominal). Concentrations at 96 h were 0.416, 0.778, 1.70, 3.36, 5.82 and 12.6 µg/L, representing relatively minor losses of triclosan of 3%-13% when compared to the initial measured concentrations (and other ecotoxicity studies undertaken with algae). Mean measured concentrations (0.42, 0.81, 1.7, 3.4, 6.3 and 13 µg/L) were used to calculate EC50 values, which is considered appropriate.

At test completion, test concentrations of 1.7, 3.4, 6.3 and 13 µg/L inhibited cell growth rates by 55%, 76%, 95% and 99%, respectively.

Microscopic analysis of test solutions indicated there were no signs of clumping, flocculation or adherence of the algae to the test flasks, or changes to cell colour or morphology indicative of algicidal properties. A few cells in the 3.4, 6.3, and 13 µg/L treatment groups were enlarged.

To assess recovery post-exposure, at 96 h aliquots of test solutions (3.4, 6.3, 13 µg/L) were diluted with culture medium to concentrations of test substance that theoretically would not limit growth and monitored. After 9 days the algal cells resumed normal growth indicating algistatic rather than algicidal properties of triclosan. Results are presented in Table 21.5.

Carolina Ecotox Inc (1997) study

The phytotoxicity of triclosan to several aquatic plant species including *S. capricornutum*, *A. flos-aquae*, *Navicula pelliculosa*, *Skeletonema costatum* and duckweed *Lemna gibba* has been investigated by Carolina Ecotox Inc (1997). The test method followed a non-standard protocol based on methods developed by US EPA (1971, 1974, 1978, 1985d, 1987), Miller et al. (1978), Holst and Ellwanger, (1982), ASTM (1990, 1991) and supplemented by in-house procedures, and under GLP.

Stock solutions were prepared by weighing an appropriate quantity of triclosan and diluting in acetone, which was then mixed and sonicated. Stock solution was a clear liquid. Secondary stock solutions for each test were prepared, in acetone, by serial dilutions. The solvent controls contained an amount of solvent (acetone) equivalent to the amount present in each test treatment (0.5 mg/L). In the algae toxicity tests, 25 mL of test solution was used in 125 mL flasks, and 200 mL of test solution was used in 500 mL flasks for the duckweed test.

For each test, the test treatments were prepared by quantitatively diluting aliquots of the appropriate stock solutions, with culture medium, in flasks to yield nominal concentrations as follows:

- *S. capricornutum* and *A. flos-aquae*: 0.496, 2.48, 12.4 and 69 µg/L;
- *N. pelliculosa* and *S. costatum*: 0.500, 2.51, 12.6 and 66 µg/L; and
- *L. gibba*: 0.500, 2.50, 12.5 and 62.5 µg/L.

Reasons for the selection of these test concentrations were not provided. No range-finding tests were performed. Test concentrations and test substance stability were not verified by analytical testing. Results from other studies indicate that some loss of triclosan would probably have occurred during these tests. Calculation of EC50 values on the basis of initial nominal test concentrations may under-estimate ecotoxicity of triclosan to the species tested.

The no-treatment controls contained test medium only. Several test media were used, which were prepared by adding, for each litre, aliquots of the appropriate stock solutions to type I water. The pH was adjusted to 7.5±0.1 with 0.1 N or 1.0 N NaOH and HCl as necessary and the volume brought up to 1 L. Medium was then filtered (0.22 µm) into a sterile container. To prepare medium for the marine species, a commercial salt mix was added to type I water to reach a salinity of 30‰ and then filtered (0.22 µm). Nutrients were added to the sterile synthetic salt water. Stock culture contained ~10⁶ cells/mL and test vessels contained ~10⁴ cells/mL at Day 0. Algae cell density was monitored daily using an electronic particle counter (3 replicates/treatment). Samples of *A. flos-aquae* (filamentous algae) were sonicated prior to counting.

The inoculum for duckweed consisted of 12 d old stock culture. Three plants, consisting of 4 fronds each, were added to each replicate test vessel at Day 0. Fronds were counted daily during the 7 d test. Discoloured fronds were noted but not included in the frond counts (i.e. growth).

Test conditions were as follows:

- *S. capricornutum*: Temp. 24±2°C, continuous shaking (100 rpm) and light 3790-4780 lux, Day 0 pH 7.32-7.53, Day 4 pH 7.34-8.26;

- *A. flos-aquae*: Temp. 24±2°C, shaken once daily, continuous light 2153±15% lux, Day 0 pH 7.32-7.40, Day 4 pH 7.26-7.4;
- *N. pelliculosa*: Temp. 24±2°C, continuous shaking (100 rpm) and light 4306±15% lux, Day 0 pH 7.15-7.46; pH, Day 4 pH 7.41-7.84;
- *S. costatum*: Temp. 20±2°C, shaken once daily, 14 h photoperiod with 4306±15% lux, Day 0 pH 7.99-8.23, Day 4 pH 8.51-8.54; and
- *L. gibba*: Temp. 25±2°C, not shaken, continuous light 5000±15% lux, Day 0 pH 7.71-7.76, Day 4 pH 7.58-8.92.

Results are presented below and summarised in Table 21.5.

- *S. capricornutum* test: Inhibition in the control (45%) was significantly greater than the solvent control. The solvent appeared to enhance growth. Exposure to triclosan at concentrations of 0.496, 2.48, 12.4 and 69 µg/L inhibited the growth of *S. capricornutum* by 27.8, 22.5, 93.4 and 98.8%, respectively, when compared to the solvent control.
- *A. flos-aquae* test: Inhibition in the control was -32% when compared to the solvent control, i.e. the solvent appeared to inhibit growth. Exposure to triclosan at concentrations of 0.496, 2.48, 12.4 and 69 µg/L inhibited the growth by 11.4%, 95.6%, 100%, and 100%, respectively, when compared to the solvent control.
- *N. pelliculosa* test: Inhibition in the control was not significantly different to the solvent control. Exposure to triclosan at concentrations of 0.5, 2.51, 12.6 and 66 µg/L inhibited the growth of *S. capricornutum* by 10.8%, 14.6%, 34.7% and 93.2%, respectively, when compared to the pooled controls.
- *S. costatum* test: Inhibition in the control was not significantly different to the solvent control. Exposure to triclosan at concentrations of 0.5, 2.51, 12.6 and 66 µg/L inhibited the growth of *S. costatum* by 2.71%, 4.92%, 4.47% and 13.2%, respectively, when compared to the pooled controls.
- *L. gibba* test: Frond count in the control was not significantly different to the solvent control. Exposure to triclosan at concentrations of ≤12.5 µg/L stimulated growth up to 16.2%, while a concentration of 62.5 µg/L inhibited the growth by 20.9%, respectively, relative to the pooled controls. Since no test concentration resulted in inhibition >25%, no EC50 could be calculated.

In this above comparative study, *A. flos-aquae* was the most sensitive aquatic plant species tested. The results compare closely with the other study of this species, and with *S. capricornutum*.

Phytotoxicity data for aquatic plants, algae are presented in Table 21.5.

Freshwater algae are the most sensitive freshwater organisms tested to date, with the NOEC values of 0.5-0.69 µg/L and 72-96 h EC50 values of 0.7-1.4 µg/L. Results were only available for tests conducted under alkaline test solution conditions (e.g. pH ≥7.3) whereas the neutral form, predominant at pH values <8.0, is clearly the most toxic from daphnia studies.

Table 21.5 - Phytotoxicity data for algae and freshwater plants

Species	Conditions	Endpoint	Result ($\mu\text{g/L}$)	Reference		
Green algae <i>Scenedesmus subspicatus</i>	72 h (acetone carrier)	EbC50	0.7 (0.7-0.8) (M)	RCC (1995)		
		LOEC	1.2 (M)			
		NOEC	0.5 (M)			
	96 h (NaOH carrier)	ErC50	2.8 (2.3-3.7) (M)	ABC Laboratories Inc. (1997c)		
			LOEC		1.2 (M)	
			NOEC		0.5 (M)	
		ErC80	1.8 (M)			
			ErC50		1.4 (M)	
			ErC20		1.2 (M)	
		NOEC	0.69 (M)			
			ErC90		2.3 (1.8-2.9) (M)	Wildlife International Ltd (1999)
					ErC50	
		ErC10			0.78 (0.78-2.0) (M)	
		NOEC	0.742 (M)			
			ErC90		7.0 (1.6-7.0) (M)	Wildlife International Ltd (1999)
ErC50	3.5 (3.2-3.7) (M)					
ErC10	2.4 (1.5-2.8) (M)					
NOEC	2.38 (M)					
	ErC90	5.6 (4.8-5.8) (M)	Wildlife International Ltd (1998)			
		ErC50		1.6 (1.5-1.7) (M)		
ErC10		0.97 (0.85-0.99) (M)				
NOEC	0.81 (M)					
	ErC90	0.97 (0.72-1.30) (N)	Carolina Ecotox Inc (1997)			
		EbC25		0.67 (0.45-0.98) (N)		
Diatom <i>Navicula pelliculosa</i>	96 h	EbC50	19.1 (15.3-23.8) (N)			
		EbC25	10.7 (7.93-14.5) (N)			
Green algae <i>Pseudokirchneriella subcapitata</i>	96 h	EbC50	4.46 (2.06-9.66) (N)			
		EbC25	2.44 (0.82-7.29) (N)			
(formerly called <i>Selenastrum capricornutum</i>)	96 h	IC50	2.6	Ferrari et al. (2002)		
		EC25	3.4			
	72 h	EC50	4.7	Tatarazako et al. (2004)		
		IC50	0.53			
	72 h	NOEC	0.20	Yang et al. (2008)		
		7 d	ErC50	>62.5 (N)	Carolina Ecotox Inc (1997)	

N = nominal concentration, M = measured concentration.

Wilson et al. (2003) found natural algal assemblages changed when exposed to triclosan in laboratory bioassays. Test algae were collected from filtered water samples from Cedar Creek (collected at 1-1.5 m depth), ~500 m upstream (unimpacted) and 25 m downstream (sewage impacted) from the Olathe, Kansas WWTP. While exponential growth rate was unaffected in vitro, biomass yields were significantly different and triclosan caused marked shifts in community structure of attached and suspended algae at sites both upstream and downstream. Increasing triclosan concentration (0.015, 0.15 and 1.5 $\mu\text{g/L}$) caused a decline in algal biodiversity (genera richness) in the bioassays. Algal genera affected by

triclosan included *Chlamydomonas*, *Scenedesmus*, *Melosira*, *Navicula* and *Synedra*. *Chlamydomonas*, and cyanobacteria were significantly affected at a concentration of ≥ 0.15 $\mu\text{g/L}$.

21.4.5 Methyl-triclosan

The influence of the methyl-triclosan on the growth of the green algal species *Scenedesmus subspicatus* was investigated in a 72 h static test according to the EU Commission Directive 92/69/EEC, C.3 (1992) and the OECD Guideline No. 201 (1984) (Bätscher 2006b).

A supersaturated dispersion of the test item with the loading rate of 100 mg/L was continuously stirred at room temperature in the dark over 24 hours. This dispersion was filtered. The undiluted filtrate of the dispersion and the dilutions 1:2.2, 1:4.6, 1:10 and 1:22 were used as test media. Additionally, a control was tested in parallel.

The measured concentrations for the dilutions were 0.041, 0.086, 0.17 and 0.40 mg/L, respectively, at the start of the test. The values found at the end of the test ranged from 91 to 107% of the initially measured values. The reported biological results were based on the (arithmetic) mean measured test item concentrations of 0.040 mg/L (dilution 1:10), 0.082 mg/L (dilution 1:4.6), 0.18 mg/L (dilution 1:2.2) and 0.39 mg/L (undiluted filtrate).

Table 21.6 – Ecotoxicological endpoints for methyl-triclosan to algae

Endpoint	Biomass b (mg/L)	Growth rate (mg/L)
EC90	0.26	0.39
EC50	0.12	0.17
EC10	0.055	0.076
LOEC	0.082	0.082
NOEC	0.040	0.040

21.4.6 Marine organisms

Ecotoxicity data available for marine organisms has been described above (Carolina Ecotox Inc, 1997) and summarised in Table 21.6. No ecotoxicity data are available for marine species of fish, coral species or their algae symbiotes (zooxanthellae).

Delorenzo et al. (2008) investigated the effects of triclosan on marine species. The focus of this study was to examine the effects, primarily on survival, and to investigate the formation of the degradation product, methyl-triclosan, in the estuarine environment. Acute toxicity was assessed using the bacterium *Vibrio fischeri* (using Microtox), the phytoplankton species *Dunaliella tertiolecta* (according to ASTM standar static algal toxicity guidelines), and three life stages of the grass shrimp *Palaemonetes pugio* (according to the US EPA method published by Mayer 1987). *P. pugio* larvae were more sensitive to triclosan than adult shrimp or embryos. Acute aqueous toxicity values (96 h LC50) were 305 $\mu\text{g/L}$ for adult shrimp, 154 $\mu\text{g/L}$ for larvae, and 651 $\mu\text{g/L}$ for embryos. The presence of sediment decreased triclosan toxicity in adult shrimp (24 h LC50s were 620 $\mu\text{g/L}$ with sediment, and 482 $\mu\text{g/L}$ without sediment). The bacterium was more sensitive to triclosan than the grass shrimp, with a 15 min aqueous IC50 value of

53 µg/L and a 15 min spiked sediment IC50 value of 616 µg/kg. The phytoplankton species was the most sensitive species tested, with a 96 h EC50 value of 3.55 µg/L (95% CI 3.19-3.91 µg/L), with no significant effects observed at the lowest test concentration (1.6 µg/L).

Adult grass shrimp were found to accumulate methyl-triclosan after a 14-day exposure to 100 µg/L triclosan (at levels ranging from 137-704 pg/g with an average level of 411(± 221) pg/g). This study indicates the formation of methyl-triclosan as a metabolite in the seawater environment and its potential to bioaccumulate in higher organisms.

Tatarazako et al. (2004) have also investigated the toxicity of triclosan to a freeze-dried bioluminescent bacterium *V. fischeri*. The experiment was carried out in accordance with the test conditions and standard operating protocol of the Microtox[®] acute toxicity test method. Luminescence was measured with a Microtox Model 500 photometer (Azur Environmental) in the acute mode. Various concentrations of triclosan solution (0.9, 0.45, 0.23, 0.11, 0.056, 0.028, 0.014, 0.007 and 0.0035 mg/L along with a control) were prepared as test solutions in duplicate. The study found an IC25 of 70 µg/L and an IC50 of 150 µg/L.

Ferrari et al. (2002) reported a 30 min study on the bacterium *V. fischeri* in a poster presented at SETAC Europe 2002. The poster quotes a EC50 of 246 µg/L for a study conducted according to AFNOR T90- 320-3 (1999) using the Microtox method. No further details of the study are available.

Table 21.7 - Ecotoxicity data for marine organisms

Species	Conditions	Endpoint	Result (µg/L)	Reference
<i>Palaemonetes pugio</i>	96 h	LC50	305 (adult) 154 (larvae) 651 (embryos)	Delorenzo et al. (2008)
	24 h	LC50	482	
	24 h with sediment	LC50	620	
Bacterium <i>Vibrio fischeri</i>	15 min	IC50	53	Delorenzo et al. (2008)
	-	IC25	70	Tatarazako et al. (2004)
	-	IC50	150	
-	30 min	EC50	246	Ferrari et al. (2002)
<i>Dunaliella tertiolecta</i>	96 h	EC50	3.55	Delorenzo et al. (2008)
Diatom <i>Skeletonema costatum</i>	96 h	ErC50	>66 (N)	Carolina Ecotox Inc (1997)

N = nominal concentration.

21.4.7 Aquatic ecotoxicity of treated sewage effluent

Laboratory studies

The ecotoxicity of triclosan in treated effluent from a laboratory-scale continuous activated sludge (CAS) unit was investigated in *C. dubia* and fathead minnows by

Orvos et al. (2002). Static renewal tests were conducted with *C. dubia* over 48 h using methods adapted from US EPA (1985a-b). Seven day static renewal tests were conducted with minnows using the larval growth assay (US EPA, 1985b). Test solution renewals were conducted at 24 hour intervals. Organisms were exposed to CAS treated effluent at dilutions from 0-100%. CAS influent triclosan concentrations ranged from 40-1000 µg/L; however, effluent (exposure) concentrations of triclosan were not determined. Treated effluents from both the control and triclosan-treatments each produced effects to *C. dubia* and minnows and the effect levels were similar. While the data suggest that the ecotoxicity of triclosan in wastewater effluent was being attenuated by wastewater constituents and/or conditions, no definitive conclusions can be made without information on the actual exposure concentrations. No data were available for algae species, which are considered more sensitive to triclosan than the animal species tested.

Field studies

Sydney Water Corporation has investigated the toxicity of the effluent from 17 STPs across the Hawkesbury-Nepean River catchment (Sydney Water Corporation 2000b). Samples were collected from the STPs on a minimum of three occasions during 1998-1999. The toxicity of the effluent samples were tested on the freshwater cladoceran *Ceriodaphnia dubia* and the unicellular green alga *Selenastrum capricornutum*. The levels of triclosan were not determined in the samples as this was not part of the study.

Overall, 50% of the samples tested exhibited acute toxicity to *C. dubia*, while 74% exhibited chronic toxicity to the cladoceran. Further investigation indicated that in most cases the observed toxicity to *C. dubia* was attributed to the presence of organophosphorus pesticides (such as diazinon and chlorpyrifos).

The growth of *S. capricornutum* was inhibited in 18% of the samples tested. Further investigation was unable to identify the toxicant responsible as the toxic effect dissipated. The investigations were able to show that the toxicant was a non- or moderately-polar organic and was not associated with the particulate phase.

While triclosan is a non- to moderately-polar organic which is very highly toxic to algae, the levels of triclosan were not determined in the samples and it is not possible to determine whether triclosan was contributing to these results.

21.4.8 Sediment dwelling organisms

Water column exposure

Dussault et al. (2008) have recently reported the toxicity of triclosan to two sediment dwelling organisms, the midge *Chironomus tentans* and the freshwater amphipod *Hyaella azteca* in 10 day waterborne exposures according to the U.S. EPA guidelines (US EPA 2000).

All experiments were conducted in 300-mL tall-form beakers, to which 50 mL of sand (particle size, 250–500 µm) were added in the *C. tentans* experiments. A small piece of cotton gauze was added in the *H. azteca* experiments to serve as substrate. All tests were conducted under static-renewal conditions, with water renewals performed every 48 h. The test containers were aerated continuously during the *C. tentans* assay, and pH, temperature, dissolved oxygen, and conductivity were monitored throughout the experiments. Water hardness,

alkalinity and ammonia were measured by colourimetric assay at the beginning of the experiment. Water samples were collected for residue analysis. On experiment completion, surviving animals were counted, dried, and weighed for growth calculation using ashfree dry weight for *C. tentans* and dry weight for *H. azteca*. Results are summarised in Table 21.8.

Table 21.8 - Toxicity endpoints (mg/L) for triclosan to sediment dwelling organisms for exposure through the water column

Endpoint	<i>Chironomus tentans</i>		<i>Hyalella azteca</i>	
	Survival	Growth	Survival	Growth
EC50	0.4 (0.27–0.44)	0.28 (0.208–0.362)	0.20 (0.144–0.257)	0.25 (0.09–0.40)
EC25	0.1 (0.09–0.14)	0.15 (0.088–0.212)	0.06 (0.039–0.084)	0.12 (0.05–0.20)
EC10	0.02 (0.011–0.055)	0.08 (0.027–0.131)	0.005 (0.028–0.039)	0.05 (0.02–0.08)

The above results indicate that triclosan is highly acutely toxic to sediment dwelling organisms when exposed through the water column.

Sediment exposure

Toxic effects of triclosan on the development of sediment-dwelling larvae of the midge *Chironomus riparius* in water-sediment systems were investigated according to the OECD Guidelines for Testing of Chemicals, 218: Sediment-Water Chironomid Toxicity Test Using Spiked Sediment (adopted 13 April 2004).

The radiolabelled test item was applied to the sediment in static water-sediment systems (Mommert 2006).

Triclosan was dissolved in acetone and applied to a portion of sand. Application solutions were prepared in acetone with concentrations of 0.56, 1.10, 2.22 4.43 and 8.86 mg/mL, before spiking the sediment. For spiking the sediment, volumes of 1.0 to 1.25 mL of the corresponding application solution were applied to 10 g of sand in a glass flask. The solvent acetone was completely evaporated by a stream of nitrogen at room temperature under a hood over night. Thereafter, 120 g of the wet sediment was weighed to the 10 g sand/test item mixture in the glass flask. To improve the mixing procedure of the spiked sediment, 10 mL of the test water were added. This spiked sediment was intensely shaken by hand and then mixed in the closed glass flasks on a roller mixer for about 2 hours. Afterwards the sediment was filled into the test beakers. The nominal initial test item concentrations in the sediments were 6.3, 12.5, 25, 50 and 100 mg Triclosan per kg dry sediment. A control (water-sediment systems without test item application) and a solvent control group (acetone) were tested in parallel. The spiked sediments were kept for two days under the test conditions to reach equilibrium between sediment and aqueous phases as pore water and overlying water. Then, first-instar larvae of *Chironomus riparius* were exposed for a period of 28 days until full maturation of the larvae to adult midges. The test parameters used were development time/rate of the midges and emergence ratio (sum of fully emerged

midges divided by the number of inserted larvae). The numbers were determined separately for males and females and both together.

The analytically measured concentrations of triclosan in the sediment samples ranged from 92 to 97% of the nominal values. The concentrations of triclosan in the sediment were constant over the test period of 28 days. The concentrations of triclosan and the radioactive residues in the overlying water columns were very low throughout the test period (<1% of applied radioactivity). Also in the pore water samples very low amounts of radioactivity was found ($\leq 0.1\%$ of applied radioactivity). This means that triclosan was mainly bound to the sediment, but most of this fraction was extractable.

Up to five different metabolites were detected, but no individual metabolite accounted for more than 4% of the applied radioactivity.

The mean emergence ratios and the mean development rates of the midges were not significantly lower than in the solvent control at any of the test concentrations. Thus, the 28 d NOEC of Triclosan in this sediment study was at least 100 mg/kg dry sediment. The 28 d LOEC was higher than 100 mg/kg dry sediment.

21.5 Micro-organisms

Triclosan has a specific mode of antimicrobial action in some bacteria; however, for others the mode of action is unclear. Several microbes are able to degrade triclosan, either through detoxification or as a sole carbon source (Hay et al., 2001).

21.5.1 Laboratory cultures

Inhibitory levels for various micro-organisms in various types of laboratory agar cultures include (Ciba Specialty Chemicals, 20003b):

- gram-positive bacteria 1 to >1000 ppm
- gram-negative bacteria 0.01 to >1000 ppm
- moulds and yeasts 1 to >1000 ppm

In some bacteria, triclosan blocks fatty acid synthesis by interacting with the NADP binding site of the enoyl-ACP reductase, FabI in *Escherichia coli* and InhA in *Mycobacterium tuberculosis* (Levy et al., 1999; McMurry et al., 1998, 1999; Heath and Rock, 2000; Hay et al., 2001). *Streptococcus pneumoniae*, which is sensitive to triclosan, does not contain the FabI homolog but does contain FabK, an isofunctional FAD-dependent enoyl-ACP reductase which is not sensitive to triclosan. This suggests another target in *S. pneumoniae*. *Pseudomonas aeruginosa*, which is highly resistant to triclosan, contains both FabI and FabK, in addition to an efflux pump capable of transporting triclosan out of the cell (Hay et al., 2001).

Microbial resistance mechanisms include up-regulation of *fabI* expression and spontaneous arising mutations in the *fabI* gene (Heath et al., 1998).

No data were available on the antimicrobial effects of triclosan on soil micro-organisms or processes (e.g. respiration, nitrification). Considering that triclosan is an anti-bacterial agent, adverse effects may be expected.

Fungicidal properties

In a 2-year study, Mmbaga and Sauve (2004) investigated the effect of topically applied products containing triclosan to powdery mildew (*Erysiphe pulchra* and *Phyllactinia guttata*) growing on the plant species flowering dogwood (*Cornus florida*). Products used in the study included Palmolive® Original Dish Soap, Equate® Antibacterial Liquid Hand Soap and Ajax® Antibacterial Dish Soap, each containing 0.2% triclosan (2 mg/mL) and other proprietary constituents. In addition to these biorational products, conventional fungicides and a blank (water) control were also tested. The treatments were applied in a randomised block design at a rate of 18.3 mL/L (36.6 mg triclosan/L) until leaf run-off occurred and when powdery mildew symptoms were first observed on the plants. Applications were made weekly or fortnightly using an 8002 flat fan nozzle and CO₂-pressurised backpack sprayer (275 kPa). Applications were made during 2 growing seasons (2000 and 2001). Effects on powdery mildew were made bi-weekly using a visual scale (0-5) of percent plant foliage showing disease symptoms. Although the control was heavily infested with powdery mildew, each of the treatments was effective against powdery mildew particularly when applied weekly. Mmbaga and Sauve (2004) indicated that in a separate study (unpublished), application of soap products containing no triclosan was ineffective at controlling powdery mildew, indicating that the effects observed in this study are likely attributable to triclosan. Currently, no soap products containing triclosan are registered for use as fungicides in agricultural situations.

21.5.2 Freshwater microbial populations

The general microbial ecosystem effects from environmental release of antimicrobial compounds into the aquatic environment have been discussed by Costanzo et al. (2005) and Summers (2002). The release of antimicrobial agents such as triclosan into the environment has the potential to change microbial communities and their genetics through selection of resistant individuals and promoting a negative effect on important ecosystem bacteria (through death or inhibition). The occurrence of triclosan-resistant microbes in the environment may potentially arise from concentrated sources (e.g. STPs) or from exposure to triclosan in the aquatic environment, although STP point sources are probably more prolific sources due to the higher triclosan concentration and microbial abundance. Given the past use of the products containing triclosan in Australia and the predominant sewer discharge pattern, microbial populations in the Australian aquatic environment are likely to have already been exposed to triclosan.

Once acquired, resistance genes are likely to be only slowly dissipated, if at all, from these microbial populations after cessation of exposure. Transfer of resistant genes among populations is also possible (e.g. plasmids) leading to a widespread reservoir of genetic material containing resistant traits away from the initial source. Resistance may not only occur in ecologically-beneficial (benign) microbial species but also those that are pathogenic to livestock and humans, thereby reducing the effectiveness of antibiotics on disease. Also at risk are aquatic ecosystems, which are largely controlled by, and dependent upon, micro-organisms for a suite of crucial processes (e.g. denitrification), association (e.g. nitrogen fixation) and services (e.g. organic matter breakdown), all of which can potentially be hindered by antibiotic substances. Although only limited studies of antimicrobial resistance have been conducted in natural microbial ecosystems in Australia, and none have included triclosan, the few studies that have been

conducted have detected antibiotics in discharges that are capable of influencing biotic processes (e.g., denitrification) and promoting resistance in these receiving environments (Costanzo et al., 2005).

Junker and Hay (2004) investigated the potential effect of triclosan that had been incorporated into acrylonitrile-butadiene-styrene (ABS) plastic on biofilm communities. Biofilms were cultivated on triclosan-incorporated ABS plastic (5% w/w or 5000 mg/kg) and control plastics in continuous flow culture reactors operated at 20°C to 22°C, with drinking water as the growth medium and inoculum. After 1-3 weeks of exposure, the plastics were removed and the biofilms aseptically harvested. There were no significant differences in community composition, direct cell counts, culturability and numbers of triclosan-resistant organisms that attached to the plastic surfaces. No triclosan (<0.1 µg/L) was detected in the water from the reactor vessels used, indicating that the leaching of triclosan was very limited if at all from the impregnated plastic.

21.5.3 Marine micro-organisms

As noted above in Section 21.4.5 several studies have been conducted on the marine bacterium *Vibrio fischeri*.

21.5.4 Sewage sludge organisms

There have been several studies conducted to evaluate the potential impacts of triclosan to the operation of sewage treatment plants.

The effect of triclosan on the respiration of activated sludge (as O₂ consumption) has been investigated under laboratory conditions by Miyazawa et al. (1983), finding effect levels in the relatively high concentration range of 50-150 mg/L.

Offhaus et al. (1978) reported that 2 mg/L of triclosan could inhibit the biodegradation of peptides by sewage microbes. However, inhibition is negligible at 2 mg/L if acclimation of sewage sludge occurs, thereby increasing the population of triclosan degrading micro-organisms in the sludge (Federle et al., 2002).

Ciba-Geigy Limited (1990g) investigated the effect of 3-h exposure to triclosan on a mixed culture of activated sludge organisms using OECD TG 209 Inhibition of Oxygen Consumption. A reference toxicant (3,5-dichlorophenol) was also tested, with an IC₅₀ value within acceptable criteria. Test concentrations (nominal) were 0.032, 0.1, 0.32, 1, 3.2, 10, 32 and 100 mg/L. The test was conducted at 21°C. The oxygen consumption (respiration rate) of each test concentration was measured with an oxygen-sensitive electrode system as a percentage of the mean of the controls. The percent inhibition of test concentrations ≥10 mg/L were 25.2, 68.3 and 84.5%, respectively. A median inhibition concentration (IC₅₀) of 20 mg/L was calculated.

Based on glucose utilisation (sludge activity) as the endpoint, Roy F. Weston Inc. (1990) reported a 15-minute median inhibition of heterotroph activity (HA₅₀) of 239 mg/L (95% CI 203-280) or 102 mg/g Volatile Suspended Solids (95% CI 87-120). The study, conducted using a non-standard method, was conducted at room temperature, in 100 mL polypropylene containers containing 1 mL of the appropriate test/reference substance or tap water. 100 µL of HCl was added to the 0 time controls. 23 mL of activated sludge mixed liquor was added to each beaker for

a 10 minute incubation period. 1 mL of a ^{14}C -d-glucose stock solution (500 mg active/L) was then added to the beaker for the 15-minute test period (continuously mixed). The test was terminated by the addition of 10 μL of HCl and the content of each container was allowed to settle before filtration (0.45 μm) and ^{14}C -assay. Exposure concentrations (nominal) were 3, 10, 30, 100, 300 and 1000 mg/L.

Stamatelatou et al. (2003) reported the effect of triclosan on biological processes undertaken by sewage sludge organisms in 2-hour batch-scale experiments involving activated sludge (1500 mg/L). The feeding medium contained acetate (chemical oxygen demand COD 300 mg/L, N and P source, buffer phosphate salts) and triclosan (0, 2, 4, 6, 8, and 10 mg/L). Triclosan treatments resulted in a small effect (25%-30% reduction in dissolved COD) on the activated sludge processes.

Nitrification is an important microbial process within the sewage treatment plant process, and the second step of nitrification; oxidation of nitrite to nitrate is particularly sensitive. Inhibition of this microbial process under uncontrolled conditions may lead to the accumulation of nitrite nitrogen in the STP effluent, a toxic form of nitrogen (Dokianakis et al., 2004). Batch tests have been conducted by Stamatelatou et al. (2003) to assess the effect of triclosan on the nitrification process. Four batch tests (6 h duration) were conducted in 250 mL flasks inoculated with nitrite oxidisers and fed a synthetic solution (NaNO_2 , NaHCO_3 , phosphate salts, trace elements) and triclosan (2, 6 and 10 mg/L). Triclosan caused significant inhibition of the nitrification process at all concentrations tested. The effect of triclosan on a mixed culture of nitrate oxidising bacteria has also been investigated by Dokianakis et al. (2004). Inoculum, consisted of mixed liquor from the aerobic stage of a STP, University of Patras (Greece), and this was used to isolate nitrite oxidising bacteria. In 250 mL batch reactors, the bacteria were exposed to one of four triclosan concentrations (0, 2, 6 and 10 mg/L) and the nitrification rate was measured over a 5-hour period at 25°C. The pH of the test solutions remained between 7.4 and 8.4. When compared to the control, triclosan had a substantial inhibitory effect on the substrate (nitrite) reduction rate at all test concentrations. The long-term effect of triclosan on nitrite-oxidising bacteria was also assessed using two completely stirred tank reactors, one a control, for 70 days (550 mL working volume with 12 days of retention time and with 60 mg/L of N-NO_2 in the feed). The initial triclosan concentration was 1 mg/L and this was increased to 5 mg/L (day 10) and 10 mg/L for the last 5 days of the test. As in the batch test, triclosan caused significant inhibition of nitrate oxidation during the first days of operation; however, no inhibition was observed for longer periods of operation and for higher concentrations of triclosan. Therefore, nitrite oxidising bacteria were able to adapt to the presence of triclosan in the culture medium at exposure concentrations up to 10 mg/L.

In a lab-scale continuous reactor experiment, Stamatelatou et al. (2003) investigated the effect of triclosan on the anaerobic sludge digestion process by COD measurement. The reactors operated at 35°C with a sludge retention time of 20 days. The synthetic feed included glucose, nutrients and trace metals and 10 mg/L of triclosan. Triclosan had a significant inhibitory effect on the anaerobic digestion process. Triclosan was persistent in acclimated activated sludge and anaerobically-digested sludge.

Neumegen et al. (2005) considered the toxicity of triclosan against activated sludge micro-organisms in a 5 day BOD test. An acclimated mixed cultors (seed) was the toxicity test system. The wastewater was prepared fresh and diluted by mixing

800 mL of distilled water with 200 mL of wastewater. The experiment used 12 BOD bottles and two separate BODTrak units. Each bottle contained 95 mL. Two bottles contained only the seed, and each of the remaining 10 bottles had 85.5 mL of diluted wastewater and 9.5% (10% seed by volume) at 5 concentrations (2 replicates at each concentration). Triclosan was tested at a concentration range of 0-2 mg/L. An additional control of wastewater and DMSO was run to observe the effects of the solvent. The BOD bottles were incubated at 20°C for 6 days and the data recorded continuously. DMSO had no toxicity at the tested concentration. Triclosan had a calculated EC50 of 1.82±0.1 mg/L.

21.5.5 Soil micro-organisms

Some preliminary results have been reported by Kookana (personal communication, 2006). The effect on soil biotic processes was investigated using two different soils types, a sandy loam and a clay soil. The soils were spiked with various concentrations of triclosan (0-100 mg/kg) and incubated. The microbial endpoints examined were: General microbial activity (Substrate Induced Respiration (SIR)); Specialist microbes (Substrate Induced Nitrification (SIN)); Enzymes - Acid Phosphatase Enzymes (P cycling by microbes); - Alkali Phosphatase Enzymes (P cycling by plant roots); and Beta-Glucosidase Enzymes (C cycling, breakdown of simple sugars). No effect was observed on the SIR in either soil. Some effects on the SIN were observed in both soils, with effects occurring at 5 mg/kg in the sandy loam soil and 50 mg/kg in the clay soil. An increase in acid phosphatase activity was observed at 5 mg/kg in sandy loam soil. No effect on alkali phosphatase activity was observed in either soil. No visible effect on Beta-Glucosidase activity was observed.

It should be noted that these are preliminary results and the details of the studies are insufficient to assess the impact of these results.

More recently, Völkel has investigated the effect triclosan on soil respiration (Völkel 2007a) and nitrification (Völkel 2007b). Both studies used the same soil. The properties of of the sandy loam soil are summarized below in Table 21.9.

The influence of triclosan on soil microorganisms was determined by measuring the microbial respiration in soil (Völkel 2007a) according to OECD Test Guideline 217. In the study, one fresh agricultural sandy loam soil, was moistened to 45% of its maximum water-holding capacity and incubated in the dark at 20 ± 2°C following treatment with the test item. Control soil was not treated with the test item, but was incubated in parallel under identical conditions as for the treated soil.

Soil samples were treated with the test item at rates corresponding to concentrations of 0.125 mg, 0.25 mg, 0.5 mg, 1.0 mg and 2.0 mg triclosan per kg dry soil (treatments I, II, III, IV and V, respectively).

After 28 days of incubation, the rate of respiration was 6.77 mg CO₂/h for the control and for the treated samples 6.13 mg (treatment I), 6.00 mg (II), 5.96 mg (III), 5.85 mg (IV) and 5.87 mg CO₂/h (V). In comparison to the untreated control, increasing deviations in respiration of -9.4% (treatment I), -11.3% (II), -12.0% (III), -13.5% (IV) and -13.2% (V) were observed for the treated samples.

Table 21.9 – Properties of soil used in soil microorganism toxicity studies

Parameters	Speyer 2.3
Soil Type (USDA)	Sandy loam
- Organic C (%)	1.02 ± 0.15
- Nitrate content (mg/kg dry soil)	95.4
- Total nitrogen (Ntot) (%)	0.06
- pH (CaCl ₂)	6.2 ± 0.3
- pH (water)	7.4
- Cation exchange capacity (mval/100 g soil)	9 ± 1
- Maximum water holding capacity (MWC) %	34.90 ± 3.0
- Bulk density (g/1000 mL)	1315 ± 84
Particle size analyses (mm):	
a) Classification USDA:	
< 0.002 (clay) %	9.2
0.002-0.05 (silt) %	29.8
> 0.05 (sand) %	61.0
b) Classification DIN:	
< 0.002 (clay) %	8.9
0.002-0.063 (silt) %	31.5
> 0.063 (sand) %	57.4
Microbial biomass (mg microbial C/kg dry soil)	134.2

The test item had no detrimental effect on soil microbial respiration after 28 days of incubation with triclosan, up to a concentration of 2.0 mg/kg dry soil. The reference item dinoseb acetate had a significant influence on the respiration (i.e., inhibition of -70.2% at day 28), thereby confirming the sensitivity of the test system and validity of the experimental design.

The influence of triclosan on the nitrification of lucerne meal in soil was investigated (Völkel 2007b) according to OECD Test Guideline 216. In this study, one fresh agricultural sandy loam soil was moistened to 45% of its maximum water-holding capacity and incubated in the dark at 20 ± 2°C following treatment with the test item. Control soil was not treated with the test item, but was incubated in parallel under identical conditions as for the treated soil.

Soil samples were treated with the test item at the same rates as the respiration study described above (Völkel 2007a).

For the control, the mean initial concentration of nitrite was 0.645 mg NO₂-/kg dry soil and for treatments I to V it was 0.606 mg/kg (treatment I), 0.637 mg/kg (II), 0.617 mg/kg (III), 0.620 mg/kg (IV), and 0.661 mg/kg (V), respectively. On day 28, no nitrite was detected for all treatments.

The nitrate concentration on Day 28 was 116.3 mg NO₃⁻/kg dry soil for the control and 105.4 mg/kg, 94.6 mg/kg, 105.0 mg/kg, 110.1 mg/kg and 107.4 mg/kg mg NO₃⁻/kg dry soil for the five treatment rates I to V, respectively. The calculated deviations to control were -9.3%, -18.6%, -9.7%, -5.4% and -7.6%, respectively.

A deviation of -7.6% from the control (nitrate) was obtained for the highest concentration tested, i.e. 2.0 mg a.i./kg dry soil after 28 days of incubation indicating that triclosan had no detrimental effect on the nitrification up to and including this concentration.

Furthermore, additional samples were treated with a reference compound, nitrapyrin (at a rate of 5 mg/kg soil), to show the sensitivity of the test system and method used. After 28 days of incubation, the calculated deviation to control was -82.4% for nitrate formation, confirming the validity of the test.

Appendix A - Australian Sewerage System

This Appendix provides a description of the Australian sewerage system, per capita and total wastewater generation rates, and uses for STP products (effluent and sludge).

1. Sewerage system processes, wastewater generation and effluent management

Currently, Australia has ~891 municipal STPs, mostly in New South Wales, Queensland and Victoria (Table A-1).

Table A-1. Estimated number of municipal STPs in Australia.

State/Territory	Number
NSW	318
QLD	259
VIC	174
WA	96
SA	23
TAS	30
ACT	2
NT	8
Estimated total	891

Source: ASTE (2004).

A range of municipal STPs are operated in Australia. Prior to the 1990's, no major Australian city had any more advanced sewage treatment than secondary treatment (generally screening of large solids, aeration to separate grit and promote settling, oil/floatables collection, microbiological treatment). Some were discharging primary treated effluent (generally the above without microbiological treatment) to high-energy ocean coastlines (Dillon, 2000).

Municipal STPs comprise a range of designs and operational features; however, general levels of treatment may be broadly described as (in sequential order) preliminary, primary, secondary, tertiary/advanced treatments processes (refer below).

- Preliminary treatment: Untreated wastewater (e.g. raw sewage) entering a STP, it undergoes preliminary treatment by passing through bar screens and a grit chamber(s) to remove large objects and grit that may interfere with other processes and equipment.

- Primary treatment: Primary treatment removes a fraction of the settleable material, floatable material and biological oxygen demand (BOD) from the wastewater passing the preliminary treatment using settling tanks (clarifiers) with baffles, weirs and skimmers. The treated effluent is referred to as primary effluent and the solids collected in the settling tanks are referred to as primary (raw) sludge.
- Secondary treatment: Secondary treatment removes much of the remaining suspended solids and biologically (aerobically) lowers the BOD of the effluent (secondary effluent). The two most common aerobic systems used include trickling filter (TF) and activated sludge (AS) processes. Each method produces secondary sludges (TF and AS sludge).
- Tertiary and more advanced treatment processes remove more of the solids, BOD, and nutrients from the wastewater, using processes such as sand filters, bioreactor tanks and/or ponds. Chemicals may also be used to enhance treatment processes.
- Disinfection: Most commonly, chlorine is added to the treated effluent to kill pathogens. Effluent may also be dechlorinated. Disinfection may also include exposing effluent to ultraviolet (UV) light.
- Digested sludge: Sludge collected in sedimentation tanks/clarifiers (primary, secondary, other) may be further anaerobically digested in a digester to microbiologically stabilise the biodegradable solids in the sludge (e.g. cellulose, lignin, proteins, lipids) to simpler compounds (e.g. methane, CO₂). Stabilised sludge (biosolids) is used for soil conditioning, landfilled or incinerated.

A summary of wastewater generation and re-use rates in Australia is presented in Tables A-2 and A-3.

As indicated in Table A-3, the proportion of treated sewage effluent re-used in Australia varies by State/Territory. In 1998-9, only three of the largest 21 water utilities re-used greater than 10% of their treated effluent; Goulburn Valley Water re-used 72%, Coliban Water 41%, and Melbourne Water 19%. In the same year, three minor urban utilities achieved 100% effluent re-use; Albury, Bathurst and Lower Murray. In dry low-density cities such as Perth, Canberra and Adelaide, effluent discharge is about 50% of mains water inflow as the other half is used on gardens and parks. However, areas with wetter climates have a higher ratio (e.g. <25% in Sydney). Some country towns with sewerage or common effluent schemes re-use up to 100% of reclaimed water for watering golf courses, ovals and parks, as well as local commercial crops (Dillon, 2000). Although the majority of treated effluent from the Australian sewerage system will continue to be discharged to surface waters (creeks, rivers, ocean) in the foreseeable future, the level of treatment and diversion for re-use are increasing and several operations utilize the majority of their effluent.

Table A-2. Annual wastewater generation and re-use from STPs in Australia

Period	Wastewater (GL/y)	Effluent Re-use (GL/y)	Percentage (%)	Reference
1997*	1350	Unknown	---	ASTE (2004)
1996-9	1538	113	7.3	ASTE (2004)
1998	1614	113	7.0	Dillon (2000)
2000	1824	167	9.0	ASTE (2004)
2008**	1700	328	20	Dillon (2000)

* Major Australian cities. ** Predicted estimates.

On a per capita basis, in 2000 wastewater generation was ~250 L/person/day (population ~20 million) and by 2008, the value is estimated to decline to ~220 L/p/d (population ~ 21 million). By interpolation, estimated average values for 2002, 2003 and 2004 are ~246, 241 and 237 L/p/d, respectively (mean 241 L/p/d).

Table A-3. Wastewater generation and re-use in Australia in 2000.

State/Territory	Wastewater (GL/y)	Effluent Re-use (GL/y)	Percentage Re-use (%)
NSW	694	61.5	8.9
VIC	448	30.1	6.7
Qld	339	38	11.2
WA	126	12.7	10.0
SA	101	15.2	15.1
TAS	65	6.2	9.5
ACT	30	1.7	5.6
NT	21	1.1	5.2
Total	1824	166.5	Average 9.0

Source: ASTE (2004).

In consultation with States/Territories, Environment Australia (2003) has developed a simplified STP model for estimating wastewater generation in Australia. The model assumes an Australian population of 20.1 million people generated 200 Litres of wastewater per person per day (4020 ML/d), or ~1470 GL/annum, and the estimate slightly underestimates the generation rate for 2003-4 of 237 L/person/day derived above.

1.1 NSW

Although the Sydney regions' 27 STPs generate ~1400 ML/d, most of the effluent (~98%) is not re-used, but is discharged to either inland rivers or the ocean (ASTE, 2004). The level of treatment of wastewater varies and most STPs provide secondary or greater treatment. However, three large STPs (Malabar, North Head and Bondi) that treat around 75% of Sydney's wastewater provide only high flow primary treatment before the effluent is discharged to offshore ocean outfall.

In regional NSW, coastal STPs typically discharge to ocean outfalls or coastal rivers. In the Hunter Region, ~10% of the effluent generated from 22 STPs was re-used, with uses including industrial applications and irrigation of parks, gardens, golf courses and woodlots. Wastewater is treated for re-use using oxidation ditches with extended aeration, extended aeration or trickling filter processes. Throughout the remainder of NSW, the level of wastewater treatment varies from primary to tertiary (e.g. primary pasveer ditches, oxidation ponds/ditches, trickling filter, activated sludge, extended aeration and combinations of processes; ASTE, 2004).

1.2 Victoria

Victoria has 19 water authorities operating 174 STPs, 15 with coastal discharges. Most STPs discharge to inland waters, and about 50% reclaim all of their treated effluent, representing a relatively small volume compared to the coastal STPs discharge (ASTE, 2004). Approximately 30 GL/y of the effluent produced in Victoria (448 GL/y) is reclaimed, and 6 GL/y (2%) of the 295 GL/y generated in Melbourne is reclaimed. The level of wastewater treatment varies widely in Victoria from primary to tertiary (e.g. high rate oxidation lagoon, aerated lagoon, extended aeration, oxidation pond/ditch, trickling filter, activated sludge, biological nutrient removal).

1.3 Queensland

In Queensland, most of the wastewater generated each year (340 GL/y) is disposed of into waterways, and mostly rivers and estuaries (Rhyne and Dart, 1997). Brisbane's 10 STPs generate ~106 GL of effluent annually, with ~5.3 GL (5%) re-used; golf courses, landscaping and industrial purposes. Most of the effluent re-used in Queensland (38 GL/y) originates from conventional activated sludge and trickling filter operations. An industrial application in Brisbane uses tertiary (reverse osmosis) treated effluent. Some reclaimed water derives from oxidation ditches or Imhoff tanks followed by lagoons, biological nitrogen reduction and claridigestors. The majority of the effluent is disinfected using chlorine (77%) or ultraviolet light (4%) individually or combined (2%). A further 11% use lagoons or ponds in series for disinfection (Rhyne and Dart, 1997). Treated effluent is used at STPs (e.g. wash down water, irrigation), or for irrigation of golf courses, parkland, gardens or woodlots and agriculture (e.g. sugarcane; ASTE, 2004; Rhyne and Dart, 1997).

1.4 Western Australia

In Western Australian, Perth's wastewater (~102 GL/y) is mostly secondary treated at one of nine STPs and discharged to ocean outfall. Only ~3.3% is reclaimed for re-use mainly at STPs or for industrial purposes. About 15% of Perth's households are not connected to the sewerage system. Several smaller STPs discharge ~2 GL/y of treated effluent to surface infiltration channels, with a potential for infiltration to groundwater. Regional STPs reclaim ~41% of effluent for uses including woodlots, pasture, sporting grounds, parkland, mine rehabilitation, golf courses and industrial uses (ASTE, 2004).

1.5 South Australia

In Adelaide, the four metropolitan STPs (Bolivar, Port Adelaide, Glenelg, Christies Beach) treat ~90-95 GL/y, 85% being discharged via ocean outfall after secondary

or greater treatment (e.g. activated sludge with dissolved air flotation, integrated fixed film activated sludge). Reclaimed effluent is used for agricultural crops and municipal parks. A further 19 regional STPs (14 inland, 5 coastal) treat ~10 GL/y, with discharges to inland waterways (~28%) and ocean (57%) and ~15% is reclaimed. The majority that is reclaimed originates from STPs providing primary or secondary treatment (e.g. oxidation ponds/ditches, aerated ponds, trickling filter, or STEDS/oxidation pond) (ASTE, 2004).

1.6 Tasmania

Historically, ~80% of treated effluent in Tasmania has been discharged to waterways (estuaries 61%, coastal 21%, inland 11%, bays 7%). However, it is likely that 70%-80% of wastewater generated in Tasmania will be reclaimed and re-used by 2005, and all new systems require some form of recycling under State Policy. Most STPs in Tasmania treat effluent to at least secondary, with some tertiary systems. Many STPs have schemes for up to 100% effluent re-use. Uses include irrigation of golf courses, sporting fields, parks and agriculture (e.g. dairy; ASTE, 2004).

1.7 Australian Capital Territory

In the ACT, practically all wastewater generated is treated at the Lower Molonglo Water Quality Control Centre (activated sludge; ~30 GL/y), with most of the treated effluent (~94%) discharged to the Molonglo River (ACT Commissioner for the Environment, 2000). Approximately 6% of effluent is re-used for irrigation of vineyards and golf courses (ASTE, 2004). A smaller STP at Fyshwick (~0.6 GL/y) operates oxidation ponds and microfiltration, with effluent re-used for parks and gardens (ASTE, 2004).

1.8 Northern Territory

Approximately 21 GL of effluent is generated each year in the Northern Territory. Most is discharged into waterways and most of the effluent re-used (1.1 GL/y) derives from oxidation ponds or activated sludge processes (ASTE, 2004). Effluent is re-used for irrigation of sporting fields, golf courses, rail corridors, woodlots, native bushland and pasture at cattle feedlots.

2 Uses of treated effluent

Potential options for reclaimed effluent include:

- Irrigation: domestic gardens, parks, landscaped areas, racecourses, sporting ovals, school grounds, cemeteries, golf courses, agricultural crops (orchards, cut flowers, sugar cane, tea-trees, stonefruit, olives, grapes), forestry (e.g. woodlots), pastures for livestock production (beef, dairy, sheep), turf farms, nurseries, army firing ranges, bowling greens and hydroponic systems;
- Industrial: timber mills, truck washing, mining process water, dust suppression, paper mills, power stations, tanneries, commercial car washes, petroleum refineries, manufacturing facilities (concrete, bricks, textiles, metals, paints), road construction and distilleries; and
- Environmental flows, wetland rehabilitation and dune stabilization.

- Use of effluent as cooling water in con-generation plants. This water gets hot and contaminants in the water tend to become concentrated prior to discharge.

A fraction of reclaimed effluent may not be re-used and may subsequently be discharged to waterways, typically under regulatory authority license conditions.

3 STP sludge management

Long (2001) estimated that major urban water authorities in Australia produce 185 000 tonnes of biosolids per annum. Traditionally, sewage sludge was disposed of to landfill or incinerated and these practices continue in parts of Australia (e.g. incinerated in ACT). However, an increasingly larger proportion is being reclaimed as biosolids and re-used for soil conditioning. In Sydney in 2002-3, Sydney Water Corporation captured solids to the equivalent of ~51000 dry tonnes of biosolids of which 100% was used for soil conditioning applications in agriculture (60%), forestry (20%-35%), land rehabilitation, landscaping and horticulture (5%-20%). In 2005-2006, Sydney Water produced 50489 dry tonnes (191 296 wet tonnes) of biosolids, 100% of which was used for agricultural or horticultural purposes (Sydney Water Corporation 2006). In Victoria, about 70000 tonnes (dry) of biosolids is produced annually, and there is almost 2 Mt stockpiled, mainly at 2 metropolitan STPs. Allowable uses of biosolids in Victoria include soil conditioning of agricultural, lands (cropping systems, grazing lands), landscaping, forestry, land restoration, and energy recovery (Victorian Natural Resources and Environment, 2002). In Western Australia, practically all biosolids collected at Perth's STPs are re-used for soil conditioning (Water Corporation, 2003) and a similar use is likely in Tasmania (DPIWE, 2003).

Appendix B - Wildlife Exposure Model

This Appendix provides a description of the wildlife exposure model used for this assessment.

In general, wildlife may potentially be exposed to one or more environmental media (e.g. surface waters, sediments, soils, air), each of which may potentially contain triclosan, and multi-media exposure may occur concurrently (e.g. oral, dermal and/or inhalation). Triclosan has a high affinity to lipids and a high propensity for bioaccumulation, as indicated by biological tissue residue monitoring conducted in other parts of the world, and wildlife may be exposed to triclosan through consumption of foods (foodchain or secondary exposure).

The predominantly sewer disposal route for products containing triclosan and the predominant discharge of effluent to the aquatic compartment highlights the potential for triclosan to be released into aquatic ecosystems. Wildlife species associated with these aquatic environments may potentially be exposed to triclosan following effluent discharge to surface waters as follows:

Untreated wastewater storage/treatment in surface waterbodies (e.g. lagoons, ponds)	<ul style="list-style-type: none">• Consumption (as drinking water)• Skin contact and absorption
Effluent discharge to surface waters (primary, secondary, tertiary)	<ul style="list-style-type: none">• Consumption (as drinking water)• Skin contact and absorption
Sedimentation arising from primary, secondary and tertiary effluent	<ul style="list-style-type: none">• Incidental consumption of sediment (e.g. during foraging)• Skin contact and absorption
Bioaccumulation in aquatic organisms	<ul style="list-style-type: none">• Consumption of biota (food)

The main recycled products from the sewerage system include biosolids and effluent, each of which may potentially contain triclosan. Biosolids are used for soil conditioning (e.g. agricultural lands, land rehabilitation), potentially providing a pathway for triclosan to enter the soil environment. Reclaimed effluent is used for irrigation (e.g. golf courses, parklands, crops), potentially providing a pathway for release of triclosan into wildlife habitats.

Wildlife species associated with terrestrial environments may potentially be exposed to triclosan following re-use of effluent or biosolids as follows:

- | | |
|---|--|
| Effluent irrigated to soil (primary, secondary, tertiary) | <ul style="list-style-type: none">• Consumption (as drinking water)• Skin contact and absorption |
| Biosolids application to soil (primary, secondary, tertiary sludge) | <ul style="list-style-type: none">• Incidental consumption of soil during foraging, preening, dust bath activities• Skin contact and absorption |
| Bioaccumulation in soil organisms (from effluents and/or biosolids application) | <ul style="list-style-type: none">• Consumption of organisms as food |

For this assessment, it is assumed that wildlife obtain all of their food and water within the area of contamination based on the calculated PEC values. A more detailed level of assessment is beyond the scope of this assessment. However, wildlife that have home ranges of size greater than the area of contamination will likely have less exposure than animals with smaller home ranges. Exposure may be seasonal or intermittent for migratory species of wildlife relative to sedentary species. In addition, their prey may move in and out of contaminated areas, thereby the potential for bioaccumulation of triclosan in prey may be less than for sedentary prey.

The potential for exposure by wildlife to triclosan has been evaluated using bird and mammal examples as most of the data available relates to these taxonomic groups.

Wildlife exposure model

Total exposure to environmental media by wildlife may be estimated using the following model equation:

$$\text{Exposure}_{\text{total}} = \text{Exposure}_{\text{oral}} + \text{Exposure}_{\text{dermal}} + \text{Exposure}_{\text{inhalation}} \quad (\text{Eq. 1})$$

In the above equation, oral exposure routes are considered more likely to occur or be relatively more significant for triclosan. Although all potential pathways for exposure to triclosan have been considered in this assessment, oral exposure routes are of greatest importance (e.g. food consumption, drinking water, incidental sediment ingestion). Triclosan is not volatile and inhalation exposure is unlikely to be a significant exposure pathway for wildlife. Although dermal absorption of triclosan can potentially occur, there is considerable uncertainty in estimation of dermal uptake rates by wildlife from exposure to solutions containing triclosan. In general, features such as oily fur and feathers and toughened skin, are likely to reduce the potential for skin contact with environmental media and absorption (Sample et al., 1997).

Daily exposure by wildlife to triclosan through oral routes, normalised to body weight, may be estimated using the following general equation:

$$\text{Total Exposure (E}_j\text{)} = \sum_{i=1}^m (I_i \times C_{ij} \times B_{ij})/\text{bw} \quad (\text{Eq. 2})$$

Where:

E_j = total exposure to contaminant (j) (mg/kg bw/day);

m = total number of media (e.g. food, water, sediment);

I_i = intake (ingestion) for medium (i) kg/kg bw/day or L/kg;

C_{ij} = concentration of contaminant (j) in medium (i) mg/kg or mg/L;

B_{ij} = relative bioavailability of the contaminant (assumed to be 1);

bw = body weight.

Note that soil/sediment consumption rates are expressed in dry weight. All other intake rate units are fresh, live or wet weight (Sample and Suter, 1994).

Values for contact rate factors such as food and water ingestion rates (I) have been measured for few wildlife species. As such, exposure by wildlife species has been estimated using models based on allometric equations of intake parameters. Allometry is defined as the study of the relationships between the growth and size of one body part to the growth and size of the whole organism; however, allometric relationships also exist between body size and other biological parameters (e.g. metabolic rate, food and water consumption rates; US EPA, 1993; refer below).

The assessment endpoint (goal) for this risk assessment involves wildlife protection in general. In order to assess the risks to all wildlife species, a range of body weights covering the range of wildlife species with the potential to be exposed to environmental media containing triclosan have been assessed (i.e. 0.01-1.5 kg bw). In general, smaller animals have a greater exposure per unit body weight than larger animals.

As a range of species have been considered, a range of animal body weights from 0.01-1.0 kg have been used in the model to calculate exposure by the routes of drinking water ingestion, diet and sediment ingestion.

Estimated environmental media concentrations of triclosan (C_j).

Surface waters

PEC values for triclosan in fresh and marine waters and freshwater and marine fish have been presented in Tables B-2 and B-3, respectively. A range of PEC values have been used that reflect the broad levels of wastewater treatment.

Exposure regimes are assumed to be at equilibrium and therefore concentrations in environmental media to which wildlife are exposed are assumed to be relatively constant. Most environmental release scenarios for triclosan support this view (e.g. continuous STP release of effluent to waterways). Concentrations of triclosan, and therefore potential for greater exposure by wildlife, is likely to be greater nearer sources of triclosan (e.g. STP discharge outlets).

Food intake rate

Food ingestion rates by animals vary with many factors, including metabolic rate, the energy devoted to growth and reproduction, and composition of the diet, which

may vary daily, seasonally or lifestage. The metabolic rate of free-ranging animals is a function of several factors, including ambient temperature, activity levels and body weight. In birds and mammals, thermoregulation can considerably increase metabolic requirements during winter in cold climates, and reproductive efforts can replace thermoregulation as the predominant extra metabolic expenditure in the breeding season (US EPA, 1993).

Measured food intake rates for most Australian wildlife are not available, and food intake rates have been estimated in this assessment using allometric equations (US EPA, 1993). Nagy (1987) calculated food ingestion rates from metabolisable energy and field metabolic rates and developed the following allometric equations:

Birds:

$$\text{Food Ingestion (kg}_{\text{food[dry wt]}}/\text{kg-bw/day)} = (0.0582 \times \text{bw}^{0.651})/\text{bw} \quad (\text{Eq. 1})$$

Mammals:

$$\text{Food Ingestion (kg}_{\text{food[dry weight]}}/\text{kg-bw/day)} = (0.0687 \times \text{bw}^{0.822})/\text{bw} \quad (\text{Eq. 2})$$

In the above equations, bw is body weight in kilograms live weight. Food intake rate is initially calculated on a dry weight basis. Before estimation of contaminant dose, the units for food intake rate must correlate to the units for concentration of contaminant in food items. This may involve adjustment for moisture content of food items (US EPA, 1993).

Drinking water intake rates

Most wildlife drink water, and intake rates vary within and among species. However, few data are available on drinking water intake rates of Australian wildlife. Daily water requirements of wildlife depend on their rate of loss of water to the environment due to evaporation and excretion, which may vary spatially and temporally for individual animals. Water evaporation and excretion rates depend on several factors including body size, ambient air temperature, and physiological and behavioural adaptations for conserving water. Many drier climate species have physiological adaptations to reduce drinking water requirements.

Sources of water for animals include free (drinking) water, metabolic water derived from the breakdown of food, and water moisture in food, and the total contribution of water intake may be derived from one or more sources concurrently. Taking into account dietary and metabolic water intake rates, Calder and Braun (1993) developed a general allometric equation for drinking water intake (I_{water}) by birds that is based on body weight as follows:

Birds:

$$\text{Water Intake Rate (I}_{\text{water}}; \text{L/kg-bw/day)} = (0.059 \times \text{bw}^{0.67})/\text{bw} \quad (\text{Eq. 3})$$

Where bw = body weight (kg wet weight).

Calder and Braun (1993) obtained data from 21 avian species of between 11 to 3150 grams body weight to develop Equation 3.

Based on measured body weights and drinking water intake from Calder (1981) and Skadhauge (1975), Calder and Braun (1993) developed an allometric equation for drinking water intake rates for mammals as follows:

Mammals:

$$\text{Water Intake Rate (I}_{\text{water}}; \text{L/kg-bw/day}) = (0.099 \times \text{bw}^{0.90})/\text{bw}$$

(Eq. 4)

Where bw = body weight (kg wet weight).

Equations 3 and 4 have been used to estimate drinking water intake rates for avian and mammalian wildlife species for this assessment.

These water intake rates are considered estimates only and daily water intake by birds and mammals may be more or less than estimated by Calder and Braun (1993), particularly depending on environmental conditions (e.g. temperature).

Drinking by wildlife may occur once or at a number of times during the day, and subsequently the amount consumed at a particular time may be all or part of the total daily requirement. The frequency and time of drinking water depends on the individual (e.g. condition, gender, size, reproductive status), species and environmental conditions. Furthermore, the daily dose of contaminant received may potentially be less where uncontaminated sources of drinking water are also accessible to wildlife.

For this assessment, it is assumed that the daily water requirements for wildlife are obtained only from the specific contaminated sources being evaluated. This assumption incorporates all possible wildlife exposure scenarios.

Sediment ingestion

In general, animals may incidentally ingest soils and sediments during daily activities (e.g. foraging, preening, nesting, burrowing) and through consumption of foods, and may also ingest soils/sediments intentionally to obtain minerals (e.g. salt; Weeks, 1978).

Ingestion of soils/sediments by animals during daily activities provides a pathway for exposure to the contaminants that may be present in these environmental media (Arthur and Alldredge, 1979; Garten, 1980; Beyer et al., 1994, 1998; Blus et al., 1999; Johnson et al., 1999).

Beyer et al. (1994) indicated that animals that prey on soil/sediment invertebrates might ingest relatively more soil/sediment than other animals with different foraging behaviour. Waterbirds that may be relatively more exposed include species that probe or dabble in, or pick invertebrates from, sediments. Due to their foraging regime, waterbirds such as herons, cormorants and pelicans may not be as exposed to sediments. However, even predatory species that would normally not be exposed to sediments may be exposed during foraging on invertebrate or vertebrate carcasses trapped in sediment.

In general, the sediment ingestion rates by wildlife cited in the literature should be viewed as estimates only (Beyer et al., 1994). Furthermore, due to the methods of determination used, these estimates should be viewed as the total sediment/soil intake from all sources. Site-specific studies are preferred in order to accurately

estimate soil/sediment ingestion by wildlife. However, the information available from literature sources provides a basis for estimating soil/sediment ingestion.

Mammals vary in their intake of soil or sediment. Estimates available indicate an intake rate, presented as a percentage of total food intake rates, of <2% to 9.4%, with most estimates being <3% (US EPA, 1993). Intake values for food and sediment are presented on a dry weight basis and the units must be directly comparable to analyte concentrations for risk characterisation.

Within the waterbird group, there is insufficient information to allow prediction of which species consistently ingests the most sediment. Furthermore, features such as feeding habits (Reeder, 1951) or bill length (Hui and Beyer, 1998) are poor indicators of sediment ingestion rates. Few studies reported in the literature have investigated temporal variability in sediment or soil ingestion rates by the same species, and fewer have correlated sediment or soil ingestion with other factors including nutritional requirements, weather, relative prey abundance and prey micro-habitat. However, studies of mallards from various areas (Connor, 1993; Beyer et al., 1994) demonstrate intra-species sediment ingestion variation.

Table B-1 presents estimates of sediment ingestion rates as a percentage of total daily food intake rates by waterbirds. As indicated in Table B-1, estimated sediment consumption rates may vary, ranging from 0 to 71% of food intake (by weight). An average sediment intake rate equivalent to approximately 20% of dietary intake has been assumed for this assessment. This estimate is within the range of estimates for various probing and dabbling shorebirds (i.e. 0 to 30%) but may under- or over-estimate the estimated intake by other species. As sediment intake rate has been estimated as a percentage of food intake rate, estimation of food intake rate is required and methods to estimate these have been presented above. For this assessment, daily sediment/soil ingestion by birds is assumed to represent 0 to 20% of the food intake rate each day (refer Table B-1). For mammals, the estimated range of sediment intake rate is 0 to 3% of food intake rate (US EPA, 1993). As indicated above, incidental sediment intake may vary depending on individuals and species.

Table B-1. Estimates of sediment ingestion rates by various waterbirds

Group and Species	Estimated Sediment Ingestion rate as a percentage of total dietary intake (%)	Source
<i>Probing Shorebirds</i>		
Non-specific (8 spp.)	10 to 60%	Reeder (1951)
Sandpipers <i>Calidris</i> spp.	7 to 30%	Beyer et al. (1994)
Black-bellied Plover <i>Pluvialis squatarola</i>	29%	Hui and Beyer (1998)
Willetts <i>Cataporphorus semipalmatus</i>	3%	
<i>Waterfowl</i>		
Non-specified species	0.1 to 71% of diet, mean of 19%	Heinz et al. (1999)
Mallards <i>Anas platyrhynchos</i>	7.5% (n = 28 mallards) 11.7% (n = 30 mallards) 3.3% (n = 88 mallards)	Conner (1993) Beyer et al. (1994)
Wood Ducks <i>Aix sponsa</i>	<2%	Beyer et al. (1994)
Blue-winged Teal <i>Anas discolor</i>	<2%	
Tundra swans <i>Cygnus columbianus</i>	9% (average), 22% (90 th p'tile)	Beyer et al. (1998)
American Widgeon <i>Anas americana</i>	5.9%	Beyer et al. (2000)
Green-winged Teal <i>Anas crecca</i>	1.9%	
Northern Pintail <i>Anas acuta</i>	1.6%	
American Black Duck <i>Anas rubripes</i>	1.4% (Average of 2.4%)	

Table B-2. Potential bird intakes of triclosan from the freshwater aquatic environment

Effluent Source	Maximum Freshwater PEC (mg/L)	Freshwater Biota PEC ^a (mg/kg dry weight)	Body weight (kg live weight)	PEC Drinking Water Exposure (mg/kg bw/d)	PEC Food Exposure ^b (mg/kg bw/d)	PEC Sediment Exposure (mg/kg bw/d) ^c	Total PEC ^d (mg/kg bw/d)
Untreated wastewater	0.0174	434	0.01	0.00469	126	3.59	130
			0.1	0.00219	56.5	1.61	58.1
			1.0	0.00103	25.3	0.720	26.0
Primary Treatment	0.0170	425	0.01	0.00458	123	3.51	127
			0.1	0.00214	55.2	1.57	56.8
			1.0	0.00100	24.7	0.704	25.4
Trickling Filter	0.00730	183	0.01	0.00197	53.0	1.51	54.5
			0.1	0.000921	23.7	0.676	24.4
			1.0	0.000431	10.6	0.302	10.9
Activated Sludge	0.00782	196	0.01	0.00211	56.8	1.62	58.4
			0.1	0.000986	25.4	0.724	26.1
			1.0	0.000461	11.4	0.324	11.7
Activated sludge (SimpleTreat)	0.00678	170	0.01	0.00183	49.2	1.40	50.6
			0.1	0.000855	22.0	0.627	22.7
			1.0	0.000400	9.86	0.281	10.1
Tertiary treatment	0.00226	56.5	0.01	0.000609	16.4	0.467	16.9
			0.1	0.000285	7.34	0.209	7.55
			1.0	0.000133	3.29	0.094	3.38
Measured Australian Data	0.00074	19	0.01	0.00020	5	0.15	6
			0.1	0.00009	2.4	0.07	2.5
			1.0	0.00004	1.1	0.031	1.1

a. BCF value used = 5000 .b. Wildlife exposure is calculated by multiplying the body weight-normalised food intake rate (kg dry wt/kg bw live wt/day) for each body weight range by the food concentration (Biota PEC). c. Based on the sediment forming 20% of dietary intake. d. Determined by summing the water food and sediment exposure.

Table B-3. Potential bird intakes of triclosan from the marine aquatic environment

Effluent Source	Maximum Marine PEC C (mg/L)	Marine Biota PEC ^a (mg/kg dry weight)	Body weight (kg live weight)	PEC Drinking Water Exposure (mg/kg bw/d)	PEC Food Exposure ^b (mg/kg bw/d)	PEC Sediment Exposure (mg/kg bw/d) ^c	Total PEC ^d (mg/kg bw/d)
Untreated wastewater	0.00174	43.4	0.01	0.000469	12.61	0.359	13.0
			0.1	0.000219	5.65	0.161	5.81
			1.0	0.000103	2.53	0.0720	2.60
Primary Treatment	0.00170	42.5	0.01	0.000459	12.3	0.351	12.7
			0.1	0.000215	5.52	0.157	5.68
			1.0	0.000100	2.47	0.0704	2.54
Trickling Filter	0.000730	18.3	0.01	0.000197	5.30	0.151	5.45
			0.1	0.0000920	2.37	0.0676	2.44
			1.0	0.0000431	1.06	0.0302	1.09
Activated Sludge	0.000782	19.6	0.01	0.000211	5.68	0.162	5.84
			0.1	0.0000986	2.54	0.0724	2.61
			1.0	0.0000461	1.14	0.0324	1.17
Activated sludge (SimpleTreat)	0.000678	17.0	0.01	0.00018	4.92	0.140	5.06
			0.1	0.0000855	2.20	0.0627	2.27
			1.0	0.0000400	0.986	0.0281	1.01
Tertiary treatment	0.000226	5.65	0.01	0.0000609	1.64	0.0467	1.69
			0.1	0.0000285	0.734	0.0209	0.755
			1.0	0.0000133	0.329	0.00936	0.338
Measured Australian Data	0.000074	2	0.01	0.000020	0.5	0.015	0.6
			0.1	0.000009	0.24	0.007	0.25
			1.0	0.000004	0.11	0.003	0.11

a. BCF value used = 5000 .b. Wildlife exposure is calculated by multiplying the body weight-normalised food intake rate (kg dry wt/kg bw live wt/day) for each body weight range by the food concentration (Biota PEC). c. Based on the sediment forming 20% of dietary intake. d. Determined by summing the water food and sediment exposure.

Table B-4. Potential mammal intakes of triclosan from the freshwater aquatic environment

Effluent Source	Maximum Freshwater PEC C (mg/L)	Freshwater Biota PEC ^a (mg/kg dry weight)	Body weight (kg live weight)	PEC Drinking Water Exposure (mg/kg bw/d)	PEC Food Exposure ^b (mg/kg bw/d)	PEC Sediment Exposure (mg/kg bw/d) ^c	Total PEC ^d (mg/kg bw/d)
Untreated wastewater	0.0174	434	0.01	0.00273	68.2	0.291	68.4
			0.1	0.00217	54.1	0.231	54.4
			1.0	0.00172	43.0	0.184	43.2
Primary Treatment	0.0170	425	0.01	0.00267	66.7	0.285	67.0
			0.1	0.00212	53.0	0.226	53.2
			1.0	0.00168	42.1	0.180	42.3
Trickling Filter	0.00730	183	0.01	0.00115	28.6	0.122	28.8
			0.1	0.000910	22.7	0.0972	22.8
			1.0	0.000723	18.1	0.0772	18.15
Activated Sludge	0.00782	196	0.01	0.00123	30.7	0.131	30.8
			0.1	0.000975	24.4	0.104	24.5
			1.0	0.000774	19.4	0.083	19.4
Activated sludge (SimpleTreat)	0.00678	170	0.01	0.00106	26.6	0.114	26.7
			0.1	0.000845	21.1	0.090	21.2
			1.0	0.000671	16.8	0.072	16.85
Tertiary treatment	0.00226	56.5	0.01	0.000355	8.87	0.038	8.90
			0.1	0.000282	7.04	0.0301	7.07
			1.0	0.000224	5.59	0.0239	5.62
Measured Australian Data	0.00074	19	0.01	0.000116	2.9	0.012	2.9
			0.1	0.000092	2.31	0.010	2.32
			1.0	0.000073	1.83	0.0078	1.84

a. BCF value used = 5000 .b. Wildlife exposure is calculated by multiplying the body weight-normalised food intake rate (kg dry wt/kg bw live wt/day) for each body weight range by the food concentration (Biota PEC). c. Based on the sediment forming 3% of dietary intake. d. Determined by summing the water food and sediment exposure.

Table B-5. Potential mammal intakes of triclosan from the marine aquatic environment

Effluent Source	Maximum Marine PEC C (mg/L)	Marine Biota PEC ^a (mg/kg dry weight)	Body weight (kg live weight)	PEC Drinking Water Exposure (mg/kg bw/d)	PEC Food Exposure ^b (mg/kg bw/d)	PEC Sediment Exposure (mg/kg bw/d) ^c	Total PEC ^d (mg/kg bw/d)
Untreated wastewater	0.00174	43.4	0.01	0.000273	6.82	0.029	6.84
			0.1	0.000217	5.41	0.023	5.44
			1.0	0.000172	4.30	0.018	4.32
Primary Treatment	0.00170	42.5	0.01	0.000267	6.67	0.028	6.70
			0.1	0.000212	5.30	0.023	5.32
			1.0	0.000168	4.21	0.018	4.23
Trickling Filter	0.000730	18.3	0.01	0.000115	2.86	0.012	2.88
			0.1	0.0000910	2.27	0.010	2.28
			1.0	0.0000723	1.81	0.008	1.81
Activated Sludge	0.000782	19.6	0.01	0.000123	3.07	0.013	3.08
			0.1	0.0000975	2.44	0.010	2.45
			1.0	0.0000774	1.94	0.008	1.94
Activated sludge (SimpleTreat)	0.000678	17.0	0.01	0.000106	2.66	0.011	2.67
			0.1	0.0000845	2.11	0.009	2.12
			1.0	0.0000671	1.68	0.007	1.69
Tertiary treatment	0.000226	5.65	0.01	0.0000355	0.887	0.004	0.890
			0.1	0.0000282	0.704	0.003	0.707
			1.0	0.0000224	0.559	0.002	0.562
Measured Australian Data	0.000074	2	0.01	0.000012	0.29	0.001	0.3
			0.1	0.000009	0.23	0.001	0.23
			1.0	0.000007	0.18	0.001	0.18

a. BCF value used = 5000 .b. Wildlife exposure is calculated by multiplying the body weight-normalised food intake rate (kg dry wt/kg bw live wt/day) for each body weight range by the food concentration (Biota PEC). c. Based on the sediment forming 3% of dietary intake. d. Determined by summing the water food and sediment exposure.

Appendix C - Occupational Exposure Calculations

1 EASE estimation of occupational exposure to triclosan

Table C-1 presents occupational exposure estimations using the EASE model and the various parameters input to the model to represent the different workplace scenarios. The exposure estimations generated from the EASE model represent continuous exposure to the process under consideration. The process temperature used in the EASE estimation is 25°C.

Table C-1: EASE estimations of occupational exposure to triclosan

Exposure Type: dust inhalation; Particle size: respirable / inhalable¹			
Operation	Dust Type	Pattern of control	Exposure
Dry manipulation	Non-fibrous, does not aggregate	Local exhaust ventilation present	2-5 mg/m ³
		Local exhaust ventilation absent	5-50 mg/m ³

1.1 Dry manipulation

This category includes any manipulation of the dry material.

Substances which are waxy in texture or which are in some other way sticky so that particles of the solid readily aggregate will give rise to less dust than those solid particles of which do not readily aggregate. Triclosan powder is not considered to aggregate readily.

Exposure Type: dermal			
Use pattern	Dermal contact level		Exposure
Non-dispersive	Direct handling	Intermittent (2-10 times per day)	0.1-1 mg/cm ² /day

¹ the model predicts the same exposure for respirable and inhalable dust under the parameters shown

1.2 Non-dispersive use

Non-dispersive use refers to processes in which substances are used in such a way that only certain groups of workers, with the knowledge of the processes, come into contact with these chemicals. Procedures are normally worked out to achieve adequate control of exposure commensurate with the risk. This category is intended to cover most occupational use not specifically assignable to other categories.

1.3 Intermittent

Intermittent exposure is assumed to be 2 to 10 events per day involving exposure as part of a process; for example, material transfer by a device which involved judgment, such as at a weighing plant.

1.4 Direct handling

In the absence of any other control procedures it is assumed that the worker handles the substance directly without precautions. The effect of personal protective equipment including respiratory protective equipment needs to be adjudged separately.

2 Calculations of internal dose following inhalation exposure

The internal dose arising from inhalation (D_i) is calculated using the following formula:

$$D_i = \frac{C \times R \times E \times B}{BW}$$

Where:

- D_i = Internal inhalation exposure dose ($\mu\text{g}/\text{kg}$ bw/day)
- C = Concentration of a substance in air (mg/m^3)
- R = Inhalation rate (m^3/hour)
- E = Exposure duration (hour/day) incorporated with frequency
- B = Bioavailability (%)
- BW = Average body weight of workers (kg)

In the algorithm, the values for:

- R (inhalation rate) = $1.3 \text{ mg}/\text{m}^3$, selected to represent light working activities (EC, 2003a) and,
- BW (bodyweight) = 70 kg.

2.1 Repacking

In the calculating internal dose arising from inhalation of triclosan while repacking the following additional assumptions are used:

- E = 0.25 hour per day (i.e 15 min a day) with a frequency of 10 days per year
- B = 100%
- C = $2 \text{ mg}/\text{m}^3$ – $5 \text{ mg}/\text{m}^3$ with LEV; and $5 \text{ mg}/\text{m}^3$ - $50 \text{ mg}/\text{m}^3$ without LEV, as estimated using the EASE model.

With local exhaust ventilation

$$D_i = \frac{2 \text{ mg} / \text{m}^3 \times 1.3 \text{ m}^3 / \text{hr} \times 0.25 \text{ hr} / \text{day} \times \frac{10 \text{ days}}{365 \text{ days}} \times 100\%}{70 \text{ kg}} = 0.25 \mu\text{g} / \text{kg} / \text{day}$$

$$D_i = \frac{5 \text{ mg/m}^3 \times 1.3 \text{ m}^3/\text{hr} \times 0.25 \text{ hr/day} \times \frac{10 \text{ days}}{365 \text{ days}} \times 100\%}{70 \text{ kg}} = 0.64 \text{ } \mu\text{g/kg/day}$$

Without local exhaust ventilation

$$D_i = \frac{50 \text{ mg/m}^3 \times 1.3 \text{ m}^3/\text{hr} \times 0.25 \text{ hr/day} \times \frac{10 \text{ days}}{365 \text{ days}} \times 100\%}{70 \text{ kg}} = 6.36 \text{ } \mu\text{g/kg/day}$$

The internal doses (Di) using these values range from 0.25-0.64 $\mu\text{g/kg bw/day}$ (with LEV); and 0.64 – 6.36 $\mu\text{g/kg bw/day}$ (without LEV)

2.2 Formulation of personal care/cosmetic products

In calculating the internal dose arising from inhalation of triclosan while formulating personal health care/cosmetic or therapeutic products the following additional assumptions are used:

- E=1 hour per day with a frequency of 156 days per year (3 days/week)
- B=100%
- C= 2 mg/m^3 – 5 mg/m^3 with LEV; and 5 mg/m^3 -50 mg/m^3 without LEV, as estimated using the EASE model.

With local exhaust ventilation

$$D_i = \frac{2 \text{ mg/m}^3 \times 1.3 \text{ m}^3/\text{hr} \times 1 \text{ hr/day} \times \frac{156 \text{ days}}{365 \text{ days}} \times 100\%}{70 \text{ kg}} = 15.9 \text{ } \mu\text{g/kg/day}$$

$$D_i = \frac{5 \text{ mg/m}^3 \times 1.3 \text{ m}^3/\text{hr} \times 1 \text{ hr/day} \times \frac{156 \text{ days}}{365 \text{ days}} \times 100\%}{70 \text{ kg}} = 39.7 \text{ } \mu\text{g/kg/day}$$

Without local exhaust ventilation

$$D_i = \frac{50 \text{ mg/m}^3 \times 1.3 \text{ m}^3/\text{hr} \times 1 \text{ hr/day} \times \frac{156 \text{ days}}{365 \text{ days}} \times 100\%}{70 \text{ kg}} = 397 \text{ } \mu\text{g/kg/day}$$

The calculated internal dose (Di) using these values is 15.9-39.7 $\mu\text{g/kg bw/day}$ (with LEV); and 39.7-397 $\mu\text{g/kg bw/day}$ (without LEV).

2.3 Addition of triclosan additives to textiles

In calculating the internal dose arising from inhalation of a triclosan powder additive containing 13.5% triclosan while adding the additive to textiles baths the following additional assumptions are made:

- E=1 hour a day with a frequency of 156 days per year (3 days/week)
- B=100%
- C= 0.27 mg/m³ – 0.675 mg/m³ with LEV; and 0.675 mg/m³ – 6.75 mg/m³ without LEV, when taking account the triclosan concentration in the powder is 13.5%.

With LEV

$$D_i = \frac{0.27 \text{ mg/m}^3 \times 1.3 \text{ m}^3/\text{hr} \times 1 \text{ hr/day} \times \frac{156 \text{ days}}{365 \text{ days}} \times 100\%}{70 \text{ kg}} = 2.14 \text{ } \mu\text{g/kg/day}$$

$$D_i = \frac{0.675 \text{ mg/m}^3 \times 1.3 \text{ m}^3/\text{hr} \times 1 \text{ hr/day} \times \frac{156 \text{ days}}{365 \text{ days}} \times 100\%}{70 \text{ kg}} = 5.36 \text{ } \mu\text{g/kg/day}$$

Without LEV

$$D_i = \frac{6.75 \text{ mg/m}^3 \times 1.3 \text{ m}^3/\text{hr} \times 1 \text{ hr/day} \times \frac{156 \text{ days}}{365 \text{ days}} \times 100\%}{70 \text{ kg}} = 53.6 \text{ } \mu\text{g/kg/day}$$

The calculated internal doses (Di) using these assumptions ranges from 2.14-5.36 $\mu\text{g/kg bw/day}$ (with LEV), and 5.36-53.6 $\mu\text{g/kg bw/day}$ (without LEV).

3 Calculations of internal dose following dermal exposure for repacking, formulation, textile and plastic workers

The internal dose from dermal exposure (D_d) is calculated using the following formula:

$$D_d = \frac{W \times C \times A \times F}{BW} \times \frac{S}{100}$$

Where:

- D_d = Internal dermal exposure dose (mg/kg bw/day)
- C = EASE estimated dose (mg/cm²/day)
- W = Weight fraction of substance in products (%)
- A = Skin surface area exposed (cm²)
- BW = Average body weight of workers (kg)

S = Skin absorption rate (%)
 F = frequency of occupational exposure (day/year)

In using this algorithm values for:

- A is assumed to be 1000 cm², to represent both hands or a hand and a forearm,
- BW (bodyweight) is assumed to be 70 kg; and
- S (skin absorption) is assumed to be 14%

3.1 Repacking

In the calculations for internal dose arising from dermal exposure to triclosan while repacking, the following additional assumptions are used in the calculation:

- W = 100%
- C = 0.1-1 mg/cm²/day, as estimated using the EASE model
- F = 10 days per year

$$D_d = \frac{100\% \times 0.1 \text{ mg/cm}^2/\text{day} \times 1000 \text{ cm}^2 \times \frac{10 \text{ days}}{365 \text{ days}} \times 14\%}{70 \text{ kg}} = 5.48 \text{ } \mu\text{g/kg/day}$$

$$D_d = \frac{100\% \times 1 \text{ mg/cm}^2/\text{day} \times 1000 \text{ cm}^2 \times \frac{10 \text{ days}}{365 \text{ days}} \times 14\%}{70 \text{ kg}} = 54.8 \text{ } \mu\text{g/kg/day}$$

The calculated internal doses (D_d) range from 5.5 – 55 μg/kg bw/day.

3.2 Formulation of personal care/cosmetics/therapeutic products

In calculating the internal dose arising from dermal exposure to triclosan while formulating personal health care/cosmetic or therapeutic products the following additional assumptions are used in the calculation:

- W = 100%
- C = 0.1-1 mg/cm²/day, as estimated using the EASE model
- F = 156 days per year (3 days/week)

$$D_d = \frac{100\% \times 0.1 \text{ mg/cm}^2/\text{day} \times 1000 \text{ cm}^2 \times \frac{156 \text{ days}}{365 \text{ days}} \times 14\%}{70 \text{ kg}} = 85.5 \text{ } \mu\text{g/kg/day}$$

$$D_d = \frac{100\% \times 1 \text{ mg/cm}^2/\text{day} \times 1000 \text{ cm}^2 \times \frac{156 \text{ days}}{365 \text{ days}} \times 14\%}{70 \text{ kg}} = 855 \text{ } \mu\text{g/kg/day}$$

The calculated internal doses (D_d) range from 85.5 – 855 μg/kg bw/day

3.3 Addition of triclosan additives to textiles

In the calculations for internal dose arising from dermal exposure to triclosan while adding triclosan additives to textile baths, the following additional assumptions are made:

- W = 13.5% (powdered additive);
- C = 0.1-1 mg/cm²/day, as estimated using the EASE model
- F = 156 days per year (3 days/week)

$$D_d = \frac{13.5\% \times 0.1 \text{ mg/cm}^2 / \text{day} \times 1000 \text{ cm}^2 \times \frac{156 \text{ days}}{365 \text{ days}} \times 14\%}{70 \text{ kg}} = 11.5 \text{ } \mu\text{g/kg/day}$$

$$D_d = \frac{13.5\% \times 1 \text{ mg/cm}^2 / \text{day} \times 1000 \text{ cm}^2 \times \frac{156 \text{ days}}{365 \text{ days}} \times 14\%}{70 \text{ kg}} = 115 \text{ } \mu\text{g/kg/day}$$

The calculated internal doses (D_d) range from 11.5 – 115 μg/kg bw/day

In the calculations for internal dose arising from dermal exposure to triclosan while adding triclosan additives to textile baths, the following additional assumptions are made:

- W = 20% (liquid additive)
- C = 0.1-1 mg/cm²/day, as estimated using the EASE model
- F = 156 days per year (3 days/week)

$$D_d = \frac{20\% \times 0.1 \text{ mg/cm}^2 / \text{day} \times 1000 \text{ cm}^2 \times \frac{156 \text{ days}}{365 \text{ days}} \times 14\%}{70 \text{ kg}} = 17.1 \text{ } \mu\text{g/kg/day}$$

$$D_d = \frac{20\% \times 1 \text{ mg/cm}^2 / \text{day} \times 1000 \text{ cm}^2 \times \frac{156 \text{ days}}{365 \text{ days}} \times 14\%}{70 \text{ kg}} = 171 \text{ } \mu\text{g/kg/day}$$

The calculated internal doses (D_d) range from 17.1 – 171 μg/kg bw/day

3.4 Plastics compounding

In the calculations for internal dose arising from dermal exposure to triclosan while adding triclosan powder during compounding process the following additional assumptions are made:

- W = 100%
- C = 0.1-1 mg/cm²/day, as estimated using the EASE model
- F = 156 days per year (3 days/week)

$$D_d = \frac{100\% \times 0.1 \text{ mg/cm}^2 / \text{day} \times 1000 \text{ cm}^2 \times \frac{156 \text{ days}}{365 \text{ days}} \times 14\%}{70 \text{ kg}} = 85.5 \text{ } \mu\text{g/kg/day}$$

$$D_d = \frac{100\% \times 1 \text{ mg/cm}^2 / \text{day} \times 1000 \text{ cm}^2 \times \frac{156 \text{ days}}{365 \text{ days}} \times 14\%}{70 \text{ kg}} = 855 \text{ } \mu\text{g/kg/day}$$

The calculated internal doses (D_d) range from 85.5 – 855 $\mu\text{g/kg bw/day}$

In the calculations for internal dose arising from dermal exposure to triclosan while adding triclosan liquid additives during compounding process, the following additional assumptions are made

- $W = 10\%$
- $C = 0.1\text{-}1 \text{ mg/cm}^2/\text{day}$, as estimated using the EASE model
- $F = 156 \text{ days per year (3 days/week)}$

$$D_d = \frac{10\% \times 0.1 \text{ mg/cm}^2 / \text{day} \times 1000 \text{ cm}^2 \times \frac{156 \text{ days}}{365 \text{ days}} \times 14\%}{70 \text{ kg}} = 8.55 \text{ } \mu\text{g/kg/day}$$

$$D_d = \frac{10\% \times 1 \text{ mg/cm}^2 / \text{day} \times 1000 \text{ cm}^2 \times \frac{156 \text{ days}}{365 \text{ days}} \times 14\%}{70 \text{ kg}} = 85.5 \text{ } \mu\text{g/kg/day}$$

The calculated internal doses (D_d) range from 8.55 – 85.5 $\mu\text{g/kg bw/day}$

4 Calculations of internal dose following dermal exposure for end users

The estimation of internal dose exposure for end users is determined using the following formula from the European Commission's Technical Guidance on Risk Assessment (EC, 2003a)

$$U_{der} = \frac{C_{dermal} \times (TH_{der} \times AREA_{der})}{BW} \times TF$$

$$U_{i-der} = U_{der} \times S$$

where:

U_{der} = Potential uptake (mg/kg bw/day)

C_{dermal} = Dermal concentration of substance on skin (0.3%)

$AREA_{der}$ = Area of contact between product and skin (1000 cm^2)

TH_{der} = Thickness of product layer on skin (0.01 cm)

BW = Body weight (70 kg)

TF = Time factor (exposure duration)

S = Skin absorption rate (14%)

U_{i-der} = Internal dermal exposure dose (mg/kg bw/day)

The values provided for C_{dermal} (0.3%) is the maximum concentration of triclosan in an industrial end product reported as being in use in Australia, and the determination of internal dose below represents the worst-case scenario. The duration is estimated to be 8 h per day and 5 days per wk.

$$U_{\text{der}} = \frac{0.3\% \times 1000 \text{ cm}^2 \times 0.01 \text{ cm}}{70 \text{ kg}} \times \frac{8 \text{ h}}{24 \text{ h}} \times \frac{5 \text{ days}}{7 \text{ days}} = 119 \mu\text{g} / \text{kg} / \text{day}$$

$$U_{i\text{-der}} = 119 \mu\text{g} / \text{kg} / \text{d} \times 14\% = 16.7 \mu\text{g} / \text{kg} / \text{day}$$

Appendix D - Consumer Exposure Calculations

1 Inhalation exposure to consumer products

The estimations of internal dose arising from inhalation are calculated using the following formula from the Technical Guidance Document on Risk Assessment of the European Chemicals Bureau (EC, 2003a):

$$C_{inh} = \frac{Q_{prod} \times FC_{prod}}{V_{room}} \quad \text{and}$$

$$I_{inh} = \frac{F_{resp} \times C_{inh} \times IH_{air} \times T_{contact} \times n}{BW}$$

where:

Parameter	Explanation	Unit
BW	Body weight	kg
C_{inh}	Concentration in air of room	kg/m ³
FC_{prod}	Weight fraction of substance in product	%
F_{resp}	Respirable fraction of inhaled substance	-
IH_{air}	Ventilation rate of person	m ³ /day
I_{inh}	Inhalation uptake of substance	kg/kg bw/day
n	Mean number of events per day	-
Q_{prod}	Amount of product used per event	mg
$T_{contact}$	Duration of contact per event	day
V_{room}	Room volume	m ³

In these calculations the following assumptions are consistently made: the ventilation rate is 23 m³/day as provided in the Australian Exposure Assessment Handbook (EnHealth Council, 2003), an adult weighs 60 kg, and 100% is absorbed (i.e. F_{resp}). All other parameters are variable.

For transparency and as examples of calculations, inhalation exposure calculations are detailed below using the values available from information submitted for assessment and use data for the various products from the Technical Guidance Document on Risk Assessment of the European Chemicals Bureau (EC, 2003a). Dermal exposure calculations have not been detailed for children but not adults. The results of the dermal exposure calculations for adults are presented in Table D-1, D-2 and D-4.

1.1 Calculations of inhalation exposure from use of anti-perspirant/deodorant spray products

For the inhalation exposure calculation, the concentration of triclosan in body spray product is taken as 0.3%, and the duration per application is assumed to be 15 min. A room volume of 2 m³ is taken to represent the volume of air immediately surrounding the user (EC, 2003a).

$$C_{inh} = \frac{3000 \text{ mg} \times 0.3\%}{2 \text{ m}^3} = 4.5 \text{ mg} / \text{m}^3 \quad \text{and}$$

$$I_{inh} = \frac{1 \times 4.5 \text{ mg} / \text{m}^3 \times 23 \text{ m}^3 \times \left(\frac{0.25 \text{ h}}{24 \text{ h}}\right) \times 1}{60 \text{ kg}} = 18 \text{ } \mu\text{g} / \text{kg} / \text{day} \quad (n=1)$$

$$I_{inh} = \frac{1 \times 4.5 \text{ mg} / \text{m}^3 \times 23 \text{ m}^3 \times \left(\frac{0.25 \text{ h}}{24 \text{ h}}\right) \times 3}{60 \text{ kg}} = 53.9 \text{ } \mu\text{g} / \text{kg} / \text{day} \quad (n=3)$$

The inhalation exposure of triclosan from body spray is estimated to be 18 to 53.9 $\mu\text{g}/\text{kg}/\text{day}$.

1.2 Calculations of inhalation exposure from use of surface disinfectant/cleaner spray products

i) when using 5 g surface disinfectant/cleaner products and 1 min per event, and 1 event/day:

$$C_{inh} = \frac{5000 \text{ mg} \times 0.25\%}{4 \text{ m}^3} = 3.13 \text{ mg} / \text{m}^3 \quad \text{and}$$

$$I_{inh} = \frac{1 \times 3.13 \text{ mg} / \text{m}^3 \times 23 \text{ m}^3 \times \left(\frac{0.0333 \text{ h}}{24 \text{ h}}\right) \times 1}{60 \text{ kg}} = 1.66 \text{ } \mu\text{g} / \text{kg} / \text{day}$$

ii) when using 30 g surface disinfectant/cleaner products and 10 min per event, and 7 event/day:

$$C_{inh} = \frac{30000 \text{ mg} \times 0.25\%}{4 \text{ m}^3} = 18.75 \text{ mg} / \text{m}^3 \quad \text{and}$$

$$I_{inh} = \frac{1 \times 18.75 \text{ mg} / \text{m}^3 \times 23 \text{ m}^3 \times \left(\frac{0.1667 \text{ h}}{24 \text{ h}}\right) \times 7}{60 \text{ kg}} = 349.5 \text{ } \mu\text{g} / \text{kg} / \text{day}$$

The inhalation exposure of triclosan from surface cleaning spray is estimated to be 1.66 to 349.5 µg/kg/day.

1.3 Calculation of inhalation exposure from textile and plastic products and painted surfaces

It should be noted that when determining the internal dose following inhalation exposure from a textile/plastic article or painted surface, exposure is assumed to be continuous (i.e. 24 hours per day) and that the concentration in the air of the room is 0.01 mg/m³ (as determined using the OECD Environmental Directorate model – OECD, 1993).

Inhalation exposure from textile and plastic articles and painted surfaces for adults is calculated as:

$$C_{inh} = 0.01 \text{ mg} / \text{m}^3 \quad \text{and}$$

$$I_{inh} = \frac{1 \times 0.01 \text{ mg} / \text{m}^3 \times 23 \text{ m}^3 \times 1 \times 1}{60 \text{ kg}} = 3.83 \text{ } \mu\text{g} / \text{kg} / \text{day}$$

The inhalation exposure of triclosan from textile and plastic products and painted surfaces is estimated to be 3.83 µg/kg/day.

Inhalation exposure from textile and plastic articles and painted surfaces for <1 year babies is calculated as:

$$C_{inh} = 0.01 \text{ mg} / \text{m}^3 \quad \text{and}$$

$$I_{inh} = \frac{1 \times 0.01 \text{ mg} / \text{m}^3 \times 4.5 \text{ m}^3 \times 1 \times 1}{7.4 \text{ kg}} = 6.08 \text{ } \mu\text{g} / \text{kg} / \text{day}$$

The inhalation exposure of triclosan from textile and plastic products and painted surfaces is estimated to be 6.08 µg/kg/day.

Inhalation exposure from textile and plastic articles and painted surfaces for 1-2 years old children is calculated as:

$$C_{inh} = 0.01 \text{ mg} / \text{m}^3 \quad \text{and}$$

$$I_{inh} = \frac{1 \times 0.01 \text{ mg} / \text{m}^3 \times 6.8 \text{ m}^3 \times 1 \times 1}{12.9 \text{ kg}} = 5.27 \text{ } \mu\text{g} / \text{kg} / \text{day}$$

The inhalation exposure of triclosan from textile and plastic products and painted surfaces is estimated to be 5.27 µg/kg/day.

Inhalation exposure from textile and plastic articles and painted surfaces for 3-5 years old children is calculated as:

$$C_{inh} = 0.01 \text{ mg} / \text{m}^3 \quad \text{and}$$

$$I_{inh} = \frac{1 \times 0.01 \text{ mg} / \text{m}^3 \times 8.3 \text{ m}^3 \times 1 \times 1}{19.4 \text{ kg}} = 4.28 \text{ } \mu\text{g} / \text{kg} / \text{day}$$

The inhalation exposure of triclosan from textile and plastic products and painted surfaces is estimated to be 4.28 $\mu\text{g}/\text{kg}/\text{day}$.

2 Dermal exposure for consumer products

2.1 Calculation of internal dose following dermal exposure to cosmetic/personal care products

The estimations of internal dose arising from dermal exposure are calculated using formula in the Technical Guidance Document on Risk Assessment of the European Chemicals Bureau (EC, 2003a) and the Guidance Notes for the Testing of Cosmetic Ingredients and their Safety Evaluation of the (EU) Scientific Committee on Cosmetic Products and Non-Food Products Intended for Consumers (SCCNFP, 2003):

$$U_{der} = \frac{A_{der} \times n}{BW} = \frac{(Q_{prod} \times C_{prod} \times RF) \times n}{BW} \text{ and}$$

$$U_{i-der} = U_{der} \times BIO_{der}$$

where:

Parameter	Explanation	Units
A_{der}	Amount of substance on skin per event	kg
BIO_{der}	Dermal absorption	%
BW	Body weight	kg
C_{prod}	Concentration of substance in product	%
n	Mean number of events per day	-
RF	Retention factor after wash-off	-
U_{der}	Amount of substance that can be potentially taken up	kg/kg bw/day
U_{i-der}	Internal dose from dermal exposure	kg/kg bw/day
Q_{prod}	Amount of product used	kg/event

For the dermal exposure calculation, concentrations of triclosan in the cosmetic and personal care products (C_{prod}) are assumed to be the maximum concentration of triclosan in the product category.

The values for amount of product used per event (Q_{prod}), number of events per day (n) and retention factor (RF) come from the SCCNFP's Notes of Guidance for the Testing of Cosmetic Ingredients and Their Safety Evaluation (SCCNFP, 2003). The body weight is assumed to be 60 kg, and the bioavailability for dermal uptake is 14%.

Calculations of dermal exposure are similar to that of inhalation exposure. Estimation of dermal exposure of triclosan from the use of cosmetic and personal care products is presented in Table D-1 and D-2 for adults and D-3 for children.

Table D-1: The estimation of dermal exposure from the use of cosmetic and personal care products

Product Type	Q _{prod} (mg/event)	n (events/day)	RF	C _{prod} (%)	U _{der} (µg/kg/d)	U _{i-der} (µg/kg/day)
Body lotion	8000	0.71	1	0.3	284	39.76
Face cream / Moisturizer	800	2	1	0.3	80	11.2
Colognes	5000	0.29	1	0.1	24.17	3.38
Sun cream / lotion	8000	3	1	0.1	400	56
Nail polish / remover	250	0.28	1	0.2	2.33	0.33
Face cream	800	1	1	0.5	66.67	9.33
Antiperspirant/ deodorant	500	1	1	0.31	25.83	3.62
Foot spray / body deodorant	3000	2	1	0.2	200	28
Bath Products	17000	0.29	0.001	0.5	0.41	0.058
Shower gel	5000	1.07	0.01	0.5	4.46	0.62
Toilet soap	800	6	0.01	1	8	1.12
Make-up remover	2500	1	0.1	0.3	12.5	1.75
Facial masks	3700	0.1	0.1	0.5	3.08	0.43

Table D-2: The estimation of dermal exposure from the use of cosmetic and personal care products applied to the eye-region

Product Type	Q _{prod} (mg/event)	n (event/day)	RF	C _{prod} (%)	U _{der} (µg/kg/d)	U _{i-der} (µg/kg/day)
Shadow	10	2	1	0.1	0.33	0.047
Mascara	25	1	1	0.1	0.42	0.058
Liner	5	1	1	0.1	0.083	0.012
Eyebrow pencil	10	1	1	0.1	0.17	0.023
Concealer	60	1	1	0.1	1	0.14
Total	110					0.28
Removal lotion	500	1	0.1	0.1	0.83	0.12

The Q_{prod} in children use is adjusted based on the ratio of total surface area of an adult to the amount of use in adults. The surface areas of <1, 1-2, 3-5 years old children and adults are 0.487, 0.833, 0.761 and 2.538 m², respectively, based on the surface area/body weight ratios provided from the *Child-Specific Exposure Factors Handbook* and the body weight of each age group.

$$Q_{prod} = \frac{8 \text{ g}}{60 \text{ kg} \times 0.0423 (\text{m}^2 / \text{kg})} \times 0.0641 (\text{m}^2 / \text{kg}) \times 7.4 \text{ kg} = 1.5 \text{ g} (< 1 \text{ year group})$$

$$Q_{prod} = \frac{8 \text{ g}}{60 \text{ kg} \times 0.0423 (\text{m}^2 / \text{kg})} \times 0.0641 (\text{m}^2 / \text{kg}) \times 12.9 \text{ kg} = 2.6 \text{ g} (2 \text{ years group})$$

$$Q_{prod} = \frac{8 \text{ g}}{60 \text{ kg} \times 0.0423 (\text{m}^2 / \text{kg})} \times 0.0423 (\text{m}^2 / \text{kg}) \times 19.4 \text{ kg} = 2.5 \text{ g} (5 \text{ years group})$$

Table D-3: The estimation of dermal exposure from the use of body lotion in children

Age (year)	Q _{prod} (mg/event)	n (event/day)	RF	C _{prod} (%)	U _{i-der} (µg/kg/day)
<1	1500	1	1	0.3	85
2	2600	1	1	0.3	84
5	2600	1	1	0.3	56

2.2 Calculation of internal dose following dermal exposure to household cleaning products

The estimations of internal dose arising from dermal exposure are calculated using the following formula from the Technical Guidance Document on Risk Assessment of the European Chemicals Bureau (EC, 2003a) that has been modified to incorporate a duration factor:

$$C_{der} = \frac{C_{prod}}{D} \quad C_{der} = \frac{Q_{prod} \times FC_{prod}}{D}$$

$$U_{der} = \frac{C_{der} \times V_{appl} \times \frac{n}{7}}{BW} \times T_{contact} = \frac{C_{der} \times (TH_{der} \times AREA_{der}) \times \frac{n}{7}}{BW} \times T_{contact}$$

$$U_{i-der} = U_{der} \times BIO_{der}$$

where:

Parameter	Explanation	Units
AREA _{der}	Area of contact between product and skin	m ²
BIO _{der}	Dermal absorption	%
BW	Body weight	kg
C _{der}	Dermal concentration of substance on skin	kg/m ³
C _{prod}	Concentration of substance in product	%
D	Dilution factor	-
FC _{prod}	Weight fraction of substance in product	%

n	Mean number of events per week	event/week
Q _{prod}	Amount of product used	kg
T _{contact}	Duration of contact per event	day
TH _{der}	Thickness of product layer on skin	m
U _{der}	Amount of substance that can potentially be taken up	kg/kg bw/day
U _{i-der}	Internal dose from dermal exposure	kg/kg bw/day
V _{appl}	Volume actually contacting the skin	m ³

For the dermal exposure calculation, concentrations of triclosan in the household cleaning products (C_{prod}) are assumed to be the maximum concentration of triclosan in the product category.

The values for amount of product used per event (Q_{prod}), number of events per day (n) and retention factor (RF) come from the SCCNFP's Notes of Guidance for the Testing of Cosmetic Ingredients and Their Safety Evaluation (SCCNFP, 2003). The body weight is assumed to be 60 kg, and the bioavailability for dermal uptake is 14%.

Calculations of dermal exposure are similar to that of inhalation exposure. Estimation of dermal exposure of triclosan from the use of household cleaning products is presented in Table D-4.

2.3 Calculation of dermal exposure from painted tile and cabinet/cupboard surfaces

Triclosan concentration on painted surfaces is 8.3 x 10⁻⁵ kg/ m². Time spent in the kitchen and bathroom is 2 hours per day (enHealth, 2003). The sole area that comes in contact with the floor surface is estimated to be a third of the surface area of adult feet (3.5 x 10⁻² m²).

$$U_{der} = \frac{C_{der} \times AREA_{der} \times T_{der} \times BIO_{der}}{BW}$$

$$C_{der} = 8.3 \times 10^{-5} \text{ kg/m}^2$$

$$U_{der} = \frac{8.3 \times 10^{-5} \text{ kg/m}^2 \times 0.035 \text{ m}^2 \times \frac{2 \text{ hrs}}{24 \text{ hrs/day}} \times 0.14}{60 \text{ kg}} = 0.56 \text{ } \mu\text{g / kg / day}$$

For infants, time spent in the kitchen and bathroom is 1.5 hours per day. The total skin surface area of infants less than 1 yo is 0.35 m² (enHealth, 2003) 13.7% of which is the arm area (US EPA, 2002) and 20.6%, the leg area (US EPA, 2002). Assuming only half of the legs and arms are in contact with floor surfaces, 0.06 m² of an infant's skin is directly exposed to triclosan.

Dermal exposure from painted tile and cabinet/cupboard surfaces for <1 year babies is calculated as:

$$U_{der} = \frac{8.3 \times 10^{-5} \text{ kg/m}^2 \times 0.06 \text{ m}^2 \times \frac{1.5 \text{ hrs}}{24 \text{ hrs/day}} \times 0.14}{7.4 \text{ kg}} = 5.90 \text{ } \mu\text{g / kg / day}$$

Table D-4: The estimation of dermal exposure from the use of household products

Product Type	Amount applied per application (g)		n (events/week)		T _{contact} (min)		C _{prod} (%)	C _{der} (mg/cm ³)		U _{der} (µg/kg/ bw/d)		U _{i-der} (µg/kg/day)	
	min	max	min	max	min	max		min	max	min	max	min	max
Hand dishwashing													
Liquid regular	3	10	3	21	10	45	0.2	0.0012	0.004	0.000595	0.0625	0.0000833	0.00875
Liquid concentrate	2	5	3	21	10	45	0.1	0.0004	0.001	0.000199	0.0156	0.0000278	0.00219
Hand laundry detergent													
Liquid	78	230	1	18	10	10	0.3	0.003	0.03	0.000496	0.0893	0.000069	0.0125
Surface cleaners													
Liquid	30	110	1	7	10	20	0.2	2.0	2.0	0.165	2.315	0.0231	0.324
Gel	20	40	1	7	10	20	0.04	0.4	0.4	0.0331	0.463	0.0046	0.065
Spray	5	30	1	7	2	10	0.25	2.5	2.5	0.0414	1.447	0.0058	0.203

Time spent in the kitchen and bathroom is 1 hour per day for children 1-2 and 3-5 years old (enHealth, 2003). The total skin surface area of children 1-2 yo is 0.59 m² (enHealth, 2003); feet comprise 6.27% of surface area (US EPA, 2002). The total skin surface area of children 3-5 yo is 0.69 m² (enHealth, 2003); feet comprise 7.25% of surface area (US EPA, 2002). The sole area that comes in contact with the floor surface is estimated to be a third of the surface area of feet. The skin surface area exposed to triclosan is 0.012 m² and 0.017 m² for 1-2 yo and 3-5 yo children, respectively.

Dermal exposure from painted tile and cabinet/cupboard surfaces for children 1-2 yo is calculated as:

$$U_{der} = \frac{8.3 \times 10^{-5} \text{ kg/m}^2 \times 0.012 \text{ m}^2 \times \frac{1.0 \text{ hr}}{24 \text{ hrs/day}} \times 0.14}{12.9 \text{ kg}} = 0.45 \text{ } \mu\text{g/kg/day}$$

Dermal exposure from painted tile and cabinet/cupboard surfaces for children 3-5 yo is calculated as:

$$U_{der} = \frac{8.3 \times 10^{-5} \text{ kg/m}^2 \times 0.017 \text{ m}^2 \times \frac{1.0 \text{ hr}}{24 \text{ hrs/day}} \times 0.14}{19.4 \text{ kg}} = 0.42 \text{ } \mu\text{g/kg/day}$$

3 Oral exposure for consumer products

3.1 Calculation of internal dose following oral exposure to cosmetic and personal care products

The estimations of internal dose arising from oral exposure are calculated using the following formula from the Technical Guidance Document on Risk Assessment of the European Chemicals Bureau (EC, 2003a) that has been modified to incorporate a retention factor:

$$I_{oral} = \frac{F_{oral} \times Q_{prod} \times C_{prod} \times n}{BW}$$

$$I_{i-oral} = I_{oral} \times BIO_{oral}$$

where:

Parameter	Explanation	Units
BW	Body weight	kg
BIO _{oral}	Oral absorption	%
C _{prod}	Concentration of substance in product	%
F _{oral}	Retention factor after use	-
I _{oral}	Amount of substance that can be potentially	kg/kg bw/day

	absorbed	
I _{i-oral}	Internal dose from oral exposure	kg/kg bw/day
n	Mean number of events per day	-
Q _{prod}	Amount of product used per event	kg

For toothpaste, mouthwash, and lipstick products, no dilution of the product is assumed before use. The use pattern and the fraction of the product that is ingested (F_{oral}) are in accordance with the Colipa data (SCCNFP, 2003). Bodyweight is assumed to be 60 kg, and the absorption rate of oral membrane is 14%. The concentrations of triclosan in lipstick, toothpaste and mouthwash are assumed to be 0.1%, 0.3% and 0.3%, respectively.

Calculations of oral exposure are similar to that of inhalation exposure. Estimation of oral exposure of triclosan from the use of cosmetic and personal care products is presented in Table D-5 for adults and D-6 for children.

Table D-5: The estimation of oral exposure from the use of cosmetic and personal care products

Product Type	Q _{prod} (mg/event)	n (event/day)	RF	C _{prod} (%)	I _{oral} (µg/kg/d)	I _{i-oral} (µg/kg/day)
Lipstick	10	4	1.0	0.1	0.67	0.093
Toothpaste	1400	2	0.17	0.3	23.8	3.33
Mouthwash	10000	3	0.1	0.3	150	21

Table D-6: The estimation of oral exposure from the use of cosmetic and personal care products in children

Product Type	Q _{prod} (mg/event)	n (event/day)	RF	C _{prod} (%)	BW (kg)	I _{i-oral} (µg/kg/day)
Toothpaste						
2 years old	1400	2	0.17	0.3	12.9	15.5
5 years old	1400	2	0.17	0.3	19.4	10.3

3.2 Exposure to triclosan in breast-fed babies

The estimations of internal dose arising from ingestion of breast milk are calculated using the following formula where absorption of triclosan is considered to be 100%. The concentration of triclosan in breast milk is 19 µg/kg milk. The values below are for a baby aged < 1 year old.

$$EDI = \frac{C_{milk} \times Q_{milk}}{BW} = \frac{19 \mu\text{g/kg} \times 751 \text{ g/day}}{4.7 \text{ kg}} = 3.04 \mu\text{g/kg bw/day}$$

where:

Parameter	Explanation	Units
BW	Body weight	kg
C_{milk}	Concentration of triclosan in breast milk	$\mu\text{g}/\text{kg}$ milk
EDI	Estimated daily intake of triclosan	$\mu\text{g}/\text{kg}$ bw/day
Q_{milk}	Breast milk intake per day	g/day

Appendix E -

Determination of triclosan in the Australian population by analysis of human breast milk

1. Objectives

The objectives of this project were to determine triclosan levels in individual human breast milk samples collected from various regions of Australia between 2003 and 2005.

2. Methodology

2.1 Sample collection/Sample numbers

In the last 5 yrs the consultants have undertaken a range of studies investigating the levels of organic pollutants including polychlorinated dibenzo-para-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), polychlorinated biphenyls (PCBs), organochlorine pesticides (OCPs) and polybrominated diphenyl ethers (PBDEs) in breast milk. During the course of these studies over 200 breast milk samples have been collected from sites located throughout Australia. These samples were progressively collected between 2000 and 2005. Full details of the criteria used for the collection of these samples and information related to the samples themselves can be found in the following publications: Harden et al., 2005a, Dioxins in the Australian Population: Levels in Human Milk, National Dioxins Program Technical Report No.10, Australian Government Department of the Environment and Heritage, Canberra; Harden et. al., 2005b, Organochlorine Pesticides (OCPs) and Polybrominated Diphenyl Ethers (PBDEs) in the Australian Population: Levels in Human Milk, Environment Protection and Heritage Council of Australia and New Zealand. Briefly, samples were collected during the period 2-8 wks post partum from primipara mothers from 12 regions throughout Australia. The regions included Brisbane, Sydney, Melbourne, Adelaide, Perth, Hobart, rural inland NSW (Dubbo), rural inland Queensland (Dalby), rural Victoria (Bendigo, Ballarat, Lakes Entrance), Newcastle, Wollongong and Darwin.

From these samples 151 individual breast milk samples were selected for the analysis of the level of triclosan, with an inter-laboratory comparison undertaken on 10 of these samples.

Ethics approval

Ethical approval was granted by the University of Queensland Medical Research Committee (see Appendice E-1). The approval Clearance Number was H/308/NRCET/00. An amendment to this was approved on 10th November 2004. All participants signed informed consent forms agreeing that their sample be retained

and used for future research on pollutants. Full details regarding other Ethics Committees can be found in the Harden et al., 2005a, Dioxins in the Australian Population: Levels in Human Milk, National Dioxins Program Technical Report No.10, Australian Government Department of the Environment and Heritage, Canberra; and Harden et al., 2005b, Organochlorine Pesticides (OCPs) and Polybrominated Diphenyl Ethers (PBDEs) in the Australian Population: Levels in Human Milk, Environment Protection and Heritage Council of Australia and New Zealand.

2.2 Sample analysis

Analyte identification and quantification criteria

Chemicals

Solvents used in the extraction and cleanup of samples: n-hexane (hexane) (LiChrosolv) (Merck, Darmstadt, Germany) was of liquid chromatography grade; acetone (Suprasolv) (Merck) was of gas chromatography grade; hydrochloric acid (HCl, 37%, w/w), sodium chloride (NaCl) (Scharlau, Barcelona, Spain), sulphuric acid (H₂SO₄, 98%) (Fisher Scientific, Loughborough, UK) and potassium hydroxide (KOH) (Eka Chemicals, Bohus, Sweden) were of pro analysis quality. Ethanol (99.5%) (Kemetyl, Haninge, Sweden). Pentafluorobenzoyl chloride (PFBCl, ≥ 98.5%) (Fluka, UK). Water was purified employing a Milli-Q Reagent Water System (Millipore Corporation, US). Universal indicator (Merck) was used for pH measurement.

¹³C-labeled triclosan was purchased from Cambridge Isotope Laboratories (Andover, USA). Triclosan (Irgasan DP300) (calibration standard) was a gift from Ciba-Geigy.

Methods

Test tubes were machine washed, using RBS detergent, and heated to 420°C for 4 h before use. The test tubes were sealed with a double layer of aluminium foil before carefully capping, to avoid triclosan contamination from the Teflon coated lining of screw caps, which has been found to be a source of triclosan. Centrifugation was done for 5 min at 2000 rpm. Mixing was done for 10 seconds using a vortex mixer.

Extraction and clean up

The milk sample (3 g) was transferred to a 15 ml screw capped test tube together with ¹³C-labeled triclosan (97.3 pg/μl in EtOH, 100 μl) as the surrogate standard. The contents were mixed. For the hydrolysis of metabolic conjugates of triclosan, H₂SO₄ (13.7 M, 5.7 ml) was added to the sample to obtain a 9 M H₂SO₄ solution. After mixing the solution was incubated for 30 min on a heating unit at 60°C. The test tube was cooled to room temperature, hexane/acetone (9:1, v/v, 6 ml) was added and the tube inverted for 15 min on rotary mixer. Following centrifugation the organic phase was transferred to a second test tube. The sample was then extracted with hexane/acetone (9:1, v/v, 4 ml), which was also transferred to the second test tube. H₂SO₄ (13.7 M, 2 ml) was added to the extract and the tube inverted 60 times by hand. Following centrifugation the extract was transferred to a third test tube and the H₂SO₄-layer reextracted with hexane/acetone (9:1, 2 ml). Triclosan was separated from the organic phase by adding aqueous KOH solution (0.5 M, 50% ethanol, 2 ml) to the extract, mixing two times and inverting the test tube for 3 min on rotary mixer.

Following centrifugation, the organic phase was discarded. The KOH solution was acidified with HCl (2 M, 1 ml) and a pH of 1 was established. Hexane/acetone (9:1, v/v, 4 ml) was added and after mixing and centrifuging, the organic phase was transferred to a fourth test tube. The aqueous phase was then extracted with hexane/acetone (9:1, v/v, 3 ml), which was combined with the organic fraction in the fourth test tube. The solvent volume was reduced to 3 ml under a gentle flow of nitrogen gas at room temperature prior to derivatization.

Derivatization and clean up for all extracts and standards

H₂O (Milli-Q, 2 ml), KOH (2 M, 50 µl), NaCl (0.3 g; more NaCl was added if emulsion was formed upon mixing) and pentafluorobenzoyl chloride (PFBCl) (10% in toluene, 10 µL) was added to extracts and calibration standards. The contents were mixed and after centrifugation the organic layer was transferred to a fifth test tube. The aqueous phase was re-extracted with hexane (2 ml).

H₂SO₄ (98%, 2 ml) was added to the derivatized extract and the tube was inverted 60 times. Following centrifugation the extract was transferred to a sixth test tube. The H₂SO₄-layer was reextracted with hexane (2 ml). The final extract volume was reduced to 2 ml under a gentle flow of nitrogen gas at room temperature. Approximately 0.5 ml of the extract was transferred to a GC/MS vial and analyzed as described below.

Gas chromatography/Mass spectrometry

Analysis was performed using gas chromatography mass spectrometry (GC/MS), applying electron capture negative ionization (ECNI) with single ion monitoring (SIM). The ions monitored were *m/z*: [287; 289; 482] for the triclosan pentafluorobenzoyl derivative, [299; 301; 494] for ¹³C-labeled for the ¹³C-labeled triclosan pentafluorobenzoyl derivative.

The instruments used for analysis were a Finnigan A200S autosampler on a HP5890A gas chromatograph with a DB5-MS capillary column (15 m; i.d 0.25 mm; 0.10 µm film thickness; J&W, USA) connected to a Finnigan SSQ 7000 quadrupole mass spectrometer. The temperature of the split/splitless injector in splitless mode was 280°C and the transfer line temperature was 300°C. The column temperature program was: 90°C (2 min); 20°C min⁻¹ to 315°C and held for 10 min. Ion source temperature was 180°C. Electron energy was 70 eV. Helium was used as the carrier gas and ammonia as the reagent gas.

Quantification

The triclosan concentration in the samples was quantified using the internal standard method. ¹³C-labeled triclosan was added to the samples prior to analysis.

The LOQ was defined as the lowest triclosan calibration standard that fitted the calibration curve. The lowest calibration standard used was excluded from the calibration curve because the calculated amount in the standard deviated more than 10% from the specified amount. The second lowest calibration standard defined the LOQ. The level in this standard was corrected for the blanks and divided by the average amount of milk sample used in the analysis to give the LOQ.

The LOQ was 0.019 and 0.016 ng/g milk for the first and second batch, respectively.

All blank amounts were low and below the LOQ. Blanks, although below the LOQ, were quantified using the calibration curve and all samples were corrected for blanks.

2.3 Alternative method of analysis (NMI method)

For comparative purposes, ten samples were analysed by the National Measurement Institute (NMI), Sydney Australia using a different analytical method. Samples of milk (1 g) were mixed with 9 mL of dilute sodium hydroxide solution (0.02M) and passed through solid phase extraction (SPE) cartridges containing an anion exchange resin to retain triclosan. The triclosan trapped on the resin was released by methylation with methyl iodide. After eluting the methyl triclosan from the resin it was further purified by SPE on a reverse phase resin cartridge. Determination was by electron impact GC/MS. Triclosan concentration in the sample was calculated by an isotope dilution procedure employing the response of ¹³C-triclosan added to the milk sample before extraction. The reporting limit of this method was set at the average concentration of triclosan in reagent blanks plus ten times the standard deviation of these blanks. All results were corrected for the average triclosan concentration in the blanks.

2.4 Results reporting and statistics

All concentrations are reported as fresh weight concentrations (ng/g freshweight) as reported by the analytical laboratory. Comparisons of concentrations on the basis of age, region and infant age were made using ANOVA (SigmaStat).

3. Results

3.1 Inter-laboratory comparison

Inter-laboratory comparison was conducted by having 10 duplicate samples analysed at NMI (Sydney, Australia). The results are reported as fresh weight concentrations in ng/g fresh weight and are shown in Table E-1. The reporting limit (0.6 ng/g milk) for the samples analysed at NMI was, while conservative, considerably higher than the limits of quantification (LOQ), reported by ITM (0.019 and 0.016 ng/g milk). However, for reported concentrations above the NMI reporting limit the triclosan concentrations were in good agreement with the greatest difference being 43.9% for sample 136. All other comparisons were within 20%.

Table E-1. Inter-laboratory comparison data from NMI and ITM.

Sample Number	Triclosan (ng/g milk)	
	NMI	ITM
6	< 0.6	≤ 0.019
104	< 0.6	1.1
140	9.4	9.5
142	14	14
101	0.9	1
95	0.8	0.73
54	< 0.6	0.15
1	< 0.6	≤ 0.019
125	2	2.5
136	4.1	5.9

3.2 The levels of triclosan in the breast milk of Australian women

One hundred and fifty-one human breast milk samples and two cow milk samples were analysed. The age of the women varied from 16 to 45 yrs of age and the age of the infants varied from 1 week to 6 months.

The samples were analysed in two batches at different times. The determined values in the present study are presented as the sum of unconjugated triclosan and contents of possible metabolic triclosan conjugates in the milk.

Triclosan was detected in 141 samples. In 18 samples the levels were below the LOQ. Figure E-1 shows the results for samples with a concentration of less than 1.0 ng/g milk and Figure E-2 show the results for samples with a concentration greater than 1.0 ng/g milk. The concentration of triclosan varied from the LOQ to a maximum value of 19ng/g milk (equivalent to 19 µg/kg milk). The data were not normally distributed. Full details are shown in Appendice E-2.

Figure E-1. Concentration of triclosan in breast milk obtained from Australian women - Results for 97 samples containing less than 1.0ng/g milk are shown

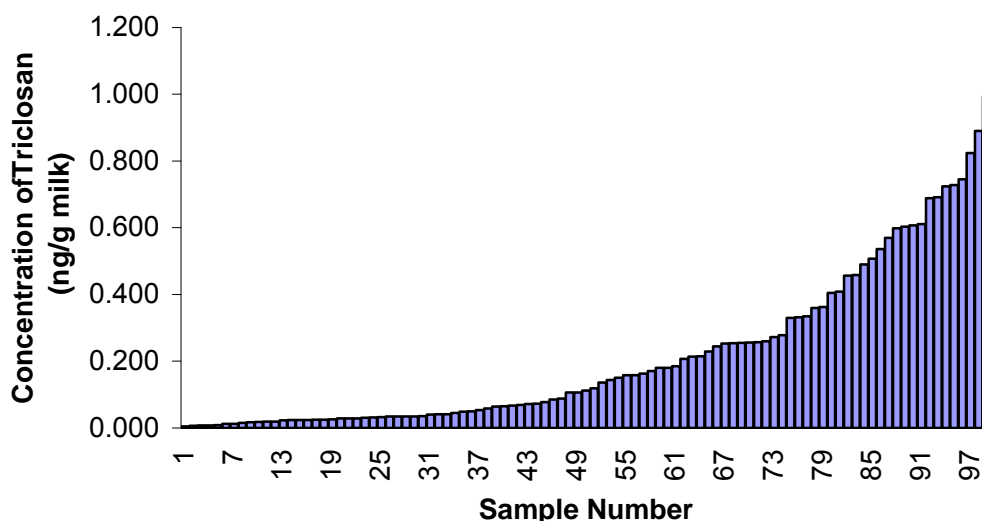
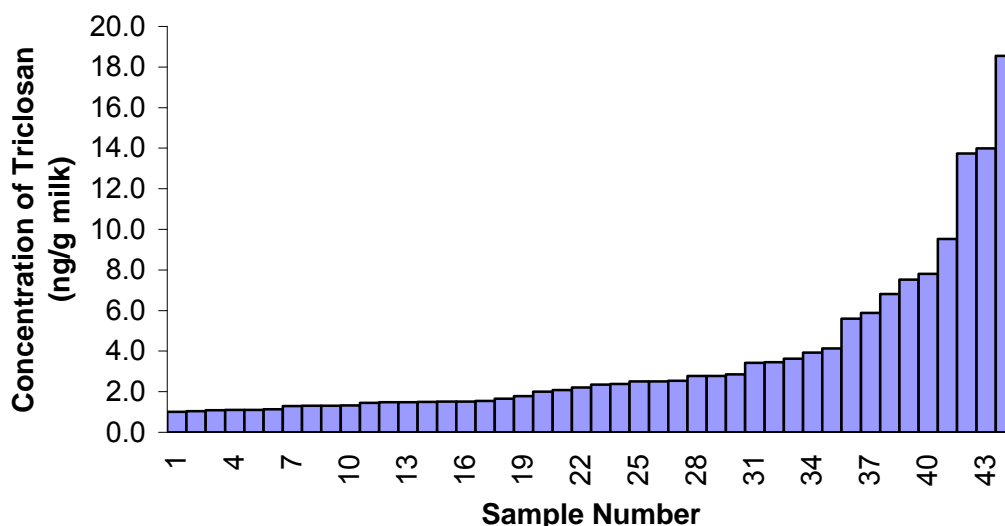


Figure E-2. Concentration of triclosan in breast milk obtained from Australian women - Results for 44 samples containing greater than 1ng/g milk are shown.



Analysis of variance showed that triclosan levels were not dependent on maternal age ($p>0.05$), age of the infant at the time of collection ($p>0.05$) or the region from which the sample was collected ($p>0.05$). Therefore, it is likely that the levels of triclosan in human milk are influenced by the individual's exposure to or use of triclosan containing products. Thus, exposure is unlikely to be affected by any of the other factors but rather is a reflection of an individual's product preference. This means that any assessment of exposure would require an investigation of an individual's use of triclosan containing products. Assessment of the potential intake of triclosan by the participants was not part of the requirements for this study.

Two other studies have investigated levels of triclosan in human breast milk samples (Adolfsson-Eric et al., 2002, and Plautz, 2005). The earliest study analysed the levels in five individual samples that were randomly collected from the Mothers' Milk Centre in Stockholm (Adolfsson-Eric et al., 2002). Triclosan was detected in three of the five samples at levels of 60, 130 and 300 $\mu\text{g}/\text{kg}$ lipid weight (equivalent to 0.9, 1.6 and 2.0 $\mu\text{g}/\text{kg}$ milk respectively). For the other two samples the levels were below the limit of detection. Comparisons between the two studies are difficult because of the small sample size of the Swedish study.

A further study analysed a total of 62 samples collected from two milk banks from two US states (Plautz, 2005). Triclosan was detected in all samples above the 5 ng/g lipid weight limit of quantification: ranging from 6 to approximately 2200 $\mu\text{g}/\text{kg}$ lipid weight (equivalent to 0.2 to approximately 55 $\mu\text{g}/\text{kg}$ milk respectively). Thus, the maximum observed triclosan level in a US breast milk sample was over twice that seen in an Australian, though as with the present study no information was available on the general characteristics of the milk donors or their use of products containing triclosan. However, as seen in the present study US triclosan concentrations were highly variable though similar ranges of concentration were seen between regions.

The method used in the present study makes no distinction between unconjugated triclosan and metabolic triclosan conjugates (i.e. triclosan glucuronide and triclosan sulphate) in the milk. Therefore the fraction of triclosan conjugates in the milk is not known. However, in the interlaboratory comparison, NMI determined the unconjugated fraction of triclosan and ITM the sum of the conjugated and unconjugated triclosan. Taking account of the considerably higher reporting limit for the NMI compared to ITM, then overall the triclosan contents in the ten samples analysed by the two laboratories suggests that the conjugated fraction of triclosan in the milk was negligible.

In summary the concentrations of triclosan detected in breast milk samples collected from Australian women were variable. This study has provided the first data on the concentration of triclosan in human breast milk in Australia, and provides a baseline against which any future monitoring can be compared to.

Appendix E.1 - Ethics Approval Letter

OFFICE OF RESEARCH AND POSTGRADUATE STUDIES

DIRECTOR
JAN MASSEY

Tel: (07) 3365 3924
Fax: (07) 3365 4455
Email: humanelthics@research.uq.edu.au



THE UNIVERSITY OF QUEENSLAND

Cumbræ-Stewart Building
Research Road
Brisbane Qld 4072 Australia
Telephone (07) 3365 3560, (07) 3365 4584
International +61 7 3365 3560, +61 7 3365 4584
Facsimile (07) 3365 4455

Friday, 6 December 2002

Dr Jochen Mueller
National Research Centre for Environmental Toxicology

Dear Dr Mueller

Concerning: Ethical clearance for project:- *Dioxinlike Compounds In Human Milk - 25/11/02 - AMENDMENT*

Clearance No: H/308/NRCET/00

The Medical Research Ethics Committee has approved your project.

Please note that:-

- (i) The Clearance number should be quoted on the protocol coversheet when applying to a granting agency and in any correspondence relating to ethical clearance;
- (ii) Clearance will normally be for the duration of the project unless otherwise stated in the institutional clearance;
- (iii) Adverse reaction to treatment by subjects, injury or any other incident affecting the welfare and/or health of subjects attributable to the research should be promptly reported to the Head of Department and the Behavioural and Social Sciences Ethical Review Committee.
- (iv) Amendments to any part of the approved protocol, documents or questionnaires attached to this clearance are to be submitted to the Behavioural and Social Sciences Ethical Review Committee for approval.

H/308/NRCET/00

- (v) Advisers on 'Integrity in Research'
As part of the University's commitment to the institutional statement, *Code of conduct for the Ethical Practice of Research (1990)*, and the NH&MRC's *National Statement on Ethical Conduct in Research Involving Humans (1999)*, designated positions have been appointed as advisers on integrity in research. The Chairperson of each ethics committee acts in an advisory capacity to provide confidential advice on such matters as misconduct in research, the rights and duties of postgraduate supervisors, and procedures for dealing with allegations on research misconduct within the University. The contact number for the Chairperson of each ethics committee can be obtained from the Ethics Officer.
- (vi) The Committee reserves the right to visit the research site and materials at any time during the project.
- (vii) It is the Committees expectation whenever possible, this work should result in publication and the Committee would require details to be submitted for our records.

Staff and students are also encouraged to contact either the Ethics Officer (3365 3924), or Chairperson on other issues concerning the conduct of experimentation/research (e.g. involvement of children, informed consent) prior to commencement of the project and throughout the course of the study.

Yours sincerely



Michael Tse
Ethics Officer

Encs:
cc: Head of School, National Research Centre for Environmental Toxicology



**Institutional Approval Form For Experiments On
Humans Including Behavioural Research**

Chief Investigator: Dr Jochen Mueller
Project Title: Dioxinlike Compounds In Human Milk - 25/11/02 - AMENDMENT
Supervisor: None
Co-Investigator(s): Dr Fiona Harden
Department(s): National Research Centre for Environmental Toxicology
Project Number: H/308/NRCET/00
Granting Agency/Degree: Environment Australia
Duration: March 2002 – March 2003

Comments:

**Name of responsible Committee:-
Medical Research Ethics Committee**

This project complies with the provisions contained in the *National Statement on Ethical Conduct in Research Involving Humans* and complies with the regulations governing experimentation on humans.

Name of Ethics Committee representative:-

**Dr Bill Vicenzino
Chairperson
Medical Research Ethics Committee**

Date

4-Dec-2002

Signature

Appendix E.2 - Levels of Triclosan in Australian Breast Milk Samples

Levels of triclosan in Australian breast milk samples. Two samples taken from cows milk are also shown. These were samples 14 and 15.

Sample No.	1	2	3	4	5	6	7	8	9
Triclosan ng/g	≤0.019	≤0.016	≤0.019	≤0.019	≤0.019	≤0.019	≤0.016	≤0.016	0.017
Sample No.	10	11	12	13	14	15	16	17	18
Triclosan ng/g	0.018	0.019	0.019	0.023	0.024	0.024	0.024	0.025	0.025
Sample No.	19	20	21	22	23	24	25	26	27
Triclosan ng/g	0.025	0.029	0.029	0.029	0.031	0.032	0.032	0.034	0.034
Sample No.	28	29	30	31	32	33	34	35	36
Triclosan ng/g	0.035	0.035	0.036	0.040	0.041	0.042	0.045	0.049	0.050
Sample No.	37	38	39	40	41	42	43	44	45
Triclosan ng/g	0.053	0.058	0.065	0.065	0.067	0.069	0.072	0.073	0.077
Sample No.	46	47	48	49	50	51	52	53	54
Triclosan ng/g	0.085	0.089	0.11	0.11	0.11	0.12	0.14	0.14	0.15
Sample No.	55	56	57	58	59	60	61	62	63
Triclosan ng/g	0.16	0.16	0.16	0.17	0.18	0.18	0.19	0.21	0.21
Sample No.	64	65	66	67	68	69	70	71	72
Triclosan ng/g	0.22	0.23	0.24	0.25	0.25	0.25	0.26	0.26	0.26
Sample No.	73	74	75	76	77	78	79	80	81
Triclosan ng/g	0.27	0.28	0.33	0.33	0.33	0.36	0.36	0.40	0.41
Sample No.	82	83	84	85	86	87	88	89	90
Triclosan ng/g	0.46	0.46	0.49	0.51	0.54	0.57	0.60	0.60	0.61
Sample No.	91	92	93	94	95	96	97	98	99
Triclosan ng/g	0.61	0.69	0.69	0.72	0.73	0.75	0.82	0.89	0.99
Sample No.	100	101	102	103	104	105	106	107	108
Triclosan ng/g	1.0	1.0	1.1	1.1	1.1	1.1	1.3	1.3	1.3
Sample No.	109	110	111	112	113	114	115	116	117
Triclosan ng/g	1.3	1.4	1.5	1.5	1.5	1.5	1.5	1.5	1.7
Sample No.	118	119	120	121	122	123	124	125	126
Triclosan ng/g	1.8	2.0	2.1	2.2	2.4	2.4	2.5	2.5	2.5
Sample No.	127	128	129	130	131	132	133	134	135
Triclosan ng/g	2.8	2.8	2.9	3.4	3.5	3.6	3.9	4.1	5.6
Sample No.	136	137	138	139	140	141	142	143	
Triclosan ng/g	5.9	6.8	7.5	7.8	9.5	14	14	19	

Appendix F - Classification under the Globally Harmonized System of Classification and Labelling of Chemicals and the Stockholm Convention on Persistent Organic Pollutants

In this report, triclosan has been classified against the NOHSC *Approved Criteria for Classifying Hazardous Substances* (Approved Criteria) (NOHSC, 2004) and, in the case of physicochemical hazards, the *Australian Code for the Transport of Dangerous Goods by Road and Rail* (ADG Code) (FORS, 1998). However, classifications under the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) (OECD 2003) will come into force when the GHS is adopted by the Australian Government and promulgated into Commonwealth legislation. GHS documentation is available at

http://www.unece.org/trans/danger/publi/ghs/ghs_rev01/01files_e.html

1.1 GHS Classification

Based on the data presented in this assessment triclosan is toxic by inhalation, irritating to the skin, eyes and respiratory system, highly toxic to fish and aquatic invertebrates (EC/LC50 < 1 mg/L) and very highly toxic to algae (EC50 < 0.1 mg/L). While BCFs >5000 and log Kow values are between 4.76-4.8.

The classification of triclosan to the GHS is presented below in Table F-1. As yet, the GHS for environmental toxicity only addresses acute and chronic aquatic toxicity.

1.2 Persistent Organic Pollutants (POPs) Assessment



The Stockholm Convention on Persistent Organic Pollutants (POPs) is a global treaty to protect human health and the environment. The convention contains criteria which address persistence, bioaccumulation potential, long-range transport and toxicity concerns. These criteria are used to identify substances that may be candidates for inclusion in the treaty. The Stockholm Convention on Persistent Organic Pollutants (POPs) entered into force on 17 May 2004. Australia ratified the Convention on 20 May 2004, and obligations of the POPs Convention entered into force for Australia on 18 August 2004. The Stockholm Convention requires parties under the Convention to take into account POPs characteristics when conducting assessments on new and existing chemicals.

Persistence

- (i) Evidence that half life in water is >two months, in soil is >six months and in sediment is >six months; or
- (ii) Evidence that the chemical is otherwise sufficiently persistent.

Table F-1 Classification of triclosan under the GHS

Health and Environmental Hazards	Classification	Hazard Communication
<u>Health hazard</u>		
Acute inhalation toxicity	Category 3	<p>Symbol:</p>  <p>Signal Word: Danger</p> <p>Hazard Statement: Toxic if inhaled (dust aerosol)</p>
Skin irritation	Category 2	<p>Symbol:</p>  <p>Signal Word: Warning</p> <p>Hazard Statement: Causes skin irritation</p>
Eye irritation	Category 2A	<p>Symbol:</p>  <p>Signal Word: Warning</p> <p>Hazard Statement: Causes serious eye irritation</p>
Respiratory irritation	Category 3	<p>Symbol:</p>  <p>Signal Word: Warning</p> <p>Hazard Statement: May cause respiratory irritation</p>

Health and Environmental Hazards	Classification	Hazard Communication
<u>Environmental hazard</u>		
Acute toxicity	Category 1	<p>Symbol:</p>  <p>Signal Word: Warning</p> <p>Hazard Statement: Very toxic to aquatic life</p>
Chronic toxicity	Category 1	<p>Symbol:</p>  <p>Signal Word: Warning</p> <p>Hazard Statement: Very toxic to aquatic life with long lasting effects</p>

Triclosan is not considered readily biodegradable. Singer et al. (2002) have found significant levels of triclosan have been found in sediments dating back to 1970 in lake sediments. Tixier et al. (2002) have determined photolytic half lives ranging from 2-2000 days depending on the latitude and time of year. These data suggest that while triclosan is persistent in the environment under some conditions i.e. anaerobic conditions, under other conditions it is degraded. Therefore, it is unlikely to adequately meet the persistence criteria for a POP chemical.

Bioaccumulation

- (i) Evidence that bio-concentration factor or bio-accumulation factor in aquatic species >5000 or $\log Kow > 5$
- (ii) Evidence of other reasons for concern (high bio-accumulation in other species, high toxicity or ecotoxicity); or
- (iii) Sufficient monitoring data in biota indicating that the chemical is bio-accumulative.

Ciba-Geigy Limited (1991) and Orvos et al. (2002) reported on the bioconcentration and depuration of ^{14}C -triclosan in zebra fish (*Brachydanio rerio*). The test followed the method of OECD TG 305C. BCFs have been measured between 905-10779, with the highest concentrations occurring in the intestines. Triclosan was detected in the fish two weeks post-exposure although concentrations had declined by $\geq 98\%$ from

levels experienced during the exposure period. Depuration rate constants at 3 and 30 µg/L were reported by Orvos et al. (2002) as 0.142 d⁻¹ and 0.141 d⁻¹, respectively.

Bioconcentration of triclosan in zebra fish, and potentially other fish species, in water has been shown to be pH-dependent, with higher uptake at low pH. With exposure to 35-50 µg triclosan/L for 250 days in waters of different pH, BCF values were as follows (Schettgen et al., 1999):

<u>pH</u>	<u>BCF</u>
9	3700
8	6350
7	8150
6	8700

After termination of exposure, triclosan was eliminated at a rate (half-life) of 16.8 to 19.9 hours. Although the uptake rate is pH dependent, the elimination rate is pH independent (Schettgen, 2000).

Based on the above measured bioaccumulation factors triclosan would meet the bioaccumulation criterion for POP chemicals (BCF>5000). However, the rapid depuration would limit the potential sustained levels in exposed organisms once exposure ceases.

Potential for long-range environmental transport

- (i) Measured levels of the chemical in locations distant from the sources of its release that are of potential concern;*
- (ii) Monitoring data showing that long-range environmental transport, with the potential for transfer to a receiving environment, (via air, water or migratory species); or*
- (iii) Environmental fate properties and/or model results that demonstrate that the chemical has a potential for such transportation, with the potential for transfer to a receiving environment in locations distant from the sources of its release. For a chemical that migrates significantly through the air, its half-life in air should be greater than two days.*

While there is a considerable volume of monitoring data for triclosan it is restricted to media close to the STP sources. No data are available for measured levels in locations distant from sources.

The low solubility and volatility of triclosan coupled with the relatively short predicted atmospheric half life (7.96 h) and adsorption to sediments would suggest that it unlikely to undergo long range environmental transport through air or water.

The measured BCFs would indicate potential for accumulation in migratory species, but the rapid depuration rate would indicate that high concentrations within migratory species would not be expected to persist for sufficient duration to afford long range transport of triclosan through migratory species.

Based on the above, long range transport of triclosan through air, water or migratory species is unlikely to occur. Hence triclosan would not meet this criterion for a POP chemical.

Adverse environmental effects

- (i) Evidence of adverse effects to human health or to the environment that justifies consideration of the chemical within the scope of this Convention; or*
- (ii) Toxicity or ecotoxicity data that indicate the potential for damage to human health or to the environment.*

Triclosan is highly toxic to fish and aquatic invertebrates (EC/LC50 < 1 mg/L) and very highly toxic to algae (EC50 < 0.1 mg/L) indicating that potential for damage to the environment. Hence, triclosan would meet the adverse environmental effects criterion of POP chemicals.

Summary

Triclosan is not considered to meet the criteria for it to be considered a candidate for listing as a potential POP chemical.

Appendix G - Wildlife Risk Quotients

The wildlife risk quotients for the various modes of oral exposure are summarised in Table G-1 and G-2 and are based on the comparison of the avian and mammalian TRVs (Table 14.6) with the potential exposure as determined in Section 8.5.10.

Table G-1. Estimated Risk Quotients (PEC/TRV) for birds (0.01-1.0 kg bw) potentially exposed to freshwater and marine ecosystems containing triclosan released in STP effluent, based on removal rates for sewage treatment levels

Effluent Source	Body weight (kg live wt)	PEC/TRV Water intake		PEC/TRV Food Intake		PEC/TRV Sediment Intake		PEC/TRV Total Oral Intake	
		Freshwater	Marine	Freshwater	Marine	Freshwater	Marine	Freshwater	Marine
Untreated wastewater	0.01 kg	<0.01	<0.01	21	2.1	0.6	0.06	22	2.2
	0.1 kg	<0.01	<0.01	9.4	0.94	0.3	0.03	9.7	1.0
	1.0 kg	<0.01	<0.01	4.2	0.42	0.1	0.01	4.3	0.43
Primary Treatment	0.01 kg	<0.01	<0.01	21	2.1	0.6	0.06	21	2.1
	0.1 kg	<0.01	<0.01	9.2	0.92	0.3	0.03	9.5	0.95
	1.0 kg	<0.01	<0.01	4.1	0.41	0.1	0.01	4.2	0.42
Trickling Filter	0.01 kg	<0.01	<0.01	8.8	0.88	0.3	0.03	9.1	0.91
	0.1 kg	<0.01	<0.01	4.0	0.40	0.1	0.01	4.1	0.41
	1.0 kg	<0.01	<0.01	1.8	0.18	0.1	<0.01	1.8	0.18
Activated Sludge	0.01 kg	<0.01	<0.01	9.5	0.95	0.3	0.03	9.7	1.0
	0.1 kg	<0.01	<0.01	4.2	0.42	0.1	0.01	4.4	0.44
	1.0 kg	<0.01	<0.01	1.9	0.19	0.1	<0.01	2.0	0.20
Activated sludge (SimpleTreat)	0.01 kg	<0.01	<0.01	8.2	0.82	0.2	0.02	8.4	0.84
	0.1 kg	<0.01	<0.01	3.7	0.37	0.1	0.01	3.8	0.38
	1.0 kg	<0.01	<0.01	1.6	0.16	0.0	<0.01	1.7	0.17
Tertiary treatment	0.01 kg	<0.01	<0.01	2.7	0.27	0.1	<0.01	2.8	0.28
	0.1 kg	<0.01	<0.01	1.2	0.12	0.0	<0.01	1.3	0.13
	1.0 kg	<0.01	<0.01	0.5	0.05	0.0	<0.01	0.6	0.06
Measured Australian Data	0.01 kg	<0.01	<0.01	0.9	0.09	0.0	<0.01	0.9	0.09
	0.1 kg	<0.01	<0.01	0.4	0.04	0.0	<0.01	0.4	0.04
	1.0 kg	<0.01	<0.01	0.2	0.02	<0.01	<0.01	0.2	0.02

Table G-2. Estimated Risk Quotients (PEC/TRV) for mammals (0.01-1.0 kg bw) potentially exposed to freshwater and marine ecosystems containing triclosan released in STP effluent, based on removal rates for sewage treatment levels

Effluent Source	Body weight (kg live wt)	PEC/TRV Water intake		PEC/TRV Food Intake		PEC/TRV Sediment Intake		PEC/TRV Total Oral Intake	
		Freshwater	Marine	Freshwater	Marine	Freshwater	Marine	Freshwater	Marine
Untreated wastewater	0.01 kg	<0.01	<0.01	55	5.5	0.23	0.02	55	5.5
	0.1 kg	<0.01	<0.01	43	4.3	0.18	0.02	43	4.3
	1.0 kg	<0.01	<0.01	34	3.4	0.15	0.01	35	3.5
Primary Treatment	0.01 kg	<0.01	<0.01	53	5.3	0.23	0.02	54	5.4
	0.1 kg	<0.01	<0.01	42	4.2	0.18	0.02	43	4.3
	1.0 kg	<0.01	<0.01	34	3.4	0.14	0.01	34	3.4
Trickling Filter	0.01 kg	<0.01	<0.01	23	2.3	0.10	<0.01	23	2.3
	0.1 kg	<0.01	<0.01	18	1.8	0.08	<0.01	18	1.8
	1.0 kg	<0.01	<0.01	14	1.4	0.06	<0.01	15	1.5
Activated Sludge	0.01 kg	<0.01	<0.01	25	2.5	0.10	0.01	25	2.5
	0.1 kg	<0.01	<0.01	19	1.9	0.08	<0.01	20	2.0
	1.0 kg	<0.01	<0.01	15	1.5	0.07	<0.01	16	1.6
Activated sludge (SimpleTreat)	0.01 kg	<0.01	<0.01	21	2.1	0.09	<0.01	21	2.1
	0.1 kg	<0.01	<0.01	17	1.7	0.07	<0.01	17	1.7
	1.0 kg	<0.01	<0.01	13	1.3	0.06	<0.01	13	1.3
Tertiary treatment	0.01 kg	<0.01	<0.01	7.1	0.71	0.03	<0.01	7.1	0.71
	0.1 kg	<0.01	<0.01	5.6	0.56	0.02	<0.01	5.7	0.57
	1.0 kg	<0.01	<0.01	4.5	0.45	0.02	<0.01	4.5	0.45
Measured Australian Data	0.01 kg	<0.01	<0.01	2.3	0.23	<0.01	<0.01	2.3	0.23
	0.1 kg	<0.01	<0.01	1.8	0.18	<0.01	<0.01	1.9	0.19
	1.0 kg	<0.01	<0.01	1.5	0.15	<0.01	<0.01	1.5	0.15

Appendix H - BurrliOZ Modelling

A species sensitivity distribution (SSD) for triclosan has recently been published by Capdeville et al. (2008). This modeling relied on chronic data collected from the literature and determined an HC5,50 (the concentration estimated to affect the survival, reproduction and/or growth of 5% of species with a 50% confidence interval). The value reported for the HC5 was 1.551 µg/L.

The data provided or available were used to generate a SSD using the BurrliOZ software (CSIRO 2002). The BurrliOZ software is used by environmental managers responsible for implementing the Australian and New Zealand Water Quality Guidelines for Fresh and Marine Waters to generate 'trigger values' (ie the maximum concentration of a chemical that should be maintained to permit the integrity and function of the aquatic environments) for local conditions within Australia. The BurrliOZ software is designed to estimate the protecting concentrations of chemicals such that a given percentage of species will survive. The estimations of the protecting concentrations are computed by fitting a certain distribution to the input data, called the Burr III distribution. This methodology has been applied to the aquatic toxicity data listed in Table H-1 (from the available acute LC/EC50 and NOEC values from the acute studies with aquatic species presented in Tables 21.3-21.5).

Table H-1 - Summary of acute aquatic toxicity data used in BurrliOZ modeling

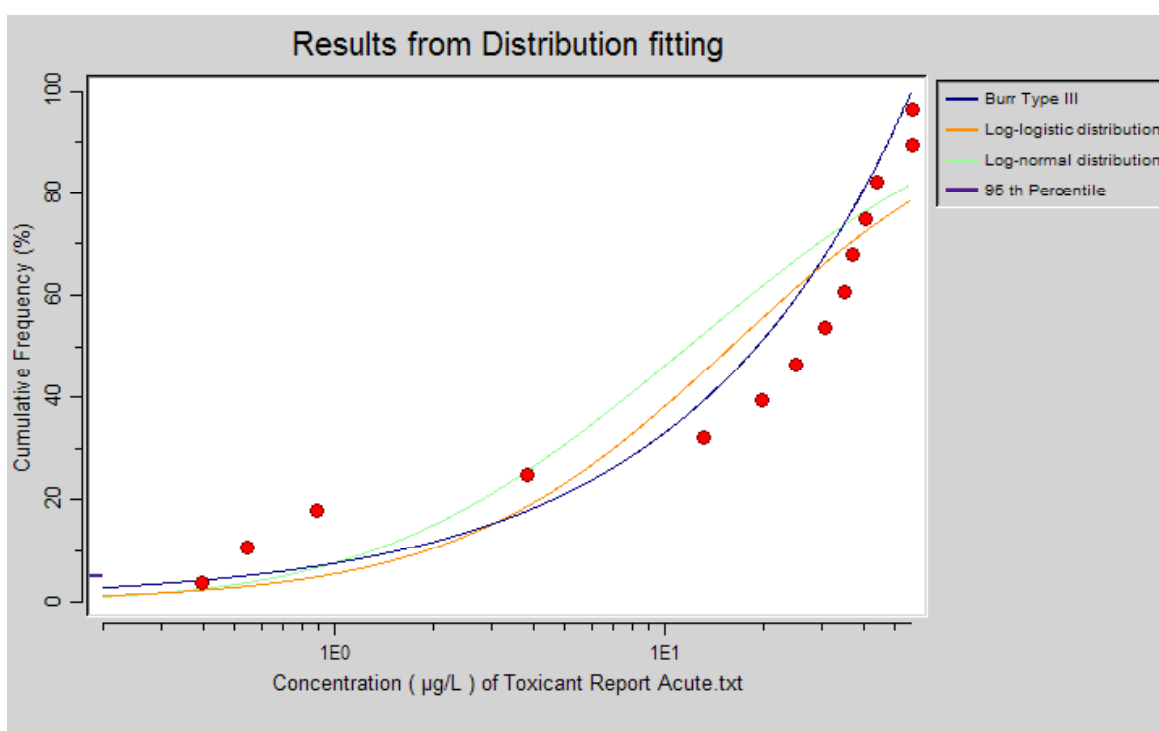
Species	Duration/Conditions	Endpoint	Result (µg/L)
<i>Pimephales promelas</i>	96 h	LC50	260
	96 h	LC50	360
<i>Leuciscus idus</i>	96 h	LC50	560
<i>Lepomis macrochirus</i>	96 h	LC50	370
<i>Oryzias latipes</i>	48 h	LC50	352
	96 h (ELS)	LC50	602
	96 h (embryos)	LC50	399
<i>Danio rerio</i>	96 h	LC50	540
<i>Oncorhynchus mykiss</i>	96 h	LC50	350
<i>Daphnia magna</i>	48 h	EC50	550
	48 h	EC50	303
<i>Ceriodaphnia dubia</i>	48 h, pH 6.8-7.0	EC50	130
	48 h, pH 7.4-7.6	EC50	180
	48 h, pH 8.0-8.2	EC50	240
	48 h, pH 8.2-8.5	EC50	420
	48 h	EC50	123
<i>Scenedesmus subspicatus</i>	72 h	NOEC	0.5
	96 h	NOEC	0.69
	96 h	NOEC	0.742
	96 h	NOEC	2.38
<i>Anabaena flos-aquae</i>	96 h	NOEC	0.81
	96 h	EbC50	0.97
<i>Navicula pelliculosa</i>	96 h	EbC50	19.1
<i>Pseudokirchneriella subcapitata</i>	96 h	EbC50	4.46
	96 h	IC50	2.6
	72 h	EC50	4.7
	72 h	NOEC	0.2
<i>Vibrio fischeri</i>	15 min	IC50	53
	-	IC50	150

	30 min	EC50	246
<i>Skeletonema costatum</i>	96 h	ErC50	66

In undertaking the modeling, an acute chronic ratio (ACR) of 10 to fish and invertebrate data and, 5 to algal and bacterial data were used for LC/EC50 values. No assessment has been applied to the NOEC values in the table. For multiple endpoints for the same organism the geometric mean of the values has been used in the modeling.

The results of the distribution fitting are presented in Figure H-1 for all aquatic species. The model predicts a protective concentration of 0.53 µg/L to protect 95% of species (equivalent to the HC5).

Figure H-1 Results of BurrliOZ distribution fitting acute toxicity data for aquatic organisms exposed to TCS

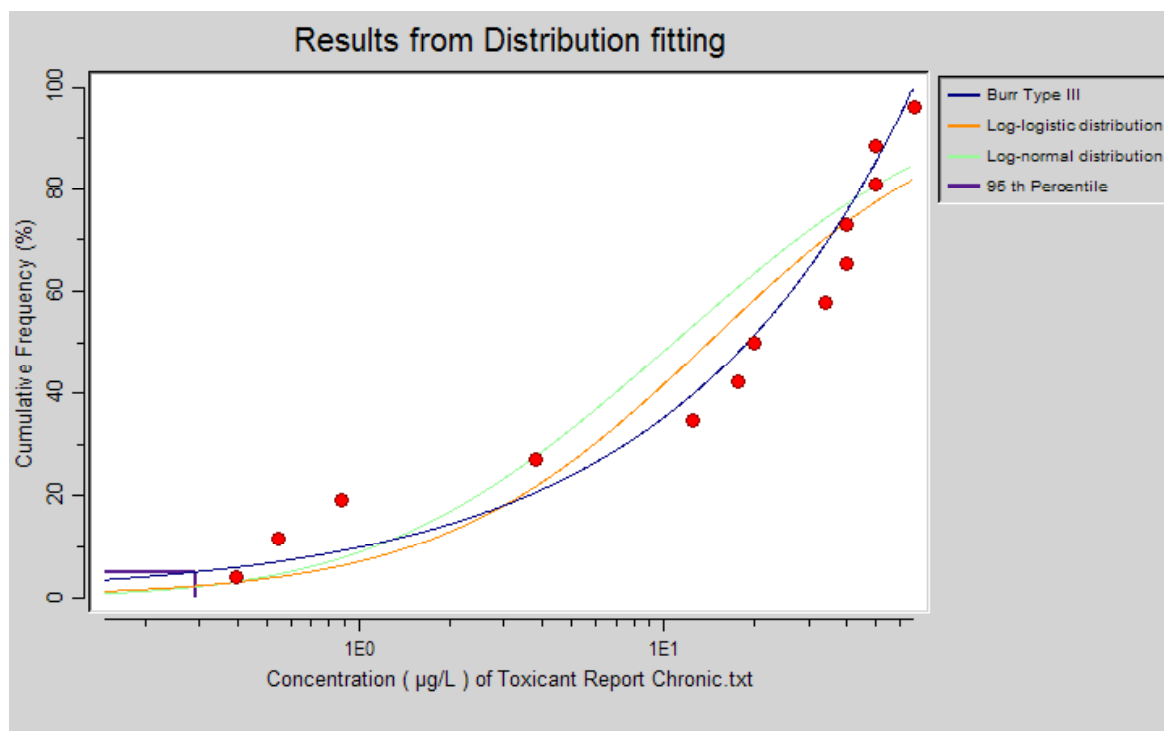


Repeating the modelling as above using chronic data presented in Tables 21.3-21.5 (summarized in Table H-2), the distribution and fitting are presented in Figure H-2 for all aquatic species. The model predicts a protective concentration of 0.29 µg/L to protect 95% of species. From this value a PNEC of 0.058 µg/L can be determined by applying an assessment factor of 5 in accordance with the EC Technical Guidance Document (EC 2003b).

Table H-2 Summary of chronic aquatic toxicity data used in BurrliOZ modelling

Species	Duration/Conditions	Endpoint	Result (µg/L)
Oryzias latipes	14 d (ELS)	IC50	400
Brachydanio rerio	10 d (ELS)	NOEC	200
	9 d (ELS)	IC50	220
Oncorhynchus mykiss	96 d (ELS)	NOEC	34.1
Daphnia magna	22 d	NOEC (reprod.)	40
Ceriodaphnia dubia	7 d	NOEC (reprod.)	6
	7 d	NOEC (reprod.)	182
	7 d	NOEC	4
	7 d	IC50	220
Brachionus calyciflorus	48 h	NOEC	50
Scenedesmus subspicatus	72 h	NOEC	0.5
	96 h	NOEC	0.69
	96 h	NOEC	0.742
	96 h	NOEC	2.38
Anabaena flos-aquae	96 h	NOEC	0.81
	96 h	EbC50	0.97
Navicula pelliculosa	96 h	EbC50	19.1
Pseudokirchneriella subcapitata	96 h	EbC50	4.46
	96 h	IC50	2.6
	72 h	EC50	4.7
	72 h	NOEC	0.2
Lemna gibba	7 d	ErC50	62.5
Chironomus tentans	10 d	EC10	200
Hyalella azteca	10 d	EC10	50

Figure H-2 Results of BurrliOZ distribution fitting chronic toxicity data for aquatic organisms exposed to TCS



Appendix I - Sample Material Safety Data Sheet for Triclosan

This sample MSDS only presents information on the raw material, not products containing triclosan. The information presented in this sample MSDS is based on the findings of this assessment and takes into account information in MSDSs provided by applicants. Also, where relevant, guidance-only information (text in italic) is provided. Industry is required to create accurate text in accordance with the guidance, by consultation of the relevant documents and/or organisations. Information placed in Section 15 of the MSDS should reflect the hazard classification for triclosan recommended in this assessment. (see Recommendations section: Recommendation 1).

Page 1	of Total 7
--------	------------

Section 1 - Identification of the Material and Supplier	
Product name	Triclosan
Other names	Phenol, 5-chloro-2-(2,4-dichlorophenoxy)- (AICS Name) 2,4,4,-trichloro-2,-hydroxydiphenyl ether
Recommended use	Antimicrobial treatment agent used in a wide range of products.
Company name	
Address	
State	Postcode
Telephone number	Emergency telephone number

Section 2 - Hazard Identification

HAZARDOUS SUBSTANCE. DANGEROUS GOODS.

Classified as hazardous according to the criteria of NOHSC

Risk phrases

R23 – Toxic by inhalation
 R36 – Irritating to eyes
 R37 – Irritating to respiratory system
 R38 – Irritating to skin

Safety phrases

S22 – Do not breathe dust
 S26 – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice
 S37 – Wear suitable gloves
 S38 – In case of insufficient ventilation, wear suitable respiratory equipment
 S39 – Wear eye/face protection
 S45 – In case of accident or if you feel unwell seek medical advice immediately (show the label where possible)
 S60 – This material and its container must be disposed of as a hazardous waste

Poison Schedule

Not Scheduled

Section 3 - Composition/Information on Ingredients

Chemical entity	Proportion	CAS Number
Phenol, 5-chloro-2-(2,4-dichlorophenoxy)-	> 99%	3380-34-5

Section 4 - First Aid Measures

Swallowed: If swallowed do NOT induce vomiting. Wash out mouth with water. Drink plenty of water. Seek medical advice.

Eyes: If in eyes, hold eyelids apart and flush the eye continuously with clean running water for at least 15 minutes, or until advised to stop by the Poisons Information Centre or a doctor.

Skin: If skin contact occurs, remove contaminated clothing. Clean contaminated area with soap and water, and flush skin with running water. Seek medical attention.

Inhalation: If inhaled remove from contaminated area. Apply artificial respiration if not breathing. Seek medical advice.

First aid facilities: Ensure eye bath and safety showers are available and ready for use. For advice, contact a Poisons Information Centre (131 126) or a doctor at once.

Advice to doctor: Treat symptomatically and supportively, no specific antidote known.

Section 5 - Fire Fighting Measures

Suitable extinguishing media

Water spray, carbon dioxide, foam or dry powder - no restrictions.

Hazard from combustion products

Vapours of carbon and nitrogen oxides, and hydrochloric acid can be released in a fire.

Under extreme conditions such as high alkalinity and high temperature triclosan can release chlorinated dibenzo-*p*-dioxines.

Precautions for fire fighters and special protective equipment

Fire fighters wear full protective gear including self-contained breathing apparatus.

Section 6 - Accidental Release Measures

Emergency procedures

Avoid eye or skin contact. Wear protective clothing including impervious gloves, overalls, and eye protection.

Avoid creating dust. Dampen down spill, and collect into marked containers for disposal.

Do not hose spills down drains, sewers or waterways.

Highly toxic to aquatic organisms, prevent entry into drains and surface waters.

Methods and materials for containment and clean up

Sweep up spills, then absorb/vacuum up all remaining residue using small quantities of water and detergent if necessary. Clean up personnel should wear full protective equipment.

Refer to Section 8 for personal protection equipment.

Section 7 - Handling and Storage

Precautions for safe handling

Avoid ingestion, inhalation, eye or skin contact. Wash hands and face thoroughly after handling and before eating, drinking or smoking. Avoid dust formation: equipment should be adequately grounded to reduce risk of dust explosion.

Conditions for safe storage, including any incompatibilities

Store in a sealed container in a cool, dry, ventilated area away from sources of heat, ignition and moisture, and incompatibles such as chlorinating agents.

Section 8 - Exposure Controls/Personal Protection

National exposure standards

No exposure standard allocated

Engineering controls

Ensure adequate ventilation. Local exhaust ventilation may be necessary for some operations.

Personal protective equipment

Use suitable protective clothing and gloves to avoid skin contact. Wear eye protection. When using triclosan powder, if no local exhaust ventilation is available, wear respiratory protection.

Please refer to relevant Australian Standards and consult with manufacturers of personal protective equipment for accurate information on suitable protective equipment.

Section 9 - Physical Description and Properties

Appearance

Fine white crystalline powder with a slight aromatic odour

Boiling point

Not known

Melting point

54 – 57.3 °C

Vapour pressure

4×10^{-6} mm Hg at 20 °C

Specific gravity

1.58 ± 0.03 g/cm³

Flash point

Not known

Flammability limits

Not applicable

Solubility in water

0.1 g/L at 20 °C

Section 10 - Stability and Reactivity

Chemical stability

Triclosan decomposes at temperatures ≥ 280 °C. In solution it is unstable in strong sunlight.

Conditions to avoid

Moisture, light and excessive heat

Incompatible materials

Chlorinating and oxidising agents.

Hazardous decomposition products

Vapours of carbon and nitrogen oxides, and hydrochloric acid are likely to be released in a fire.

Under extreme conditions such as high alkalinity and high temperature triclosan can release chlorinated dibenzo-*p*-dioxines.

Hazardous reactions

No data

Section 11 - Toxicological Information

Acute effects:

Animal data indicates that triclosan has low acute toxicity by the oral and dermal route. The LC50 value in rats was less than 1300 mg/m³ after 2 h exposure indicating moderate inhalation toxicity.

Triclosan is a skin, eye and respiratory irritant.

Chronic effects:

Animal data indicate triclosan causes mild hepatic effects following long-term ingestion or application to the skin. Irritation to the skin and nasal tract has been observed in animals following repeated dermal application and inhalation exposure respectively.

Section 12 - Ecological Information

Overall

Very toxic to aquatic life (Category: Acute I).

Very toxic to aquatic life with long lasting effects (Category: Chronic I).

Persistent under anaerobic conditions and its rapid depuration would limit its potential to bioaccumulate. Do NOT allow to enter water, wastewater or the soil.

Ecotoxicity

Triclosan is very toxic to fish, LC50 96 hr values ranging from 260 – 560 µg/L

Acute Fish Toxicity LC50 (Fathead Minnow, 96 hrs): 260 µg/L

Acute Fish Toxicity LC50 (Rainbow Trout, 96 hrs): 350 µg/L

Triclosan is very toxic to invertebrates, with algae the most sensitive species.

Acute Invertebrate Toxicity EC50 (Daphnia Magna, 48 hrs): 550 µg/L

Acute Bacterial Aquatic Toxicity EC50 (Anabaena flos-aquae, 96 hr) 1.6 µg/L

Acute Algae Aquatic Toxicity EC50 (Scenedesmus subspicatus, 72 hr): 0.7 µg/L

Persistence

Triclosan is persistent in the environment only under some conditions i.e. anaerobic conditions, under other conditions it is degraded.

Mobility

Low mobility in soils. When saturation or binding capacity is reached, mobility may potentially increase.

Bioaccumulative potential

Triclosan has the potential to bioaccumulate, however, its rapid depuration would limit the potential sustained levels in exposed organisms once exposure ceases.

Section 13 - Disposal Considerations

Disposal methods and containers

Dispose of all waste by high temperature incineration in accordance with State waste regulations.

Empty containers must be disposed of as a chemical waste.

Special precautions for landfill or incineration

Contact local waste disposal authority for advice or pass to a licensed waste disposal company for disposal.

Section 14 - Transport Information

UN Number

2811 for triclosan powder (100%) or,
3077 (solid)/3082 (liquid) if the 1-h LC50 is > 4mg/L

UN proper shipping name

'Toxic solid, organic' or 'Environmentally hazardous substance, solid, not otherwise specified' or 'Environmentally hazardous substance, liquid, not otherwise specified'.

Class and subsidiary risk

Class 6.1 (or Class 9 based on the concentration)

Packing group

III

Special precautions for user

Not available

Hazchem code

2X

Section 15 - Regulatory Information

Australian regulatory information

Triclosan is listed on the Australian Inventory of Chemicals Substances (AICS).

Section 16 - Other Information

Date of preparation

Abbreviations/Acronyms

ASSC – Australian Safety & Compensation Council
HSIS – Hazardous Substances Information System
NOHSC – National Occupational Health and Safety Commission

Literature references

National Industrial Chemicals Notification and Assessment Scheme (NICNAS)
Assessment Report on Triclosan: Priority Existing Chemical Assessment Report.

The full report can be downloaded from: <http://www.nicnas.gov.au>

Appendix J - Material Safety Data Sheet Assessment Summary

Data/information	Details	MSDS number						
		1	2	3	4	5	6	7
NOHSC hazard statement		√	√	√	√	√	X	√
Product name		√	√	√	√	√	√	√
UN number		I	I	I	I	I	X	I
ADG Code Class		I	I	I	I	I	X	I
Hazchem Code		√	√	√	√	I	X	√
Formulation	P	√	√	√	√	√	√	√
	R	√	√	√	√	√	√	√
Health effects ¹		I	I	I	I	I	I	I
First aid		√	√	√	√	√	I	√
Exposure standard ²		NA	NA	NA	NA	NA	X	NA
Advice on PPE		√	√	√	√	√	X	√
Safe handling	S/T	√	√	√	√	√	I	√
	S/D	√	√	√	√	I	X	√
	F/E	√	√	√	√	I	X	√
Company details		√	√	√	√	I	X	√

Key:

√ = Adequate. I = Addressed but inadequate or incomplete. X = No data or not present. NA = Not allocated (as stated in MSDS).

¹ = According to ASCC Hazardous Substances Information System. ² = According to NOHSC Occupational Exposure Standard (1995). P = Reporting presence of triclosan. R = Data on concentration/range triclosan. S/T = Storage/transport. S/D = Spills/disposal. F/E = Fire/explosion.

Appendix K - Applicants

Following the declaration of triclosan as a priority existing chemical, seventy-two companies, one government authority and one association applied for assessment of the chemical. Applicants supplied information on the properties, import quantities and uses of the chemical. In accordance with the *Industrial Chemicals (Notification and Assessment) Act (1989)*, NICNAS provided the applicants with a draft copy of the report for comments during the corrections/variation phase of the assessment. The applicants were:

3M Australia Pty Ltd

950 Pacific Hwy
PYMBLE NSW 2073

Amtrade International Pty Ltd

Level 6, 574 St Kilda Road
MELBOURNE VIC 3004

ACCORD

Suite 4.02 (Level 4)
22-36 Mountain Street
ULTIMO NSW 2007

Apisant Pty Ltd

12 – 18 Victoria Street East
LIDCOMBE NSW 2141

Aeris Technologies Ltd

24/566 Gardeners Road
ALEXANDRIA NSW 2015

Avon Products Pty Ltd

120 Old Pittwater Road
BROOKVALE NSW 2100

Aeropack Australia Pty Ltd

14 – 16 Potter Close
WETHERILL PARK NSW 2125

Barry Luke & Associates Pty Limited

68 The Ridge
MT ELIZA VIC 3930

Aerosol Products Ltd

134 – 144 Felton Mathew Avenue
GLEN INNES, AUCKLAND,
NEW ZEALAND 1006

Beauty & Care Australia Pty Ltd

Suite 1502, Level 15, 207 Kent St
SYDNEY NSW 2000

Boots Healthcare Australia Pty Ltd

101 Waterloo Road
NORTH RYDE NSW 2113

Campbell Industrial Products

32 Perivale Street
DARRA QLD 4076

Canpoint International Pty Ltd

PO Box 375
LIDCOMBE NSW 1825

C B Fleet Co (Aust) Pty Ltd

25 Macbeth Street
BRAESIDE VIC 3195

Cartigny Pty Ltd

45 Huntingwood Drive
HUNTINGWOOD NSW 2148

Chanel (Australia) Pty Ltd

Level 12, 121 Walker St
NORTH SYDNEY NSW 2060

Church & Dwight (Aust) Pty Ltd

1/108 Pittwater Rd
BROOKVALE nsw 2100

Ciba (Australia) Pty Ltd

235 Settlement Road
THOMASTOWN VIC 3074

Clarient (Australia) Pty Ltd

675 Warrigal Road
CHADSTONE VIC3148

Colgate-Palmolive Pty Ltd

345 George Street
SYDNEY NSW 2000

Combe International Ltd

10/1 Milton Parade
MALVERN VIC 3144

Cosmeceutical Creations Corporation Ltd

391 Rosebank Rd
AVONDALE 1007
NEW ZEALAND

Cosmetech Pharmaceuticals

38 Donegal Road
LONSDALE SA 5160

Custom Chemicals International Pty Ltd

103 – 107 Potassium Street
NARANGBA QLD 4504

Deb Australia Pty Ltd
73 Alfred Rd
CHIPPING NORTON NSW 2170

Dominant (Australia) Pty Ltd
12 Coglin St
BROMPTON SA 5007

Down Under Chemicals
7 Lansdown Parade
OATLEY NSW 2223

Ecolab Pty Ltd
6 Hudson Avenue
CASTLE HILL NSW 2154

Elizabeth Arden
Level 1, 1 Epping Rd
NORTH RYDE NSW 1670

Ensign Laboratories Pty Ltd
490 Wellington Road
MULGRAVE VIC 3170

Estee Lauder
21 Rosebery Avenue
ROSEBERY NSW 2018

Frostbland Pty Ltd
1/47 – 53 Moxon Road
PUNCHBOWL NSW 2196

**Glaxo Smith Kline Consumer
Healthcare**
82 Hughes Avenue
ERMINGTON NSW 2115

**Guerlain Oceania Australia Pty
Ltd**
1/13 Lord Street
BOTANY NSW 2019

**Hair Advisory Centre Pty Ltd
t/as Queensland Cosmetic
Laboratories**
28 Horizon Drive
BEENLEIGH QLD 4207

Halas Dental Limited
44 O’Dea Avenue
WATERLOO NSW 2017

Hallas Trading Co Pty Ltd
2 Lambs Road
ARTARMON NSW 2064

HyAust Pty Ltd
Unit 1/15 Dunstan St
WINGFIELD, SA 5013

Innox Pty Ltd
6/106 Old Pittwater Road
BROOKVALE NSW 2100

Jalco Group Pty Ltd

6 Ash Road
PRESTONS NSW 2170

L'Oreal Australia Pty Ltd

266 Bay Road
SANDRINGHAM VIC 3191

Johnson & Johnson Medical Pty Ltd

1 – 5 Khartoum Road
NORTH RYDE NSW 2113

LVMH Perfumes and Cosmetics Group Pty Ltd

1/13 Lord Street
BOTANY NSW 2019

Johnson & Johnson Pacific Pty Ltd

Level 3, 1 Bay Street
BROADWAY NSW 2007

McPherson's Consumer Products

105 Vanessa St
KINGSGROVE NSW 2208

JohnsonDiversey Australia Pty Ltd

29 Chifley St
SMITHFIELD NSW 2164

Milpharma Pty Ltd

13B Clearview Place
BROOKVALE NSW 2100

Juvena Australia Pty Ltd

75 Epping Roadf
NORTH RYDE NSW 2113

Nimue Skin Technology Pty Ltd

7/153 Beauchamp Road
MATRAVILLE NSW 2036

Key Sun Laboratories Pty Ltd

2/10 Ponderosa Parade
WARRIEWOOD NSW 2102

Nowra Chemical Manufacturers Pty Ltd

112 Albatross Road
NOWRA NSW 2541

Kimberly-Clark Australia Pty Ltd

52 Alfred St
MILSONS POINT NSW 2061

NSW Department of Environment and Climate Change

59 – 61 Goulburn Street
SYDNEY NSW 2000

Nuplex Industries (Aust) Pty Ltd

49-61 Stephens Road
BOTANY, NSW 2019

Nutrimetics International (Australia) Pty Ltd

102 Elliott Street
BALMAIN NSW 2041

Optigen Ingredients Pty Ltd

308 St Vincent Street
PORT ADELAIDE, SA 5015

PAX Australia

9 Williamson Road
INGLEBURN NSW 2565

Proarma Pty Ltd

3 Tipperary Mews
Subiaco WA 6008

Procter & Gamble Australia Pty Ltd

320 Victoria Road
RYDALMERE NSW 2116

Protective Technology Pty Ltd

1/208 Whitehorse Road
BLACKBURN VIC 3130

Pryme Australia Pty Ltd

2/12 Sudbury St
DARRA, QLD 4076

Reckitt Benckiser Healthcare Australia Pty Ltd

44 Warf Road
WEST RYDE, NSW 2114

Redox Pty Ltd

2 Swettenham Road
Minto, NSW 2566

Revlon Australia Pty Limited

12 Julius Avenue
NORTH RYDE NSW 2113

Ross Cosmetics Aust Pty Ltd

14 – 22 Carrick Drive
TULLAMARINE VIC 3034

Sabco Australia

461 Plummer Street
PORT MELBOURNE, VIC 3207

Sara Lee Household & Body Care (Australia) Pty Ltd

610 Heatherton Road
CLAYTON SOUTH VIC 3169

Saraya Australia Pty Ltd

Unit 12, 2-4 Northumberland Rd
CARINGBAH, NSW 2229

**Semal Pty Ltd t/as Consolidated
Chemical Company**

52 – 62 Waterview Close

DANDENONG SOUTH VIC
3175

SSL Australia Pty Ltd

225 Beach Road

MORDIALLOC VIC 3195

SUN-CHEM

64 Violet Street

GYMPIE QLD 4570

**The Australian Perfume
Company**

14 Barcrest Drive

YANDINA QLD 4561

Trimex Pty Ltd

5 Crewe Place

ROSEBERY NSW 2018

Unilever Australasia

219 North Rocks Road

NORTH ROCKS NSW 2151

Wilfrid Owen (Sales) Pty Ltd

15 – 16/167 Prospect Highway

SEVEN HILLS NSW 2147

References

Aardema MJ, Albertini S, Arni P, Henderson LM, Kirsch-Volders M, Mackay JM, Sariff AM, Stringer SA and Taalman RDF (1998). Aneuploidy: a report of an ECETOC task force. *Mutation Research*, **410**:3–79.

ABC Laboratories Inc. (1990a) Acute toxicity of D1063.01 to Fathead Minnow (*Pimephales promelas*). Analytical Bio-Chemistry Laboratories, Inc. Unpublished report, Project ID. 38655, Proctor & Gamble Company.

ABC Laboratories Inc. (1990b) Acute toxicity of D1063.01 to *Daphnia magna*. Analytical Bio-Chemistry Laboratories, Inc. Unpublished report, Proctor & Gamble Company.

ABC Laboratories Inc. (1996) Early life-stage toxicity of triclosan to Rainbow Trout (*Oncorhynchus mykiss*) under flow through conditions. Analytical Bio-Chemistry Laboratories, Inc. Unpublished study No. 42726R, Unilever Research, NJ, USA.

ABC Laboratories Inc. (1997a) Adsorption of ¹⁴C-Triclosan to suspended solids. Analytical Bio-Chemistry Laboratories, Inc. Unpublished final report N0. 43356, Ciba-Geigy Corporation, NC, USA.

ABC Laboratories Inc. (1997b) FDA seedling growth phytotoxicity test. Analytical Bio-Chemistry Laboratories, Inc. Unpublished test report, Colgate-Palmolive Company.

ABC Laboratories Inc. (1997c) Acute toxicity of triclosan to *Scenedesmus subspicatus*. Analytical Bio-Chemistry Laboratories, Inc. Unpublished Report No. 43118, Ciba-Geigy Corporation.

ACT Commissioner for the Environment (2000). Australian Capital Territory State of the Environment Report 2000. <http://www.environmentcommissioner.act.gov.au/SoE2000/ACT/IndicatorResults/Dischargestowaters.htm>

Achari RG and Chin D (1981) HPLC analysis of some bacteriostats in deodorant sticks and soaps. *Journal of the Society of Cosmetic Chemists*, **32**:163–173.

Adam D (2007) ¹⁴C-Triclosan: degradation and metabolism in three soils incubated under aerobic conditions. Unpublished study report, RCC Study Number B12835. RCC Ltd, Zelgliweg 1, 4452 Itingen, Switzerland.

Adam D (2006) ¹⁴C-Triclosan: route and rate of degradation in aerobic aquatic sediment systems. Unpublished study report, RCC Study Number A33300. RCC Ltd, Zelgliweg 1, 4452 Itingen, Switzerland.

Adams RM and Maibach HI (1985) A five-year study of cosmetic reactions. *Journal of the American Academy of Dermatology*, **13**:1062–1069.

Adolfsson-Erici M, Pettersson M, Parkkonen J and Sturve J (2002) Triclosan, a commonly used bactericide found in human milk and in the aquatic environment in Sweden. *Chemosphere*, **46**:1485–1489.

Agrisearch Inc. (1993) Aqueous photolysis of triclosan. Unpublished study report, Project No. 12208. Ciba-Geigy Corporation, North Carolina, USA.

Aguera A, Fernandez-Alba AR, Piedra L, Mezcua M and Gomez JM (2003) Evaluation of triclosan and biphenylol in marine ediments and urban wastewaters by pressurized liquid extraction and solid phase extraction followed by gas chromatography mass spectrometry and liquid chromatography mass spectrometry. *Analytica Chimica Acta*, **480**:193–205.

Aiello AE, Marshall B, Levy SB, Della-Latta P and Larson E (2004) Relationship between triclosan and susceptibilities of bacteria isolated from hands in the community. *Antimicrobial Agents and Chemotherapy*, **48**:2973–2979.

Aiello AE, Marshall B, Levy SB, Della-Latta P, Lin SX and Larson E (2005) Antibacterial cleaning products and drug resistance. *Emerging Infectious Diseases*, **11**:1565–1570.

Alaee M, D'Sa I, Bennet E and Letcher R (2003) Levels of triclosan and methyl-triclosan in the plasma of fish from the Detroit River. 23rd International Symposium on Halogenated Environmental Pollutants and POPs (DIOXIN'2003), Aug. 24-29, Boston, U.S.A; Organohalogen Compounds (Published Aug. 2003, Organohalogen Compounds, **62**:136–139).

Allard AS, Remberger M and Neilson AH (1987) Bacterial O-methylation of halogen-substituted phenols. *Applied and Environment Microbiology*, **53**(4):839-845.

Allmyr A, Adolfsson-Erici M, McLachlan MS and Sandborgh-Englund G (2006) Triclosan in plasma and milk from Swedish nursing mothers and their exposure via personal care products. *Science of the Total Environment*, **372**(1):87–93.

Alongi DM (1994) The role of bacteria in nutrient recycling in tropical mangrove and other coastal benthic ecosystems. *Hydrobiologia*, **285** (1-3):19-32.

Alonso A, Morales G, Escalante R, Campanario E, Sastre L and Martinez JL (2004) Overexpression of the multidrug efflux pump SmeDEF impairs *Stenotrophomonas maltophilia* physiology. *Journal of Antimicrobial Chemotherapy*, **53**:432–434.

Amemiya T, Sakai M, Mori K, Suzuki S and Kazama M (1984) Hygenic chemical studies on household necessities (XI), high performance liquid chromatography of Irgan DP-300 and thiabendazole used in sanitary finishing agent in textile products. Annual Report of Tokyo Metropolitan Research Laboratories, **35**:133–137.

Annex 1 of Directive 67548EEC (2005) Update of Annex 1 up to Adaptations to Technical Progress 29. Accessed at: <http://ecb.jrc.it/classification-labelling/> in February 2006.

Anon. (1971) Pollution by detergents. Paris, Publications de l'OCDE, 2 rue Andre-Pascal. Cited in Voets et al., (1976).

ANZECC / ARMCANZ (Australian and New Zealand Environment and Conservation Council and the Agriculture and Resource Management Council of Australia and New Zealand). (2000). Australian and New Zealand Guidelines for Fresh and Marine Water Quality. National Water Quality Management Strategy, Environment Australia, Department of Environment and Heritage, Canberra. Internet. Accessed at: <http://www.ea.gov.au/water/quality/nwqms/volume1.html> in May 2006.

Argus Research Laboratories Inc. (1992a) Dosage-range developmental toxicity (embryo-fetal toxicity and teratogenic potential) study of C-P sample No. 38328 administered orally via the diet to CrI:CD-1(ICR)BR presumed pregnant mice. Unpublished protocol No: 403-010P, study No: 91-016, Argus Research Laboratories Inc., Pennsylvania, USA.

Argus Research Laboratories Inc. (1992b) Developmental toxicity (embryo-fetal toxicity and teratogenic potential) study of C-P sample No. 38328 administered orally via the diet to

CrI:CD-1(ICR)BR presumed pregnant mice. Unpublished protocol No: 403-010, study No: 92-001, Argus Research Laboratories Inc., Pennsylvania, USA.

Arni P and Muller D (1978a). *Salmonella*/mammalian-microsome mutagenicity test with FAT 80 023/A. Unpublished experiment No. 78/2511. Ciba-Geigy Limited, Basel, Switzerland.

Arni P and Muller D (1978b) Mutagenicity test on *Saccharomyces cerevisiae* MP-1 *in vitro* with FAT 80 023/A. Unpublished experiment No. 78/3402. Ciba-Geigy Limited, Basel, Switzerland.

Arni P and Muller D (1979) Intravascular host-mediated assay with *S. typhimurium* with FAT 80 023/A. Unpublished experiment No. 78/2803. Ciba-Geigy Limited, Basel, Switzerland.

Arnold WA, McNeill K, Packer JL, Latch DE and Boreen AL (2003) Photochemical fate of pharmaceutical compounds discharged and detected in natural waters. Department of Chemistry, University of Minnesota, USA. URL. Accessed at <http://wrc.umn.edu/research/competitivegrants/reports/2003arnold.pdf> in April 2006.

Arnott C (2003) A study of residual pharmaceutical concentrations in Virginia wastewater effluent via High Pressure Liquid Chromatography and Gas Chromatography/Mass Spectrometry. Unpublished Senior Honours Thesis, Sweet Briar College, VA.

Arthur III WJ and Alldredge AW (1979) Soil ingestion by mule deer in north central Colorado. *Journal of Rangeland Management*, **32**:67-70.

ASCC (2005) Hazardous Substances Information System (HSIS) Australian Safety and Compensation Council. <http://hsis.ascc.gov.au/Default.aspx>, accessed in February 2006.

ASTE (Australian Academy of Technology Sciences and Engineering) (2004) Water recycling in Australia. BPA Digital, Victoria, Australia.

ASTM (American Society for Testing and Materials) (1990) Standard guide for conducting static 96-hour toxicity tests with microalgae. E1218-90. Annual Book of ASTM Standards, Vol. 11.04.

ASTM (American Society for Testing and Materials) (1991) Standard guide for conducting static toxicity tests with *Lemna gibba* G3. E1415-91. Annual Book of ASTM Standards, Vol. 11.04.

Baert JH, Veys RJ, Ampe K, and De Boever A (1996) The effect of sodium lauryl sulphate and triclosan on hamster cheek pouch mucosa. *International Journal of Experimental Pathology*, **77**:73-78.

Balmer ME, Poiger T, Droz C, Romanin K, Bergqvist P-A, Muller MD and Buser H-A (2004) Occurrence of methyl triclosan, a transformation product of the bactericide triclosan, in fish from various lakes in Switzerland. *Environmental Science and Technology*, **38**:390-395.

Barkvoll P and Rolla G (1994) Triclosan protects the skin against dermatitis caused by sodium lauryl sulphate exposure. *Journal of Clinical Periodontology*, **21**:717-719.

Barnes E (1991) Mentadent P toothpaste: background study in man haematological and biochemical data. Unpublished test report: Project reference D91/052. Unilever Research, Sharnbrook, Bedford, UK.

Bätscher, R (2006a) Methyl-triclosan: toxicity to *Scenedesmus subspicatus* in a 72-hour algal growth inhibition test. RCC Ltd. Environmental Chemistry & Pharamalytics, Ittingen, Switzerland, Study Number A34918, Date: 2006-07-24.

Bätscher, R (2006b) Methyl-triclosan: acute toxicity to *Daphnia magna* in a 48-hour immobilization test. RCC Ltd. Environmental Chemistry & Pharamanalytics, Ittingen, Switzerland, Study Number A34931, Date: 2007-07-19.

Beiswanger BB and Tuohy MA (1990) Analysis of blood samples for free triclosan, triclosan glucuronide, triclosan sulphate and total triclosan from subjects using a triclosan dentifrice, bar soap and deodrant. Unpublished study report: OHRI study #89-A-111. Indiana University School of Dentistry, Indiana, USA.

Bendig JWA (1990) Surgical hand disinfection: comparison of 4 % chlorhexidine detergent solution and 2 % triclosan detergent solution. *Journal of Hospital Infection*, **15**:143–148.

Bester K (2003) Triclosan in a sewage treatment process – balances and monitoring data. *Water Research*, **37**:3891-3896.

Bester K (2005) Fate of triclosan and triclosan-methyl in sewage treatment plants and surface waters. *Archives of Environmental Contamination and Toxicology*, **49**:9-17.

Beyer NW, Audet DJ, Morton A, Campbell JK and LeCaptain L (1998) Lead exposure of waterfowl ingesting Coeur d'Alene River Basin Sediments. *Journal of Environmental Quality*, **27**:1533-1538.

Beyer NW, Connor EE and Gerould S (1994) Estimates of soil ingestion by wildlife. *Journal of Wildlife Management*, **58** (2):375-382.

Beyer WN, Audet DJ, Heinz GH, Hoffman DJ and Day D (2000) Relation of waterfowl poisoning to sediment lead concentrations in the Coeur d'Alene River Basin. *Ecotoxicology*, **9**:207-218.

Bhargava HN and Leonard PA (1996) Triclosan: applications and safety. *American Journal of Infection Control*, **24** (3):209–218.

BIBRA International (1988) The free and conjugated triclosan concentrations, clinical chemical analysis and haematology of blood samples from a human volunteer study (Beecham's Project SR 396). Unpublished test report: 720/3/88, BIBRA, Carshalton, Surrey, UK.

BIBRA International (1997) A study to determine the pharmacokinetics of triclosan in healthy subjects following 14 days of four times daily tooth-brushing with a dentifrice containing triclosan. Unpublished test report: 3133/1/3/97, BIBRA, Carshalton, Surrey, UK.

Biodynamics Inc. (1992a) A range-finding study to evaluate the toxicity of Irgacare MP (C-P sample No: 38328) in the pregnant rat. Unpublished final test report 91-3654, Colgate-Palmolive study 91-013, Biodynamics Inc., New Jersey, USA.

Biodynamics Inc. (1992b) A segment II teratology study in rats with Irgacare MP (C-P sample No.: 38328). Unpublished final test report 91-3665, Colgate-Palmolive study 91-005, Biodynamics Inc., New Jersey, USA.

Biodynamics Inc. (1992c) A range-finding study to evaluate the toxicity of Irgacare MP (C-P sample No: 38328) in the pregnant rabbit. Unpublished final test report 91-3655, Colgate-Palmolive study 91-014, Biodynamics Inc., New Jersey, USA.

Biodynamics Inc. (1992d) A segment II teratology study in rabbits with Irgacare MP (C-P sample No: 38328). Unpublished final test report 91-3666, Colgate Palmolive study 91-006, Biodynamics Inc., New Jersey, USA.

- Bio-Life Associates Ltd. (1993a) Triclosan (IRGASAN DP300[®]): 14-day acute oral LD50 study in Mallard Ducks. Unpublished Report No. 102-023-04. Ciba-Geigy Corporation.
- Bio-Life Associates Ltd. (1993b) Triclosan (IRGASAN DP300[®]): 14-day acute oral LD50 study in Bobwhite Quail. Unpublished Report No. 102-024-03. Ciba-Geigy Corporation.
- Bio-Life Associates Ltd. (1993c) Triclosan (IRGASAN DP300[®]): 8-day acute dietary LC50 study in Bobwhite Quail. Unpublished Report No. 102-022-01. Ciba-Geigy Corporation.
- Birkel W, Erking W and Wetzelsberger N (1993) Improved internally standardised GC-ECD method for the determination of free and conjugated triclosan (Irgasan DP300) in human plasma. *Methods and Findings in Experimental and Clinical Pharmacology*, **15** (9):623–627.
- Black JG and Howes D (1975) Percutaneous absorption of triclosan from toilet preparations. *Journal of the Society of Cosmetic Chemicals*, **26**:205–215.
- Black JG, Howes D and Rutherford T (1975) Percutaneous absorption and metabolism of Irgasan DP300. *Toxicology*, **3**:33–47.
- Blus LJ, Henny CJ, Hoffman DJ, Sileo L and Audet DJ (1999) Persistence of high lead concentrations and associated effects in Tundra Swans captured near a mining and smelting complex in Northern Idaho. *Ecotoxicology*, **8**:125-132.
- Boehmer W, Ruedel H, Wenzel A and Scroeter-Kermani C (2004) Retrospective monitoring of triclosan and methyl-triclosan in fish: Results from the German Environmental Specimen Bank. *Organohalogen Compounds*, **66**:1516 - 1521.
- Boyd GR, Reemtsma H, Grimm DA and Mitra S (2003) Pharmaceuticals and personal care products (PPCPs) in surface and treated waters of Louisiana, USA and Ontario, Canada. *The Science of the Total Environment*, **311**:135–149.
- Boyd GR, Palmeri JM, Zhang S and Grimm DA (2004) Pharmaceuticals and personal care products (PPCPs) and endocrine disrupting chemicals (EDCs) in stormwater canals and Bayou St. John in New Orleans, Louisiana, USA, *Science of the Total Environment*, **333**: 137-148.
- Braoudaki M and Hilton AC (2004a) Low level of cross-resistance between triclosan and antibiotics in *Escherichia coli* K-12 and *E.coli* O55 compared to *E. coli* O157. *FEMS Microbiology Letters*, **235**:305–309.
- Braoudaki M and Hilton AC (2004b) Adaptive resistance to biocides in *Salmonella enterica* and *Escherichia coli* O157 and cross-resistance to antimicrobial agents. *Journal of Clinical Microbiology*, **42** (1):73–78.
- Braoudaki M and Hilton AC (2005) Mechanisms of resistance in *Salmonella enterica* adapted to erythromycin, benzalkonium chloride and triclosan. *International Journal of Antimicrobial Agents*, **25**:31–37.
- Brenwald NP and Fraise AP (2003) Triclosan resistance in methicillin-resistant *Staphylococcus aureus* (MRSA). *Journal of Hospital Infection*, **55**:141–144.
- Brezonik PL and Fulkerson-Brekken J (1998) Nitrate-induced photolysis in natural waters: Controls on concentrations of hydroxyl radical photo-intermediates by natural scavenging agents. *Environmental Science and Technology*, **32**:3004-3010.

- Bringmann G (1973) Bestimmung der biologischen Schädlichkeit wasser gefährdender Stoffe aus der Hemmung der Glucose-Assimilation des Bakterium. *Pseudomonas fluorescens*. Gesundheitsingenieur, **94**:366. Cited in Voets et al., 1976.
- Broeckx W, Blondeel A, Dooms-Goossens A and Achten G (1987) Cosmetic intolerance. Contact Dermatitis, **16**:189–194.
- Brooker PC, Gray VM and Howell A (1988) Triclosan, analysis of metaphase chromosomes obtained from CHO cells cultured *in vitro*. Unpublished test report: ULR 214/88731 Huntingdon Research Centre, England - Unilever test No. KC 880171.
- Burns J (1996) 14-Day repeated dose dermal study of triclosan in mice. Unpublished test report: CHV 6718-101 Hazelton Laboratories, Wisconsin, USA.
- Burns J (1997a) 14-Day repeated dose dermal study of triclosan in CD-1 mice. Unpublished test report: CHV 6718-101 Hazelton Laboratories, Wisconsin, USA.
- Burns J (1997b) 14-Day repeated dose dermal study of triclosan in rats. Unpublished test report: CHV 6718-102 Corning Hazelton Inc., Virginia, USA.
- Butte NF, Garza C, Smith EO et al. (1984) Human milk intake and growth in exclusively breast-fed infants. *Journal of Pediatrics*, **104**:187–195. As cited in EPA (2002).
- Cadden R and West P (1995) The design and implementation of strategies to manage dry weather and wet weather wastewater flows in the Sydney region. In: Proceedings of the 16th Australian Water and Wastewater Association Federal Convention, Sydney, p461 - 468.
- Calafat AM, Ye X, Wong L, Reidy JA and Needham LL (2007) Urinary concentrations of triclosan in the U.S. population: 2003 – 2004. *Environmental Health Perspectives*, National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health, US Department of Health and Human Services, 7 December 2007.
- Calder WA (1981) Scaling of physiological processes in homeothermic animals. *Annual Review of Physiology*, **43**:301-322. (Cited in US EPA, 1993).
- Calder WA and Braun EJ (1993) Scaling of osmotic regulation in mammals and birds. *American Journal of Physiology*, **244**: R601-R606.
- Canosa P, Rodriguez I, Rubi E and Cela R (2005a) Optimization of solid-phase microextraction conditions for the determination of triclosan and possible related compounds in water samples. *Journal of Chromatography A*, **1072** (1):107–115.
- Canosa P, Morales S, Rodriguez I, Rubi E, Cela R and Gomez M (2005b) Aquatic Degradation of triclosan and formation of toxic chlorophenols in presence of low concentrations of free chlorine. *Analytical and Bioanalytical Chemistry*, **383**(7-8):1119-1126.
- Capdevielle M, van Egmond R, Whelan M, Versteeg D, Hofmann-Kamensky M, Inauen J, Cunningham V, Woltering D (2008) Consideration of exposure and species sensitivity of triclosan in the freshwater environment. *Integr Environ. Assess Manag* **4**, 15-23.
- Carolina Ecotox Inc. (1997) Effects of triclosan on the growth and reproduction of aquatic plants. Unpublished study report No. 21-02-1, Ciba Specialty Chemicals, NC, USA.
- Caudal F, Grimault D and Sioufi A (1974) Urinary excretion (free and glucuronide) in man after topical application of CGP.433 cream. Unpublished report No: C.R.B. R 4/1974. Ciba-Geigy Biopharmaceutical Research Centre.

Caudal F, Grimault D and Sioufi A (1975) GP. 41 353, FAT 80 023A: Triclosan, free and conjugated GP. 41 353 plasma concentration in baboons at the end of a one-year chronic toxicity study. Unpublished study report: C.R.B.R 12/1975.

CCR Cytotest Cell Research (1990) Chromosome aberration assay in Chinese Hamster V79 cells *in vitro* with FAT 80'023/Q. Unpublished test report: CCR Project No. 179100, CCR Cytotest Cell Research GMBH & Co. KG D-6101 Roßdorf.

CCR Cytotest Cell Research (1991) Chromosome aberration assay in bone marrow cells of the rat with FAT 80'023/Q. Unpublished test report: CCR Project No. 218305, CCR Cytotest Cell Research GMBH & Co. KG D-6101 Roßdorf.

Champlin FR, Ellison ML, Bullard JW and Conrad RS (2005) Effect of outer membrane permeabilisation on intrinsic resistance to low triclosan levels in *Pseudomonas aeruginosa*. *International Journal of Antimicrobial Agents*, **26**:159–164.

Chasseaud LF, Allen GD, Major RM, Holding JD, Assinder D and Greathead HMR (1999) Toxicokinetics of FAT 80'023/S after prolonged dietary administration to hamsters. Unpublished report. Huntingdon Life Sciences Ltd., Huntingdon, Cambridgeshire, England.

Chow AYK, Hirsch GH and Buttar HS (1977) Nephrotoxic and hepatotoxic effects of triclosan and chlorhexidine in rats. *Toxicology and Pharmacology*, **42**:1–10.

Chuanchuen R, Karkhoff-Schweizer RA and Schweizer HP (2003) High-level triclosan resistance in *Pseudomonas aeruginosa* is solely a result of efflux. *American Journal of Infection Control*, **31**:124–127.

Ciba-Geigy Corporation (1972a) Hexachlorophene-Irgasan DP-300 blood level pilot study (full body bathing). Unpublished laboratory report: Notebook # 239 (Spitzer, C). Ciba-Geigy Corporation, Ardsley, NY, USA.

Ciba-Geigy Corporation (1972b) Irgasan DP-300 skin absorption pilot study. Unpublished report No: CS 239. Ciba-Geigy Corporation, Ardsley, NY, USA.

Ciba-Geigy Corporation (1973a) Irgasan DP-300 and hexachlorophene content of plasma samples: 21 day handwashing study. Unpublished report No: 73-019 and 73-034. Ciba-Geigy Corporation, Greensboro, N.C, USA.

Ciba-Geigy Limited (1973b) GP 41 353: Report on the two weeks neurotoxicity study – oral administration to albino rats. Unpublished test report. Ciba-Geigy Ltd., Basel, Switzerland.

Ciba-Geigy Limited (1974) Irgasan DP 300 (FAT 80023/A) 21-day inhalation study on the rat. Unpublished test report: Toxicology/Pathology PH 2.635, Ciba-Geigy Ltd., Basel, Switzerland.

Ciba-Geigy Limited (1975a) GP 41'353: Excretion in the biliary-fistula rat and enterohepatic circulation in the rat. Unpublished study report No: B 8/1975. Ciba-Geigy Limited, Basel, Switzerland.

Ciba-Geigy Limited (1975b) 1-Year oral toxicity study in baboons with compound FAT 80 023/A. Unpublished test report: Toxicology Department, Wilmslow, UK.

Ciba-Geigy Limited (1976a) Investigations of percutaneous absorption in the rat and rabbit. Unpublished report: B 4/1976. Ciba-Geigy Limited, Basel, Switzerland.

Ciba-Geigy Limited (1976b) Isolation and identification of the main metabolites in the blood of the beagle dog and the baboon and in the urine of the latter following oral administration of

14C-labelled triclosan. Unpublished report No: B 14/1976. Ciba-Geigy Limited, Basel, Switzerland.

Ciba-Geigy Limited (1976c) Pharmacokinetic and metabolic studies in man following oral administration of a ¹⁴C-labelled preparation. Unpublished report No: B 6/1976. Ciba-Geigy Limited, Basel, Switzerland.

Ciba-Geigy Limited (1977a) Irgasan DP 300 (triclosan) skin absorption in the rabbit. Unpublished test report. Huntingdon Research Centre, New York, USA.

Ciba-Geigy Limited (1977b) Comparison of pharmacokinetic and metabolic parameters of triclosan and HCP in the mouse, rat, beagle dog and baboon, Part A: Survey of findings, Part B: Detailed account of the study. Unpublished report No: B 1/1977. Ciba-Geigy Limited, Basel, Switzerland.

Ciba-Geigy Corporation (1986) FAT 80'023: 2-Year oral administration to rats. Unpublished report No. MIN 83305, Pharmaceuticals Division, Ciba-Geigy Corporation, NJ, USA.

Ciba-Geigy Limited (1987) FAT 80023. 28-Day toxicity study in mice (administration in feed) with special reference to histopathology. Unpublished test report: GU Project No. 864005.

Ciba-Geigy Limited (1989). Report on the test for ready biodegradability of PBS 5357.0 in the modified Sturm Test. OECD Guideline No. 301B. Unpublished report No. 880122. Bader, U. and de Morsier, A. (eds).

Ciba-Geigy Limited (1990a) Report on density of solids - OECD Guideline for testing of chemicals No 109. Unpublished test report: Anal. Test. No. FC-90/1T. Ciba-Geigy Limited, Basel, Switzerland.

Ciba-Geigy Limited (1990b) Report on partition coefficient – by OECD TG 107. Unpublished test report: Anal. Test. No. FC-90/1T. Ciba-Geigy Limited, Basel, Switzerland.

Ciba-Geigy Limited (1990c) Report on water solubility of triclosan. Unpublished test report, Ciba-Geigy Limited, Basel, Switzerland. .

Ciba-Geigy Limited (1990d) Report on vapour pressure curve of triclosan. Unpublished test report, Ciba-Geigy Limited, Basel, Switzerland.

Ciba-Geigy Limited (1990e) Report on dissociation constant in water of triclosan. Unpublished test report, Ciba-Geigy Limited, Basel, Switzerland.

Ciba-Geigy Limited (1990f) Report on hydrolysis of triclosan as a function of pH. Unpublished test report, Ciba-Geigy Limited, Basel, Switzerland.

Ciba-Geigy Ltd (1990g) Report on the determination of the IC50 (Inhibitory Concentration) of FAT-80'023/Q – by OECD TG 209. Unpublished test report: D&C Product Ecotoxicology, Test No. G 069 05. Ciba-Geigy Limited, Basel, Switzerland.

Ciba-Geigy Limited (1991) Report on the Bioaccumulation of FAT-80'023/Q. Unpublished test report No. G 069 09. Ciba-Geigy Limited, Basel, Switzerland.

Ciba Specialty Chemicals (1998a) Irgasan, DP 300, Irgacare MP. Toxicological and ecological data. Official Registrations. Technical Brochure 2521. Ciba Specialty Chemicals, Basel, Switzerland.

Ciba Speciality Chemicals (1998b) In vitro human skin penetration and distribution of ¹⁴C-labelled triclosan from a w/o emulsion. Unpublished report No: CSC/4e1/98. An-ex Analytical Services, Cardiff CF1 3XF, UK.

Ciba Speciality Chemicals (1998c) In vitro human skin penetration and distribution of ¹⁴C-labelled triclosan from a dishwashing liquid. Unpublished report No: CSC/4e2/98. An-ex Analytical Services, Cardiff CF1 3XF, UK.

Ciba Speciality Chemicals (1998d) In vitro human skin penetration and distribution of ¹⁴C-labelled triclosan from a deodorant formulation. Unpublished report No: CSC/4e3/98. An-ex Analytical Services, Cardiff CF1 3XF, UK.

Ciba Speciality Chemicals (1998e) In vitro human skin penetration and distribution of ¹⁴C-labelled triclosan from a soap solution. Unpublished report No: CSC/4e4/98. An-ex Analytical Services, Cardiff CF1 3XF, UK.

Ciba Specialty Chemicals (1999) Triclosan in WWTP samples of Slough and Chertsey, United Kingdom. Schatowitz B. (ed). Trace analysis & occupational hygiene. Prepared by Ciba Specialty Chemicals for Proctor & Gamble, UK. Order No. 99.014.

Ciba Speciality Chemicals (2001a) Ciba IRGASAN DP 300 Ciba IRGACARE MP Ciba IRGACIDE LP 10 General information on chemical, physical and microbiological properties. Pub. No. AgB2520e.02.2001. Edited in Switzerland.

Ciba Specialty Chemicals (2001b) Ciba IRGASAN DP 300 Ciba IRGACARE MP Antimicrobials: toxicological and ecological data official registrations. Pub. No. AgB2521e.01.2001. Edited in Switzerland.

Ciba Specialty Chemicals (2003a) Notifier's submission. Correspondence from Mr. Graham Dickinson. Environment Health & Safety Manager. Triclosan – Priority Existing Chemical. 1 July 2003.

Ciba Specialty Chemicals (2003b) Notifier's submission. Correspondence from Mr. Graham Dickinson. Environment Health & Safety Manager. Triclosan in textiles. July 2003.

Ciba Speciality Chemicals Corporation (2002) A pilot study for the in vivo evaluation of the percutaneous absorption of triclosan. Unpublished report No: CIBA-03-01-0131. Arizona Clinical Research Centre, Tuscon, Arizona, USA.

Cole EC, Addison RM, Rubino JR, Leese KE, Dulaney PD, Newell MS, Wilkins J., Gaber DJ, Wineinger T and Criger DA (2003) Investigation of antibiotic and antibacterial agent cross-resistance in target bacteria from homes of antibacterial product users and nonusers. *Journal of Applied Microbiology*, **95**:664–676.

Colgate Palmolive Co. (1972) P-300 soap bar (primary irritation or sensitisation and repeated insult patch test in humans) (Reference Number 5). Unpublished study summary. Colgate Palmolive Company.

Colgate Palmolive Co. (1989) Steady-state blood levels of triclosan (DP-300) following dentrifice and aqueous solution administration in 18 normal subjects. Unpublished test report: Protocol No. 87-01. Colgate Palmolive Technology Centre, NJ, USA.

Colgate-Palmolive Company (1997a) Pharmacokinetic study of triclosan solution in healthy children 8 to 12 years of age. Unpublished study report No: 97-8504.

Colgate-Palmolive Company (1997b) Pharmacokinetic study of a triclosan dentrifice in healthy adult subjects: A) single-dose phase; B) multiple-dose phase. Unpublished report No: 97-1563-70; HSL Study No. 97-8503. Hill Top Research.

Commission Regulation [EC] No 2032/2003, 2003. Official Journal of the European Union – on the second phase of the 10-year work programme referred to in Article 16(2) of Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market, and amending Regulation (EC) No 1896/2000. Accessed at

http://europa.eu.int/eur-lex/pri/en/oj/dat/2003/l_307/l_30720031124en00010096.pdf in February 2006.

Concordia Research Laboratories Inc (1997a) A pilot study to determine triclosan plasma levels in children following a single oral administration of a triclosan containing product. Unpublished study report No: 97-8502A. Concordia Research Laboratories Inc., Cedar Knolls, NJ, USA.

Concordia Research Laboratories Inc (1997b).A pilot study to determine triclosan plasma levels in humans following a single oral administration of triclosan containing products. Unpublished study report No: 97-8502. Concordia Research Laboratories Inc., Cedar Knolls, NJ, USA.

Connor EE (1993) Soil ingestion and lead concentration in wildlife species. M.Sc. Thesis. Virginia Polytechnic Institute and State University, Blackburg, VA, USA. (Cited in Heinz et al., 1999).

Coogan MA and La Point TW (2008) Snail bioaccumulation of triclocarban, triclosan, and methyltriclosan in a north Texas, USA, stream affected by wastewater treatment plant runoff. *Environmental Toxicology and Chemistry*, 27(8), pp. 1788–1793.

Costanzo SD, Murby J and Bates J (2005) Ecosystem response to antibiotics entering the aquatic environment. *Marine Pollution Bulletin*, 51(1-4):218-223.

CSIRO (2002) Environmetrics-BurrliOZ-A Flexible Approach to Species Protection. <http://www.cmis.csiro.au/envir/burrlioz/>

Danish Environmental Protection Agency (2003a) Information Collection: Antibacterial compounds in clothing articles. <http://glwww.mst.dk/chemi/01081901.htm>

Danish Environmental Protection Agency (2003b) Fate and effects of triclosan. Samsøe-Petersen L, Winther-Nielsen M and Madsen T (eds), DHI Water Environment, Danish Environmental Protection Agency, Danish Ministry of the Environment.

De Groot AC, Liem DH, Nater JP and van Ketel WG (1985) Patch tests with fragrance materials and preservatives. *Contact Dermatitis*, 12:87–92.

De Groot AC, Weyland JW, Bos JD and Jagtman BA (1986) Contact allergy to preservatives (I). *Contact Dermatitis*, 14(2):120–122.

Delorenzo ME, Keller JM, Arthur CD, Finnegan MC, Harper HE, Winder VL, Zdankiewicz DL (2008) Toxicity of the antimicrobial compound triclosan and formation of the metabolite methyl-triclosan in estuarine systems. *Environ Toxicol.*;23: 224-32.

DeSalva SJ, Kong BM and Lin Y-J (1989) Triclosan: a safety profile. *American Journal of Dentistry*, 2:185–196.

Denning HJ, Sliwa S and Willson GA (1992) Triclosan: effects of pregnancy and post-natal development in rats. Unpublished test report: D92/105, study RT/3/84, Environmental Safety Laboratory Unilever Research, Bedford, England.

Dillon PJ (2000) Water reuse in Australia: current status, projections and research. Proc. Water Recycling Australia 2000, Adelaide, 19-21 October 2000. (Ed. PJ Dillon) p99 - 104.

Dokianakis SN, Kornaros ME and Lyberatos G (2004) On the effect of pharmaceuticals on bacterial nitrite oxidation. *Water, Science and Technology*, **50**(5):341-346.

Dorner RL (1973) The systemic toxicological effects of three bacteriostats topically applied to the skin of young canines. Unpublished test report: L.R.E study #301-002 Laboratory Research Enterprises Inc., Michigan, USA.

DPIWE (Department of Primary Industries, Water and Environment) (2003) Biosolids. Tasmanian Government. <http://www.dpiwe.tas.gov.au/inter.nsf>

Duchosal F and Thevenaz Ph (1990) 4-Hour acute inhalation toxicity study with FAT 80'023/Q. Unpublished study report: RCC Project Number 254597, Research & Consulting Company AG, Carouge, Switzerland.

Durbize E, Vigan M, Puzenat E, Girardin P, Adessi B, Desprez PH, Humbert PH, Laurent R and Aubin F (2003) Spectrum of cross-photosensitisation in 18 consecutive patients with contact photoallergy to ketoprofen: associated photoallergies to non-benzophenone-containing molecules. *Contact Dermatitis*, **48**:144–149.

Dussault EB, Balakrishnan VK, Sverko, E, Solomon KR, and Sibley PK (2008) Toxicity of human pharmaceuticals and personal care products to benthic invertebrates. *Environmental Toxicology and Chemistry*, **27**(2) 425–432.

EC (European Commission) (2003a) Technical guidance document on risk assessment in support of Commission Directive 93/67/EEC on risk assessment for new notified substances, Commission Regulation (EC) No 1488/94 on risk Assessment for existing substances, Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market. Part 1. Luxembourg, Office for Official Publications of the European Communities.

EC (2003b) Technical guidance document on risk assessment in support of Commission Directive 93/67/EEC on risk assessment for new notified substances, Commission Regulation (EC) No 1488/94 on risk Assessment for existing substances, Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market. Part II. Luxembourg, Office for Official Publications of the European Communities.

ECB (2002) Spanish comments on classification of triclosan. Accessed at http://ecb.jrc.it/classlab/1802a3_E_15-7-02_triclosan.doc in May 2006.

ECB (2004) Environmental aspects of triclosan. ECBI/18/02 Add. 22. Accessed at http://ecb.jrc.it/classlab/1802a22_IND_triclosan.pdf in April 2006.

ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) (1999) GREAT-ER 1.0 Software, Brussels, Belgium.

ECETOC (2003) Aquatic hazard assessment II (Technical Report No. 91). Brussels, European Centre for Ecotoxicology and Toxicology of Chemicals.

Eldridge S (1993) Cell proliferation in rodent liver. Final report. Unpublished test report: Pathology Associates Inc., Durham, NC, USA.

EnHealth Council (2003) Australian exposure assessment handbook: Consultation Draft. Canberra, Department of Health and Ageing.

Environ (2006) Environmental Risk Assessment for Triclosan in Europe (May 2006) Environ International Corporation Ohio USA; 221 pages (unpublished).

Environ (2008) Addendum to Aquatic Ecological Risk Assessment for All Triclosan Use, Technical Memorandum (June 2008) Environ International Corporation Ohio USA; 75 pages (unpublished).

Environment Agency (2004) Briefing note: Triclosan briefing. Bristol, United Kingdom. <http://www.environment-agency.gov.uk>

Environment Australia (2003) Model and guidance for estimating predicted environmental concentrations to surface water and soil from chemicals released to the environment through a sewage treatment plant.

Environment Protection and Heritage Council (2005) National Dioxins Program – National Action Plan for addressing Dioxins in Australia. Accessed at: http://www.ephc.gov.au/pdf/EPHC/final_NAP_october_2005_rev.pdf in October 2006.

Eriksson E, Auffarth K, Eilersen A-M, Henze M and Ledin A (2003) Household chemicals and personal care products as sources for xenobiotic organic compounds in grey water. *Water SA*, 29 (2), p135 - 149.

Escalada MG, Harwood JL, Maillard J-Y and Ochs D (2005) Triclosan inhibition of fatty acid synthesis and its effect on growth of *Escherichia coli* and *Pseudomonas aeruginosa*. *Journal of Antimicrobial Chemotherapy*, **55**:879–882.

European Commission (1999) The rules governing cosmetic products in the European Union. Volume 1 Cosmetic legislation – cosmetic products. Accessed at http://www.leffingwell.com/cosmetics/vol_1en.pdf in February 2006.

European Commission Health & Consumer Protection Directorate-General (2002a) Opinion on triclosan – adopted by the Scientific Steering Committee at its meeting of 27 – 28 June 2002. Accessed at http://www.europa.eu.int/comm/food/fs/sc/ssc/out269_en.pdf in January 2006.

European Commission Health & Consumer Protection Directorate-General (2002b) Report on triclosan antimicrobial resistance: report prepared by K Jones (rapporteur), J Fink-Gremmels, T.Hardy, R.Hay, W.Klein, A.Knaap, J.Vives-Rego and I.White. Accessed at http://www.europa.eu.int/comm/food/fs/sc/ssc/out269_en.pdf in January 2006.

Facino RM, Carini M, Sala S and Minghetti P (1990) Identification of preservative composition in finished cosmetic formulations by collisionally activated decomposition mass-analysed ion kinetic energy spectrometry. *Biomedical and Environmental Mass Spectrometry*, **19**:493–505.

Fahrig R (1978a) Genetic activity of Krgasan DP 300 in the MP-1 strain of *S. cerevisiae*. Unpublished test report: Zentrallobratum fuf Mutagenitatsprufung der Deutschen Forschungsgemeinschaft.

Fahrig R (1978b) The effect of Irgasan DP 300 in the “Mammalian Spot Test”, an in vivo method for the detection of genetic alterations in somatic cells of mice. Unpublished test report: Zentrallobratum fuf Mutagenitatsprufung der Deutschen Forschungsgemeinschaft.

- Fan F, Yan K, Wallis NG, Reed S, Moore TD, Rittenhouse SF, DeWolf Jr WE, Huang J, McDevitt D, Miller WH, Seefeld MA, Newlander KA, Jakas DR, Head MS and Payne DJ (2002) Defining and combating the mechanisms of triclosan resistance in clinical isolates of *Staphylococcus aureus*. *Antimicrobial Agents and Chemotherapy*, **46**:3343–3347.
- Federle TW, Kaiser SK and Nuck BA (2002) Fate and effects of triclosan in activated sludge. *Environmental Toxicology and Chemistry*, **21**:1330-1337.
- Ferrari B, Paxeus N, Pollio A, Andreozzi R, Marotta R, Vogna D, Lyberatos G, Garric J (2002): Fate and effect of triclosan in the aquatic ecosystems: data for a risk assessment [poster]. In: Society of Environmental Toxicology and Chemistry Annual Meeting in Europe; 2002 May 12 – 16; Vienna, Austria. Brussels (BE): SETAC Europe. Poster 73-04.
- Ferrer I, Mezcua M, Jose Gomez M, Thurman ME, Aguera A., Hernando MD, Fernandez-Alba AR (2004) Liquid chromatography/time-of-flight mass spectrometric analyses for the elucidation of the photodegradation products of triclosan in wastewater samples. *Rapid Communications in Mass Spectrometry* **18**: 443-450.
- Fiege H, Voges H-W, Hamamoto T, Umemura S, Iwata T, Miki H, Fujita Y, Buysch H-J, Garbe D, Paulus W (2000) Phenol derivatives. IN: Ullmann's Encyclopedia of Industrial Chemistry, Sixth Edition, 2002. John Wiley & Sons Inc, online edition http://www.mrw.interscience.wiley.com/ueic/articles/a19_313/sect7-fs.html (Accessed January 2006)
- Fishman SK (1993) Laboratory Safety Report - Clinical effects of fluoride dentrifices on dental caries in three thousand adults. Unpublished study No 1988-5A/DP89-001. Colgate-Palmolive Company, Piscataway, New Jersey, USA.
- Foran CM, Bennett ER and Benson WH (2000) Developmental evaluation of a potential non-steroidal estrogen: triclosan. *Marine Environmental Research*, **50**(1-5):153-156.
- FORS (1998) Australian code for the transport of dangerous goods by road or rail (ADG Code), 6th ed. Canberra, ACT, Federal Office of Road Safety.
- Fort DJ (2008) 21-d Amphibian Metamorphosis Assay. Fort Environmental Laboratories, Inc. 515 South Duncan Street, Stillwater, OK 74074, U.S.A., Study Number CSCH01-00140, Date: 2008-05-01.
- Fraker SL and Smith GR (2004) Direct and interactive effects of ecologically relevant concentrations of organic wastewater contaminants on *Rana pipiens* tadpoles. *Environmental Toxicology*, **19**:250-256.
- Fritz H (1971) Dominant lethal study. Unpublished test report: Experiment No. 32710200. Ciba-Geigy Limited, Basel, Switzerland.
- Garten CT Jnr, (1980) Ingestion of soil by hispid cotton rats, white-footed mice and eastern chipmunks. *Journal of Mammalogy*, **6**:136-137.
- Gilbert RJ, Fraser SB and van der Ouderaa FJG (1987) Oral disposition of triclosan (2,4,4'-trichloro-2'-hydroxydiphenyl ether) delivered from a dentrifice. *Caries Research*, **21**:29–36.
- Gocke E, King MT, Eckhardt K and Wild D (1981) Mutagenicity of cosmetic ingredients licensed by the European Communities. *Mutation Research*, **90**:91–109.
- Goh CL and Yuen R (1994) A study of occupational skin disease in the metal industry (1986 – 1990). *Ann Acad Med Singapore*, **23**:639 – 644.

- Gold LS, Sawyer CB, Magaw R, Backman GM, De Veciana M., Levinson R., Hooper NK, Havender WR, Bernstein L, Peto R, Pike MC and Ames BN (1984) A carcinogen potency database of the standardised results of animal bioassays. *Environmental Health Perspectives*, **58**:92–98.
- Gosford City Council (2002) State of the Environment Report. Gosford, NSW.
- Graovac M, Todorovic M, Trtanj MI, Kopečni MM and Comor JJ (1995) Gas chromatographic determination of 5-chloro-2-(2,4-dichlorophenoxy)-phenol in the waste water of a slaughterhouse. *Journal of Chromatography A*, **705**:313–317.
- Grattan CEH, English JSC, Foulds S.I and Rycroft RJG (1989) Cutting fluid dermatitis. *Contact Dermatitis*, **20**:372–376.
- Greynshock A and Vikesland P (2006) Triclosan reactivity in chloraminated waters. *Environmental Science and Technology*, **40**(8):2615–2622.
- Hagedorn-Leweke U and Lippold BC (1998) Accumulation of sunscreens and other compounds in keratinous substrates. *European Journal of Pharmaceutics and Biopharmaceutics*, **46**:215 – 221.
- Hagglblom MM, Janke D, Middeldorp PJM and Salkinoja-Salonen M (1989) *Archives of Microbiology*, **152**:6-9.
- Hale RC, Smith CL, de Fur PO, Harvey E, Bush EO, La Guardia MA and Vadas GG (2000) Nonylphenols in sediments and effluents associated with diverse wastewater outfalls. *Environmental Toxicology and Chemistry*, **19**(4):946-952.
- Hannuksela M, Kousa M and Pirila V (1976) Allergy to ingredients of vehicles. *Contact Dermatitis*, **2**:105–110.
- Hansen H and Källqvist T (2001) Miljøvurdering av Triclosan [Environmental assessment of Triclosan]. Report from Norsk Institut for Vattenforskning (NIVA). In Norwegian. Cited in Danish EPA (2003).
- Hanstveit AO and Hamwijk C (2003) Environmental Report. V5330/01. Unpublished report Ciba Specialty Chemicals Inc.
- Harden et al., (2005a) Dioxins in the Australian population: levels in human milk, National Dioxins Program Technical Report No.10, Australian Government Department of the Environment and Heritage, Canberra.
- Harden et al., (2005b) Organochlorine pesticides (OCPs) and polybrominated diphenyl ethers (PBDEs) in the Australian population: levels in human milk, Environment Protection and Heritage Council of Australia and New Zealand.
- Hay AG, Dees PM and Saylor GS (2001) Growth of bacterial consortium on triclosan. *FEMS Microbiology Ecology*, **36**:105-112.
- Hazleton Laboratories (1979) 90-Day bathing of newborn rhesus monkeys with triclosan soap solution. Unpublished test report: Hazleton Laboratories America Inc., Virginia, USA.
- Health Canada (2005) Consumer Product Safety: Cosmetic Ingredient Hotlist – May 2005. Accessed at http://www.hc-sc.gc.ca/cps-spc/person/cosmet/prohibited_e.html in February 2006.
- Heath RJ and Rock C (2000) A triclosan-resistant bacterial enzyme. *Nature*, **406**:145.

- Heath RJ, Yu Y, Shapiro MA, Olson E and Rock C (1998) Broad spectrum antimicrobial biocides target the FabI component of fatty acid synthesis. *Journal of Biological Chemistry*, **273**(46):30316-30320.
- Heim S, Schwarzbauera J, Kronimusa A, Littkea R, Wodab C and Manginib A (2004) Geochronology of anthropogenic pollutants in riparian wetland sediments of the Lippe River (Germany). *Organic Geochemistry*, **35**(11-12):1409–1425.
- Heinz GH, Hoffman DJ, Sileo L, Audet DJ and LeCaptain LJ (1999) Toxicity of lead-contaminated sediment to mallards. *Arch. Environ. Toxicol*, **36**:323-333.
- Henderson LM, Ransome SJ, Brabbs CE, Tinner AJ, Davies SE and Lloyd A (1988a) An assessment of the mutagenic potential of triclosan using the mouse lymphoma tk locus assay. Unpublished test report: ULR 216/88644, KM 880170 Huntingdon Research Centre, England.
- Henderson LM, Proudlock RJ, Haynes P and Meaking K (1988b) Triclosan mouse micronucleus test. Unpublished test report: HRC Study No. ULR 213/88492 Huntingdon Research Centre, England – Unilever study No. KC 880168.
- Hindson TC (1975) Irganon DP300 in a deodorant. *Contact Dermatitis*, **1**: 328.
- Hing-Biu L, Peart T and Svoboda M (2005) Determination of endocrine-disrupting phenols, acidic pharmaceuticals, and personal-care products in sewage by solid-phase extraction and gas chromatography-mass spectrometry. *Journal of Chromatography A*, **1094**:122-129.
- Hohensee GH and Berke MS (1991) Concentrations of triclosan, triclosan glucuronide, and triclosan sulfate in dog plasma, urine and fecal samples. Unpublished study report: 425 – 015 HWI 6252 – 112. Hazleton Wisconsin, Wisconsin, USA.
- Holst RW and Ellwanger TC (1982) Pesticide assessment guidelines. Subdivision J Hazard Evaluation: Non-target Plants. EPA-540/9-82-020.
- Hong C, Hall RT, Smith NL and Kurz ND (1976) Chemical analyses of hexachlorophene (HCP), tribromsalan (TBS), triclosan (DP-300), triclocarban (TCC) and cloflucarban (CF₃) in tissues, blood and urine of animals and humans. Unpublished research report: # 2764. Colgate-Palmolive Co. Inc., Piscataway, NJ, USA.
- Hool G, Strasser F and Muller D (1978) Chromosome studies in male germinal epithelium, FAT 80 023/A, Mouse. Unpublished test report: Experiment No. 78-2903. Ciba-Geigy Limited, Basel, Switzerland.
- Hool G, Strasser F and Muller D (1979) Chromosome studies in male germinal epithelium, FAT 80 023/A, Mouse. Unpublished test report: Experiment No. 78-2904. Ciba-Geigy Limited, Basel, Switzerland.
- Houtman C, Van Oostveen AM, Brouwer A, Lamoree MH and Legler J (2004) Identification of estrogenic compounds in fish bile using bioassay-directed fractionation. *Environmental Science and Technology*, **38**:6415-6423.
- Hovander L, Malmberg T, Athanasiadou M, Athanassiadis I, Rahm S, Bergman A and Klasson Wehler E (2002) Identification of hydroxylated PCB metabolites and other phenolic halogenated pollutants in human blood plasma. *Archives of Environmental Contamination and Toxicology*, **42**:105–117.
- Howes D, Moule RC and York M (1989a) Toxicokinetics of triclosan. Part 1. Fate of triclosan in the Swiss-S mouse. Unpublished project report No: 47980. IMIS numbers: 14-95-10-611. Unilever Research, Sharnbrook, Bedford MK44 1LQ, England.

- Howes D, Moule RC and York M (1989b) Toxicokinetics of [14C] triclosan. Part 2. Fate of triclosan in the C-57 mouse. Unpublished study report No: 47980. IMIS numbers: 14-95-10-611. Unilever Research, Sharnbrook, Bedford MK44 1LQ, England.
- Howes D and Moule RC (1989) Toxicokinetics of [14C] triclosan. Part 3. Fate of triclosan in the Syrian hamster. Unpublished study report No: 47980. IMIS numbers: 14-95-10-611. Unilever Research, Sharnbrook, Bedford MK44 1LQ, England.
- Hua W, Bennett E and Letcher R (2005) Triclosan in waste and surface waters from the upper Detroit River by Liquid chromatography-electrospray-tandem quadrupole mass spectrometry. *Environment International*, **31**(5):621-630.
- Hui CA and Beyer NW (1998) Sediment ingestion by two sympatric shorebird species. *Science of the Total Environment*, **224**:227-223.
- Hundt K, Martin D, Hammer E, Jonas U, Kinderman MK and Schauer F (2000) Transformation of triclosan by *Trametes versicolor* and *Pycnoporus cinnabarinus*. *Applied and Environment Microbiology*, **66**(9):4157-4160.
- Huntingdon Life Sciences Ltd (1999) FAT 80'023/S: Potential tumorigenic and chronic toxicity effects in prolonged dietary administration to hamsters. Unpublished Report No.: CBG 756/972896. Huntingdon Life Sciences Ltd., Huntingdon, England.
- Ishibashi H, Matsumura N, Hirano M, Matsuoka M, Shiratsuchi H, Ishibashi Y, Takao Y and Arizono K (2004) Effects of triclosan on the early life stages and reproduction of medaka *Oryzias latipes* and induction of hepatic vitellogenin. *Aquatic Toxicology*, **67**(2):167-179.
- Johnson GD, Audet DJ, Kern JW, LeCaptain LJ, Strickland MD, Hoffman DJ and McDonald LM (1999) Lead exposure in passerines inhabiting lead-contaminated floodplains in the Coeur d'Alene River Basin, Idaho, USA. *Environmental Toxicology and Chemistry*, **18**(6):1190-1194.
- Jones E and Wilson LA (1988) Triclosan, Ames metabolic activation test to assess the potential mutagenic effect. Unpublished test report: ULR 215/88704 Huntingdon Research Centre, England - Unilever study No. KA 880169.
- Jordan SL, Taylor LT, McPherson B and Rasmussen HT (1996) Identification of an anti-bacterial agent in toothpaste via liquid chromatography – fourier transform infrared spectrometry mobile phase elimination. *Journal of Chromatography A*, **755**:211–218.
- Jungclaus GA, Lopez-Avila V and Hites RA (1978) Organic compounds in an industrial wastewater: a case study of their environmental impact. *Environmental Science and Technology*, **12**(1):88-97.
- Junker LM and Hay AG (2004) Effects of triclosan incorporation into ABS plastic on biofilm communities. *Journal of Antimicrobial Chemotherapy*, **53**:989-996.
- Kanda R, Griffin P, James HA and Fothergill J (2003) Pharmaceutical and personal care products in sewage treatment works. *Journal of Environmental Monitoring*, **5**(5):823-830.
- Kanetoshi A, Ogawa H, Katsura E and Kaneshima H (1987) Chlorination of Irganon DP300 and formation of dioxins from its chlorinated derivatives. *Journal of Chromatography*, **389**:139- 53.
- Kanetoshi A, Ogawa H, Katsura E and Kaneshima H (1988a) Formation of polychlorinated dibenzo-p-dioxins upon combustion of commercial textile products containing 2,4,4'-

- trichloro-2'-hydroxydiphenyl ether (Irgasan® DP300). *Journal of Chromatography*, **442**:289-299.
- Kanetoshi A, Ogawa H, Katsura E, Okui T and Kaneshima H (1988b) Disposition and excretion of Irgasan DP300 and its chlorinated derivatives in mice. *Archives of Environmental Contamination and Toxicology*, **12**:637–644.
- Kanetoshi A, Katsura E, Ogawa H, Ohyama T, Kaneshima H and Miura T (1992) Acute toxicity, percutaneous absorption and effects on hepatic mixed function oxidase activities of 2, 3, 4'-trichloro-2'-hydroxydiphenyl ether (Irgasan DP300) and its chlorinated derivatives. *Archives of Environmental Contamination and Toxicology*, **23**:91–98.
- Kawashima K, Nakaura S, Yamaguchi M, Tanaka S and Takanaka A (1987) Effect of triclosan on foetal development of rats (translation from original). *Eisei Shikenjo Hokoku*, **105**:28–32.
- Kligman AM (1969) Report to Geigy chemical corporation on phototoxicity and photoallergy study on L-2.
- Kolpin DA, Furlong ET, Meyer MT, Thurman EM, Zaugg SD, Barber LB and Buxton HT (2002) Pharmaceuticals, hormones and other organic wastewater contaminants in U.S streams, 1999 – 2000: A national reconnaissance. *Environmental Science & Technology*, **36**:1202–1211.
- Kronimus A, Schwarzbauer J, Dsikowitzky L, Heim S and Littke R (2004) Anthropogenic organic contaminants in sediments of the Lippe river, Germany. *Water Research*, **38**:3473-3484.
- Krueger B, Hunter S and Serena M (1992) Husbandry, diet and behaviour of platypus *Ornithorhynchus anatinus* at Healesville Sanctuary. *International Zoo Yearbook*, 31:64-71. Cited in Hundt et al. (2000).
- Kusnick C (1998) Isolierung und Charakterisierung antibiotisch aktiver Verbindungen aus dem marinen Pilz *Kirschsteiniothelia maritima* LINDER (D. Hawksw). Ph.D. thesis. University of Greifswald, Greifswald, Germany. Cited in Hundt et al. (2000).
- Lachapelle JM and Tennstedt D (1979) Low allergenicity of triclosan. Predictive testing in Guinea Pigs and Humans. *Dermatologica*, **158**:379–383.
- Lambert RJW (2004) Comparative analysis of antibiotic and antimicrobial biocide susceptibility data in clinical isolates of methicillin-sensitive *Staphylococcus aureus*, methicillin-resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa* between 1989 and 2000. *Journal of Applied Microbiology*, **97**:699–711.
- Langauer M and Muller D (1974) Nucleus anomaly test on somatic interphase nuclei, GP 41 343 (Triclosan), Chinese hamster. Unpublished test report. Ciba-Geigy Limited, Basel, Switzerland.
- Langauer M and Muller D (1978) Nucleus anomaly test in somatic interphase nuclei, long-term study with FAT 80023/A, Chinese hamster. Unpublished test report: Experiment No. 78-3005. Ciba-Geigy Limited, Basel, Switzerland.
- Latch D, Packer J, Stender B, Van Overbeke J, Arnold W and McNeill K (2005) Aqueous photochemistry of triclosan: Formation of 2,4-dichlorophenol, 2,8-dichlorodibenzo *p*-dioxin, and oligomerisation Products. *Environmental Toxicology and Chemistry*, **24**(3):517–525.

- Latch DE, Packer JL, Arnold WA and McNeill K (2003) Photochemical conversion of triclosan to 2,8-dichlorodibenzo-p-dioxin in aqueous solution. *Journal of Photochemistry and Photobiology A: Chemistry, Short Communication*, **158**:63066.
- LeClerc EJ, Li B, Payne WL and Cebula TA (1996). High mutation frequencies among *Escherichia coli* and *Salmonella* pathogens. *Science*, **272**:1208–1211.
- Lee H and Peart TE (2002) Organic contaminants in Canadian municipal sewage sludge. Part I. Toxic or endocrine-disrupting phenolic compounds. *Water Quality Research Journal of Canada*, **37**(4):681-696.
- Lee H-B, Sarafin K, Peart TE and Svoboda ML (2003) Acidic pharmaceuticals in sewage – methodology, stability test, occurrence, and removal from Ontario samples. *Water Quality Research Journal of Canada*, **38**(4):667–682.
- Legler J, Jonas A, Lahr J, Vethaak AD, Brouwer A and Murk AJ (2002) Biological measurement of estrogenic activity in urine and bile conjugates with the in vitro ER-CALUX reporter gene assay. *Environmental Toxicology and Chemistry*, **21**:473-479.
- Leuschner F, Leuschnerm A, Schwerdtfeger W and Dontenwill W (1970a) 90 Days oral toxicity study in New Zealand White rabbits with CH 3565. Unpublished test report: Laboratorium Fur Pharmakologie Und Toxikologie.
- Leuschner F, Leuschnerm A, Schwerdtfeger W and Dontenwill W (1970b) 90 Days oral toxicity study in Beagle dogs with CH 3565. Unpublished test report: Laboratorium Fur Pharmakologie Und Toxikologie.
- Levy CW, Roujeinikova A, Sedelnikova S, Baker PJ, Stuitje AR, Slabas AR, Rice DW and Rafferty JB (1999) Molecular basis of triclosan activity. *Nature*, **398**:383-384. Cited in McBain AJ, Rickard AH and Gilbert P (2002) Possible implications of biocide accumulation in the environment on the prevalence of bacterial antibiotic resistance. *Journal of Industrial Microbiology and Biotechnology*, **29**:326 - 330.
- Lim HW, Cohen D and Soter NA (1998) Chronic actinic dermatitis results of patch and photopatch tests with compositae fragrances and pesticides. *Journal of the American Academy of Dermatology*, **38**(1):108–111.
- Lin YJ (1988) Triclosan dentifrice plaque clinical study. Unpublished study No: 87-03.
- Lin YJ (1989) Triclosan Canada study. Unpublished study report. Hazleton Blood Report HLA study No. 6002-773.
- Lin Y-J (1994) Statistical evaluation for triclosan dentifrice study in Canada (Study No. HLCL 565-27-001), Memo Subject: Liver function tests of triclosan dentifrice study (HLCL 565-27-001). Unpublished Hazleton Report and Memo dated April 25, 1994.
- Lin YJ (2000) Buccal absorption of triclosan following topical mouthrinse application. *American Journal of Dentistry*, **13**(4):215–217.
- Lin YJ, Fung KK, Kong BM and DeSalva SJ (1994) Gingival absorption of triclosan following topical mouthrinse application. *American Journal of Dentistry*, **7**(1):13–16.
- Lin YJ and Smith NL (1990) Pharmacokinetics of triclosan in rats following a single oral administration. Unpublished research report: # 3803. Colgate-Palmolive Company, Piscataway, NJ, USA.

- Lindstrom A, Buerge IJ, Poiger T, Bergqvist P-A, Muller MD and Buser H-R (2002) Occurrence and environmental behaviour of the bactericide triclosan and its methyle derivative in surface waters and in wastewater. *Environmental Science & Technology*, **36**:2322–2329.
- Litchfield JT and Wilcoxon FW (1949) Evaluating dose-effect experiments. *Journal of Pharmacology and Experimental Therapeutics*, **96**:99–113.
- Litton Bionetics Inc. (1983). 90-Day oral toxicity study in rats with Fat 80-023/H Final Report. Unpublished test report: Project No. 22188. Litton Bionetics Inc., Maryland, USA.
- Long K (2001) The use of biosolids (sewage sludge) as a fertiliser/soil conditioner on dairy pastures. A review from a dairy food safety perspective. Dairy Food Safety Victoria.
- Lopez-Avila A and Hites RA (1980) Organic compounds in an industrial wastewater. Their transport into sediments. *Environmental Science and Technology*, **14**:1382-1390.
- Lucker PW, Wetzelsberger N and Sturm Y (1990) Safety (tolerance) and pharmacokinetics of triclosan (TCS) (study report). Unpublished test report: Study No 27419. Institut für Klinische Pharmakologie Bobenheim, Grunstadt, Federal Republic of Germany.
- Luke B, Graham R and James P (1996) The detection of 5-chloro-2(2,4 dichlorophenoxy)phenol in sewage biosolids Oral Presentation 16th Conference of Residue Chemists, World Trade Centre, Melbourne, Australia.
- Luke B (1999) Residues of 5-chloro-2 (2,4dichlorophenoxy)phenol in biosolids Oral Presentation Envirottox International Conference, Geelong, Australia.
- Lyman FI and Furia T (1969) Toxicology of 2,4,4'-trichloro-2'-hydroxy-diphenyl ether. *Ind. Medicine*, **38**(2):45–52.
- Magnusson J (1979) Mutagenic effects of "Irgasan" on *Drosophila melanogaster*. Unpublished brief test report. Wallenberg Laboratory, Stockholm, Sweden.
- Maibach HI (1969) Percutaneous absorption of Irgasan CH 3565 in a soap solution. Unpublished report. Dept of Dermatology, University of California Medical Centre, San Francisco, USA.
- Manufacturabrasil (2004) Secco – high performance – the smart pillow. Accessed at http://www.manufaturabrasil.com.br/secco_en.html in July 2004.
- Marzulli FN and Maibach HI (1973) Antimicrobials: Experimental contact sensitisation in man. *J. Soc. Cosmet. Chem.*, **24**:399–421.
- Marzulli FN and Maibach HI (1974) The use of graded concentrations in studying skin sensitisers: experimental contact sensitisation in man. *Fd Cosmet.Toxicol.*, **12**:219–227.
- Matsumura N, Ishibashi H, Hirano M, Nagao Y, Watanabe N, Shiratsuchi H, Kai T, Nishimura T, Kashiwagi A and Arisono K (2005) Effects of nonylphenol and triclosan on production of plasma vitellogenin and testosterone in male South African Clawed Frogs (*Xenopus laevis*). *Biological and Pharmaceutical Bulletin*, **28**(9):1748-1751.
- Maurer T, Thomann P, Weirich EG and Hess R (1979) Predictive evaluation in animals of the contact allergenic potential of medically important substances: II. Comparison of different methods of cutaneous sensitisation with 'weak' allergens. *Contact Dermatitis*, **5**:1–10.

- Mayer FLJ and Ellersieck MR (1986) Manual of acute toxicity: Interpretation and data base for 410 Chemicals and 66 Species of freshwater animal. Resource Publication 160, US Department of Interior, US Fish and Wildlife Service, Washington, DC.
- Mayer FL (1987) Acute toxicity handbook of chemicals to estuarine organisms. EPA 600/8-87/017. U.S. Environmental Protection Agency, Gulf Breeze, FL.
- McAvoy DC, Schatowitz B, Jacob M, Hauk A and Eckhoff WS (2002) Measurement of triclosan in wastewater treatment systems. *Environmental Toxicology and Chemistry*, **21**(7):1323–1329.
- McBain AJ, Bartolo RG, Catrenich CE, Charbonneau D, Ledder RG, Price BB and Gilbert P (2003) Exposure of sink drain microcosms to triclosan: population dynamics and antimicrobial susceptibility. *Applied and Environmental Microbiology*, **69**:5433–5442.
- McBain AJ, Ledder RG, Sreenivasan P and Gilbert P (2004) Selection for high-level resistance by chronic triclosan exposure is not universal. *Journal of Antimicrobial Chemotherapy*, **53**:727–777.
- McMurry LM, Mcdermott PF and Levy SB (1999) Genetic evidence that InhA of *Mycobacterium smegmatis* is a target for triclosan. *Antimicrobial Agents and Chemotherapy*, **43**, p711 - 713. Cited in McBain AJ, Rickard AH and Gilbert P (2002) Possible implications of biocide accumulation in the environment on the prevalence of bacterial antibiotic resistance. *Journal of Industrial Microbiology and Biotechnology*, **29**:326-330.
- McMurry LM, Oethinger M and Levy SB (1998) Triclosan targets lipid synthesis. *Nature*, **394**:531-532. Cited in McBain AJ, Rickard AH and Gilbert P (2002) Possible implications of biocide accumulation in the environment on the prevalence of bacterial antibiotic resistance. *Journal of Industrial Microbiology and Biotechnology*, **29**: 326-330.
- Meade MJ, Waddell RL and Callahan TM (2001) Soil bacteria *Pseudomonas putida* and *Alcaligenes xylosoxidans* subsp. *denitrificans* inactivate triclosan in liquid and solid substrates. *FEMS Microbiology Letters*, **204**:45-48.
- Memmert U (2006): Triclosan: Effects on the development of sediment-dwelling larvae of *Chironomus riparius* in a water-sediment system with spiked sediment. RCC Ltd., Itingen, Switzerland, Report No. A34896, date: 2006-07-17.
- Menoutis J and Parisi AI (2002) Testing for dioxin and furan contamination in triclosan. *Cosmetics & Toiletries Magazine*, **117**(10):75–77.
- Merck Index (1983) The Merck Index, an encyclopedia of chemicals, drugs and biologicals. 10th Edition. Windholz et al (ED). Merck & Co. Inc., Rahway, N.J., USA.
- Mensink BJWG, Montforts M, Wijkhuizen-Maslankiewicz H, Tibosch H and Linders JBHJ (1995) Manual for summarising and evaluating the environmental aspects of pesticides. Report number 679101022.
- Mezcua M, Gomez MJ, Ferrer I, Aguera A, Hernando MD and Fernandez-Alba A. R (2004) Evidence of 2,7/2,8-dibenzodichloro-p-dioxin as a photodegradation product of triclosan in water and wastewater. *Analytica Chimica Acta*, **524**:241-247.
- Mill T (1999) Predicting photoreaction rates in surface waters. *Chemosphere*, **38**:1379-1390.
- Miller TR, Heidler J, Chillrud SN, DeLaquil A, Ritchie JC, Mihalic JN, Bopp R, Halden RU (2008) Fate of triclosan and evidence for reductive dechlorination of triclocarban. *Environ Sci Technol* **42**:4570-6.

Miller WE, Greene JC and Shiroyama T (1978) The *Selenastrum capricornutum* Printz Algal Assay Bottle Test. EPA-600/9-78-018.

Ministry of Health and Welfare Notification No.331 (2000) Standards for Cosmetics – Appendix 3. Accessed at <http://www.mhlw.go.jp/english/topics/cosmetics/index.html> in February 2006.

Mitchell JC, Adams RM, Glendenning WE, Fischer A, Kanof N, Larse W, Maibach HI, Rudner EJ, Schnorr W, Storrs F and Taylor J.S (1982) Results of standard patch tests with substances abandoned. Contact Dermatitis, **8**:336–337.

Miyazaki T, Yamagishi T and Matsumoto M (1984) Residues of 4-chloro-1-(2,4-dichlorophenoxy)-2-methoxybenzene (triclosan methyl) in aquatic biota. Bulletin of Environment Contamination and Toxicology, **32**:227-232.

Miyazawa U, Magane H and Matsushima H (1983) Proc. Tokai Society for Public Health 29: 89. Cited in Matsushima H. (1988) A selected ion monitoring assay for triclosan in medical waste water. Biomedical and Environmental Mass Spectrometry, **16**:255-257.

Mmbaga MT and Sauve RJ (2004) Management of powdery mildew in flowering dogwood in the field with biorational and conventional fungicides. Canadian Journal of Plant Science, **84**:837-844.

Molitor E and Persohn E (1993) The effects of FAT 80'023/Q (Irgasan DP 300) on selected biochemical and morphological liver parameters following dietary administration to males rats. Unpublished test report: No. CB 92/28. Ciba-Geigy Limited, Basel, Switzerland.

Molitor E, Persohn E and Thomas H (1992) The effect of FAT 80'023/Q (Irgasan DP 300) on selected biochemical and morphological liver parameters following subchronic dietary administration to male and female mice. Unpublished test report: No. CB 91/18. Ciba-Geigy Limited, Basel, Switzerland.

Morrall D, McAvoy D, Schatowitz B, Inauen J, Jacob M, Hauk A and Eckhoff W (2004) A field study of triclosan loss rates in river water (Cibolo Creek, TX). Chemosphere, **54**:653-660.

Morita M, Ishigaki M and Abe T (1981) Mutagenicity of materials related with cosmetics. J. Soc. Cosmet. Chem. Japan, **15**(3):243–253.

Morseth SL (1988) Two-generation reproduction study in rats FAT 80'023. Unpublished final test report 2386-100. Hazleton Laboratories America Inc., Virginia, USA.

Moss T, Howes D and Williams FM (2000) Percutaneous penetration and dermal metabolism of triclosan (2,4,4'-trichloro-2'-hydroxydiphenyl ether). Food and Chemical Toxicology, **38**:361 – 370.

Muller D and Strasser FF (1973) Chromosome studies on somatic cells-GP 41 353 (Triclosan), Chinese hamster. Unpublished test report. Ciba-Geigy Limited, Basel, Switzerland.

Muller SR, Singer HP and Canonica S (2000) Fate and behaviour of the biocide triclosan in the aquatic environment. American Chemical Society, Division of Environmental Safety, **40** (1):166–167.

Nagy KA (1987) Field metabolic rate and food requirement scaling in mammals and birds. Ecological Monographs, **57**:111-128.

National Dioxins Program Technical Report No. 12 (2005) Human health risk assessment of dioxins in Australia. Accessed at: <http://www.deh.gov.au/settlements/publications/chemicals/dioxins/report-12/pubs/report-12.pdf> in December 2006.

National Health & Medical Research Council (2004) National water quality management strategy – Australian drinking water guidelines. Accessed at http://www.nhmrc.gov.au/publications/_files/awgfull.pdf in February 2006.

NDPSC (2003) Standard for the Uniform Scheduling of Drugs and Poisons. Canberra, Commonwealth Department of Health and Ageing.

Neilson AH, Lindgren C, Hynning PA and Remberger M (1988) Methylation of halogenated phenols and thiophenols by cell extracts of gram-positive and gram-negative bacteria. *Applied and Environment Microbiology*, **54**:524-530.

Neumegen R, Fernandez-Alba A and Chisti Y (2005) Toxicities of triclosan, phenol and copper sulfate in activated sludge. *Environmental Toxicology*, **20**(2):160-164.

Nilsson C-A, Anderson K, Rappe C and Westermark S-O (1974) Chromatographic evidence for the formation of chloro-dioxins from chloro-2-phenoxyphenols. *Journal of Chromatography*, **96**:137-147.

NOHSC (1994) National code of practice for the control of workplace hazardous substances [NOHSC:2007 (1994)]. Australian Government Publishing Service, Canberra, ACT.

NOHSC (1994a) National code of practice for the labelling of workplace hazardous substances [NOHSC:2012 (1994)]. Australian Government Publishing Service, Canberra, ACT.

NOHSC (1994b) National code of practice for the preparation of material safety data sheets [NOHSC:2011 (1994)]. Australian Government Publishing Service, Canberra, ACT.

NOHSC (1994c) National model regulations for the control of workplace hazardous substances [NOHSC:1005 (1994)]. Australian Government Publishing Service, Canberra, ACT.

NOHSC (1994d) Guidance note for the assessment of health risks arising from the use of hazardous substances in the workplace [NOHSC:3017 (1994)]. Australian Government Publishing Service, Canberra, ACT.

NOHSC (1995) Exposure standards for atmospheric contaminants in the occupational environment [NOHSC;1003 (1995)]. Australian Government Publishing Service, Canberra, ACT.

NOHSC (2002) Control of major hazard facilities - National Standard [NOHSC:1014(2002)], National Code of Practice [NOHSC:2016(1996)], Australian Government Publishing Service, Canberra. Available at: http://www.ascc.gov.au/NR/rdonlyres/C4246822-C5C6-4AEF-9E09-C8F6D1874413/0/MajorHazardFacilities_2ed_2002.pdf

NOHSC (2003) National code of practice for the preparation of material safety data sheets 2nd Edition [NOHSC:2011 (2003)]. Australian Government Publishing Service, Canberra, ACT.

NOHSC (2004) Approved criteria for classifying hazardous substances, 3rd edition [NOHSC:1008 (2004)]. National Occupational Health and Safety Commission. Accessed at http://www.nohsc.gov.au/pdf/Standards/approved_criteriaNOHSC1008_2004.pdf in December 2005

Noel PRB, Mawdesley-Thomas LE, Squires PF and Street AE (1969) Oral toxicity study in baboons. Repeated dose for 4 and 13 weeks. Irgasan DP 300. GP 41353. Unpublished test report: Huntingdon Research Centre, England.

OECD (1993) Occupational and Consumer Exposure Assessments, Environment Monograph No 70, Environment Directorate. Accessed at: [http://www.olis.oecd.org/olis/1993doc.nsf/LinkTo/ocde-gd\(93\)128](http://www.olis.oecd.org/olis/1993doc.nsf/LinkTo/ocde-gd(93)128) in March 2006.

OECD (2004). The 2004 OECD list of High Production Volume Chemicals. Accessed at <http://www.oecd.org/dataoecd/55/38/33883530.pdf> in February 2006.

Offhaus K, Klingl H, Scherb K and Wachs B (1978) Untersuchungen zum eines bakteriostatikums in klaranlagen. Muech Beitr Abwasser-Fisch Flussbiol., **30**:29-71. Cited in Federle et al. (2002).

Okumura T and Nishikawa Y (1996) Gas chromatography – mass spectrometry determination of triclosans in water, sediment and fish samples via methylation with diazomethane. *Analytical Chimica Acta*, **325**:175–184.

Onodera S, Takahashi M, Ogawa M and Suzuki S (1995) Mutagenicity of polychlorophenoxyphenols (predioxins) and their photo-degradation products in aqueous solution. *Jpn. Journal of Toxicology and Environmental Health*, **41**(3):212–219.

Orvos DR, Versteeg DJ, Inauen J, Capdevielle M, Rothenstein A. and Cunningham V (2002) Aquatic Toxicity of Triclosan. *Environmental Toxicology and Chemistry*, **21**(7):1338-1349.

Oshima H, Kawahara D, Kosugi H, Nakamura M, Sugai T and Tamaki T (1991) Epidemiologic study on occupational allergy in the dental clinic. *Contact Dermatitis*, **24**:138–139.

Palmquist H (2003) Hazardous substances in wastewater systems: A delicate issue for wastewater management. Department of Environmental Engineering, Division of Sanitary Engineering, Lulea, University of Technology, Sweden. Licentiate thesis 2001:65. Swedish Foundation for Strategic Environmental Research, Sustainable Urban Water Management Programme.

Palmquist H and Hanaeus J (2005) Hazardous substances in grey- and blackwater from households at Vibyasan housing area, Sweden. *Science of the Total Environment*, **348**(1-3):151-163.

Pao EM, Hines JM and Roche AF (1980) Milk intakes and feeding patterns of breast-fed infants. *Journal of the American Dietetic Association*, **77**:540–545.

Parkes D (1978a) Pilot study. Single dose dermal absorption of triclosan in three days old rhesus monkeys, analyses of blood and soap samples. Unpublished test report. Ciba-Geigy Corporation, Greensboro, North Carolina, USA.

Parkes D (1978b) Irgasan DP300 oral dose kinetic study in adult rhesus monkeys. Unpublished study report. Ciba-Geigy Corporation, Greensboro, North Carolina, USA.

Parkes D (1979) Irgasan DP 300 ninety day bathing study in newborn rhesus monkeys. Final analytical report. Unpublished report. Ciba-Geigy Corporation, Greensboro, North Carolina, USA.

Parkes D (1986) Determination of FAT 80'023 (Irgasan DP 300) in blood and tissue samples taken during a two-year chronic oral toxicity/oncogenicity study in albino rats. Unpublished test report. Ciba-Geigy Corporation, Greensboro, North Carolina, USA.

- Paterson RA (1967) 91-day oral toxicity study in dogs, final report. Irgasan DP 300. Unpublished test report: Ciba Geigy, Wilmslow, England.
- Paterson RA (1969) 13-Week oral toxicity study in rabbits, final Report. Irgasan DP 300. GP 41 353. Unpublished test report: Ciba Geigy, Wilmslow, England.
- Paterson RA, Chapman TM and Porter M (1998). Re-use Potential from septage receival and treatment facilities The Australian-Indonesian International Conference on Water Quality and Waste Treatment. 19-22 October, 1998. Lombok, Indonesia.
- Paxeus N (1996) Organic pollutants in the effluents of large wastewater treatment plants in Sweden. *Water Research*, **30**:1115-1122.
- Paxeus N (2004) Removal of selected non-steroidal anti-inflammatory drugs (NSAIDS), gemfibrozil, carbamazepine, β -blockers, trimethoprim and triclosan in conventional wastewater treatment plants in five EU countries and their discharge to the aquatic environment. *Water, Science and Technology*, **50**(5):253-260.
- PBT Profiler (2004) Persistent, bioaccumulative, and toxic profiles estimated for organic chemicals on-line. Accessed at <http://www.pbtprofiler.net/> in May 2006.
- Pedersen BM and Neilsen U (2003) Maleprogram for Renseanlaeg Lynetten – Husholdningkemikalier og hormonforstyrrende stoffer [Monitoring Program for wastewater treatment plant Lynetten, household chemicals and endocrine disrupting substances], Report to Lynettefaellesskabet I/S. in Danish. (Cited in Danish Environmental Protection Agency, 2003b).
- Pemberton RM and Hart JP (1999) Electrochemical behaviour of triclosan at a screen-printed carbon electrode and its voltametric determination in toothpaste and mouthrinse products. *Analytica Chimica Acta*, **390**:107–115.
- Perrenoud D, Bircher A, Hunziker T, Suter H, Bruckner-Tuderman L, Stager J, Thurlimann W, Schmid P, Suard A and Hunziker N (1994) Frequency of sensitisation to 13 common preservatives in Switzerland. *Contact Dermatitis*, **30**(5):276–269.
- Persohn E (1994) FAT 80'023/R, assessment of replicate DNA synthesis in the course of a 13-week oral toxicity study in the hamster. Unpublished test report: RCC Project 356490, Ciba Limited, Toxicology Services, Basel, Switzerland.
- Persohn E and Molitor E (1993) The effect of FAT 80'023/Q (Irgasan DP 300) on replicative DNA synthesis in hepatocytes following dietary administration to male rats. Unpublished test report: CB 92/28-2. Ciba-Geigy Limited, Basel, Switzerland.
- Peters RJB (2005) Man-made chemicals in maternal and cord blood, TNO report B&O-A R 2005/129, Laan van Westenenk 501, PO Box 342, 7300 AH Apeldoorn, The Netherlands, March 2005.
- Pharmacon USA (1993a) Ames/*Salmonella* plate incorporation assay on test article 39316 (CC# 14663-09). Unpublished amended final report, Pharmakon Study No. PH 301-CP-001-93, Colgate Palmolive Study No.CP-93-012.
- Pharmakon USA (1993b) Rat hepatocyte primary culture/DNA repair test on 39317. Unpublished test report, Pharmakon Study No. PH 311-CP-001-93, Colgate Palmolive Study No. 93-013

- Piekacz H (1978) Effect of certain preservative agents on the course of pregnancy and foetal development in experimental animals with preliminary toxicological characteristics (translated from original). *Rocznik Panstw Zakl Higieny*, **29**(5):469–481.
- Plautz JR (2005) Triclosan in human mother's milk: Summary of existing sample analysis results and safety assessment for nursing infants. Unpublished report: 7 February 2005. Ciba Speciality Chemicals, Basel, Switzerland.
- Poiger T, Lindstrom A, Buerge IJ, Buser H, Bergqvist P-A and Muller MD (2003) Occurrence and environmental behaviour of the bactericide triclosan and its methyl derivative in surface waters and in wastewater. *Chimia*, **57**(1-2):26-29.
- Quercia V, Tucci B, Pierini N, Schrieber L, Biasci R and Caruso P (1979) Identification and determination of Irgasan DP-300 and hexachlorophene in cosmetic formulations using HPLC. *Bollettino Chimico Farmaceutico*, **118**:748–756.
- Quintana JB and Reemtsma T (2004) Sensitive determination of acidic drugs and triclosan in surface and wastewater by ion-pair reverse-phase liquid chromatography/tandem mass spectrometry. *Rapid Communications in Mass Spectrometry*, **18**:765-774.
- Ramachandran T, Rajendrakumar K and Rajendran R (2004) Antimicrobial textiles – an overview. *Institute of Engineers (India) Journal – Textiles*, 84 (Feb. 2004 issue) Accessed at <http://www.ieindia.org/publish/tx/0204/feb04tx4.pdf> in January 2005.
- Randall LP, Cooles SW, Piddock LJV and Woodward MJ (2004) Effect of triclosan or a phenolic farm disinfectant on the selection of antibiotic-resistant *Salmonella enterica*. *Journal of Antimicrobial Chemotherapy*, **54**:621–627.
- Rappe C and Nilsson C-A (1972) An artefact in the gas chromatographic determination of impurities in pentachlorophenol. *Journal of Chromatography*, **67**:247-253.
- Rasmussen HT, McDonough R, Gargiullo RJ and McPherson B.P (1996) Determination of triclosan in human dental plaque by gas chromatography with atomic emission detection. *HRC – Journal of High Resolution Chromatography*, **19**:359–361.
- RCC (1990a) Influence of FAT 80'023/Q on the reproduction of *Daphnia magna*. RCC Umweltchemie AG, CH-4452 Itingen, Switzerland. Unpublished report, Ciba-Geigy Corporation.
- RCC (1990b) Acute toxicity (LC50) study of FAT 80'023/Q to earthworms. RCC Umweltchemie AG, CH-4452 Itingen, Switzerland. Unpublished report, Ciba-Geigy AG.
- RCC (1995) Toxicity of ¹⁴C-FAT 80'023/R to *Scenedesmus subspicatus* (OECD – Algae Growth Inhibition Test). RCC Umweltchemie AG, CH-4452 Itingen, Switzerland. Unpublished Report No. 385637, Ciba-Geigy Limited.
- Reeder WG (1951) Stomach analysis of a group of shorebirds. *The Condor*, **53**:43-45.
- Reiss R, Mackay N, Habig C and Griffin J (2002) An ecological risk assessment for triclosan in lotic systems following discharge from wastewater treatment plants in the United States. *Environmental Toxicology and Chemistry*, **21**(11):2483-2492.
- Reither LL (2003) Detection of triclosan in geographically-diverse wastewater samples and the isolation of triclosan-resistant bacteria. Unpublished Senior Honours Thesis, Sweet Briar College, VA.

Remberger M, Allard A and Neilson AH (1986) Biotransformation of chloroguaiacols, and chloroveratroles in sediments. *Applied and Environmental Microbiology*, **51**(3):552-558.

Remberger M, Sternbeck J and Stromberg K (2002) Screening of triclosan and some brominated phenolic substances in Sweden. IVL Svenska Miljoinstitutet AB (In Swedish; cited in Danish EPA, 2003b).

Rhynne FG and Dart P (1997) Effluent reuse in Queensland: A survey of current treatment and reuse practices. CIRM Water Renewal Consortium. University of Qld, St. Lucia, Qld. June 1997.

Riach CG (1988) Triclosan: Assessment of genotoxicity in an unscheduled DNA synthesis assay using adult rat hepatocyte primary cultures. Unpublished Inveresk Research International Project No. 738388, Unilever Study No. KU 880258.

Roed-Petersen J, Auken G and Hjorth N (1975) Contact sensitivity to Irgasan DP 300. *Contact Dermatitis*, **1**:293-294.

Rotterdam Convention Annex III (2006) Information on chemicals subject to the PIC procedure. Accessed at <http://www.pic.int/en/Table7.htm> in February 2006.

Roy F. Weston Inc. (1990) Bacterial toxicity test on D1063.01. Marks KH, Crapo KC, Ziegenfuss PS and Marks PJ (eds) Unpublished Project No. 90-034, Proctor & Gamble Company.

Roy F. Weston Inc. (1992) Assessing the removal of the test substance during secondary wastewater treatment. D1063.01. Marks KH, Crapo KC, Doi J and Marks PJ (eds) Unpublished Study Report No. 90-117, Proctor & Gamble Company, Cincinnati, OH, USA.

Roy F. Weston Inc. (1998) Assessing the removal of the test substance during secondary wastewater treatment. Irgasan DP 300. Marks KH, Crapo KC and Doi J (eds) Unpublished Study Report No. 97-018, Ciba Specialty Chemicals, NC, USA.

Rule K, Ebbett V and Vikesland P (2005) Formation of chloroform and chlorinated organics by free-chlorine-mediated oxidation of triclosan. *Environmental Science and Technology*, **39**(9):3176-3185.

Russell LB and Montgomery CS (1980) Use of the mouse spot test to investigate the mutagenic potential of triclosan (Irgasan DP300). *Mutation Research*, **79**:7-12.

Sabaliunas D, Webb SF, Hauk A, Jacob M and Eckhoff WS (2003) Environmental fate of triclosan in the River Aire Basin, UK. *Water Research*, **37**:3145-3154.

Sachsse and Ullmann L (1975) Skin irritation in the rabbit after a single application of FAT 80'023/A - Toxicology/Pathology PH 2.63. Unpublished Project report Siss 4719. Ciba-Geigy Limited, Basle, Switzerland.

Safety and Security Centre (2003) Silver coated anti-sars mask actually kill pathogens. Accessed at <http://www.safetyandsecuritycenter.com/phsisama.html> in September 2003.

Safford B (1991) A critical assessment of the 65-week in-use human trial with toothpaste containing 0.2 % triclosan. Unpublished test report: Project reference D91/007. Unilever Research, Sharnbrook, Bedford, UK.

Sagelsdorff P and Busner G (1995) Investigation of the binding of Irgasan DP300 to human, hamster and mouse plasma proteins in vitro. Unpublished final report No: CB95/07. Ciba-Geigy Limited, Basel, Switzerland.

Sample BE and Suter II GW (1994) Estimating exposure of terrestrial wildlife to contaminants. Draft report. Prepared by the Environmental Sciences Division, Oak Ridge National Laboratory, Oak Ridge, TN. ES/ER/TM-125.

Sample BE, Aplin MS, Efrogmson RA, Suter II GW and Welsh CJE (1997) Methods and tools for estimation of the exposure of terrestrial wildlife to contaminants. Oak Ridge National Laboratory, Oak Ridge TN. ORNL/TM-13391.

Sanches-Silva A, Sendon-Garcia R, Lopez-Hernandez JL and Paseiro-Losada P (2005) Determination of triclosan in foodstuffs. *Journal of Separation Science*, **28**:65–72.

Sanchez P, Linares JF, Ruiz-Diez B, Campanario E, Nava A, Baquero F and Martinez JL (2002) Fitness of in vitro selected *Pseudomonas aeruginosa nalB* and *nfxB* multidrug resistant mutants. *Journal of Antimicrobial Chemotherapy*, **50**:657–664.

Sanchez P, Moreno E and Martinez J.L (2005) The biocide triclosan selects *Stenotrophomonas maltophilia* mutants that overproduce the SmeDEF multidrug efflux pump. *Antimicrobial Agents and Chemotherapy*, **49**:781–782.

Sanchez-Prado L, Llompарт M, Lores M, Fernandez-Alvarez M, Garcia-Jares C and Cela R (2006) Further research on the photo-SPME of triclosan. *Analytical and Bioanalytical Chemistry*, **384**(7-8):1548-57.

Sauer J, Antusch E. and Ripp C (1997) Monitoring of lipophilic organic pollutants in sewer systems by sewer slime analysis. *Vom Wasser*, **88**:49-69. (German).

SCCNFP (2003) The SCCNFP's notes for guidance for the testing of cosmetic ingredients and their safety evaluation (5th revision). European Commission - Scientific Committee on Cosmetic Products and Non-Food Products Intended for Consumers.

Schenkel A and Furia T (1965) The absorption of CH3565 through intact human skin from soap solutions. Unpublished test report No: 65-16-W221. Geigy Industrial Chemicals, Ardsley, NY, USA.

Schettgen C (2000) Bioakkumulation von Triclosan bei verschiedenen pH-Werten des Wassers und der Pyrethroide Cyfluthrin, Cypermethrin, Deltamethrin und Permethrin. 126 Bl. - Oldenburg, Univ., Diss. (In German).

Schettgen C, Schmidt A and Butte W (1999) Variation of accumulation and clearance of the predioxin 5-chloro-2-(2,4-dichlorophenoxy)-phenol (Irgasan DP 300, Triclosan) with the pH of water. *Organohalogen Compounds*, **43**:49-52.

Schmid MB and Kaplan N (2004) Reduced triclosan susceptibility in methicillin-resistant *Staphylococcus epidermidis*. *Antimicrobial Agents and Chemotherapy*, **48**:1397–1399.

Schmid A, Dotti A, Keller G, Kouchakji G, Luetkemeier H, Wilson J, Biedermann K and Marbot H (1994) 13-Week oral toxicity (feeding) study with FAT 80'023/R in the hamster. Final report. Unpublished test report: Project Number 356490. RCC Group, Itingen, Switzerland.

Schnuch A, Geier J, Uter W and Frosch PJ (1998) Patch testing with preservative, antimicrobials and industrial biocides. Results from a multi-centre study. *British Journal of Dermatology*, **138**:467–476.

Shanghai Municipal Prevention Medical Institution (2002a) Rabbit acute dermal irritation test report, sample No. YAN2002-9. Unpublished test report.

Shanghai Municipal Prevention Medical Institution (2002b) Human patch test report, sample No. YAN2002-9. Unpublished test report.

Shiraishi F, Shiraishi N, Nishikawa J, Nishihara T and Morita M (2000) Development of a simple operational estrogenicity assay system using the yeast two-hybrid system. *Journal of Environmental Chemistry*, **10**:57-64.

Siddiqui WH and Buttar HS (1979) Pharmacokinetics of triclosan in rat after intravenous and intravaginal administration. *Journal of Environmental Pathology and Toxicology*, **2**:861–871.

Singer H, Muller S, Tixier C and Pillonel L (2002) Triclosan: Occurrence and fate of a widely used biocide in the aquatic environment: field measurements in wastewater treatment plants, surface waters, and lake sediments. *Environmental Science and Technology*, **36**:4998–5004.

Sioufi A, Caudal F and Grimault D (1977) GLC determination of free and conjugated triclosan in human plasma and urine. *Journal of Pharmaceutical Sciences*, **66**(8):1166–1168.

Skaare A, Eide G, Herlofson B and Barkvoll P (1996) The effect of toothpaste containing triclosan on oral mucosal desquamation. *Journal of Clinical Periodontology*, **23**:1100–1103.

Skaare A, Kjaerheim V, Barkvoll P and Rolla G (1997a) Skin reactions and irritation potential of four commercial toothpastes. *Acta Odontol Scand*, **55**:133–136.

Skaare AB, Rolla G and Barkvoll P (1997b) The influence of triclosan, zinc or propylene glycol on oral mucosa exposed to sodium lauryl sulphate. *European Journal of Oral Sciences*, **105**:527–533.

Skadhauge R (1975) Renal and cloacal transport of salt and water. *Symposia of the Zoological Society London*, **35**:97-106. (Cited in US EPA, 1993).

Springborn Laboratories (1992) (D1063) - Determination of Effects on Seedling Growth of Six Plant Species. Unpublished Report No. 90-12-3574. Proctor & Gamble Company.

Springborn Laboratories (1993) Chronic toxicity evaluation of D1063.02R using *Ceriodaphnia dubia* under Static-renewal Conditions. Jop, K. M (ed). Unpublished Report No. 92-01-4080, Proctor & Gamble Company.

Springborn Laboratories Inc. (1994a) Triclosan – Determination of anaerobic aquatic biodegradation. Christensen KP (ed) Unpublished Report No. 93-12-5076, Colgate-Palmolive Company, NJ, USA.

Springborn Laboratories Inc. (1994b) Triclosan – Determination of aerobic biodegradation in soils. Christensen KP (ed) Unpublished Report No. 93-5-4770, Colgate-Palmolive Company, NJ, USA.

Stamatelatou K, Dokianakis SN, Fountoulakis M, Frounda K, Kornaros ME and Lyberatos G (2003) On the effect of pharmaceuticals on biological processes. Oral presentation, Envirpharma Conference, Lyon, France, 4-16 April, 2003.

Stasinakis AS, Petalas AV, Mamais D, Thomaidis NS (2008) Application of the OECD 301F respirometric test for the biodegradability assessment of various potential endocrine disrupting chemicals. *Bioresour Technol*.99:3458-67.

Steinkjer B and Braathen LR (1998) Contact dermatitis from triclosan (Irgasan DP 300). *Contact Dermatitis*, **18**(4):243–244.

Sterling Fibres (2005) Biofresh antibacterial fiber. Accessed at <http://www.fabriclink.com/hf/biofreshhf/homehf.html> in March 2005.

- Stierlin H (1972a) Study of pharmacokinetics and metabolism in mouse, rat, rabbit and dog. Unpublished study report No: 33/1972. Ciba-Geigy Limited, Basel, Switzerland.
- Stierlin H (1972b) Exploratory study of the percutaneous absorption of GP 41 353 in man following topical application in a cream base. Unpublished study report No: 34/1972. Ciba-Geigy Limited, Basel, Switzerland.
- Strasser FF and Muller D (1978) Point mutation assay with mouse lymphoma cells I. In vitro test II. Host-mediated assay. Unpublished Experiment No. 782305. Ciba-Geigy Limited, Basel, Switzerland.
- Strasser FF and Muller D (1979) Chromosome studies in somatic cells, long-term study with FAT 80 023/A, Chinese hamster. Unpublished Experiment No. 78 - 3105. Ciba-Geigy Limited, Basel, Switzerland.
- Struijs J (1996) SimpleTreat 3.0: a model to predict the distribution and elimination of chemicals by sewage treatment plants. Report nr. 719101025. National Institute of Public Health and Environmental Protection (RIVM), Bilthoven, The Netherlands.
- Sullivan A, Wretling B and Nord CE (2003) Will triclosan in toothpaste select for resistant oral streptococci? *Clinical Microbiology and Infection*, **9**:306–309.
- Summers AO (2002) Generally overlooked fundamentals of bacterial genetics and ecology. *Clinical Infectious Diseases*, **34**(Supplement 3):S85-92
- SUSDP (2008) Standard for the Uniform Scheduling of Drugs and Poisons, No 23. National Drugs and Poisons Schedule Committee, Canberra, Australian Government Publishing Service.
- Svensson A (2002) Ecotoxic substances in sewage sludge – A study of 19 WWTPs in Vastra Gotaland, Sweden. Lansstyrelsen I Vastra Gotaland, Report 2002:39. In Swedish.
- Sydney Water Corporation (2000a) Sydney Water's 2000-2005 Environment Plan. NSW.
- Sydney Water Corporation (2000b) Assessment of STP effluent toxicity: Hawkesbury-Nepean River Report August 2000. Sinclair Knight Mertz Pty Ltd, St Leonards, NSW.
- Sydney Water Corporation (2003) Sydney Water Ecologically Sustainable Development Indicators & Environment Plan Report 2003. NSW.
- Sydney Water (2006) Sydney Water Annual Report 2006, Sydney Water. <http://www.sydneywater.com.au/Publications/Reports/SydneyWaterAnnualReport2006.cfm>
- Tatarazako N, Ishibashi H, Teshima K, Kishi K, Arizono K (2004) Effects of triclosan on various aquatic organisms. *Environ Sciences* **11**, 130-133.
- Terizzi A, Riccola S, Contos N and Canaletti M (1999) Cutaneous tolerability (irritation patch test) of a new liquid disinfectant based on triclosan 1 %: clinical trial on 12 healthy volunteers. *Acta Toxicologica et Therapeutica*, **20**(2):81–89.
- Therapeutic Goods Administration (2004) Regulation of anti-bacterial hand washes. Accessed at <http://www.tga.gov.au/docs/html/antihawa.htm> in June 2004.
- Therapeutic Goods Administration (2008) Interim Guidelines for the National Drugs and Poisons Schedule Committee, Department of Health and Ageing, January 2008.
- Thomann P and Maurer T (1978) Experiments in guinea pigs with Irgasan DP 300. Unpublished test report (test laboratory not reported).

- Thomas H (1994) The effect of FAT 80'023/R and the model inducers phenobarbitone, 3-methylcholanthrene, pregnenolone-16 α -carbonitrile and nafenopin on selected biochemical and morphological parameters in the Syrian hamster. Unpublished laboratory report. CB 93/40. Ciba-Geigy Limited, Basel, Switzerland.
- Thomas PM and Foster GD (2005) Tracking acidic pharmaceuticals, caffeine, and triclosan through the wastewater treatment process. *Environmental Toxicology and Chemistry*, **24**(1):25–30.
- Thompson TA (1975) Triclosan – Results to date of multiple scrub studies with GP 41353 surgical scrub. Unpublished test report: Ciba-Geigy Medical Research.
- Thompson RD (2001) Determination of phenolic disinfectant agents in commercial formulations by liquid chromatography. *Journal of AOAC International*, **84**(3):815–822.
- Thompson TA, Goodblatt RS and Borman CH (1975a) Triclosan (Report 1): A method for determining triclosan in human plasma and urine, and results of a pilot handwashing study. Unpublished drug metabolism report 1975-17. Ciba-Geigy Corporation, Ardsley, NY, USA.
- Thompson TA, Borman CH and Goodblatt RS (1975b) Triclosan (Report 2): Concentration in human plasma and urinary excretion after dermal application of GP 41353 patient skin prep. Unpublished drug metabolism report 1975-18. Ciba-Geigy Corporation, Ardsley, NY, USA.
- Thompson TA, Goodblatt RS and Borman CH (1976) Triclosan (Report 3): Concentration in human plasma and urinary excretion after use of GP 41353 surgical scrub. Unpublished drug metabolism report 1976-3. Ciba-Geigy Corporation, Ardsley, NY, USA.
- Thompson A, Griffin P, Stuetz R, and Cartmell E (2005) The fate and removal of triclosan during wastewater treatment, *Water Environment Research*, **77**(1), January/February 2005, pp. 63-67(5).
- Tixier C, Singer HP, Canonica S and Muller SR (2002) Phototransformation of triclosan in surface waters: A relevant elimination process for this widely used biocide – Laboratory studies, field measurements, and modelling. *Environmental Science and Technology*, **36**:3482–3489.
- Toxicological Resources (1974) Guinea pig Buehler dermal sensitisation study. Compound 1292. Unpublished Project No. 2118-74.
- Trevisi P, Vincenzi C, Chierigato C, Guerra L and Tosti A (1994) Sunscreen sensitisation: a three-year study. *Dermatology*, **189**:55–57.
- Trimmer GW (1994) 90-Day subchronic dermal toxicity study in the rat with satellite group with Irgasan DP300 (MRD-92-399). Unpublished test report: 139910B Exxon Biochemical Sciences Inc., New Jersey, USA.
- Trutter JA (1993) 13-Week subchronic oral toxicity study of triclosan in CD-1 mice. Unpublished test report: HWA 483-287 Hazelton Washington Inc., Virginia, USA.
- Tulp MTM, Sundstrom G, Martron LBJM and Hutzinger O (1979) Metabolism of chlorodiphenyl ethers and Irgasan DP 300. *Xenobiotica*, **9**(2):65–77.
- Ullmann L (1980) Report on eye irritation in the rabbit after single application of FAT 80'023A. Unpublished Final Report: Project no. 801012. Ciba-Geigy Limited, Basle, Switzerland.

UNEP (2002) Stockholm Convention on Persistent Organic Pollutants (POPs) - Text and Annexes. Interim Secretariat for the Stockholm Convention on Persistent Organic Pollutants, United Nations Environment Programme (UNEP) Chemicals, Chatelaine, Geneva, Switzerland.

UNEP (2005) Ridding the world of POPs: A guide to the Stockholm Convention on persistent organic pollutants. Accessed at http://www.pops.int/documents/guidance/beg_guide.pdf in May 2005.

Urbach F (1973) Phototoxicity study in mice, pigs and humans, Irgasan DP-300. Unpublished test report. Temple University Skin and Cancer Hospital, Philadelphia, Pennsylvania, USA.

US ACE/US EPA (2004) Environmental Residue Effects Database. U.S. Corps of Engineers and U.S. Environmental Protection Agency. Interne URL: <http://ered1.wes.army.mil/ERED/help/hlpAbout.cfm>

US ACE/US EPA (2004) Environmental Residue Effects Database. U.S. Corps of Engineers and U.S. Environmental Protection Agency. Interne URL: <http://ered1.wes.army.mil/ERED/help/hlpAbout.cfm>

USACHPPM (United States Army Center for Health Promotion and Preventive Medicine) (2000). Standard Practice for Wildlife Toxicity Reference Values. Technical Guide No. 254. October 2000. Environmental Health Risk Assessment Program and Health Effects Research Program, Aberdeen Proving Ground, Maryland. 45 pp.

US EPA (United States Environmental Protection Agency) (1971) Algal Assay Bottle Test. National Eutrophication Research Program.

US EPA (1974) Marine algal assay procedure: Bottle test. Eutrophication and Lake Restoration Branch, Pacific Northwest Environmental Research Laboratory, OR.

US EPA (1978) Bioassay procedures for the Ocean Disposal Permit Program, Environmental research Laboratory, Gulf Breeze, FL. EPA-600/9-78-010.

US EPA (1985a) Methods for estimating the acute toxicity of effluents to freshwater and marine organisms. EPA-600/4-85/013.

US EPA (1985b) Methods for estimating the chronic toxicity of effluent and receiving Waters to freshwater organisms. EPA-600/4-85/041.

US EPA (1985c) Standard evaluation procedures for an avian dietary LC50 test. Hazard Evaluation Division. EPA-540/9-85-008.

US EPA (1985d) TSCA Environmental Effects Testing Guidelines. Subpart B, Section 797.1050, Federal Register, 50, No. 188.

US EPA (1987) TSCA Environmental Effects Testing Guidelines. Subpart B, Section 797.1050, Federal Register, 52, No. 97.

US EPA (1989a) Avian dietary LC50 test for waterfowl and upland game birds. FIFRA Pesticide Assessment Guidelines.

US EPA (1989b) Short-term method for estimating the chronic toxicity of effluents and receiving waters to freshwater organisms. EPA/600/4-89/001.

US EPA. (1993) Wildlife exposure factors handbook. Office of Research and Development. EPA/600/R-93/189.

- US EPA (1996a) Ecological Effects Test Guidelines (OPPTS Series 850.1085). Fish acute toxicity mitigated by humic acid.
- US EPA (1996b) Ecological Effects Test Guidelines (OPPTS Series 850.5400). Algal toxicity test I and II.
- US EPA (2000) Methods for measuring the toxicity and bioaccumulation of sediment-associated contaminants with freshwater invertebrates. EPA/600/R-99/064. Office of Water, Washington DC.
- US EPA (2002) Child-specific exposure factors handbook – interim report. Accessed at: <http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=55145> in March 2006.
- US EPA (2007) Dietary Risk Assessment for Triclosan for the Re-registration Eligibility Decision (RED) Process (April 5, 2007).
- US EPA (2008) 5-Chloro-2-(2,4-dichlorophenoxy) phenol (Triclosan): Risk assessment for the Reregistration Eligibility Decision (RED) Document. Case No 2340. PC Code: 054901, April 17, 2008.
- US FDA (Food and Drug Administration) (1990) Protocol for conduct of a seedling growth toxicity test. FDA Technical Assistance Documents (TAD) 4.07 (Protocol 073090).
- US NPIRS (2005) National Pesticide Information Retrieval System. Accessed at <http://aboutnpirs.ceris.purdue.edu/> in March 2005.
- USP (2004) Monograph USP 27. United States Pharmacopeial Convention Inc., Rockville, MD 20852, USA.
- Valo R and Salkinoja-Salonen M (1986) Microbial transformation of polychlorinated phenoxy phenols. *Journal of General and Applied Microbiology*, **32**:505-517. Cited in Hundt et al. (2000).
- Valters K, Li H, Alaei M, D'Sa I, Marsh G, Bergman A and Letcher R (2005) Polybrominated diphenyl ethers and hydroxylated and methoxylated brominated and chlorinated analogues in the plasma of fish from the Detroit River. *Environmental Science and Technology*, **39**(15):5612-5619.
- van Dijk A (1994) 14C-triclosan: Absorption, distribution, metabolism and elimination after single/repeated oral and intravenous administration to hamsters. Unpublished study report No: RCC project 351707. RCC Umweltchemie AG, Itingen, Switzerland.
- van Dijk A (1995) 14C-triclosan: Absorption, distribution, metabolism and elimination after single/repeated oral and intravenous administration to mice.
- van Dijk A (1996) 14C-triclosan: Absorption, distribution and excretion (ADE) after single oral and repeated oral administration to male rats. Unpublished study report No: RCC project 341998. RCC Umweltchemie AG, Itingen, Switzerland.
- van Stee LL, Leonards PEG, Vreuls RJJ and Brinkman UAT (1999) Identification of non-target compounds using gas chromatography with simultaneous atomic emission and mass spectrometric detection (GC-AED/MS): analysis of municipal wastewater. *Analyst*, **124**:1547-1552.
- van Wezel AP and Jager T (2002) Comparison of two screening level risk assessment approaches for six disinfectants and pharmaceuticals. *Chemosphere*, **47**:1113-1128.

Veldhoen N, Skirrow RC, Osachoff H, Wigmore H, Clapson DJ, Gunderson MP, Van Aggelen G and Helbing CC (2006) The bactericidal agent triclosan modulates thyroid hormone-associated gene expression and disrupts postembryonic anuran development. *Aquatic Toxicology*, **80**(3):217-227.

Veronesi S, De Padova MP, Vanni D and Melino M (1986) Contact dermatitis to triclosan. *Contact Dermatitis*, **15**:257–258.

Victorian Natural Resources and Environment (2002) Victorian biosolids market survey.

Voets JP, Pipyn P, Van Lancker P and Verstraete W (1976) Degradation of microbiocides under different environmental conditions. *Journal of Applied Bacteriology*, **40**:67-72.

Völkel W (2007a) The effects of triclosan on soil respiration. RCC Study Number: A889954, RCC Ltd Environmental Chemistry & Pharamanalytics, Itingen, Switzerland.

Völkel W (2007b) The effects of triclosan on soil nitrification. RCC Study Number: A88312, RCC Ltd Environmental Chemistry & Pharamanalytics, Itingen, Switzerland.

Wagner J (1973) Preparation GP 41,353: Binding to human serum proteins in vitro. Unpublished report No: B 34/73. Ciba-Geigy Limited, Basel, Switzerland.

Wagner WE and Le Sher A (1977) Triclosan (Irgasan DP300) soap bar plateau plasma levels in man. Unpublished Bioco report No: 1977-24. Ciba-Geigy Corporation, NJ, USA.

Wahlberg JE (1976) Routine patch testing with Irgasan DP 300. *Contact Dermatitis*, **2**(5):292.

Walsh SE, Maillard J-Y, Russell AD, Catrenich CE, Charbonneau DL and Bartolo RG (2003) Development of bacterial resistance to several biocides and effects on antibiotic susceptibility. *Journal of Hospital Infection*, **55**:98–107.

Walther WL (1968) Acute toxicity – mouse i.v. Unpublished test report GP 41 353 = CH 3565, Investigation # 327/16 025.

Wang L-H and Chu S-C (2004) Voltammetric detector for liquid chromatography: Determination of triclosan in rabbit urine and serum. *Chromatographia*, **60**:385–390.

Wang L-Q, Falany CN and James MO (2004) Triclosan as a substrate and inhibitor of 3'-phosphoadenosine 5'-phosphosulfate-sulfotransferase and UDP-glucuronyl transferase in human liver fractions. *Drug, Metabolism and Distribution*, **32**(10):1162–1169.

Water Corporation (2003) Annual Report 2002/03. Wastewater Treatment Branch, Perth, WA.

Weeks HP, Jr. (1978) Characterisation of mineral licks and behaviour of visiting White-tailed Deer in Southern Indiana. *American Midland Naturalist*, **100**:384-395.

Weigel S, Berger U, Jensen E, Kallenborn R, Hilde T and Huhnerfuss H (2004) Determination of selected pharmaceuticals and caffeine in sewage and seawater from Tromsø/Norway with emphasis on ibuprofen and its metabolites. *Chemosphere*, **56**:583-592.

Wennersten G, Thune P, Brodthagen H, Jansen C and Rystedt I (1984) The Scandinavian multicenter photopatch study. *Contact Dermatitis*, **10**:305–309.

WHO (2006) Guidelines for drinking-water quality: incorporating first addendum. Vol. 1, Recommendations. – 3rd ed. World Health Organization. Electronic version for the web, accessed at http://www.who.int/water_sanitation_health/dwq/gdwq3/en/index.html in February 2006.

- Wildlife International Ltd (1998) Triclosan: A 96-hour toxicity test with the freshwater alga (*Anabaena flos-aquae*). Unpublished Project Report No. 473A-101, Ciba Specialty Chemicals, NC, USA.
- Wildlife International Ltd (1999) Triclosan: Toxicity mitigation by humic acid during a 96-hour toxicity test with the Freshwater Algae (*Scenedesmus subspicatus*). Unpublished report.
- Wilkison DH, Armstrong DJ and Blevins DW (2002) Effects of wastewater and combined sewer overflows on water quality in the Blue River Basin, Kansas City, Missouri and Kansas, July 1998-October 2000. U.S Geological Survey report, accessed at <http://mo.water.usgs.gov/Reports/WRIR02-4107/report.pdf>
- Wilson BA, Smith VH, Denoyelles F Jnr. and Larive CK (2003) Effect of three pharmaceutical and personal care products on natural freshwater algal assemblages. *Environmental Science and Technology*, **37**:1713-1719.
- Wind T, Werner U, Jacob M and Hauk A (2004) Environmental concentrations of boron, LAS, EDTA, NTA and triclosan simulated with GREAT-ER in the river Itter. *Chemosphere*, **54**:1135-1144.
- Wnorowski G (1994a) Acute oral toxicity limit test. Unpublished Project number 2800. Product Safety Laboratory, East Brunswick, New Jersey, USA.
- Wnorowski G (1994b) Dermal sensitisation test – Buehler method for triclosan. Unpublished Project number 2635. Product Safety Laboratory, East Brunswick, New Jersey, USA.
- Wong CSM and Beck MH (2001) Allergic contact dermatitis from triclosan in antibacterial handwashes. *Contact Dermatitis*, **45**:p.307.
- Yang LH, Ying GG, SU HC, Stauber JL, Adams MS and Binet MT (2008) Growth-inhibiting effects of 12 antibacterial agents and their mixtures on the freshwater microalga *Pseudokirchneriella subcapitata*. *Environmental Toxicology and Chemistry*, **27**(5), pp. 1201–1208.
- Yarra Valley Water (2001) Environment Performance Report & Environment Improvement Plan 2000-2001. Accessed at http://www.yvw.com.au/NR/rdonlyres/D07A221D-A8F3-4C16-B957-179783D04549/0/enviro_report_2001.pdf
- Ye X, Kuklenyik Z, Needham LL and Calafat AM (2005) Automated on-line column-switching HPLC-MS/MS method with peak focusing for the determination of nine environmental phenols in urine. *Analytical Chemistry*, **77**(16):5407–5413.
- Ying GG and Kookana RS (2007) Triclosan in effluents and biosolids from Australian wastewater treatment plants. *Environment International*, **33**:199–205.
- Ying GG, Yu XY, Kookana RS (2007) Biological degradation of triclocarban and triclosan in a soil under aerobic and anaerobic conditions and comparison with environmental fate modelling, *Environmental Pollution* **150** 300-305.
- Zhang H and Huang C-H (2003) Oxidative transformation of triclosan and chlorophene by manganese oxides. *Environmental Science and Technology*, **37**:2421-2430.

Glossary

Acute exposure	A contact between an agent and a target occurring over a short period of time, generally less than a day. (Other terms such as “short-term exposure” and “single dose” are also used.)
Adverse effect	Change in the morphology, physiology, growth, development, reproduction, or life span of an organism, system or (sub) population that results in an impairment of functional capacity, an impairment of the capacity to compensate for additional stress, or an increase in susceptibility to other influences.
Agent	A chemical, biological, or physical entity that contacts a target.
Analysis	Detailed examination of anything complex, made in order to understand its nature or to determine its essential features
Assessment	Evaluation of appraisal of an analysis of facts and the inference of possible consequences concerning a particular object or process.
Assessment endpoint	Quantitative/qualitative expression of a specific factor with which a risk may be associated as determined through an appropriate risk assessment.
Background level	The amount of an agent in a medium (e.g., water, soil) that is not attributed to the source(s) under investigation in an exposure assessment. Background level(s) can be naturally occurring or the result of human activities. (Note: natural background is the concentration of an agent in a medium that occurs naturally or is not the result of human activities).
Biomarker/biological marker	Indicator of changes or events in biological systems. Biological markers of exposure refer to cellular, biochemical, analytical, or molecular measures that are obtained from biological media such as tissues, cells, or fluids and are indicative of exposure to an agent.
Bounding Estimate	An estimate of exposure, dose, or risk that is higher than that incurred by the person with the highest exposure, dose, or risk in the population being assessed. Bounding estimates are useful in developing statements that exposures, doses, or risks are "not greater than" the estimated value.
Chronic exposure	A continuous or intermittent long-term contact between an agent and a target. (Other terms, such as “long-term exposure,” are also used.)

Concentration	Amount of a material or agent dissolved or contained in unit quantity in a given medium or system.
Contact volume	A volume containing the mass of agent that contacts the exposure surface
Dose	Total amount of an agent administered to, taken up or absorbed by an organism, system or (sub) population.
Dose-effect relationship	Relationship between the total amount of an agent administered to, taken up or absorbed by an organism, system or (sub) population and the magnitude of a continuously-graded effect to that organism, system or (sub) population Related terms: <i>Effect Assessment, Dose-Response Relationship, Concentration-Effect Relationship.</i>
Dose-related effect	Any effect to an organism, system or (sub) population as a result of the quantity of an agent administered to, taken up or absorbed by that organism, system or (sub) population.
Dose-response	Relationship between the amount of an agent administered to, taken up or absorbed by an organism, system or (sub) population and the change developed in that organism, system or (sub) population in reaction to the agent. Synonymous with Dose-response relationship. Related Term: <i>Dose-Effect Relationship, Effect Assessment, Concentration-Effect Relationship.</i>
Dose-response assessment	Analysis of the relationship between the total amount of an agent administered to, taken up or absorbed by an organism, system or (sub)population and the changes developed in that organism, system or (sub)population in reaction to that agent, and inferences derived from such an analysis with respect to the entire population. Dose-Response Assessment is the second of four steps in risk assessment. Related terms: <i>Hazard Characterisation, Dose-Effect Relationship, Effect Assessment, Dose-Response Relationship, Concentration-Effect Relationship.</i>
Dose-response curve	Graphical presentation of a dose-response relationship.
Dose-Response Relationship	Relationship between the amount of an agent administered to, taken up or absorbed by an organism, system or (sub) population and the change developed in that organism, system or (sub) population in reaction to the agent. Related Terms: <i>Dose-Effect Relationship, Effect Assessment, Concentration-Effect Relationship.</i>
Effect	Change in the state or dynamics of an organism, system or (sub) population caused by the exposure to an agent.

Effect assessment	Combination of analysis and inference of possible consequences of the exposure to a particular agent based on knowledge of the dose-effect relationship associated with that agent in a specific target organism, system or (sub) population.
Expert judgement	Opinion of an authoritative person on a particular subject.
Exposure	Concentration or amount of a particular agent that reaches a target organism, system or (sub) population in a specific frequency for a defined duration.
Exposure assessment	Evaluation of the exposure of an organism, system or (sub) population to an agent (and its derivatives). Exposure Assessment is the third step in the process of Risk Assessment.
Exposure concentration	The exposure mass divided by the contact volume or the exposure mass divided by the mass of contact volume depending on the medium.
Exposure duration	The length of time over which continuous or intermittent contacts occur between an agent and a target. For example, if an individual is in contact with an agent for 10 minutes a day, for 300 days over a one-year time period, the exposure duration is one year.
Exposure frequency	The number of exposure events in an exposure duration.
Exposure mass	The amount of agent present in the contact volume. For example, the total mass of residue collected with a skin wipe sample over the entire exposure surface is an exposure mass.
Exposure model	A conceptual or mathematical representation of the exposure process.
Exposure pathway	The course an agent takes from the source to the target.
Exposure period	The time of continuous contact between an agent and a target.
Exposure route	The way an agent enters a target after contact (e.g., by ingestion, inhalation, or dermal absorption).
Exposure scenario	A set of conditions or assumptions about sources, exposure pathways, amount or concentrations of agent(s) involved, and exposed organism, system or (sub) population (i.e. numbers, characteristics, habits) used to aid in the evaluation and quantification of exposure(s) in a given situation.

Exposure surface	A surface on a target where an agent is present. Examples of outer exposure surfaces include the exterior of an eyeball, the skin surface, and a conceptual surface over the nose and open mouth. Examples of inner exposure surfaces include the gastro-intestinal tract, the respiratory tract and the urinary tract lining. As an exposure surface gets smaller, the limit is an exposure point.
Fate	Pattern of distribution of an agent, its derivatives or metabolites in an organism, system, compartment or (sub) population of concern as a result of transport, partitioning, transformation or degradation.
Guidance value	Value, such as concentration in air or water, which is derived after allocation of the reference dose among the different possible media (routes) of exposure. The aim of the guidance value is to provide quantitative information from risk assessment to the risk managers to enable them to make decisions. (See also: reference dose)
Hazard	Inherent property of an agent or situation having the potential to cause adverse effects when an organism, system or (sub) population is exposed to that agent.
Hazard assessment	A process designed to determine the possible adverse effects of an agent or situation to which an organism, system or (sub) population could be exposed. The process includes hazard identification and hazard characterization. The process focuses on the hazard in contrast to risk assessment where exposure assessment is a distinct additional step.
Hazard characterization	The qualitative and, wherever possible, quantitative description of the inherent properties of an agent or situation having the potential to cause adverse effects. This should, where possible, include a dose-response assessment and its attendant uncertainties. Hazard Characterisation is the second stage in the process of Hazard Assessment, and the second step in Risk Assessment. Related terms: <i>Dose-Effect Relationship</i> , <i>Effect Assessment</i> , <i>Dose-Response Relationship</i> , <i>Concentration -Effect Relationship</i> .
Hazard identification	The identification of the type and nature of adverse effects that an agent has inherent capacity to cause in an organism, system or (sub) population. Hazard identification is the first stage in hazard assessment and the first step in process of Risk Assessment
Intake	The process by which an agent crosses an outer exposure surface of a target without passing an absorption barrier, i.e. through ingestion or inhalation.
Measurement of end-point	Measurable (ecological) characteristic that is related to the valued characteristic chosen as an assessment point.

Medium	Material (e.g., air, water, soil, food, consumer products) surrounding or containing an agent.
Microenvironment	The rate at which the medium crosses the outer exposure surface of a target, during ingestion or inhalation.
Reference dose	An estimate of the daily exposure dose that is likely to be without deleterious effect even if continued exposure occurs over a lifetime. Related term: <i>Acceptable Daily Intake</i> .
Response	Change developed in the state or dynamics of an organism, system or (sub) population in reaction to exposure to an agent.
Risk	The probability of an adverse effect in an organism, system or (sub) population caused under specified circumstances by exposure to an agent.
Risk analysis	A process for controlling situations where an organism, system or (sub) population could be exposed to a hazard. The Risk Analysis process consists of three components: risk assessment, risk management and risk communication.
Risk assessment	A process intended to calculate or estimate the risk to a given target organism, system or (sub)population, including the identification of attendant uncertainties, following exposure to a particular agent, taking into account the inherent characteristics of the agent of concern as well as the characteristics of the specific target system. The Risk Assessment process includes four steps: hazard identification, hazard characterization (related term: dose-response assessment), exposure assessment, and risk characterization. It is the first component in a risk analysis process.
Risk characterization	The qualitative and, wherever possible, quantitative determination, including attendant uncertainties, of the probability of occurrence of known and potential adverse effects of an agent in a given organism, system or (sub) population, under defined exposure conditions. Risk Characterization is the fourth step in the Risk Assessment process.
Risk communication	Interactive exchange of information about (health or environmental) risks among risk assessors, managers, news media, interested groups and the general public.
Risk estimation	Quantification of the probability, including attendant uncertainties, that specific adverse effects will occur in an organism, system or (sub)population due to actual or predicted exposure.

Risk evaluation	Establishment of a qualitative or quantitative relationship between risks and benefits of exposure to an agent, involving the complex process of determining the significance of the identified hazards and estimated risks to the system concerned or affected by the exposure, as well as the significance of the benefits brought about by the agent. It is an element of risk management. Risk Evaluation is synonymous with Risk-Benefit evaluation
Risk management	Decision-making process involving considerations of political, social, economic, and technical factors with relevant risk assessment information relating to a hazard so as to develop, analyse, and compare regulatory and non-regulatory options and to select and implement appropriate regulatory response to that hazard. Risk management comprises three elements: risk evaluation; emission and exposure control; risk monitoring.
Risk monitoring	Process of following up the decisions and actions within risk management in order to ascertain that risk containment or reduction with respect to a particular hazard is assured. Risk monitoring is an element of risk management.
Safety	Practical certainty that adverse effects will not result from exposure to an agent under defined circumstances. It is the reciprocal of risk.
Safety factor	Composite (reductive) factor by which an observed or estimated no-observed-adverse effect level (NOAEL) is divided to arrive at a criterion or standard that is considered safe or without appreciable risk. Related terms: <i>Assessment Factor</i> , <i>Uncertainty Factor</i> .
Source	The origin of an agent for the purposes of an exposure assessment.
Subchronic exposure	A contact between an agent and a target of intermediate duration between acute and chronic. (Other terms, such as “less-than-lifetime exposure” are also used.)
Target	Any biological entity that receives an exposure or a dose (e.g., a human, human population or a human organ).
Threshold	Dose or exposure concentration of an agent below that a stated effect is not observed or expected to occur.
Time-averaged exposure	The time-integrated exposure divided by the exposure duration. An example is the daily average exposure of an individual to carbon monoxide. (Also called time-weighted average exposure.)
Tolerable daily intake	Analogous to Acceptable Daily Intake. The term Tolerable is used for agents which are not deliberately added such as contaminants in food.

Toxicity	Inherent property of an agent to cause an adverse biological effect.
Uncertainty	Imperfect knowledge concerning the present or future state of an organism, system or (sub) population under consideration.
Uncertainty factor	Reductive factor by which an observed or estimated no-observed-adverse-effect level (NOAEL) is divided to arrive at a criterion or standard that is considered safe or without appreciable risk. Related terms: <i>Assessment Factor</i> , <i>Safety Factor</i> .

Index

- ABC Laboratories Inc. (1997c) study on algal toxicity 354–6
- Abramis brama*, chronic/reproductive toxicity 347
- absorption 27, 80
 - animal studies
 - dermal 230–3
 - inhalation 230
 - oral 233–9
 - human skin, in vitro studies 247–8
 - human studies
 - buccal 246–7
 - dermal 239–43
 - gingival 246
 - inhalation 239
 - intravaginal 246
 - oral 243–5
- Acinetobacter iwoffi* 314
- acronyms and abbreviations xxvii–xxxi
- acute risks due to occupational exposure 39
 - end-use products 39
 - secondary transfer 40
- acute risks due to public exposure
 - adults 43
 - children 47
- acute toxicity
 - aquatic organisms, data used in BurliOZ modelling 428–9
 - classification 33, 323–4
 - freshwater fish 342–3
 - freshwater invertebrates 348, 351, 352
 - humans 33
 - laboratory animal studies 29, 80–1, 323–4
 - dermal 273
 - inhalation 273
 - intravenous 273
 - oral 272–3
 - methyl-triclosan, freshwater invertebrates 352
- acute toxicity profile (triclosan) 81, 330
- Adelaide, wastewater treatment and re-use 376–7
- ADG Code *see Australian Code for the Transport of Dangerous Goods by Road & Rail*
- adsorption, to soils 133
- adults
 - internal dose levels 22
 - public exposure 21–2, 42–3
 - public health risk estimates 43–7
 - routes of public exposure 106
 - sources of public exposure 106
- Advisory Group on Chemical Safety 5
- aerobic aquatic degradation 145–9
 - aerobic biodegradation 52
 - aerobic soil degradation
 - Australian soils 144–5
 - European soils 142–4
 - air, exposure via 122
 - air conditioning heat exchange coils, antimicrobial treatment agent 17
 - air monitoring data, Sweden 211
 - algae toxicity data 35, 53, 65, 352–62
 - see also* freshwater algae
 - Alicigenes xylooxidans* 140
 - amphibians, toxicity studies 338–42
 - Anabaena flos-aquae*
 - phytotoxicity studies 359–62
 - toxicity studies 358
 - anaerobic microbial degradation 52
 - analytical methods 12, 91
 - for triclosan in biological samples 93
 - for triclosan in breast milk 410–11, 412
 - for triclosan in various media 94
 - for triclosan in water 91, 92
 - animal studies *see* laboratory animal studies
 - anti-perspirant/deodorant spray products
 - dermal absorption 242–3
 - inhalation exposure 111
 - inhalation exposure calculations 399
 - antimicrobial properties, and ecological effects 64, 367–8
 - antimicrobial resistance 7, 13, 31–2, 36, 51
 - 2002 EU review 308–9
 - analysis of bacteria from clinical or natural settings 32, 312–15
 - laboratory studies of resistance and cross-resistance 31, 309–12, 366
 - overall conclusions 32
 - physiological fitness of bacteria resistant to biocides and antibiotics 32, 315–16
 - studies since 2002 EU review 309–16
 - see also* fungicidal properties
 - antimicrobial treatment agent for air conditioning heat exchange coils 17
 - applicants (to receive draft copy of report) 439–44
 - Approved Criteria for Classifying Hazardous Substances* (ASCC) xix, 33, 81, 323
 - aquatic degradation, aerobic 145–9
 - aquatic ecosystems management 76
 - aquatic ecotoxicity of treated sewage effluent
 - field studies 364
 - laboratory studies 363–4
 - aquatic environment 24–5
 - environmental risks from release to 85
 - predicted triclosan concentrations in Australia 221–5
 - aquatic organisms
 - bioaccumulation in 84, 200–10

- predicted concentrations
 - BCF-based 224–5
 - international data 225
 - risk to 65
 - toxicity data used in BurrliOZ modelling 428–30
 - toxicity to 35–6, 338–66
 - see also* specific types, eg. amphibians
- aquatic plants
 - phytotoxicity data 359–62
 - risks to 65
 - see also* cyanobacteria; freshwater algae
- aquatic risk 53–7, 84
 - predicted no effect concentrations (PNEC) 53–4
 - risk to freshwater ecosystems 54–5
 - risk to marine ecosystems 55–6
- articles
 - estimated risks from repeated exposure 46, 48
 - see also* plastic articles; textile articles; tile and laminate painted surfaces
- assessment objectives 3
- atmospheric exposure 122
- atmospheric monitoring 74, 91, 211, 226
- atmospheric occupational exposure standard 7
- atmospheric photooxidation 133
- atmospheric release 158
- Australia
 - bioaccumulation in aquatic biota 203
 - biosolid levels 181–2
 - municipal STP data on untreated and treated wastewater
 - other Australian data 161–3
 - Ying and Kookana (2007) study 159–61, 221
 - sediment levels 196
 - surface water levels 187–8
- Australian Capital Territory, wastewater treatment and re-use 377
- Australian Code for the Transport of Dangerous Goods by Road & Rail* 7, 33, 74–5, 323
 - recommendation xx
- Australian Dangerous Goods Code *see* *Australian Code for the Transport of Dangerous Goods by Road & Rail*
- Australian Drinking Water Guidelines* 7, 75
- Australian Government Department of the Environment, Water, Heritage and the Arts (DEWHA) 5
- Australian Inventory of Chemical Substances (AICS) 9
- Australian manufacturing facilities, untreated and treated wastewater data 162–3
- Australian perspective 7
- Australian Pesticides and Veterinary Medicines Authority (APVMA) xxii, 4, 7, 72
- Australian Register of Therapeutic Goods (ARTG) 17
- Australian Safety and Compensation Council (ASCC)
 - Hazardous Substances Information System xix, 7, 69, 70, 81
 - List of Designated Hazardous Substances* 7, 81, 323
 - recommendation xix
- Australian sewerage system
 - sewerage system processes 373–4
 - state and territory data on treatment and re-use 375–7
 - STP sludge management 378
 - uses of treated effluent 377–8
 - wastewater generation and re-use 374–5
- Australian soils, aerobic degradation 144–5
- Australian uses 13, 80
 - industrial applications 13–17
 - non-industrial applications 17–18
- Australian water quality guidelines 76
- avian risk *see* birds
- babies
 - dermal exposure 119
 - exposure through breast milk 22–3, 27–8, 48–9, 118, 120–1
 - inhalation exposure 118–19
- baboons, oral repeat dose toxicity studies 292–3
- baby wipes 119
- bacteria
 - from clinical or natural settings 312–15
 - marine, toxicity studies 362–3
 - physiological fitness of bacteria resistant to biocides and antibiotics 32, 315–16
 - triclosan-degrading 140–2
 - in vitro genotoxicity studies 296–7
 - see also* antimicrobial resistance
- bioaccumulation in aquatic biota 84, 200–10
 - field studies 203
 - Australia 203
 - Germany 203–6
 - Japan 206
 - the Netherlands 208
 - Sweden 206–8
 - Switzerland 208
 - United States 209
 - laboratory studies 200–1
 - bioconcentration tests 201–3
 - predicted concentrations 224–5
 - summary 209–10
- bioaccumulation criteria, Stockholm Convention on POPs 422–3
- bioaccumulation in soil biota 211
- bioaccumulation in wildlife 61
- biocidal products 7–8

- biocide resistance 313–14
- bioconcentration tests 201–3
- biodegradation 52
 - aerobic aquatic environments 24, 145–9
 - aerobic soil degradation
 - Australian soils 144–5
 - European soils 142–4
 - by sewage sludge micro-organisms
 - aerobic conditions 134–6
 - anaerobic conditions 136–7
 - laboratory-scale continuous activated sludge systems 137–40
 - products from combustion 150–2
 - reaction with metals 149–50
 - resistant micro-organisms 140
 - soil micro-organisms 140–2
- biological monitoring data 50, 91–3
- biosolids
 - adsorption of triclosan to during sewage treatment 25, 26
 - management, Australia 378
 - predicted concentrations in Australia from municipal STPs 218
 - international data 219
 - mass-balance modelling 219–20
 - risk associated with, from STPs 58–9
 - triclosan levels
 - Australian data 181–2
 - international data 182
 - use of 157
 - see also* sewage sludge
- biosolids applied as soil conditioners 25–6
 - recommendations xxiv–xxv
 - targeted study xxv
- birds
 - acute dose studies 332–3
 - potential intakes
 - freshwater aquatic environment 386
 - marine aquatic environment 387
 - repeat dose studies 333–4
 - risk quotients 62–3, 426
 - risk to 62–3, 65, 85, 332–4
 - sediment ingestion rates 385
 - toxicity reference values 60–1
 - toxicity to 35
- bleaching of textiles, chlorinated derivatives of triclosan formation 124–6
- blended polyester wadding for bedding material 100
- blow moulding 103
- bluegill sunfish, acute toxicity 342, 343
- bobwhite quail
 - acute dose studies 333
 - repeat dose studies 333–4
- body lotion 119–20
- bone marrow chromosome aberration test 30, 298, 299
- Brachydanio rerio*, bioaccumulation studies 201–3, 422–3
- brand names (for triclosan) 9, 12
- breast muscle, methyl-triclosan and triclosan bioaccumulation 203–6
- breast milk
 - babies exposure from 22–3, 27–8, 48–9, 118, 120–1
 - distribution of triclosan in 253–4, 329
 - elimination via 270
 - internal dose calculations 407–8
- breast milk analysis for triclosan in the Australian population
 - alternative NMI method 412
 - ethics approval 409–10, 416–18
 - methodology 409–10
 - objectives 409
 - results 412–15, 419
 - sample analysis 410–12
- Brisbane, wastewater treatment and re-use 376
- buccal absorption 27, 246–7
 - and excretion 270
 - and metabolism 262
- buccal exposure
 - cosmetic and personal care products 111, 112
 - toothpaste 111, 112, 121
 - see also* oral exposure
- BurliOZ modelling 428–30
- Canada
 - maximum allowable concentrations in
 - cosmetics and mouthwash 6
 - sewage sludge levels 182
 - surface water levels 189
 - untreated and treated wastewater data 163
- carcinogenicity
 - animal studies 30, 34, 81, 300–1, 328
 - classification 34, 328
- Carolina Ecotox Inc. (1997) study 359–62
- carpet tile coating 101–2
- CAS No. xiv, 9
- cast moulding of PVC films 103
- Ceriodaphnia dubia*
 - acute toxicity studies 348
 - chronic toxicity studies 349–50
 - ecotoxicity of treated sewage effluent 363–4
 - reproductive toxicity 350–1
- chemical identity (triclosan) 9
- chemical properties (triclosan) 11–12
- Child-Specific Exposure Factors Handbook* 118, 119, 402
- children
 - direct exposure 118
 - indirect exposure 118
 - public exposure 22–3, 47, 118–22

- risk estimates 47–9
- routes and sources of exposure 118
 - buccal exposure 121
 - dermal exposure 119–20, 402
 - inhalation exposure 118–19
 - oral exposure 121–2
- see also* babies
- Chironomus riparius*, sediment exposure 365–6
- Chironomus tentans*, water column exposure 364–5
- chlorinated derivatives of triclosan 124–6
 - concentrations in wastewaters 176, 181
 - photolysis 131–2
 - pyrolysis products 151–2
 - sewage sludge levels 184, 186, 187
- chlorination 123–6
- chlorophenols 124–6
- chlorophenoxy phenols 126
- chromosome aberration test
 - germ cells 300
 - mammalian cells 297–8
 - somatic cells 298, 299
- chronic risks 40–1
- chronic/reproductive toxicity
 - freshwater fish 343–7
 - freshwater invertebrates 348–52
- chronic toxicity, aquatic organisms, data used in BurrliOZ modelling 429–30
- classification and labelling for public health
 - hazards xxi, 34, 69–70, 81
 - scheduling in SUSDP 34, 330–1
- classification based on hazard *see* regulatory classification based on hazard
- classification of mixtures 70
- cleaning products 13, 14–15
 - exposure during formulation 98–9
 - exposure from xxi, 22
 - see also* household cleaning products; industrial cleaning products
- combustion products
 - chlorinated derivatives of triclosan 151–2
 - from triclosan and dioxins 150–1
- compliance with state and territory legislation (MSDS and labels) xxi
- consumer products
 - dermal exposure calculations
 - cosmetic/personal care products 401–3
 - household cleaning products 403–4, 405
 - painted tile and cabinet/cupboard surfaces 404–6
 - inhalation exposure calculations 398
 - anti-perspirant/deodorant spray products 399
 - surface disinfectant/cleaner spray products 399–400
 - textile and plastic products and painted surfaces 400–1
 - labels 75
 - leaching from 133–4
 - oral exposure calculations
 - cosmetic/personal care products 406–7
 - exposure to triclosan in breast-fed babies 407–8
- control measures, assessment 67–9
- corrosive effects, humans 33, 324–5
- cosmetic and personal care products 13–14
 - categorisation and triclosan concentrations 108
 - concentration of triclosan in 13
 - estimated amount in 13–14
 - estimated exposure data 109–12
 - buccal exposure 111, 112
 - dermal exposure 111, 112, 401–3
 - inhalation exposure 110–11, 399
 - oral exposure 406–7
 - exposure during formulation 98–9
 - inhalation exposure 392–3
 - exposure from xxi, 22, 107–12
 - children 118, 121
 - exposure pattern 107–9
 - maximum allowable concentrations 6
 - MOE 44, 45
 - plasma levels of triclosan 43–5, 109, 110
 - public health regulations 75
 - risks from repeated exposure
 - adults 45
 - children 47–8
 - types of products containing triclosan 14
 - see also* anti-perspirant/deodorant spray products; toothpaste
- critical health effects 38
- cyanobacteria
 - phytotoxicity studies 359–62
 - toxicity studies 358
- Danio rerio*, chronic/reproductive toxicity 347
- Daphnia magna*
 - acute toxicity studies 348
 - chronic toxicity studies 348–9
- data gaps
 - environmental risks 63, 64, 85–7
 - human health risks 85–7
- declaration 3
- degradation and partitioning in sewerage system 155
- degradation products
 - concentrations in wastewater 180–1
 - following photolysis 129–31
 - risk from 63, 124–6
 - sewage sludge levels 186, 187
 - see also* chlorinated derivatives of triclosan; methyl-triclosan; photolytic products

- Denmark, untreated and treated wastewater data 163–4
- deodorants
 - metabolism studies 261
 - see also* anti-perspirant/deodorant spray products
- derived risk quotients *see* risk quotients
- dermal absorption 27
 - human studies 239–43
 - laboratory animal studies 230–3
 - dogs 233
 - guinea-pigs 232
 - mice 231
 - monkeys 233
 - rabbits 232–3
 - rats 230–1
 - summary 233
 - see also* elimination and excretion; metabolism
- dermal exposure 95
 - in babies and children 119–20
 - cosmetic and personal care products 111, 112, 401–3
 - during formulation 99, 394
 - during plastics manufacture 104
 - during repacking 97, 394
 - during textile manufacture 102, 395
 - EASE model 96
 - from end-use products 104–5
 - household cleaning products 114–15, 403–4, 405
 - internal dose calculations 393–4
 - addition of triclosan additives to textiles 395
 - cosmetic/personal care products 401–3
 - formulation of personal care/cosmetics/therapeutic goods 394
 - household cleaning products 403–4, 405
 - painted tile and cabinet/cupboard surfaces 404–6
 - repacking 394
 - metabolism studies 260–1
 - textile and plastic articles 116
 - tile and laminate painted cupboards/surfaces 117, 404–6
- dermal route
 - acute toxicity, animal studies 273
 - distribution *see* distribution
 - excretion *see* elimination and excretion
 - metabolism *see* metabolism
 - repeat dose toxicity, animal studies 30, 293–6, 327
- desorption, from impregnated plastics and textiles 133–4
- detection and analysis methods *see* analytical methods
- developmental toxicity
 - animal studies 31, 81, 303–7, 329
 - hamsters 307
 - mice 305–6
 - rabbits 306–7
 - rats 303–5
 - classification 34, 329
- dibenzofurans, limits as impurities in triclosan xxii–xxiii, 10, 80
- 2,7/2,8-dichlorodibenxzo-p-dioxin (DCDD) 64
- dioxins
 - combustion products 150–1
 - formation from photolysis of triclosan 131
 - limits as impurities in triclosan xxii–xxiii, 10, 80
- disposal
 - conceptual exposure model 154
 - into sewerage system 154–5
 - to landfills 158–9
 - and waste treatment 76–7
- distribution
 - animal studies
 - dogs 252–3
 - guinea-pigs 252
 - hamsters 252
 - mice 250–1
 - monkeys 253
 - rats 248–50
 - in vitro 255
 - human studies 253–4
 - in vitro 255
 - oral and dermal routes 27–8
- dogs
 - dermal absorption studies 233
 - distribution studies 252–3
 - elimination and excretion studies 267
 - metabolism studies 259–60
 - oral absorption studies 238
 - oral repeat dose toxicity studies 291–2
- drinking water
 - Australian Drinking Water Guidelines* 7, 75
 - exposure via 122
 - intake rates, wildlife 228, 382–3
- Drosophila*, in vitro genotoxicity studies 298
- duckweed, phytotoxicity studies 359–62
- Dunaliella tertiolecta*, toxicity studies 362–3
- earthworms
 - risk from biosolids and sludge from STPs 58
 - toxicity to 35, 84, 334–5
- EASE model xv–xvi, 20, 21, 40, 41, 95–6, 99, 102
 - estimation of occupational exposure to triclosan 390–1
 - and NOAEL 42, 82
- education and training (OH&S) 73–4

effluent *see* treated effluent
 effluent for irrigation 25, 26
 risks 59–60
 elimination as control measure 67
 elimination and excretion 28, 80
 animal studies
 dogs 267
 guinea-pigs 267
 hamsters 266
 mice 265–6
 monkeys 267–8
 rabbits 267
 rats 263–5
 human studies 268–70
 summary 270–1
 emergency procedures
 handling and storage incidents 77–8
 maritime incidents 79
 road transport incidents 78–9
 end-use products, risks of occupational exposure
 39, 95, 104–5
 end users, internal dose calculations following
 dermal exposure 396–7
 engineering controls 68
Enterobacter cloacae 314
 environment, fate and transformation processes
 123–52
 Environment Protection and Heritage Council
 Chemicals Working Group *see* EPHC
 Chemicals Working Group
 environmental concentrations predicted in
 Australia 213–29
 aquatic environments 221–5
 atmosphere 226
 effluent and sludge from septic and household
 systems 220–1
 groundwater 225–6, 227
 landfill 225–6
 sludge and biosolids from municipal STPs
 218–20
 soils 226, 227
 treated effluent 215–18
 untreated wastewater 213–14
 wildlife exposure 227–9
 environmental effects, overview xvi–xvii
 environmental exposure 24–6
 data 123–229
 import and manufacture 152–3
 overview xvii–xviii
 uses, releases and disposal 153–9
 environmental fate 24
 environmental hazard assessment 35–6
 environmental hazards, discussion and
 conclusions 84–5
 environmental monitoring
 aquatic biota 200–10
 atmosphere 211
 groundwater 211
 landfill leachate 211
 sediments 196–200
 soil biota 211
 soils 211
 summary 211–13
 surface waters 187–96
 environmental regulatory controls 76
 environmental releases 24–5, 51–3, 85
 environmental risk characterisation 51–66
 aquatic risk 53–7
 conclusions 65–6
 data gaps 63
 microbial effects 64
 monitoring data 64
 degradation products 63, 124–6, 129–31
 environmental release and degradation 24–5,
 51–3
 terrestrial risk 57–63
 environmental risk management
 aquatic ecosystems management 76
 control of major hazard facilities 76
 disposal and waste treatment 76–7
 emergency procedures 77–9
 environmental regulatory controls 76
 environmental risks
 data gaps 85–7
 from release to the aquatic environment 85
 from release to the terrestrial environment 85
 environmental safety, recommendations xxiv–
 xxv
 EPHC Chemicals Working Group xxiv–xxv
Escherichia coli, resistance and cross-resistance
 310, 311, 366
 Estimation and Assessment of Substance
 Exposure (EASE) model *see* EASE model
 European Commission
 Scientific Steering Committee 7, 32, 308
 Technical Guidance for Risk Assessment 105,
 109, 113, 398
 European soils, aerobic degradation 142–4
 European Union
 classification and labelling 7
 maximum allowable concentration in
 cosmetics 6
 ‘notification’ under Biocidal Products
 Directive 7–8
 excretion *see* elimination and excretion
 exposure *see* environmental exposure;
 occupational exposure; public exposure
*Exposure Standards for Atmospheric
 Contaminants in the Occupational
 Environment* 74
 eye irritation 29, 33, 81, 95
 animal studies 275, 325

- fabric manufacture 100–1
- faecal excretion 28
- fate and transformation processes in the environment 123–52
 - adsorption and mobility 133–4
 - biodegradation and methylation 134–49
 - chlorination 123–6
 - photolysis 126–33
 - water solubility and hydrolysis 123
- fathead minnows, acute toxicity 342, 343
- Ferrari et al. (2002) study 347, 353
- fertility effects
 - animal studies 31, 81, 301–2, 328–9
 - classification 34, 329
- fish
 - methyl-triclosan bioaccumulation 203–6, 208
 - predicted concentrations 225
 - triclosan bioaccumulation 201–9
 - see also* freshwater fish; marine fish
- fish bile, triclosan concentration 206–7
- food, exposure via 122
- Foran et al. (2000) study 344
- formulation of personal care/cosmetic products/therapeutic products
 - exposure during 98–9
 - internal dose calculations
 - following dermal exposure 394
 - following inhalation exposure 392–3
- France, untreated and treated wastewater data 164, 165
- freshwater algae
 - phytotoxicity studies, Carolina Ecotox Inc. (1997) study 359–62
 - toxicity studies
 - ABC Laboratories Inc. (1997c) study 354–6
 - Ferrari et al. (2002) study 353
 - RCC (1995) study 353–4
 - Tatarazako et al. (2004) study 352
 - Wildlife International Ltd (1999) study 356–8
 - Yang et al. (2008) study 352–3
 - toxicity to 35, 53, 65
 - see also* cyanobacteria
- freshwater aquatic organisms, toxicity to 35–6
- freshwater ecosystems, risk to 54–5, 84
- freshwater fish
 - acute toxicity studies 342–3
 - chronic/reproductive toxicity 343–4
 - Ferrari et al. (2002) study 347
 - Foran et al. (2000) study 344
 - Houtman et al. (2004) study 347
 - Ishibashi et al. (2004) study 344–7
 - Tatarazako et al. (2004) study 347
 - predicted concentrations 225
 - triclosan accumulation 201–9
- freshwater invertebrates
 - acute toxicity of methyl-triclosan 352
 - acute toxicity studies 348, 351
 - chronic toxicity studies 348–52
 - toxicity to 35–6
- freshwater microbial populations 367–8
- frogs, toxicity studies 338–42
- full body bathing study, dermal absorption 243
- fungi
 - triclosan-degrading 142
 - in vitro genotoxicity studies 297
- fungicidal properties 367
- gene mutation
 - bacteria 296–7
 - Drosophila* 298
 - fungi 297
 - mammalian cells 297–8
- genotoxicity
 - classification 34, 327–8
 - in vitro 30, 81, 327
 - bacterial studies 296–7
 - Drosophila* studies 298
 - fungi studies 297
 - mammalian cells 297–8
 - in vivo 30, 81, 327–8
 - germ cells 300
 - somatic cells 298–300
- germ cells, in vivo genotoxicity 300
- Germany
 - bioaccumulation in aquatic biota 203–6
 - sediment levels 196–7
 - sewage sludge levels 182
 - surface water levels 189–90
 - untreated and treated wastewater data 164–6
- GHS classification *see Globally Harmonized System of Classification and Labelling of Chemicals*
- gingival absorption 246
- glass shrimp, toxicity studies 362–3
- Globally Harmonized System of Classification and Labelling of Chemicals* 323, 420
 - classification of triclosan 421–2
- glucuronide conjugate 28, 80, 255–63
- Greece, untreated and treated wastewater data 166
- green algae
 - methyl-triclosan toxicity 362
 - phytotoxicity studies 359–62
 - toxicity studies 352–6
- groundwater
 - levels in 211
 - predicted concentrations 225–6, 227
 - releases to 157–8
- grout 17
- guinea-pigs

- dermal absorption studies 231
- distribution studies 252
- elimination and excretion studies 267
- hamsters
 - developmental toxicity studies 307
 - distribution studies 252
 - elimination and excretion studies 266
 - metabolism studies 258–9
 - oral absorption studies 236–7
 - oral repeat dose toxicity studies 286–91
- hand washing studies
 - dermal absorption 240–2
 - elimination and excretion 268–9
 - metabolism 260–1
- handling incidents 77–8
- hazard assessment *see* environmental hazard assessment; human health hazard assessment
- hazard classification *see* regulatory classification based on hazard
- hazard communication
 - labels xix, 34, 69–70
 - MSDS 70–1
 - recommendation xx
- Hazardous Substances Information System (HSIS) xix, 7, 69, 70, 81
- health effects, overview xiv–xv
- health hazard assessment utilisation, recommendation xxii
- health hazards *see* occupational health hazards; public health hazards
- health risk characterisation methodology 37
- health risks
 - and occupational exposure xv–xvi
 - and public exposure xvi
 - see also* occupational risk; public health risk
- health surveillance 74
- hosiery manufacture 100–1
- household cleaning products 14–15
 - estimated exposure data 113–15
 - dermal exposure 114–15, 403–4, 405
 - inhalation exposure 114, 399–400
 - estimated risk from repeated exposure 45–6
 - exposure pattern 113
 - exposure to 113–15
 - MOE 45
 - products containing triclosan 113
- household wastewater treatment systems, effluent and sludge from 220–1
- Houtman et al. (2004) study 347
- human breast milk *see* breast milk
- human exposure
 - occupational exposure xv–xvi, 20–1, 37–8, 96–105, 390–6
 - public exposure xxi, 21–3, 106, 118–22, 399–408
- human health effects
 - repeat dose toxicity 33, 38, 321–2
 - sensitisation 318–21
 - photo-sensitisation 33, 320–1
 - skin 33, 34, 318–20
 - skin irritation 32, 33, 38, 317–18
 - see also* occupational health hazards; public health hazards
- human health hazard assessment 27–34
 - recommendations xxi
- human health risk characterisation 37–50
 - biological monitoring data 50
 - margin of exposure methodology 37
 - occupational risk 37–42
 - public health risk 42–50
- human health risk management
 - occupational health and safety 67–74
 - occupational monitoring and regulatory controls 74–5
 - public health regulation 75
- human health risks 80–1
 - data gaps 85–7
- human patch test 317
- human skin, absorption, in vitro studies 247–8
- human studies
 - absorption
 - buccal 246–7
 - dermal 239–43, 247–8
 - gingival 246
 - inhalation 239
 - intravaginal 246
 - oral 243–5
 - summary 248
 - distribution 253–4
 - in vitro studies 255
 - elimination and excretion 268–70
 - metabolism 260–3
- Hyalella azteca*, water column exposure 364–5
- hydrolysis 123
- identification of triclosan, methods 91
- importation of triclosan into Australia 7, 12–13, 80
 - conceptual exposure model 153
 - exposure during 95, 96, 152–3
- impurities in triclosan 10, 80
 - concentration limits on imports, recommendations xxiii
 - limits on 10
 - recommendations xxii–xxiii
 - recommendations xxii–xxiii
- in vitro dermal absorption studies 247–8
- in vitro distribution studies 255
- in vitro genotoxicity 30, 81, 327
 - bacterial studies 296–7
 - Drosophila* studies 298

- fungal studies 297
 - mammalian cell studies 297–8
- in vivo genotoxicity 30, 81, 327–8
 - germ cell studies 300
 - somatic cell studies 298–300
- Industrial Chemicals (Notification and Assessment) Act 1989* (Cwlth) xxxvi, 3, 16
- industrial cleaning products 13–14
- industrial uses 13–17
- infra-red absorption spectrum 91
- inhalation exposure 20, 22, 38, 95
 - absorption, animal studies 230
 - acute toxicity, animal studies 29, 81, 273
 - anti-perspirant/deodorant spray products 111, 399
 - in babies and children 118–19
 - during formulation 99, 392–3
 - during plastics manufacture 104
 - during repacking 97, 391–2
 - during textile manufacture 102
 - EASE model 96
 - household cleaning products 114, 399–400
 - human studies 239
 - internal dose calculations 391, 398–9
 - addition of triclosan additives to textiles 393
 - anti-perspirant/deodorant spray products 399
 - formulation of personal health care/cosmetic products 392–3
 - repacking 391–2
 - surface disinfectant/cleaner spray products 399–400
 - textile and plastic products and painted surfaces 400–1
 - laboratory animal data 29, 81, 230, 273
 - repeat dose toxicity, animal studies 29, 81, 277, 327
 - textile and plastic articles 116, 400–1
 - tile and laminate painted surfaces 117, 400–1
 - toxicity symptoms 28
 - injection moulding 103
 - international perspective 6–7
 - intravaginal absorption 246
 - intravenous route, acute toxicity, animal studies 273
 - irrigation using triclosan containing effluent 25, 26
 - risks from STP effluent 59–60
 - irritation
 - classification 34, 325
 - humans 32, 33, 38, 317–18, 324–5
 - laboratory animals 29, 30, 81, 274–5
 - see also* eye irritation; respiratory irritation; skin irritation
 - Ishibashi et al. (2004) study 344–7
 - isolation as control measure 67–8
 - Italy, untreated and treated wastewater data 167
 - Japan
 - bioaccumulation in aquatic biota 206
 - Standards for Cosmetics 6
 - Japanese medaka, chronic/reproductive toxicity studies 344–7
 - kinetics and metabolism 27–9, 230–71
 - absorption 27, 80, 230–48
 - distribution 27–8, 248–50
 - metabolism 27, 28, 80, 255–63
 - Klebsiella pneumoniae* 314
 - labels xvi, 34, 69–70
 - consumer products 75
 - recommendations xxi
 - risk phrases xix, 70
 - safety phrases xix, 70
 - laboratory animal studies
 - absorption
 - dermal 230–3
 - inhalation 230
 - oral 233–9
 - acute toxicity 29, 80–1, 272–3
 - carcinogenicity 30, 34, 81, 300–1
 - developmental toxicity 31, 81, 303–7
 - distribution 248–53
 - elimination and excretion 263–8
 - fertility effects 31, 81, 301–3
 - genotoxicity
 - in vitro 30, 81
 - in vivo 30, 81
 - irritation 29, 30, 81
 - eye 275
 - skin 274
 - metabolism 255–60
 - repeat dose toxicity
 - dermal 30, 293–6
 - inhalation 29, 81, 277
 - oral 29–30, 277–93
 - sensitisation 29, 81, 276
 - see also* specific animals, eg. mice
 - laboratory-scale continuous activated sludge systems, biodegradation studies 137–40
 - lactational effects 253–4, 270
 - classification 329
 - see also* breast milk
 - laminate painted surfaces *see* tile and laminate painted surfaces
 - landfill disposal 158–9
 - landfill leachate 211
 - predicted concentrations 225–6
 - leaching
 - from consumer products 133–4

- from landfills 211, 225–6
 - Lemna gibba*, phytotoxicity studies 359–62
 - Lepomis macrochirus*, acute toxicity 342, 343
 - lipstick 111, 112
 - List of Designated Hazardous Substances* (ASCC) 7, 81, 323
 - long-range environmental transport, potential for 423–4
- major hazard facilities, control of 76
- mallard ducks, toxicity studies 332
- mammalian cells, in vitro genotoxicity studies 297–8
- mammals
 - potential intakes
 - freshwater aquatic environment 388
 - marine aquatic environment 389
 - risk quotients 62–3, 427
 - risk to 62–3, 65, 85, 332
 - toxicity reference values 60–1
- manufacture of triclosan 12–13
 - conceptual exposure model 153
 - exposure during 152–3
- Margin of Exposure (MOE)
 - in adults, for exposure scenarios to triclosan 47
 - calculated for effects on the liver for occupational exposure scenarios 41
 - in children, for exposure scenarios to triclosan 47
 - and chronic risks 40–1
 - estimated risks from repeated exposure
 - to articles 46, 48
 - to breast milk 48–9
 - to cosmetic and personal care products 45, 48
 - to household cleaning products 45–6
 - and exposure models 83
 - from measured exposure to cosmetic and personal care products 44
 - methodology 37
 - and NOAEL/NOAEC 40, 42
- marine ecosystems, risk to 55–6, 84
- marine fish, predicted concentrations 225
- marine micro-organisms 363, 368
- marine organisms, toxicity to 36, 362–3
- maritime incidents 79
- mass-balance modelling
 - sludge triclosan content 219, 220
 - surface water triclosan concentration 222–3
 - treated effluent triclosan concentration 215
- Material Safety Data Sheet *see* MSDS
- Melbourne
 - untreated and treated wastewater data 162
 - wastewater treatment and re-use 376
- metabolism 27, 28, 80
 - animal studies
 - dogs 259–60
 - hamsters 258–9
 - mice 257–8
 - monkeys 260
 - rats 255–7
 - human studies 260–3
 - summary 263
- metal oxides, reaction with 149–50
- methicillin-resistant *Staphylococcus aureus* (MRSA) 312
- methicillin-sensitive *Staphylococcus aureus* (MSSA) 312
- methicillin-sensitive *Staphylococcus epidermidis* (MSSE) 312
- methodology
 - for deriving PNECs 53
 - for deriving TRVs for avian and mammalian oral toxicity 60
 - estimating concentration in sediment 223
 - estimating wildlife exposure 379–89
 - human breast milk study 409–12
 - human health risk characterisation 37
 - label assessment 69
 - MSDS assessment 71
 - occupational exposure assessment 95–6
 - public exposure assessment 106–7
 - see also* BurrliOZ modelling; Margin of Exposure; mass-balance modelling
- methyl-triclosan 24, 64
 - acute toxicity, freshwater invertebrates 352
 - bioaccumulation in aquatic biota 203–6, 208–10
 - concentrations in wastewaters 171, 176, 180
 - ecotoxicity, freshwater algae 362
 - photolysis 132
 - sediment levels 196–7, 200
 - sewage sludge levels 186
 - surface water levels 184, 191, 192, 195–6
- mice
 - dermal absorption studies 231
 - developmental toxicity studies 305–6
 - distribution studies 250–1
 - elimination and excretion studies 265–6
 - metabolism studies 257–8
 - oral absorption studies 235–6
 - oral repeat dose toxicity studies 277–81, 326–7
- micro-organisms
 - effects on 36, 366–72
 - freshwater 367–8
 - fungicidal properties 367
 - laboratory cultures 31, 309–12, 366
 - marine 363, 368
 - resistance *see* antimicrobial resistance
 - resistant 140

- sewage sludge 36, 134–6, 368–70
- soil 140–2, 370–3
- triclosan-resistant 140–2
- see also* bacteria; sewage sludge micro-organisms
- micronucleus assay 30, 299
- mixtures
 - risk phrases on labels xix, 70
 - safety phrases on labels xix, 70
- Model Regulations *see* *National Model Regulations for the Control of Workplace Hazardous Substances*
- MOE *see* Margin of Exposure
- monitoring data, limited amounts of 64, 85–6
- monkeys
 - dermal absorption studies 233
 - distribution studies 253
 - elimination and excretion studies 267–8
 - metabolism studies 260
 - oral absorption studies 238–9
- mouthwash 111, 112
- MSDS xvi, 70–1, 82
 - assessment summary 438
 - assessment for triclosan raw material 71–2
 - health hazard information 73
 - precautions for use 73
 - product identification 72
 - safe handling information 73
 - recommendation xx–xxi
 - recommendations for spills 77
 - sample sheet for triclosan 431–7
 - for triclosan and triclosan-containing products 71
- MSDS Code 71
- Mycobacterium tuberculosis*, sensitivity 366
- National Code of Practice for the Control of Workplace Hazardous Substances* 67
- National Code of Practice for the Labelling of Workplace Substances* xxi, 69
- National Code of Practice for the Preparation of Material Safety Data Sheets* 70
- National Code of Practice for the Preparation of Material Safety Data Sheets* (2nd edition) xx–xxi, 71
- National Dioxins Program xxiii
- National Drugs and Poisons Schedule Committee (NDPSC) xxi, 330
 - Guidelines 330
- National Health and Medical Research Council (NHMRC) xxii
- National Model Regulations for the Control of Workplace Hazardous Substances* xx, 33, 67, 70, 73, 74, 323
- National Occupational Health and Safety Commission
 - Approved Criteria for Classifying Hazardous Substances* xix, 33, 81, 323
 - Model Regulations xx, 33, 67, 70, 73, 74, 323
 - National Codes of Practice *see* *National Code of Practice ...*
 - National Standards *see* *National Standard for ...*
 - National Standard for the Control of Major Hazard Facilities* 76
 - National Standard for the Storage and Handling of Workplace Dangerous Goods* 71
 - national transportation regulations xx, 7, 33, 74
 - National Water Quality Management Strategy 76
 - natural environment
 - bioaccumulation in aquatic biota 200–10
 - occurrence in 186–212
 - surface waters and sediments 187–200
 - Navicula pelliculosa*, phytotoxicity studies 359–62
 - Netherlands
 - bioaccumulation in aquatic biota 208
 - surface water levels 192
 - untreated and treated wastewater data 172
 - New South Wales
 - sewage sludge management 378
 - wastewater treatment and re-use 375
 - see also* Sydney
 - NICNAS
 - commissioned projects for the assessment 4
 - internal peer review of the report 5
 - NOAEL/NOAEC, and MOE 40, 42, 82
 - non-industrial uses 13, 17–18
 - non-woven ‘wet wipes’ manufacture 100
 - North American bullfrog, toxicity studies 339
 - northern leopard frog, toxicity studies 339–40
 - Northern Territory, wastewater treatment and re-use 377
 - Norway
 - surface water levels 190
 - untreated and treated wastewater data 167–8
 - NSW Environment Protection Agency 76
 - occupational exposure 20–1, 37–8
 - acute risks due to 39–40
 - data 95–104
 - internal dose levels 20
 - major scenarios 96–105
 - methods for assessing exposure 95–6
 - overview xv–xvi
 - routes of exposure 95
 - standards 74
 - see also* specific situations, eg. plastics manufacture
 - occupational exposure calculations 390
 - EASE estimation 390
 - direct handling 391

- dry manipulation 390
- intermittent use 391
- non-dispersive use 390
- internal dose calculations following dermal exposure 393–4
 - addition of triclosan additives to textiles 395
 - end users 396–7
 - formulation of personal care/cosmetic products 394
 - plastics compounding 395–6
 - repacking 394
- internal dose calculations following inhalation exposure 391
 - addition of triclosan additives to textiles 393
 - formulation of personal care/cosmetic products 392
 - repacking 391–2
- occupational health hazards
 - acute toxicity 33, 323–4
 - carcinogenicity 34, 328
 - classification 33–4, 323–9
 - genotoxicity 34, 327–8
 - irritation and corrosive effects 33, 317–18, 324–5
 - repeated or prolonged exposure effects 34, 321–2
 - reproductive effects 34, 328–9
 - sensitising effects 34, 318–21, 326
- occupational health and safety
 - assessment of current control measures 67
 - elimination 67
 - engineering controls 68
 - isolation 67–8
 - personal protective equipment 68–9
 - safe work practices 68
 - substitution 67
 - education and training 73–4
 - hazard communication
 - labels 69–70
 - MSDS 70–3
 - recommendations xix–xxi
- occupational health and safety risks 81–2
- occupational monitoring and regulatory controls 74–5
- occupational risk 37–42
 - areas of concern 42
 - critical health effects 38
 - risk estimates 38–42
 - uncertainties in estimates 42
- occurrence
 - in natural environment 186–213
 - in wastewater and the sewerage systems 159–86
- oil-based paints 17
 - exposure during formulation 98–9
- oral absorption 27
 - human studies 243–5
 - laboratory animal studies
 - dogs 238
 - hamsters 236–7
 - mice 235–6
 - monkeys 238–9
 - rabbits 237–8
 - rats 233–5
 - summary 239
 - see also* elimination and excretion; metabolism
- oral exposure
 - cosmetic and personal care products 111, 112, 406–7
 - internal dose calculations
 - breast-fed babies 407–8
 - cosmetic/personal care products 406–7
 - textile and plastic articles 116–17, 121–2
 - tile and laminate painted surfaces 118
 - see also* buccal exposure
- oral route
 - acute toxicity, animal studies 29, 80, 272–3
 - distribution *see* distribution
 - excretion *see* elimination and excretion
 - metabolism *see* metabolism
 - repeat dose toxicity, animal studies 29–30, 277–93
 - baboons 292–3
 - dogs 291–2
 - hamsters 286–91
 - mice 277–81, 326–7
 - rabbits 291
 - rats 281–6
 - Oryzias latipes*, chronic/reproductive toxicity studies 344–7
 - overseas uses 18
 - overview xiv–xviii
- painted surfaces *see* tile and laminate painted surfaces
- Palaemonetes pugio*, toxicity studies 362–3
- peer review 5
- Persistent Organic Pollutants (POPs) Assessment xxii, 6, 420–4
 - adverse environmental effects 424
 - bioaccumulation 422–3
 - persistence 420–2
 - potential for long-range environmental transport 423
- personal care products *see* cosmetic and personal care products
- personal protective equipment (PPE) 68–9
- Perth, wastewater treatment and re-use 376
- pesticide uses of triclosan 8, 13

phenol, 5-chloro-2-(2,4-dichlorophenoxy)- xiv, 9
see also triclosan

photodegradation 188

photodegradation products 129–31

photolysis 24, 126–33
 atmospheric photooxidation 133
 chlorinated derivatives of triclosan 131–2
 dioxin formation 131
 factors affecting 127–8
 mechanisms 128–9
 methyl-triclosan 132

photolytic products 129–31
 concentrations in wastewaters 181

photo-sensitisation 33, 320–1

physical properties (triclosan) 11

physical state (triclosan) 10

physicochemical hazards 33, 38–9, 323
 classification 323

physiological fitness of bacteria resistant to
 biocides and antibiotics 32, 315–16

phytoplankton, ecotoxicity data 362–3

phytotoxicity data 35, 84
 aquatic plants and freshwater algae 359–62
 from soil tests 335–7
 from topical tests 337–8

Pimephales promelas, acute toxicity 342, 343

plants *see* aquatic plants; terrestrial plants

plasma levels of triclosan, cosmetic and personal
 care products 43–5, 109, 110

plastic articles
 estimated exposure data 116
 dermal exposure 116
 inhalation exposure 116, 400–1
 oral exposure 116–17, 121–2
 exposure pattern 115–16
 exposure to 115–17
 children 118, 121–2
 leaching from 133–4

plastics manufacture
 cast moulding of PVC films 103
 compounding of polyolefin masterbatches 103
 injection and blow moulding 103
 internal dose calculations following dermal
 exposure 395–6
 occupational exposure 20, 21, 39, 102–5
 types of products containing triclosan 16
 use in 13, 16–17

platypus exposure xviii, 62–3, 65–6, 228–9

PNECs *see* predicted no effect concentrations
 (PNEC) for triclosan

poison scheduling, recommendations xxi, 330
see also Standard for the Uniform Scheduling
 of Drugs and Poisons (SUSDP)

polychlorodibenzo-p-dioxins *see* dioxins

polychlorodibenzofurans *see* dibenzofurans

polychlorophenoxyphenols (PCDD/Fs)
 formation from combustion of chlorinated
 derivatives of triclosan 151–2
 formation from combustion of triclosan 150–1

polyolefin masterbatches compounding 103

pond aquatic systems, physico-chemical
 characteristics 145, 146

POPs *see* Persistent Organic Pollutants (POPs)
 Assessment
 predicted environmental concentrations in
 Australia 213–29
 predicted no effect concentrations (PNEC) for
 triclosan 53–4, 84

Prevotella nigrescens 311

proactive management actions to reduce risks
 xxv

prolonged exposure effects *see* repeat exposure
 effects; repeated exposure risks

Pseudokirchneriella subcapitata
 ecotoxicity of treated sewage effluent 364
 phytotoxicity studies 359–62
 toxicity studies 352–3

Pseudomonas aeruginosa
 physiological fitness of mutants 32, 315
 resistance and cross-resistance 309–10, 366
 as triclosan-degrading organism 140

Pseudomonas mendocina 140

Pseudomonas multocida 310

public exposure xxi
 adults 21–2, 42–3, 106
 children 22–3, 47, 118–22
 data 106–22
 indirect exposure via the environment 122
 methodology for assessing exposure 106–7
 overview xvi
 routes and sources of exposure
 adults 106
 children 118–22
see also consumer products; specific
 situations, eg. cosmetic and personal care
 products

public health hazards
 classification and labelling 34, 69–70
 scheduling in SUSDP 34, 330–1

public health regulations 75

public health risk xxi, 42–50
 areas of concern 50
 discussion and conclusion 82–3
 uncertainties in estimates 49–50

public health risk estimates (adults)
 acute risks 43
 measured plasma levels, cosmetic and
 personal care products 43–5
 risks from repeated exposure 43
 articles 46
 cosmetic and personal care products 45
 household cleaning products 45–6

- summary 46–7
- public health risk estimates (children)
 - acute risks 47
 - risks from repeated exposure 47
 - articles 48
 - breast milk 48–9
 - personal care products 47–8
 - summary 49
- public health and safety, recommendations xxi–xxiii
- PVC films, cast moulding 103
- Pycnoporus cinnabarinus* 142
- pyrolysis products
 - chlorinated derivatives of triclosan 151–2
 - from triclosan and dioxins 150–1
- quail, toxicity studies 333–4
- Queensland, wastewater treatment and re-use 376
- rabbits
 - dermal absorption studies 231–2
 - developmental toxicity studies 306–7
 - elimination and excretion studies 267
 - oral absorption studies 237–8
 - oral repeat dose toxicity studies 291
- rainbow trout, triclosan accumulation 206–7
- Rana catesbeiana*, toxicity studies 339
- Rana pipiens*, toxicity studies 339–40
- rats
 - dermal absorption studies 230–1
 - in vitro 347
 - developmental toxicity studies 303–5
 - distribution studies 248–50
 - elimination and excretion studies 263–5
 - inhalation studies 230
 - metabolism studies 255–7
 - oral absorption studies 233–5
 - oral repeat dose toxicity studies 281–6
- RCC (1995) study 353–4
- reaction with metal oxides 149–50
- recommendations xix–xxv
- regulatory classification based on hazard xix, 33, 323–9
 - occupational health hazards xix, 33–4, 323–9
 - acute toxicity 33, 323–4
 - carcinogenicity 34, 328
 - effects from repeated or prolonged exposure 34, 326–7
 - genotoxicity 34, 327–8
 - irritation and corrosive effects 33, 324–5
 - reproductive effects 34, 328–9
 - sensitising effects 34, 326
 - physicochemical hazards 33, 323
- releases
 - conceptual exposure model 154
 - environmental 24–5, 51–3, 85
 - from sewage treatment plants, recommendations xxiv
 - from sewerage systems 155
 - sewage treatment plant effluent xxiv
 - to atmosphere 158
 - to groundwater 157–8
 - to surface waters 51, 154
- repacking
 - dermal exposure, internal dose calculations 394
 - inhalation exposure 97
 - internal dose calculations 391
 - occupational exposure 20, 97
- repeat dose toxicity
 - animal studies
 - dermal 30, 293–6, 327
 - inhalation 29, 81, 277, 327
 - oral 29–30, 277–93, 326–7
 - human studies 33, 38, 321–2
- repeated exposure risks
 - articles, adults 46
 - classification 34, 326–7
 - cosmetic and personal care products
 - adults 45
 - children 47–8
 - household cleaning products, adults 45–6
 - public health risk estimates
 - adults 43–7
 - children 47–9
 - summary
 - adults 46–7
 - children 49
- reproductive effects
 - developmental toxicity 31, 81, 303–7, 329
 - fertility 31, 34, 81, 301–2, 328–9
 - lactational effects 253–4, 270, 329
- resistant micro-organisms 140
- respiratory irritation 29, 33, 325
- revised occupational hazard classification (ASCC)
 - recommendation xix
 - see also* regulatory classification based on hazard
- Rhodonobacter lindanoclasticus* 140
- risk characterisation *see* environmental risk characterisation; human health risk characterisation
- risk estimates
 - acute risks due to occupational exposure 39–40
 - chronic risks 40–1
 - physicochemical hazards 38–9, 323
- risk management *see* environmental risk management; human health risk management
- risk phrases for mixtures xix, 70

- risk quotients
 - birds 62–3, 426
 - freshwater ecosystems 54–5
 - mammals 62–3, 427
 - marine ecosystems 55–6
 - sediment dwelling organisms 56–7
 - soil dwelling organisms
 - based on use of sewage sludge as soil conditioner 59
 - based on use of treated effluent for irrigation 59
- river aquatic systems, physico-chemical characteristics 145, 146
- road transport incidents 78–9
- Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade 6
- safe work practices 68
- safety phrases xix, 70
- Salmonella enterica*, resistance and cross-resistance 310–11
- Scenedesmus subspicatus*
 - methyl-triclosan toxicity 362
 - toxicity studies 353–6
- secondary notification xxvi
- secondary transfer, risks from 40
- sediment dwelling organisms
 - risk to 56–7
 - sediment exposure 365–6
 - toxicity to 36, 364–6
 - water column exposure 364–5
- sediments
 - adsorption to 133
 - levels in
 - Australia 196
 - Germany 196–7
 - Spain 198
 - summary 200
 - Sweden 198
 - Switzerland 198–9
 - United States 199–200
 - predicted concentrations, international data 223–4
- Selenastrum capricornatum* *see* *Pseudokirchneriella subcapitata*
- sensitisation
 - animal studies 29, 81, 276, 326
 - classification 34, 326
 - human studies 318–21, 326
 - photo-sensitisation 33, 320–1
 - skin sensitisation 33, 34, 318–20
- septic and household wastewater treatment systems, effluent and sludge from 220–1
- serum levels of triclosan, maternal and cord blood 23
- sewage sludge
 - management, Australia 378
 - occurrence in 181–6
 - predicted concentrations in Australia from municipal STPs 218–20
 - risk associated with, from STPs 58–9
 - triclosan concentrations 218–20
 - comparison with Australian data 220
 - direct STP monitoring of sludge triclosan partitioning rate 219–20
 - international data 219
 - STP Model: SimpleTreat 219
 - triclosan degradation products, summary 186, 187
 - triclosan levels
 - Australian data 181–2
 - international data 182–4
 - summary 185–6
 - use of 157
 - see also* biosolids
- sewage sludge micro-organisms
 - biodegradation, aerobic conditions 134–6
 - toxicity to 36, 368–70
- sewage treatment plant systems 24–5, 51–3, 123
 - adsorption to biosolids 25
 - aerobic biodegradation 52
 - anaerobic microbial degradation 52
 - Australian municipal data on treated and untreated wastewater
 - other Australian data 161–2
 - Ying and Kookana (2007) study 159–61, 221
 - effluent releases, recommendations xxiv
 - international data on treated and untreated wastewater 163–76
 - number of municipal STPs in Australia 373
 - risk associated with effluent for irrigation 59–60, 66
 - risk associated with sludge and biosolids 58–9, 66
 - risk to birds and mammals from effluent 62–3, 85
 - triclosan removal rates by treatment 25, 52–3, 215–18
 - use of effluent, sludge and biosolids 157
 - see also* Australian sewerage system; laboratory-scale continuous activated sludge systems; wastewater treatment plant systems
- sewer disposal route, conceptual model 157
- sewerage system
 - Australian 373–8
 - degradation and partitioning 155
 - disposal into 154–5
 - overflows and leaks 156
 - releases from 155

- SimpleTreat model
 - sludge triclosan concentrations 219, 220
 - surface water triclosan concentrations 222–3
 - wastewater triclosan output 216–17
- Skeletonema costatum*, phytotoxicity studies 359–62
- skin cream
 - dermal absorption 240–1
 - metabolism 261
- skin irritation 29, 95
 - animal studies 274
 - human studies 32, 33, 38, 317–18, 324–5
- skin sensitisation 33, 34, 326
 - case reports 320
 - studies in patients 319
 - volunteer studies 318–19
- sludge *see* sewage sludge
- soil ameliorants 25–6
- soil biota, bioaccumulation in 211
- soil degradation
 - aerobic conditions
 - Australian soils 144–5
 - European soils 142–4
- soil dwelling organisms
 - risk associated from sludge and biosolids from STPs 58–9, 66
 - risk associated from treated effluent for irrigation 59, 66
 - toxicity tests xxv
- soil micro-organisms
 - in biodegradation 140–2
 - effect on 370–2
- soil tests, phytotoxicity data 335–7
- soils
 - adsorption to 133
 - aerobic degradation 142–5
 - concentrations in 211
 - predicted concentrations 226, 227
 - public exposure via 122
- solubility (triclosan) 24
- somatic cells, in vivo genotoxicity studies 298–300
- sources of information 3–4
- South African clawed frogs, toxicity studies 338–9, 340–2
- South Australia, wastewater treatment and re-use 376–7
- Spain
 - sediment levels 198
 - untreated and treated wastewater data 168–9
- Sphingomonas*, as triclosan-degrading organism 140
- Standard for the Uniform Scheduling of Drugs and Poisons* (SUSDP) 7, 75, 81
 - acute toxicity profile 81, 330
 - classification and labelling for public health hazards 34, 330–1
 - labelling 69
 - scheduling recommendation xxi, 330
- Staphylococcus aureus* 312, 314
- Staphylococcus epidermidis* 312, 314
- Stenotrophomonas maltophilia*
 - antibiotic resistance 311–12
 - physiological fitness of mutants 32, 315–16
- Stockholm Convention on Persistent Organic Pollutants *see* Persistent Organic Pollutants (POPs) Assessment
- storage
 - exposure during 97
 - incidents 77–8
- Streptococcus pneumoniae*, sensitivity 366
- substitution as control measure 67
- sulphate conjugate 28, 80, 255–63
- sunscreens 111, 112, 119
- surface disinfectant/spray cleaner products, inhalation exposure calculations 399–400
- surface waters 24
 - levels in 55, 56, 62–3, 65, 85
 - Australia 187–8
 - Canada 189
 - Germany 189–90
 - the Netherlands 192
 - Norway 190
 - summary 195–6
 - Sweden 190
 - Switzerland 190–2
 - United Kingdom 192–3
 - United States 193–5
 - predicted concentrations
 - Australian data 221, 381
 - international data 221
 - mass-balance modelling 222–3
 - releases to 51, 154
 - removal of triclosan from 221–2
- surgical scrub, dermal absorption 240–1
- SUSDP *see* *Standard for the Uniform Scheduling of Drugs and Poisons*
- Sweden
 - air monitoring data 211
 - bioaccumulation in aquatic biota 206–7
 - sediment levels 198
 - sewage sludge levels 182–3
 - soil concentrations 211
 - surface water levels 190
 - untreated and treated wastewater data 169–70
- Switzerland
 - bioaccumulation in aquatic biota 208
 - sediment levels 198–9
 - sewage sludge levels 183
 - surface water levels 190–2
 - untreated and treated wastewater data 171–2
- Sydney

- sewage sludge management 378
- untreated and treated wastewater data 161–2
- wastewater treatment and re-use 375
- synonyms 9
- Tasmania, wastewater treatment and re-use 377
- Tatarazako et al. (2004) study 347, 353
- teratogenicity 31, 81
- terrestrial environment 25–6, 84
 - environmental risks from release to 85
- terrestrial invertebrates, toxicity to 35, 334–5
- terrestrial plants
 - soil tests 335–7
 - topical tests 337–8
 - toxicity to 35, 335–8
- terrestrial risk 57–63, 84
 - sludge and biosolids from STPs containing triclosan 58–9
 - treated effluent from STPs for irrigation 59–60
 - water-associated wildlife 60–3
- textile articles
 - estimated exposure data 116
 - dermal exposure 116
 - inhalation exposure 116, 400–1
 - oral exposure 116–17, 121–2
 - exposure pattern 115–16
 - exposure to 115–17
 - children 118, 121–2
 - leaching from 133–4
- textile bleaching, chlorinated derivatives of
 - triclosan formation 124–6
- textile coatings formulation for use in vertical
 - blind manufacture 101
- textile manufacture
 - coating of carpet tiles 101–2
 - formulation of textile coatings for use in vertical blind manufacture 101
 - internal dose calculations
 - following dermal exposure 395
 - following inhalation exposure 393
 - list of products containing triclosan 15
 - manufacture of blended polyester wadding for bedding material 100
 - manufacture of fabric and hosiery 100–1
 - manufacture of non-woven ‘wet wipes’ 100
 - manufacture of top in wool processing 100
 - occupational exposure 20, 21, 39, 99–102
 - use in 13, 15–16
- textile materials impregnated with triclosan,
 - combustion products 150–1, 152
- Therapeutic Goods Act 1989* 330
- Therapeutic Goods Administration (TGA) xxii
 - impurities in triclosan xxii–xxiii
- Therapeutic Goods Regulations 1990* 330
- therapeutic uses 13, 17–18
 - types of products containing triclosan 18
- thyroid hormones, effects on 54
- tile and laminate painted surfaces 17
 - estimated exposure data 117
 - dermal exposure 117, 404–6
 - inhalation exposure 117, 400–1
 - oral exposure 118
 - exposure pattern 117
- toothpaste 111, 112, 121
- top making wool processing manufacture 100
- toxicity
 - aquatic organisms 35–6, 338–66
 - humans *see* human *headings*
 - laboratory animal studies 29, 81
 - lack of data for many environmental organisms 64, 86
 - repeat dose *see* repeat dose toxicity
 - terrestrial invertebrates 35, 334–5
 - terrestrial plants 35, 335–7
 - wildlife 35, 332–4
 - see also* genotoxicity
- toxicity reference values (TRVs), for birds and mammals 60–1
- toxicity signs, in laboratory animals 28
- toxicity tests for soil dwelling organisms xxv
- trade names 9, 12
- Trametes versicolor* 142
- transportation, exposure during 97
- treated effluent
 - aquatic ecotoxicity
 - field studies 364
 - laboratory studies 363–4
 - Australian state and territory data 374–7
 - from STPs for irrigation, terrestrial risk 59–60
 - predicted concentrations
 - Australian data 215
 - comparison with Australian data 218
 - international data 215
 - mass-balance model 215
 - treatment-specific wastewater removal rates 215–18
 - risk to soil dwelling organisms 58, 66
 - uses of 157, 377–8
 - see also* untreated and treated wastewater
- triclosan
 - Australian perspective 7
 - background 6–8
 - chemical identity 9
 - chemical properties 11–12
 - chlorinated derivatives 124–6
 - classification under GHS 421–2
 - declaration 3
 - detection and analysis methods 12, 91–4
 - impurities *see* impurities in triclosan
 - international perspective 6–7
 - manufacture and importation 7, 12–13

- overview xiv–xviii
- physical properties 11
- physical state 10
- recommendations xix–xxv
- secondary notification xxvi
- toxicity profile 330
- triclosan-degrading bacteria 140–2
- triclosan-degrading fungi 142
- triclosan raw material, MSDS assessment 71–3
- TRVs *see* toxicity reference values (TRVs)
- ultra-violet absorption spectrum 91
- United Kingdom
 - surface water levels 192–3
 - untreated and treated wastewater data 172–3
- United Kingdom Health and Safety Executive xvi, 20, 95
- United States
 - aggregated risk assessment on biological monitoring for non-EPA regulated uses 8
 - bioaccumulation in aquatic biota 209
 - Preliminary Risk Assessment of the pesticide uses of triclosan 8
 - sediment levels 199–200
 - sewage sludge levels 184
 - surface water levels 193–5
 - untreated and treated wastewater data 174–6
- United States Pharmacopeia, limits of dioxins and dibenzofurans as impurities xxii, xxiii, 6
- untreated and treated wastewater
 - Australian municipal STP data
 - Australian manufacturing facility data 162–3
 - Melbourne 162
 - Sydney 161–2
 - Wagga Wagga 162
 - Ying and Kookana (2007) study 159–61, 221
 - international data 163
 - Canada 163
 - Denmark 163–4
 - France 164, 165
 - Germany 164–6
 - Greece 166
 - Italy 167
 - the Netherlands 172
 - Norway 167–8
 - Spain 168–9
 - Sweden 169–70
 - Switzerland 171–2
 - United Kingdom 172–3
 - United States 174–6
 - summary of concentrations
 - chlorinated derivatives 181
 - methyl-triclosan 180
 - photolytic products 181
 - triclosan 176–9
 - triclosan degradation products 180–1
- untreated wastewater, predicted concentrations in Australia 213–14
- urinary excretion 28, 80
- urine samples, triclosan in 23
- uses
 - in Australia 13–18, 80
 - conceptual exposure model 154
 - industrial 13–17
 - non-industrial 17–18
 - overseas 18
 - overview xiv
 - summary 19
- veterinary uses 13, 17
- Vibrio fischeri*, toxicity studies 363, 368
- Victoria
 - sewage sludge management 378
 - wastewater treatment and re-use 376
 - see also* Melbourne
- Wagga Wagga, untreated and treated wastewater data 162
- waste treatment and disposal 76–7
- wastewater
 - disinfection using aqueous chlorine 123–4
 - occurrence in 159–86
 - treatment-specific removal rates 25, 52–3, 215–16
 - direct STP monitoring of removal rates 217–18
 - STP model: Simple Treat 216–17
 - triclosan concentrations in 176–9
 - triclosan degradation products concentrations in 180–1
 - see also* treated effluent; untreated and treated wastewater
- wastewater treatment plant systems 24–5, 51–2, 123
 - laboratory-scale continuous activated sludge system 137–40
 - microbial biodegradation processes 51–2
 - see also* septic and household wastewater treatment systems; sewage treatment plant systems
- water-associated wildlife, risks to 60–3
- water sediment system, triclosan and methyl-triclosan concentrations 145–9
- water solubility 123
- waterbirds, sediment ingestion rates 385
- Western Australia
 - sewage sludge management 378
 - wastewater treatment and re-use 376
- wildlife
 - risk quotients *see* risk quotients

- toxicity to 35, 332–4
- water-associated, risks to 60–3
- see also* birds; mammals
- wildlife exposure model 61, 227–9, 379–89
 - drinking water intake rates 228, 382–3
 - food intake rate 228, 381–2
 - potential bird intakes of triclosan
 - from freshwater aquatic environment 386
 - from marine aquatic environment 386
 - potential mammal intakes of triclosan
 - from freshwater aquatic environment 387
 - from marine aquatic environment 388
 - sediment ingestion 228, 383–5
 - surface water concentrations 381
 - see also* platypus exposure
- Wildlife International Ltd (1998) study, on cyanobacteria 358
- Wildlife International Ltd (1999) study, on green algae 356–8
- workers *see* occupational *headings*
- World Health Organization 6

- Xenopus laevis*, toxicity studies 338–9, 340–2

- Yang et al. (2008) study 352–3
- Ying and Kookana (2007) study 159–61, 221

- zebra fish
 - chronic/reproductive toxicity 347
 - triclosan bioaccumulation 201–3, 422–3