Pure Appl. Chem., Vol. 79, No. 7, pp. 1153–1344, 2007.
doi:10.1351/pac200779071153

INTERNATIONAL UNION OF PURE AND APPLIED CHEMISTRY

CHEMISTRY AND HUMAN HEALTH DIVISION*

GLOSSARY OF TERMS USED IN TOXICOLOGY, 2nd EDITION

(IUPAC Recommendations 2007)

Prepared for publication by
JOHN H. DUFFUS[1,‡], MONICA NORDBERG[2], AND DOUGLAS M. TEMPLETON[3]

[1]The Edinburgh Centre for Toxicology, Edinburgh, Scotland, UK; [2]Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden; [3]Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Canada

*Membership of the Division Committee of the Chemistry and Human Health Division during the preparation of this report (2004–2006) was as follows:

***President*:** P. W. Erhardt (USA, 2004–2006); P. Soares de Araujo (Brazil, 2006); ***Secretary*:** B. Heinzow (Germany, 2004–2005); M. S. Chorgade (USA, 2005–2006); ***Past President*:** A. Kallner (Sweden, 2004–2005); P. W. Erhardt (2002–2006); ***Members*:** M. S. Chorghade (USA, 2004–2006); J. H. Duffus (UK, 2004–2006); J. Fischer (Hungary, 2004–2006); U. Forsum (Sweden, 2004–2005); M. N. Liebman (USA, 2004–2006); M. Nordberg (Sweden, 2006); P. Soares de Araujo (Brazil, 2004–2006); D. M. Templeton (Canada, 2006); H. Timmerman (Netherlands, 2004–2006).

‡Corresponding author: John H. Duffus, The Edinburgh Centre for Toxicology, 43 Mansionhouse Road, Edinburgh EH9 2JD, Scotland, UK; E-mail: J.H.Duffus@blueyonder.co.uk

Glossary of terms used in toxicology, 2nd edition

(IUPAC Recommendations 2007)

Abstract: This glossary, a revision of the IUPAC "Glossary for Chemists of Terms Used in Toxicology" [*Pure Appl. Chem.* **65**, 2003 (1993)] incorporating new and redefined terms from the "Glossary of Terms Used in Toxicokinetics" [*Pure Appl. Chem.* **76**, 1033 (2004)], contains definitions and explanatory notes, if needed, for terms frequently used in the multidisciplinary field of toxicology. The glossary is compiled primarily for those scientists and others who now find themselves working in toxicology or requiring a knowledge of the subject, especially for hazard and risk assessment. Many medical terms are included because of their frequent occurrence in the toxicological literature. There are three annexes, one containing a list of abbreviations and acronyms used in toxicology, one containing a list of abbreviations and acronyms used by international bodies and by legislation relevant to toxicology and chemical safety, and one describing the classification of carcinogenicity according to the weight of evidence available.

Keywords: toxicology; toxicokinetics; risk assessment; hazard assessment; carcinogenicity; IUPAC Chemistry and Human Health Division.

Note: Terms for which no primary source is given have been taken verbatim from the original IUPAC "Glossary for Chemists of Terms Used in Toxicology" [1] or have been newly defined by the compilers of this paper. New or redefined terms in the "Glossary of Terms Used in Toxicokinetics" are currently referenced as in that glossary [2]. Other terms that are quoted verbatim from their sources are referenced individually. For other chemical terminology, the reader is referred to the on-line version of *Compendium of Chemical Terminology* (the "Gold Book") [3].

CONTENTS

PREFACE

IUPAC aims to promote world-wide "regulation, standardization, or codification" in relevant areas of chemistry. In 1993, the importance of toxicology to chemists was recognized by the publication in *Pure and Applied Chemistry* (*PAC*) of the "Glossary for Chemists of Terms Used in Toxicology" [1]. This glossary has been widely accepted and used, but, inevitably, with the continuing development of both chemistry and toxicology, terms have changed their meanings as a result of altered usage and new terms

have been coined. Further, some important terms were overlooked, notably those relating to toxicokinetics, and a supplementary glossary has already been published in *PAC* [2]. The revised and extended glossary presented here includes all new terms identified as relevant by the Working Party, together with those in toxicokinetics previously omitted. As before, the glossary is compiled primarily for chemists who now find themselves working in toxicology or requiring a knowledge of the subject. However, there are also many other scientists as well as regulators and managers who have to interpret toxicological information and need ready access to internationally accepted definitions of relevant terms in common use. In order to make this a convenient one-stop glossary, the terms included in this glossary have come from a wide range of disciplines which contribute to toxicology. For some of the entries, alternative definitions are given in order to display the significant differences in the use that occur in practice.

We are grateful to all those whose names are listed below who have contributed to this glossary with constructive criticism and who have suggested modifications for its improvement. Their contributions have been invaluable. The Working Group is responsible for any remaining flaws, but we hope that the final version will be sufficiently close to achieving the original objectives to justify the very widespread support that we have received.

ACKNOWLEDGMENTS

For their valuable comments and suggestions for improvements, the authors are very grateful to the following contributors to this glossary: Ole Andersen, Rick Becker, Joseph Borzelleca, Rita Cornelis, John Fowler, Philippe Grandjean, Birger Heinzow, Jane Huggins, Paul Illing, Marek Jakubowski, József Nyitrai, Stephanie Publicker, Mike Schwenck, Ron Shank, Wayne Temple, Philip Wexler, Howard Worth, and Paul Wright.

ALPHABETICAL ENTRIES

abiological
See *abiotic*.

abiotic
abiological
Not associated with living organisms.

abiotic degradation
Process in which a substance is converted to simpler products by physical or chemical mechanisms: examples include *hydrolysis* and *photolysis*.

abiotic transformation
Process in which a substance in the environment is modified by nonbiological mechanisms.

abortifacient
Substance that causes pregnancy to end prematurely and causes an abortion.

absolute lethal concentration (LC_{100})
Lowest *concentration* of a substance in an environmental medium which kills 100 % of test organisms or species under defined conditions.

Note: This value is dependent on the number of organisms used in its assessment.

absolute lethal dose (LD_{100})
Lowest amount of a substance that kills 100 % of test animals under defined conditions.

Note: This value is dependent on the number of organisms used in its assessment.

absorbance, A
Logarithm of the ratio of incident to transmitted *radiant power* through a sample (excluding the effects of sample cell walls). Depending on the base of the logarithm, decadic and Napierian absorbances are used. Symbols: A, A_{10}, A_e. This quantity is sometimes called extinction, although the term "extinction", better called *attenuance*, is reserved for the quantity which takes into account the effects of luminescence and scattering as well.
Corrected from [3]

Note: When natural logarithms are used, the Napierian absorbance is the logarithm to the base e of the incident *spectral radiant power*, essentially monochromatic, divided by the transmitted spectral radiant power, P_λ.

absorbed dose (of a substance)
internal dose
Amount (of a substance) taken up by an organism or into organs or tissues of interest.
See *absorption*, *systemic.*

absorbed dose (of ionizing radiation), D
Energy imparted by ionizing radiation to a specified volume of matter divided by the mass of that volume.

absorptance (in chemistry), α
Ratio of the absorbed to the incident radiant power. Also called *absorption factor*. When $\alpha \leq 1$, $\alpha \approx A_e$, where A_e is the Napierian absorbance.
[3]
See also *absorbance*.

absorption (general)
1. Process of one material (absorbate) being retained by another (absorbent).

   Note: The process may be the physical solution of a gas, liquid, or solid in a liquid; attachment of molecules of a gas, vapor, liquid; or dissolved substance to a solid surface by physical forces, etc.

2. Transfer of some or all of the energy of radiation to matter which it traverses.

   Note: Absorption of light at bands of characteristic wavelengths is used as an analytical method in spectrophotometry to identify the chemical nature of molecules, atoms, or ions and to measure the concentrations of these species.

Corrected from [3]

absorption (in biology)
uptake
Penetration of a substance into an organism and its cells by various processes, some specialized, some involving expenditure of energy (active transport), some involving a *carrier* system, and others involving passive movement down an electrochemical gradient.

Note: In mammals, *absorption* is usually through the respiratory tract, gastrointestinal tract, or skin into the circulatory system and from the circulation into organs, tissues, and cells.

[2]

absorption (of radiation)
Phenomenon in which radiation transfers some or all of its energy to matter which it traverses.
[3]

absorption, systemic
Uptake to the blood and transport via the blood of a substance to an organ or *compartment* in the body distant from the site of *absorption*.
[2]

absorption coefficient (in biology)
absorption factor
Ratio of the absorbed quantity (*uptake*) of a substance to the administered quantity (intake).

Note: For *exposure* by way of the respiratory tract, the absorption coefficient is the ratio of the absorbed amount to the amount of the substance (usually particles) deposited (adsorbed) in the lungs.

absorption factor
See *absorptance* (in chemistry), *absorption coefficient* (in biology).

abuse (of drugs, substances, solvents, etc.)
Improper use of drugs or other substances.

acaricide
Substance intended to kill mites, ticks, or other Acaridae.

acceptable daily intake (ADI)
Estimate by JECFA of the amount of a food additive, expressed on a body weight basis, that can be ingested daily over a lifetime without appreciable health *risk*.

Note 1: For calculation of ADI, a standard body mass of 60 kg is used

Note 2: *Tolerable daily intake* (TDI) is the analogous term used for contaminants.
[2]

acceptable daily intake (ADI) **not allocated**
See *no acceptable daily intake allocated.*

acceptable residue level of an antibiotic
Acceptable *concentration* of a residue that has been established for an antibiotic found in human or animal foods.

acceptable risk
Probability of suffering disease or injury that is considered to be sufficiently small to be "negligible".

Note: Calculated risk of an increase of one case in a million people per year for cancer is usually considered to be negligible.

accepted risk
Probability of suffering disease or injury that is accepted by an individual.

accidental exposure
Unintended contact with a substance or change in the physical environment (including, e.g., radiation) resulting from an accident.

acclimatization, biological
1. Processes, including selection and adaptation, by which a population of microorganisms develops the ability to degrade a substance, or develops a tolerance to it.
2. In animal tests, allowing an animal to adjust to its environment prior to undertaking a study.

accumulation (in biology)
See *bioaccumulation.*

accuracy
Quantity referring to the differences between the mean of a set of results or an individual result and the value which is accepted as the true or correct value for the quantity measured.

acid dissociation constant, K_a
Equilibrium constant for the following reaction of an acid HB:

$$HB(aq) \rightleftharpoons H^+(aq) + B^-(aq)$$

$$K_a = [H^+][B^-] / [HB]c^o$$

where $c^o = 1$ mol dm^{-3} is the standard amount concentration and activity coefficients have been neglected.

Note 1: This constant, because activity coefficients are neglected, is valid at a specified ionic strength. The thermodynamic dissociation constant is found by suitable extrapolation of the conditional constant to zero ionic strength. Note that it is defined as a dimensionless quantity, but sometimes it is given dimensions by omitting the standard amount concentration.

Note 2: Because this constant differs for each acid and varies over many degrees of magnitude, the acidity constant is often represented by the additive inverse of its common logarithm, represented by the symbol pK_a (using the same mathematical relationship as $[H^+]$ is to pH), viz.:

$$pK_a = -\log_{10} K_a$$

In general, a larger value of K_a (or a smaller value of pK_a) indicates a stronger acid, since the extent of dissociation is larger at the same concentration.

[4]

acidosis
Antonym: *alkalosis*
Pathological condition in which the hydrogen(1+) (hydron) amount concentration of body fluids is above normal and hence the pH of blood falls below the reference interval.

action level
1. *Concentration* of a substance in air, soil, water, or other defined medium at which specified emergency counter-measures, such as the seizure and destruction of contaminated materials, evacuation of the local population or closing down the sources of pollution, are to be taken.
2. Concentration of a pollutant in air, soil, water, or other defined medium at which some kind of preventive action (not necessarily of an emergency nature) is to be taken.

activation (abiotic)
Conversion of a *xenobiotic* to a more *toxic* derivative by modification not involving biological catalysis.

activation (in biology)
See *bioactivation.*

active ingredient
Component of a mixture responsible for the biological effects of the mixture.
Compare *inert ingredient.*

active metabolite
Metabolite causing biological and (or) toxicological effects.
After [2]
See *metabolite.*

active transport
Movement of a substance across a cell membrane against an electrochemical gradient, in the direction opposite to normal diffusion and requiring the expenditure of energy.

acute
Antonym: *chronic*
1. Of short duration, in relation to *exposure* or effect; the effect usually shows a rapid onset.

Note: In regulatory *toxicology*, "acute" refers to studies where dosing is either single or limited to one day although the total study duration may extend to two weeks to permit appearance of toxicity in susceptible organ systems.

2. In clinical medicine, sudden and severe, having a rapid onset.

After [2]

acute effect

Effect of finite duration occurring rapidly (usually in the first 24 h or up to 14 d) following a single *dose* or short *exposure* to a substance or radiation.

Note: Acute effects may occur continuously following continuous dosing or repeatedly following repeated dosing.

After [2]

acute exposure

Antonym: *chronic exposure*

Exposure of short duration.

[2]

See *acute, exposure*.

acute toxicity

Antonym: *chronic toxicity*

1. *Adverse effects* of finite duration occurring within a short time (up to 14 d) after administration of a single *dose* (or *exposure* to a given *concentration*) of a test substance or after multiple doses (exposures), usually within 24 h of a starting point (which may be exposure to the *toxicant*, or loss of reserve capacity, or developmental change, etc.).
2. Ability of a substance to cause *adverse effects* within a short time of dosing or *exposure*.

[2]

acute toxicity test

short-term toxicity test

Antonym: *chronic toxicity test*

Study in which organisms are observed during only a short part of the life span and in which there is often only a single *exposure* to the test agent at the beginning of the study.

adaptation

1. Change in an organism, in response to changing conditions of the environment (specifically chemical), which takes place without any irreversible disruptions of the given biological system and without exceeding normal (homeostatic) capacities of its response.
2. Process by which an organism stabilizes its physiological condition after an environmental change.

Note: If this process exceeds the homeostatic range, it becomes pathological and results in symptoms of disease (*adverse effects*).

added risk
Difference between the *incidence* of an *adverse effect* in a treated group (of organisms or a group of *exposed* humans) and a control group (of the same organisms or the spontaneous incidence in humans).

addiction
Surrender and devotion to the regular use of a medicinal or pleasurable substance for the sake of relief, comfort, stimulation, or exhilaration which it affords; often with craving when the drug is absent.

additive effect
Consequence that follows *exposure* to two or more physicochemical agents which act jointly but do not interact: The total effect is the simple sum of the effects of separate exposures to the agents under the same conditions.
[2]

adduct
New chemical species AB, each molecular entity of which is formed by direct combination of two separate molecular entities A and B in such a way that there is change in connectivity, but no loss, of atoms within the moieties A and B.

Note 1: Stoichiometries other than 1:1 are also possible, for example, a bis-adduct (2:1). An "intramolecular adduct" can be formed when A and B are groups contained within the same molecular entity.

Note 2: This is a general term that, whenever appropriate, should be used in preference to the less explicit term *complex*. It is also used specifically for products of an addition reaction.

[3]

adenocarcinoma
Malignant tumor originating in glandular *epithelium* or forming recognizable glandular structures.

adenoma
Benign tumor occurring in glandular *epithelium* or forming recognizable glandular structures.

adjuvant
1. In pharmacology, a substance added to a *drug* to speed or increase the action of the main component.
2. In immunology, a substance (such as aluminum hydroxide) or an organism (such as killed mycobacterium) that increases the response to an *antigen*.

administration (of a substance)
Application of a known amount of a substance to an organism in a reproducible manner and by a defined route.

adrenergic
Secreting adrenaline (epinephrine) and (or) related substances; in particular referring to sympathetic nerve fibers.
See *sympathomimetic*.

adsorption
Increase in the *concentration* of a substance at the interface of a condensed and a liquid or gaseous layer owing to the operation of surface forces.
[2]
See also *interfacial layer.*

adsorption factor
Ratio of the amount of substance adsorbed at the interface of a condensed and a liquid or gaseous phase to the total amount of the substance available for *adsorption*.
[2]

adstringent
See *astringent*.

advection (in environmental chemistry)
Process of transport of a substance in air or water solely by mass motion.
[2]

adverse effect
Change in biochemistry, physiology, growth, development morphology, behavior, or lifespan of an organism which results in impairment of functional capacity or impairment of capacity to compensate for additional stress or increase in susceptibility to other environmental influences.
After [2]

adverse event
Occurrence that causes an *adverse effect*.

Note: An adverse event in clinical studies is any untoward reaction in a human subject participating in a research project; such an adverse event, which may be a psychological reaction, must be reported to an institutional review board.

aerobe
Organism that requires dioxygen for respiration and hence for growth and life.

aerobic
Requiring dioxygen.

aerodynamic diameter (of a particle)
Diameter of a spherical particle with relative density equal to unity that has the same settling velocity in air as the particle in question.

aerosol
Mixture of small particles (solid, liquid, or a mixed variety) and a *carrier* gas (usually air).

Note 1: Owing to their size, these particles (usually less than 100 μm and greater than 0.01 μm in diameter) have a comparatively small sedimentation velocity and hence exhibit some degree of stability in the earth's gravitational field.

Note 2: An aerosol may be characterized by its chemical composition, its radioactivity, the particle size distribution, the electrical charge, and the optical properties.

[2]

aetiology
See *etiology*.

after-effect of a poison
Ability of a *poison* to produce a change in an organism after cessation of contact.

age sensitivity
Quantitative and qualitative age dependence of an effect.

agonist
Antonym: *antagonist*
Substance that binds to cell *receptor*s normally responding to a naturally occurring substance and produces an effect similar to that of the natural substance.

Note 1: A partial agonist activates a receptor but does not cause as much of a physiological change as does a full agonist.

Note 2: A co-agonist works together with other co-agonists to produce a desired effect.

air pollution
Presence of substances in the atmosphere resulting either from human activity or natural processes, in sufficient concentration, for a sufficient time and under circumstances such as to interfere with comfort, *health*, or welfare of persons or to harm the environment.

air pollution control system
1. Network of organizations that monitor air pollution.
2. Group of measures or processes used to minimize or prevent air pollution.

albuminuria
Presence of albumin, derived from *plasma*, in the urine.

algicide
algaecide
Substance intended to kill algae.

aliquot (in analytical chemistry)
Known amount of a homogeneous material, assumed to be taken with negligible *sampling error*.

Note 1: The term is usually applied to fluids.

Note 2: The term "aliquot" is usually used when the fractional part is an exact divisor of the whole; the term "aliquant" has been used when the fractional part is not an exact divisor of the whole (e.g., a 15-mL portion is an aliquant of 100 mL).

Note 3: When an aliquot is taken of a laboratory sample or test sample or the sample is otherwise subdivided, the samples have been called split samples.

[2]

alkalosis
Antonym: *acidosis*
Pathological condition in which the hydrogen(1+) (hydron) substance concentration of body fluids is below normal and hence the pH of blood rises above the reference interval.

alkylating agent
Substance that introduces an alkyl substituent into a compound.

allele
One of several alternate forms of a *gene* that occur at the same relative position (locus) on homologous *chromosome*s and which become separated during *meiosis* and can be recombined following fusion of *gamete*s.

allergen
Immunostimulant antigenic substance that may or may not cause a clinically significant effect but which is capable of producing immediate *hypersensitivity*.

allergy
Symptoms or signs occurring in sensitized individuals following *exposure* to a previously encountered substance (*allergen*) which would otherwise not cause such *symptom*s or *sign*s in non-sensitized individuals. The most common forms of allergy are *rhinitis*, *urticaria*, *asthma*, and *contact dermatitis*.

allometric
1. Pertaining to a systematic relationship between growth rates of different parts of an organism and its overall growth rate.

[2]

2. Pertaining to a systematic relationship between size, shape, and metabolism in different species.

allometric growth
Regular and systematic pattern of growth such that the mass or size of any organ or part of a body can be expressed in relation to the total mass or size of the entire organism according to the *allometric* equation:

$$Y = bx^{\alpha}$$

where Y = mass of the organ, x = mass of the organism, α = growth coefficient of the organ, and b is a constant.
[2]

allometric scaling
1. Adjustment of data to allow for change in proportion between an organ or organs and other body parts during the growth of an organism.
2. Adjustment of data to allow for differences and make comparisons between species having dissimilar characteristics (e.g., in size, shape, and metabolism).

After [2]

allometry (in biology)
Measurement of the rate of growth of a part or parts of an organism relative to the growth of the whole organism.
[2]

allomone
Semiochemical that is produced by an organism inducing a response in an organism of another species that is favorable to the emitter.
See *kairomone*, *synomone*.

all-or-none effect
See *quantal effect*.

alopecia
Baldness; absence or thinning of hair from areas of skin where it is usually present.

alveol/us (pulmonary)**, -i** pl., **-ar** adj.
Terminal air sac of the lung where gas exchange occurs.

ambient
Surrounding (applied to environmental media such as air, water, sediment, or soil).

ambient monitoring
Continuous or repeated measurement of agents in the environment to evaluate ambient *exposure* and *health risk* by comparison with appropriate reference values based on knowledge of the probable relationship between exposure and resultant *adverse* health *effects.*

ambient standard
See *environmental quality standard*.

Ames test
In vitro test for *mutagenicity* using mutant strains of the bacterium *Salmonella typhimurium* which cannot grow in a given histidine-deficient medium: *mutagen*s can cause reverse *mutation*s which enable the bacterium to grow on the medium. The test can be carried out in the presence of a given microsomal

fraction (S-9) from rat liver (see *microsome*) to allow metabolic transformation of mutagen precursors to active derivatives.

amnesic shellfish poisoning (ASP)
Serious illness that is a consequence of consumption of bivalve shellfish (mollusks) such as mussels, oysters, and clams that have ingested, by filter feeding, large quantities of microalgae containing domoic acid; acute symptoms include vomiting, diarrhea, and in some cases, confusion, loss of memory, disorientation, and even coma.

amplification (of genes)
See *gene amplification*.

anabolism
Antonym: *catabolism*
Biochemical processes by which smaller molecules are joined to make larger molecules.

anaemia
See *anemia*.

anaerobe
Antonym: *aerobe*
Organism that does not require dioxygen for life.

Note: Obligate (strict) anaerobes grow only in the absence of dioxygen. Facultative anaerobes can grow either in the presence or in the absence of dioxygen.

anaerobic
Antonym: *aerobic*
Not requiring dioxygen.

anaesthetic
See *anesthetic*.

analgesic
Substance that relieves pain, without causing loss of consciousness.

analogue metabolism
Process by which a normally non-biodegradable compound is biodegraded in the presence of a structurally similar compound which can induce the necessary enzymes.

analytic study (in epidemiology)
Study designed to examine associations, commonly putative or hypothesized causal relationships.

anaphylactoid
Of or resembling *anaphylaxis*.

anaphylaxis
Life-threatening type 1 hypersensitivity allergic reaction (see *allergy*) occurring in a person or animal *exposed* to an *antigen* or *hapten* to which they have previously been sensitized.

Note: Consequences of the reaction may include angio-edema, vascular collapse, shock, and respiratory distress.

anaplasia
Loss of normal cell differentiation, a feature characteristic of most *malignancies*.

anemia
Condition in which there is a reduction in the number of red blood cells or amount of *hemoglobin* per unit volume of blood below the reference interval for a similar individual of the species under consideration, often causing pallor and fatigue.

anesthetic
Substance that produces loss of feeling or sensation: general anesthetic produces loss of consciousness; local or regional anesthetic renders a specific area insensible to pain.

aneuploid
Cell or organism with missing or extra *chromosome*s or parts of chromosomes and thus an abnormal number of chromosomes which is not an exact multiple of the haploid number.

anoxia
Strictly total absence of oxygen but sometimes incorrectly used instead of *hypoxia* to mean a decreased oxygen supply in tissues.

antagonism (in toxicology)
Combined effect of two or more factors that is smaller than the solitary effect of any one of those factors.

Note: In *bioassays*, the term may be used when a specified effect is produced by *exposure* to either of two factors but not by exposure to both together.

antagonist (in toxicology)
Antonym: *agonist*
Substance that binds to a cell *receptor* normally responding to a naturally occurring substance and prevents a response to the natural substance.

anthelmint(h)ic
antihelminth
helminthagogue
helminthic
vermifuge
1. n., Substance intended to kill or cause the expulsion of parasitic intestinal worms, such as helminths.
2. adj., Acting to expel or kill parasitic intestinal worms.

anthracosis (coal miners' pneumoconiosis)
Form of *pneumoconiosis* caused by accumulation of anthracite carbon deposits in the lungs due to inhalation of smoke or coal dust.

anthropogenic
1. Caused by or influenced by human activities.
2. Describing a conversion factor used to calculate a *dose* or *concentration* affecting a human that has been derived from data obtained with another species (e.g., the rat).

[2]

anti-adrenergic
See *sympatholytic.*

antibiotic
Substance produced by, and obtained from, certain living cells (especially bacteria, yeasts, and molds), or an equivalent synthetic substance, which is *biostatic* or *biocidal* at low concentrations to some other form of life, especially pathogenic or noxious organisms.

antibody
Protein (*immunoglobulin*) produced by the immune system in response to *exposure* to an antigenic molecule and characterized by its specific binding to a site on that molecule (antigenic determinant or *epitope*).

[3]

anticholinergic
1. adj., Preventing transmission of *parasympathetic* (acetylcholine releasing) nerve impulses.
2. n., Substance that prevents transmission of parasympathetic nerve impulses.

anticholinesterase
See *cholinesterase inhibitor.*

anticoagulant
Substance that prevents blood clotting (e.g., warfarin).

antidote
Substance capable of specifically counteracting or reducing the effect of a potentially *toxic* substance in an organism by a relatively specific chemical or pharmacological action.

antigen
Substance or a structural part (*epitope*) of a substance that causes the immune system to produce specific *antibody* or specific cells and combines with specific binding sites (*epitopes*) on the antibody or cells.

antihistamine
Substance that blocks or counteracts the action of *histamine*.

antihelminth
See *anthelmint(h)ic.*

antimetabolite
Substance, structurally similar to a *metabolite*, which competes with it or replaces it, and so prevents or reduces its normal utilization.

antimuscarinic
1. n., Substance inhibiting or preventing the actions of muscarine and muscarine-like agents (e.g., atropine) on the muscarinic acetylcholine *receptors*.
2. adj., Inhibiting or preventing the actions of muscarine and muscarine-like agents on the muscarinic acetylcholine receptors.

antimycotic
fungicide
Substance used to kill a fungus or to inhibit its growth.

antinicotinic
1. n., Substance inhibiting or preventing the actions of nicotine and nicotine-like agents (e.g., suxamethonium chloride) on the nicotinic acetylcholine *receptors*.
2. adj., Inhibiting or preventing the actions of nicotine and nicotine-like agents on the nicotinic acetylcholine receptors.

antipyretic
Substance that relieves or reduces fever.

antiresistant
Substance used as an additive to a *pesticide* formulation in order to reduce the resistance of insects to the pesticide (e.g., an antimetabolite that inhibits metabolic inactivation of the pesticide).

antiserum
Serum containing *antibodies* to a particular *antigen* either because of immunization or after an infectious disease.

Note: Usually, the antibodies are polyclonal.

antiviral
See *virucide.*

aphasia
Loss or impairment of the power of speech or writing, or of the ability to understand written or spoken language or signs, due to a brain injury or disease.

aphicide
Substance intended to kill *aphids*.

aphid
Common name for a harmful plant parasite in the family Aphididae, some species of which are vectors of plant virus diseases.

aplasia
Lack of development of an organ or tissue, or of the cellular products from an organ or tissue.

apopto/sis n., **tic** adj.
Active process of programmed cell death, requiring metabolic energy, often characterized by fragmentation of *DNA*, and cell deletion without associated *inflammation*.
[2]
See *necrosis*.

arboricide
Substance intended to kill trees and shrubs.

area source
Widespread origin of *emissions*.

area under the concentration–time curve
See *area under the curve.*

area under the curve (AUC)
Area between a curve and the abscissa (horizontal axis), i.e., the area underneath the graph of a function: often, the area under the tissue (*plasma*) *concentration* curve of a substance expressed as a function of time.
[2]

area under the moment curve (AUMC)
Area between a curve and the abscissa (horizontal axis) in a plot of (*concentration* × time) vs. time.
[2]

argyria
argyrosis
Pathological condition characterized by gray-bluish or black pigmentation of tissues (such as skin, retina, mucous membranes, internal organs) caused by the accumulation of metallic silver, due to reduction of a silver compound which has entered the organism during (prolonged) administration or *exposure*.

arrhythmia
Any variation from the normal rhythm of the heartbeat.

arseniasis
Chronic arsenical poisoning.

artefact
Observation, effect, or result which is inaccurate because it is produced by the methodology used in scientific investigation or by experimental error

arteriosclerosis
Hardening and thickening of the walls of the arteries.
See also *atherosclerosis.*

arthralgia
Pain in a joint.

arthritis
Chronic inflammation of a joint, usually accompanied by pain and often by changes in structure.

arthropathy
arthrosis
Disease of a joint.

arthrosis
Joint or articulation.

asbestosis
Form of *pneumoconiosis* caused by inhalation of asbestos fibers.

ascaricide
Substance intended to kill roundworms (Ascaridae).

asphyxia
Condition resulting from insufficient intake of oxygen: Symptoms include breathing difficulty, impairment of senses, and, in extreme, convulsions, unconsciousness and death.

asphyxiant
Substance that blocks the transport or use of oxygen by living organisms.

Note: Examples include both physical (nitrogen gas) and chemical (carbon monoxide) asphyxiants.

assay
1. n., Process of quantitative or qualitative analysis of a component of a *sample*.
2. n., Results of a quantitative or qualitative analysis of a component of a sample.
3. v., To carry out quantitative or qualitative analysis of a component of a sample.

assimilation
Uptake and incorporation of substances by a living organism.

asthenia
Weakness; lack or loss of strength.

asthma
Chronic respiratory disease characterized by bronchoconstriction, excessive mucus secretion, and *edema* of the pulmonary alveoli, resulting in difficulty in breathing out, wheezing, and cough.

astringent
1. adj., Causing contraction, usually locally after topical application.
2. n., Substance causing cells to shrink, thus causing tissue contraction or stoppage of secretions and discharges; such substances may be applied to skin to harden and protect it.

ataxia
Unsteady or irregular manner of walking or movement caused by loss or failure of muscular coordination.

atherosclerosis
Pathological condition in which there is thickening, hardening, and loss of elasticity of the walls of blood vessels, characterized by a variable combination of changes of the innermost layer consisting of local accumulation of lipids, complex carbohydrates, blood and blood components, fibrous tissue, and calcium deposits. In addition, the outer layer becomes thickened and there is fatty degeneration of the middle layer.
See also *arteriosclerosis*.

atrophy
Wasting away of the body or of an organ or tissue, involving a decrease in size and (or) numbers of cells.

attenuation (in genetics)
Regulation of *gene* expression in bacteria by premature termination of *transcription* of a biosynthetic *operon*.

attractant
Substance that attracts animals. Some attractants fulfill natural biological functions such as mating or predation: Others may be used to attract animals for monitoring or for control.
See also *pheromone.*

attributable risk
Part of a *risk* that is identified as due to *exposure* to a defined substance.
[2]

autoimmune disease
Pathological condition resulting when an organism produces *antibodies* or specific cells which bind to constituents of its own tissues (auto*antigens*) and cause tissue injury: Examples of such disease may include rheumatoid *arthritis*, *myasthenia* gravis, systemic lupus erythematosus, and scleroderma.

autooxidation
See *autoxidation*.

autophagosome
Membrane-bound body (secondary *lysosome*) in which parts of the cell are digested.

autopsy
necropsy
Postmortem examination of the organs and body tissue to determine cause of death or pathological condition.

autosome
Any *chromosome* other than a sex chromosome.

autoxidation
Reaction with dioxygen at moderate temperatures.

autoxidation (in food chemistry)
Apparently spontaneous, usually slow reaction of foodstuff components with dioxygen in an *aerobic* environment at moderate temperatures.

auxotroph
Organism unable to synthesize an organic molecule which is required for its growth: When the compound is given to the organism with the other nutrients it requires, growth of the organism may occur.

auxotrophy
Inability of a microorganism to synthesize a particular organic compound required for its growth.

avicide
Substance intended to kill birds.

axenic animal
See *germ-free animal*.

azoospermia
1. Absence of live motile spermatozoa in semen.
2. Failure to form live spermatozoa.

back-mutation
Process that reverses the effect of a *mutation* which had inactivated a *gene*; thus, it restores the wild phenotype.

bacterial artificial chromosome (BAC)
DNA vector into which large DNA fragments can be inserted and cloned in a bacterial host.

bactericide
Substance intended to kill bacteria.

bagassosis
Lung disease caused by the inhalation of dust from sugar-cane residues.

basal lamina, pl. **-ae**
Triple-layered structure on which epithelium sits: It consists of an electron-dense layer (lamina densa) between two electron-transparent layers (lamina lucida). The lamina densa is composed of type IV collagen, and the lamina lucida contains the glycoprotein laminin.

base pairing
Linking of the complementary pair of polynucleotide chains of nucleic acids by means of hydrogen bonds between complementary purine and pyrimidine bases, adenine with thymine or uracil, cytosine with guanine.

basement membrane
Specialized layers (*basal laminae*) of extra-cellular matrix that separate epithelial tissue from underlying connective tissue: Cancer cells must break through the basement membrane in order to migrate to other parts of the body and form metastases.

Bateman function
Equation expressing the build up and decay in *concentration* of a substance (usually in *plasma*) based on first-order *uptake* and *elimination* in a *one-compartment model*, having the form

$$C = [fDk_a/V(k_a - k_e)][\exp(-k_e t) - \exp(-k_a t)]$$

where C is the concentration and D the *dose* of the substance, f the fraction absorbed, and V the *volume of distribution*. k_a and k_e are the first-order *rate constants* of uptake and elimination, respectively, and t is time.
[2]

B-cell
See *B lymphocyte.*

benchmark concentration (BMC)
Statistically calculated lower 95 % confidence limit on the *concentration* that produces a defined *response* (called the *benchmark response* or BMR, usually 5 or 10 %) for an *adverse effect* compared to background, often defined as 0 or 5 %.
[2]

benchmark dose (BMD)
Statistically calculated lower 95 % confidence limit on the *dose* that produces a defined *response* (called the *benchmark response* or BMR, usually 5 or 10 %) of an *adverse effect* compared to background, often defined as 0 or 5 %.
[2]

benchmark guidance value
Biological monitoring guidance value set at the 90th percentile of available *biological monitoring* results collected from a representative *sample* of workplaces with good occupational hygiene practices.
[2]

benchmark response
Response, expressed as an excess of background, at which a *benchmark dose* or *benchmark concentration* is set.
[2]

benefit
Advantage to or improvement in condition of an individual or a population.

benign
Antonym: *malignant*
1. Of a disease, producing no persisting harmful effects.
2. *Tumor* that does not invade other tissues (see *metastasis*), having lost growth control but not positional control.

   Note: Such a tumor is not *carcinogenic* but may cause mechanical damage to adjacent tissues.

berylliosis
See *beryllium disease.*

beryllium disease
berylliosis
Serious and usually permanent lung damage resulting from chronic inhalation of beryllium.

bias
1. Deviation of results or inferences from the truth, or processes leading to such deviation.
2. Any trend in the collection, analysis, interpretation, publication, or review of data which can lead to conclusions which are systematically different from the truth.

biased sample
Antonym: *random sample*
Any *sample* that is not a random sample.

bilirubin
Orange–yellow pigment, a breakdown product of heme-containing proteins (hemoglobin, myoglobin, *cytochrome*s), which circulates in the blood *plasma* bound to albumin or as water-soluble glucuronide conjugates, and is excreted in the bile by the liver.

bioaccessibility
Potential for a substance to come in contact with a living organism and then interact with it. This may lead to *absorption*.

Note: A substance trapped inside an insoluble particle is not bioaccessible, although substances on the surface of the same particle are accessible and may also be bioavailable. Bioaccessibility, like bioavailability, is a function of both chemical speciation and biological properties. Even surface-bound substances may not be accessible to organisms which require the substances to be in solution.

bioaccessible
Able to come in contact with a living organism and interact with it.
See *bioaccessibility.*

bioaccumulation
Progressive increase in the amount of a substance in an organism or part of an organism that occurs because the rate of intake exceeds the organism's ability to remove the substance from the body.

Note: Bioaccumulation often correlates with *lipophilicity*.

See also *bioconcentration*, *biomagnification.*

bioaccumulation potential
Ability of living organisms to concentrate a substance obtained either directly from the environment or indirectly through its food.

bioactivation
Metabolic *conversion* of a *xenobiotic* to a more *toxic* derivative or one which has more of an effect on living organisms.

bioassay
Procedure for estimating the *concentration* or biological activity of a substance by measuring its effect on a living system compared to a standard system.

bioavailability (general)
biological availability
physiological availability
Extent of *absorption* of a substance by a living organism compared to a standard system.
[2]

bioavailability (in toxico- or pharmacokinetics)
Ratio of the *systemic exposure* from extravascular (ev) exposure to that following intravenous (iv) *exposure* as described by the equation:

$$F = A_{ev}\, D_{iv}/B_{iv}\, D_{ev}$$

where F (fraction of *dose* absorbed) is a measure of the bioavailability, A and B are the *areas under the* (plasma) *concentration–time curve* following extravascular and intravenous administration, respectively, and D_{ev} and D_{iv} are the administered extravascular and intravenous *doses*.
[2]

bioavailable
Able to be absorbed by living organisms.
See *bioavailability.*

biochemical mechanism
Reaction or series of reactions, usually enzyme-catalyzed, associated with a specific physiological event in a living organism.

biochemical (biological) oxygen demand (BOD)
Amount *concentration* of oxygen taken up through the respiratory activity of microorganisms growing on organic compounds present when incubated at a specified temperature (usually 20 °C) for a fixed period (usually 5 days). It is regarded as a measure of that organic *pollution* of water which can be degraded biologically but includes the oxidation of inorganic material such as sulfide and iron(II). The empirical test used in the laboratory to determine BOD also measures the oxygen used to oxidize reduced forms of nitrogen unless their oxidation is prevented by an inhibitor such as allyl thiourea.

biocid/e n., **-al** adj.
Substance intended to kill living organisms.

bioconcentration
Process leading to a higher *concentration* of a substance in an organism than in environmental media to which it is *exposed*.
See *bioaccumulation.*

bioconcentration factor (BCF)
Measure of the tendency for a substance in water to accumulate in organisms, especially fish.

Note 1: The equilibrium *concentration* of a substance in fish can be estimated by multiplying its concentration in the surrounding water by its *bioconcentration factor* in fish.

Note 2: This parameter is an important determinant for human intake of aquatic food by the ingestion route.

bioconjugate
See *conjugate.*

bioconversion
See *biotransformation.*

biodegradation
Breakdown of a substance catalyzed by enzymes in vitro or in vivo. This may be characterized for purposes of *hazard* assessment as:
1. Primary. Alteration of the chemical structure of a substance resulting in loss of a specific property of that substance.
2. Environmentally acceptable. Biodegradation to such an extent as to remove undesirable properties of the compound. This often corresponds to primary biodegradation, but it depends on the circumstances under which the products are discharged into the environment.

3. Ultimate. Complete breakdown of a compound to either fully oxidized or reduced simple molecules (such as carbon dioxide/methane, nitrate/ammonium, and water). It should be noted that the products of biodegradation can be more harmful than the substance degraded.

bioelimination
Removal, usually from the aqueous phase, of a test substance in the presence of living organisms by biological processes supplemented by physicochemical reactions.

bioequivalen/ce n., **-t** adj.
Relationship between two preparations of the same *drug* in the same dosage form that have a similar bioavailability.

bioinactivation
Metabolic *conversion* of a *xenobiotic* to a less *toxic* derivative.
[2]

bioinformatics
Discipline encompassing the development and utilization of computational facilities to store, analyze, and interpret biological data.

biokinetics (in toxicology)
Science of the movements involved in the *distribution* of substances.
[2]

biological absorption
See *absorption*, *biological.*

biological accessibility
See *bioaccessibility.*

biological acclimatization
See *acclimatization*, *biological.*

biological assessment of exposure
See *biological monitoring.*

biological availability
See *bioavailability.*

biological cycle
Complete circulatory process through which a substance passes in the *biosphere*. It may involve transport through the various media (air, water, soil), followed by *environmental transformation*, and carriage through various *ecosystems*.

biological effect monitoring (BEM)
Continuous or repeated measurement of early biological effects of *exposure* to a substance to evaluate ambient *exposure* and *health risk* by comparison with appropriate reference values based on knowledge of the probable relationship between ambient exposure and biological effects.

biological exposure indices (BEI)
Guidance values recommended by ACGIH for assessing *biological monitoring* results.
[5]

biological half life
For a substance, the time required for the amount of that substance in a biological system to be reduced to one-half of its value by biological processes, when the rate of removal is approximately exponential.
[2]

biological half time, $t_{1/2}$
See *biological half life.*

biological indicator
Species or group of species that is representative and typical for a specific status of an *ecosystem*, which appears frequently enough to serve for monitoring and whose population shows a sensitive response to changes (e.g., the appearance of a toxicant in an ecosystem).
[6]

biological marker
See *biomarker.*

biological monitoring
biological assessment of exposure
biomonitoring
Continuous or repeated measurement of any naturally occurring or synthetic chemical, including potentially *toxic substances* or their *metabolites* or biochemical effects in tissues, secreta, excreta, expired air, or any combination of these in order to evaluate occupational or environmental *exposure* and *health risk* by comparison with appropriate reference values based on knowledge of the probable relationship between ambient exposure and resultant *adverse* health *effects*.

biological oxygen demand
See *biochemical oxygen demand.*

biological preparation
biological
biopreparation
Compound derived from living organisms and their products for use in medicine or as a *pesticide*, etc.

biological specimen
1. Organ, tissue (including blood), secretion, or excretion product taken from an organism as a *sample* reflecting the state of the whole organism.
2. Organism taken as a sample reflecting the state of a population or their environment.

biological warfare
Military operations using any organism (bacteria, virus, or other disease-causing organism) or *toxin* found in nature, to kill, injure, or incapacitate human beings, animals, or plants.

biomagnification
ecological magnification
Sequence of processes in an ecosystem by which higher *concentration*s are attained in organisms at higher trophic levels (at higher levels in the food web); at its simplest, a process leading to a higher concentration of a substance in an organism than in its food.

biomarker
Indicator signaling an event or condition in a biological system or *sample* and giving a measure of *exposure*, effect, or susceptibility.

Note: Such an indicator may be a measurable chemical, biochemical, physiological, behavioral, or other alteration within an organism.

[2]

biomarker of effect
effect biomarker
Biomarker that, depending upon the magnitude, can be recognized as associated with an established or possible *health* impairment or disease.
[2]

biomarker of exposure
exposure biomarker
Biomarker that relates *exposure* to a *xenobiotic* to the levels of the substance or its *metabolite*, or of the product of an interaction between the substance and some *target* molecule or cell that can be measured in a *compartment* within an organism.
[2]

biomarker of susceptibility
susceptibility biomarker
Biomarker of an inherent or acquired ability of an organism to respond to *exposure* to a specific substance.
[2]

biomass
1. Total amount of biotic material, usually expressed per unit surface area or volume, in a medium such as water.
2. Material produced by the growth of microorganisms, plants, or animals.

biomineralization
Complete conversion of organic substances to inorganic derivatives by living organisms, especially microorganisms.

biomolecule
Substance that is synthesized by and occurs naturally in living organisms.

biomonitoring
See *biological monitoring.*

biopesticide
Biological agent with pesticidal activity, for example, the bacterium *Bacillus thuringiensis* when used to kill insects.
After [6]

biopsy
Excision of a small piece of living tissue for microscopic or biochemical examination; usually performed to establish a diagnosis.

biosphere
Portion of the planet earth that supports and includes life.

biostatic
Adjective applied to a substance that arrests the growth or multiplication of living organisms.

biota
All living organisms as a totality.

biotransformation
bioconversion
Chemical conversion of a substance that is mediated by living organisms or *enzyme* preparations derived therefrom.

2,3-bis(sulfanyl)propan-1-ol
British anti-Lewisite
dimercaprol
2,3-dimercaptopropan-1-ol
Metal chelator that has been used in the treatment of arsenic, antimony, gold, mercury, and lead poisoning.

blastocyst
Mammalian *embryo* at the stage at which it is implanted into the wall of the uterus.
[9]

blood–brain barrier
Physiological interface between brain tissues and circulating blood created by a mechanism that alters the permeability of brain capillaries, so that some substances are prevented from entering brain tissue, while other substances are allowed to enter freely.
After [2]

blood–placenta barrier
Physiological interface between maternal and fetal blood circulations that filters out some substances which could harm the fetus while favoring the passage of others such as nutrients: Many fat-soluble substances such as alcohol are not filtered out, and several types of virus can also cross this barrier.

Note: The effectiveness of the interface as a barrier varies with species and different forms of placentation.

blood plasma
See *plasma (in biology)*.

blood substitution
See *exchange transfusion*.

blood–testis barrier
Physiological interface between the blood supply and the spermatozoa of the seminiferous tubules.

Note: This interface consists of specific junctional complexes between Sertoli cells.

After [2]

B lymphocyte
B cell
Type of *lymphocyte* that synthesizes and secretes *antibodies* in response to the presence of a foreign substance or one identified by it as foreign. The protective effect can be mediated to a certain extent by the antibody alone (contrast *T lymphocyte*).

body burden
Total amount of a substance present in an organism at a given time.

bolus
1. Single *dose* of a substance, originally a large pill.
2. Dose of a substance administered by a single rapid intravenous injection.
3. Concentrated mass of food ready to be swallowed.

botanical pesticide
Substance with activity against pests, that is produced naturally within a plant and may act as a defense against predators.

botulism
Acute food poisoning caused by botulinum toxin produced in food by the bacterium *Clostridium botulinum* and characterized by muscle weakness and paralysis; disturbances of vision, swallowing, and speech; and a high mortality rate.

brady-
Antonym: *tachy-*
Prefix meaning slow as in bradycardia or bradypnoea.

bradycardia
Antonym: *tachycardia*
Abnormal slowness of the heartbeat.

bradypnoea
Antonym: *tachypnoea*
Abnormally slow breathing.

breathing zone
Space within a radius of 0.5 m from a person's face.

British anti-Lewisite (BAL)
See *2,3-bis(sulfanyl)propan-1-ol.*

bronchoconstriction
Antonym: *bronchodilation*
Narrowing of the air passages through the bronchi of the lungs.

bronchodilation
Antonym: *bronchoconstriction*
Expansion of the air passages through the bronchi of the lungs.

bronchospasm
Intermittent violent contraction of the air passages of the lungs.

builder (in chemistry)
Material that enhances or maintains the cleaning efficiency of a surfactant, in a detergent, principally by inactivating water hardness; complex phosphates (especially sodium tripolyphosphate, i.e., pentasodium triphosphate), sodium carbonate, and sodium silicate are the builders most commonly used.

byssinosis
Pneumoconiosis caused by inhalation of dust and associated microbial contaminants and observed in cotton, flax, and hemp workers.

bystander exposure
Liability of members of the general public to come in contact with substances arising from operations or processes carried out by other individuals in their vicinity.

cacosmia
Imagined perception of vile odors, including coprosmia (smelling feces) and necrosmia (the smell of death).

calcification
Form of mineralization in which organic tissue becomes hardened by deposition of calcium salts within its substance.

calibration
Operation that, under specified conditions, in a first step establishes a relation between the quantity values with measurement *uncertainties* provided by measurement *standards* and corresponding *indications* with associated measurement uncertainties and, in a second step, uses this information to establish a relation for obtaining a measurement result from an indication.
[7]

calibration material
See *reference material.*

cancer
Disease resulting from the development of a *malignant tumor*.

carbonylhemoglobin
carboxyhemoglobin
Compound that is formed between carbon monoxide and *hemoglobin* in the blood of animals and humans and is incapable of transporting oxygen.

carboxyhemoglobin
See *carbonylhemoglobin.*

carcinogen n., **-ic** adj.
Agent (chemical, physical, or biological) that is capable of increasing the *incidence* of malignant *neoplasms*, thus causing *cancer*.

Note: Annex 3 describes the classification systems for carcinogens.

carcinogen/esis n., **-etic** adj.
Induction, by chemical, physical, or biological agents, of *malignant neoplasm*s and thus *cancer*.

carcinogenicity
Process of induction of *malignant neoplasm*s, and thus *cancer*, by chemical, physical, or biological agents.

carcinogenicity test
Long-term (*chronic*) test designed to detect any possible carcinogenic effect of a test substance.

carcinoma
epithelioma
Malignant tumor of an epithelial cell.

cardiotoxic
Chemically harmful to the cells of the heart.

carrier
1. Substance in appreciable amount which, when associated with a trace of a specified substance, will carry the trace with it through a chemical or physical process.
2. Person who is heterozygous (e.g., carries only one *allele*) for a recessive genetic character leading to *disease*, and hence does not, under most circumstances, display the disease *phenotype* but can pass it on to the next generation.

[2]

3. Gas, liquid, or solid substance (often in particulate form) used to absorb, adsorb, dilute, or suspend a substance to facilitate its transfer from one medium to another.

carrier-linked prodrug
carrier prodrug
Compound that contains a temporary linkage between a given active substance and a transient *carrier* group, the latter producing improved physicochemical or *pharmacokinetic* properties and easily removable in vivo.
[2]

carrier protein
1. Protein to which a specific *ligand* or *hapten* is *conjugated.*
2. Unlabeled protein introduced into an assay at relatively high *concentration*s that distributes in a *fractionation* process in the same manner as labeled protein analyte, present in very low concentrations.
3. Protein added to prevent nonspecific interaction of reagents with surfaces, *sample* components, and each other.
4. Protein found in cell membranes that facilitates transport of a *ligand* across the membrane.

[2]

carrier substance
Substance that binds to another substance and transfers it from one site to another.
[2]

carry-over
1. Transfer in farming and agricultural processing of a component from one system such as soil or feed to another system such as a plant, animal, or human being: Carry-over is expressed as the *concentration* of the component in the second system divided by its concentration in the first.

2. Process in analytical studies by which materials are carried into a reaction mixture in which they do not belong.
3. Persistence of a substance in soil (e.g., a *pesticide*), such that injury may occur subsequently to a new crop.
4. Persistence of a test substance in participants undergoing a cross-over clinical trial study, in which each participant randomly receives the placebo and test substance with an intervening washout period.

case cohort study
Variant of the *case control study* in which the controls are drawn from the same cohort as the cases but are identified before the cases develop; some of the controls may later become cases.

case control study
case comparison study
case compeer study
case history study
case referent study
retrospective study
Study that starts with the identification of persons with the disease (or other outcome variable) of interest, and a suitable control (comparison, reference) group of persons without the *disease*. The relationship of an attribute to the disease is examined by comparing the diseased and non-diseased with regard to how frequently the attribute is present or, if quantitative, the levels of the attribute, in the two groups.

catabolism
Antonym: *anabolism*
1. Reactions involving the oxidation of organic substrates to provide chemically available energy (e.g., ATP) and to generate metabolic intermediates.
2. Generally, process of breakdown of complex molecules into simpler ones, often providing biologically available energy.

catatonia
Behavior marked by excessive and sometimes violent motor acivity and excitement, or by generalized inhibition or stupor, that may occur in schizophrenia, mood disorders, or organic brain syndromes.

cathartic
See *laxative.*

ceiling value (CV)
Airborne *concentration* of a potentially *toxic substance* that should never be exceeded in a worker's breathing zone.

cell cycle
Regulated biochemical steps that cells go through involving *DNA* replication and cell division, usually depicted as a sequential cyclical series of events.

cell line
Defined unique population of cells obtained by culture from a primary source through numerous generations.
See also *transformed cell line.*

cell-mediated hypersensitivity
State in which an individual reacts with allergic effects caused by the reaction of *antigen*-specific *T-lymphocytes* following *exposure* to a certain substance (*allergen*) after having been *exposed* previously to the same substance or chemical group.

cell-mediated immunity
Immune response mediated by *antigen*-specific *T-lymphocytes*.

cell proliferation
Rapid increase in cell number.

cell strain
Cells having specific properties or markers derived from a primary culture or *cell line*.

censored data
Sample observations for which the complete distribution is not known: for example, a cohort study in which some persons cannot be followed to the predetermined end of the study ("right-censored data") or environmental assay data in which some results are less than the sample detection limit ("left-censored data").

certified reference material (CRM)
Reference material, accompanied by documentation issued by an authoritative body and referring to valid procedures used to obtain a specified property value with *uncertainty* and *traceability*.

Example: Human serum with assigned quantity value for the concentration of cholesterol and associated measurement *uncertainty* stated in an accompanying certificate, used as *calibrator* or measurement *trueness* control material.

[7]

chain of custody
Sequence of responsibility for a substance from the manufacturer to the distributor, to the user, or to the person(s) ultimately responsible for *waste* disposal. This term is also used in controlled transmission of *sample*s from collection to analysis, especially of samples of materials used for medico-legal or forensic purposes.

chelation therapy
Treatment with a chelating agent to enhance the *elimination* or reduce the *toxicity* of a metal ion.

chemesthesis
Sensations that arise when chemical compounds activate *receptor* mechanisms for other effectors, such as light, pain, pressure, and heat, in the eye, skin, nose, mouth, and throat; for example, the burning feel-

ing from chili pepper, the cooling from the menthol in mouthwash, and the stinging feeling of carbonation.

chemical etiologic agent
See *toxic substance.*

chemical conversion
Change from one chemical species to another.
[2]

chemical etiologic agent
See *toxic substance.*

chemical oxygen demand (COD)
Measure of the amount of oxygen, divided by the volume of the system, required to oxidize the organic (and inorganic) matter in wastewater using a chemically oxidizing agent. In practice, it is usually expressed in milligrams O_2 per litre.

chemical safety
Practical certainty that there will be no *exposure* of organisms to toxic amounts of any substance or group of substances: This implies attaining an acceptably low *risk* of exposure to potentially toxic substances.

chemical species (of an element)
Specific form of an element defined as to isotopic composition, electronic or oxidation state, and (or) complex or molecular structure.
[2]

chemical warfare
Military operations using the toxic properties of chemical agents to kill, injure, or incapacitate human beings, animals, or plants.

chemophobia
Irrational fear of chemicals.

chemosis
Chemically induced swelling around the eye caused by *edema* of the conjunctiva.

chemosterilizer
Substance used to sterilize mites, insects, rodents, or other animals.

chloracne
Acne-like eruption caused by *exposure* to certain chlorinated organic substances such as polychlorinated biphenyls or 2,3,7,8-tetrachlorodibenzo-*p*-dioxin [2,3,7,8-tetrachlorooxanthrene] and other polychlorinated dibenzo dioxins and furans.

cholinomimetic
See *parasympathomimetic.*

cholinesterase inhibitor
Substance that inhibits the action of acetylcholinesterase (EC 3.1.1.7) and related enzymes which catalyze the hydrolysis of choline esters: Such a substance causes hyperactivity in *parasympathetic* nerves.

Note: Examples include organophosphate and carbamate *pesticides*.

chromatid
Either of two filaments joined at the centromere into which a *chromosome* divides as it duplicates itself during cell division.

chromatin
Stainable complex of *DNA* and proteins present in the nucleus of a *eukaryotic* cell.

chromosomal aberration
Abnormality of *chromosome* number or structure.

chromosome
Self-replicating structure consisting of *DNA* complexed with various proteins and involved in the storage and transmission of genetic information; the physical structure that contains the *gene*s.

chronic
Antonym: *acute*
Long-term (in relation to *exposure* or effect).
1. In experimental toxicology, chronic refers to mammalian studies lasting considerably more than 90 days or to studies occupying a large part of the lifetime of an organism.
2. In clinical medicine, long-established or long-lasting.

[2]

chronic effect
long-term effect
Antonym: *acute effect*
Consequence that develops slowly and (or) has a long-lasting course; may be applied to an effect which develops rapidly and is long-lasting.
[2]

chronic exposure
long-term exposure
Antonym: *acute exposure*
Continued *exposure* or exposures occurring over an extended period of time, or a significant fraction of the test species' or of the group of individuals', or of the population's life-time.

chronic toxicity
long-term toxicity
Antonym: *acute toxicity*
1. *Adverse effects* following *chronic exposure*.
2. Effects that persist over a long period of time whether or not they occur immediately upon *exposure* or are delayed.

chronic toxicity test
long-term toxicity test
Antonym: *acute toxicity test*
Study in which organisms are observed during the greater part of the life span and in which *exposure* to the test agent takes place over the whole observation time or a substantial part thereof.

chronotoxicology
Study of the influence of biological rhythms on the *toxicity* of substances or of the influence of a toxicant on biological rhythms.

ciguateratoxin poisoning
Serious illness caused by eating carnivorous fish such as snappers and barracuda that have become contaminated by *toxins* produced by the microalga, *Gambierdiscus toxicus*; gastrointestinal symptoms may accompany a wide variety of neurological symptoms, including *ataxia*, *vertigo*, flaccid paralysis, respiratory arrest, and reversed perception of hot and cold; the neurological symptoms may persist for many years.

circadian
nychthemeral
Relating to or exhibiting an approximately 24-h periodicity.

circulation of substances in the environment
Movement of *xenobiotic* substances in the environment with air flow, river current, sediment flow, etc.

cirrhosis
1. Liver disease defined by histological examination and characterized by increased fibrous tissue, abnormal morphological and physiological changes such as loss of functional liver cells, and increased resistance to blood flow through the liver (portal *hypertension*).
2. Chronic interstitial *inflammation* and *fibrosis* of an organ.

cirrhotic
Describing an organ showing *cirrhosis*.

clastogen
Agent causing *chromosome* breakage and (or) consequent gain, loss, or rearrangement of pieces of chromosomes.

clastogenesis
Formation (or generation) of chromosomal breaks and (or) consequent gain, loss, or rearrangement of pieces of *chromosome*s.

clearance (general) $(c_o/c_i)(\Delta V/\Delta t)$
Product of the *concentration* c_o of a component in an output system and the volume flow rate of the output system divided by the concentration c_i of this component in the input system.

Note: The term "mean volume rate" is recommended for this quantity.

[2]

clearance (in physiology and toxicology)

1. Volume of blood or *plasma* or mass of an organ effectively cleared of a substance by *elimination* (*metabolism* and *excretion*) divided by time of elimination.

   Note: Total clearance is the sum of the clearances of each eliminating organ or tissue for that component.

2. (in *pulmonary toxicology*) Volume or mass of lung cleared divided by time of *elimination*; used qualitatively to describe removal of any inhaled substance which deposits on the lining surface of the lung.
3. (in *renal* toxicology) Quantification of the removal of a substance by the kidneys by the processes of filtration and secretion; clearance is calculated by relating the rate of renal excretion to the *plasma concentration*.

[2]

cleavage (of a molecule)
Splitting of a molecule into smaller molecular entities.

clinical toxicology
Scientific study involving research, education, prevention, and treatment of diseases caused by substances such as drugs and toxins.

Note: Often refers specifically to the application of toxicological principles to the treatment of human poisoning.

clon/e n., **-al** adj.

1. Population of genetically identical cells or organisms having a common ancestor.
2. To produce such a population.
3. *Recombinant DNA* molecules all carrying the same inserted sequence.

clonic
Pertaining to alternate muscular contraction and relaxation in rapid succession.

cloning vector
Small circle of *DNA* (e.g., a plasmid) or modified bacteriophage (bacterial virus) that can carry a segment of foreign DNA into an appropriate host organism (e.g., a bacterial, yeast, or mammalian cell). After [9]

cluster sampling
1. A method of sampling in which the population is divided into aggregates (or clusters) of items bound together in a certain manner. A *sample* of these clusters is taken at random, and all the items which constitute them are included in the sample.
2. A sampling method in which each unit selected is a group of persons (all persons in a city block, a family, etc.) rather than an individual.

coagonist
See *agonist.*

cocarcinogen
Chemical, physical, or biological factor that intensifies the effect of a *carcinogen*.

Codex Alimentarius
Collection of internationally adopted food standards drawn up by the Codex Alimentarius Commission, the principal body implementing the joint FAO/WHO Food Standards Program.

cohort
Component of the population born during a particular period and identified by period of birth so that its characteristics (such as causes of death and numbers still living) can be ascertained as it enters successive time and age periods. The term "cohort" has broadened to describe any designated group of persons followed or traced over a period of time, as in the term *cohort study* (*prospective study*).

cohort analysis
Tabulation and analysis of *morbidity* or *mortality* rates in relationship to the ages of a specific group of people (cohort), identified by their birth period, and followed as they pass through different ages during part or all of their life span. In certain circumstances such as studies of migrant populations, cohort analysis may be performed according to duration of residence in a country rather than year of birth, in order to relate *health* or mortality experience to duration of *exposure*.

cohort study
concurrent study
follow-up study
incidence study
longitudinal study
prospective study
Analytic study in *epidemiology* in which subsets of a defined population can be identified who are, have been, or in the future may be *exposed* or not exposed, or exposed in different degrees, to a factor or factors hypothesized to influence the probability of occurrence of a given disease or other outcome. The main feature of the method is observation of a large population for a prolonged period (years), with comparison of *incidence rates* of the given disease in groups that differ in *exposure* levels.

combined effect of poisons
Simultaneous or successive effect of two or more *poison*s on the organism by the same route of *exposure*.

cometabolism
Process by which a normally nonbiodegradable substance is biodegraded only in the presence of an additional carbon source.
See also *metabolism.*

comet assay
Means of measuring *DNA* damage, particularly DNA strand breaks. A cell is embedded in agar and exposed to a DNA-damaging agent. The cell is then permeabilized with a detergent, and an electric field is applied. If the cell's genomic DNA has been broken into small fragments, these fragments move out of the cell by electrophoresis and form a streak or "tail" leading away from the cell which looks like a comet.

comparison group
See *control group*.

comparative genomics
Study of the relationship of *genome* structure and function across different biological species.
After [9]

comparative risk
See *relative excess risk.*

compartment
Conceptualized part of the body (organs, tissues, cells, or fluids) considered as an independent system for purposes of modeling and assessment of *distribution* and *clearance* of a substance.
[2]

compartmental analysis
Mathematical process leading to a model of transport of a substance in terms of *compartments* and rate constants, usually taking the form $C = Ae^{-\alpha t} + Be^{-\beta t}\ldots$ where each exponential term represents one compartment. C is the substance *concentration*; A, B, … are proportionality constants; α, β, … are rate constants; and t is time.
[2]

compartmentalize
Separate into *compartments*.

compensation
pseudo-adaptation
Adaptation of an organism to changing conditions of the environment (especially chemical) is accompanied by the emergence of stresses in biochemical systems which exceed the limits of normal (*homeo-*

static) mechanisms. Compensation is a temporary concealed pathology which later on can be manifested in the form of explicit pathological changes (decompensation).

competent authority
In the context of European Community Council Directive 79/831/EEC, the Sixth Amendment to the European Community Council Directive 67/548/EEC relating to the Classification, Packaging and Labeling of Dangerous Substances, official government organization or group receiving and evaluating notifications of new substances.

competent bacteria
Culture of bacteria (or yeast) treated in such a way that their ability to take up *DNA* molecules without transduction or conjugation has been enhanced.

complementary DNA (cDNA)
DNA generated from an expressed m*RNA* through a process known as reverse transcription.
[9]

complete mineralization
Complete breakdown of a complex organic compound to carbon dioxide, water, oxides, and oxidative inorganic products such as nitrate or sulfate.

comprehensive effect of poisons
Simultaneous or successive effect made on an organism by *poisons* entering from different media, air, water, or food or through the skin.

computational toxicology
Application of mathematical and computer models to predict *adverse effects* and to better understand the mechanism(s) through which a given chemical causes harm.

concentration
1. Any one of a group of three quantities characterizing the composition of a mixture and defined as one of mass, amount of substance (chemical amount), or number divided by volume, giving, respectively, mass, amount (of substance), or number concentration.
2. Short form for amount (of substance) concentration (substance concentration in clinical chemistry).

[2]

concentration–effect curve
exposure–effect curve
Graph of the relation between *exposure concentration* and the magnitude of the resultant biological change.

concentration–effect relationship
exposure–effect relationship
Association between *exposure concentration* and the resultant magnitude of the continuously graded change produced, either in an individual or in a population.

concentration–response curve
exposure–response curve
Graph of the relation between *exposure concentration* and the proportion of individuals in a population responding with a defined effect.
[2]

concentration–response relationship
exposure–response relationship
Association between *exposure concentration* and the *incidence* of a defined effect in an exposed population.

concord/ance n., **-ant** adj.
Pairs or groups of individuals of identical *phenotype*.

Note: In twin studies, this is a condition in which both twins exhibit or fail to exhibit a trait under investigation.

concurrent study
See *cohort study.*

concurrent validity
Measurement and its criterion refer to the same point in time: An example would be a visual inspection of a wound for evidence of infection validated against bacteriological examination of a specimen taken at the same time.

confounding (in data analysis)
1. Situation in which the effects of two processes are not distinguishable from one another: The distortion of the apparent effect of an *exposure* on *risk* brought about by the association of other factors which can influence the outcome.
2. Relationship between the effects of two or more causal factors as observed in a set of data, such that it is not logically possible to separate the contribution which any single causal factor has made to an effect.
3. Situation in which a measure of the effect of an exposure on risk is distorted because of the association of exposure with other factor(s) which influence the outcome under study.

confounding variable
confounder
Changing factor that can cause or prevent the outcome of interest, is not an intermediate variable, and is associated with the factor under investigation.

congener
One of two or more substances related to each other by origin, structure, or function.
[2]

congenital
Trait, condition, or disorder that exists in an organism from birth.
After [9]

conjugate (in biochemistry)
1. Chemical species produced in living organisms by covalently linking two chemical moieties from different sources.

   Example: A conjugate of a *xenobiotic* with some group such as glutathione, sulfate, or glucuronic acid, to make it soluble in water or *compartmentalized* within the cell.

See also *phase II reaction.*
2. Material produced by attaching two or more substances together, for example, a *conjugate* of an antibody with a fluorochrome, or an enzyme.
[2]

conjunctiva
Mucous membrane that covers the eyeball and lines the under-surface of the eyelid.

conjunctivitis
Inflammation of the *conjunctiva*.

conservative assessment of risk
Assessment of *risk* that assumes the worst possible case scenario and therefore gives the highest possible value for risk: Risk management decisions based on this value will maximize safety.

construct validity
Extent to which a measurement corresponds to theoretical concepts (constructs) concerning the phenomenon under study; for example, if on theoretical grounds, the phenomenon should change with age, a measurement with construct validity would reflect such a change.

contact dermatitis
Inflammatory condition of the skin resulting from dermal *exposure* to an *allergen* (sensitizer) or an irritating (corrosive, defatting) substance.

contact poison
1. Chemical that injures the target organism through physical contact and skin absorption rather than through ingestion or inhalation.
[10]
2. *Pesticide (herbicide)* that causes injury to only the plant tissue to which it is applied or which is not appreciably translocated within plants.
[11]

containment
Process by which possible release, discharge, or spill of a *toxic* substance during normal use or after an accident is prevented by appropriate action.

contaminant
1. Minor impurity present in a substance.
2. Extraneous material inadvertently added to a *sample* prior to or during chemical or biological analysis
3. In some contexts, as in relation to gas cleaning equipment, used as a synonym for "*pollutant*", especially on a small scale.
4. Unintended component in food that may pose a *hazard* to the consumer.

content validity
Extent to which the measurement incorporates the domain of the phenomenon under study; for example, a measurement of functional *health* status should embrace activities of daily living, occupational, family, and social functioning, etc.

contraindication
Antonym: *indication*
Any condition that renders some particular line of treatment improper or undesirable.

control group
comparison group
Selected subjects of study, identified as a rule before a study is done, which comprises humans, animals, or other species who do not have the disease, intervention, procedure, or whatever is being studied, but in all other respects are as nearly identical to the test group as possible.

control, matched
Control (individual or group or case) selected to be similar to a study individual or group, or case, in specific characteristics: some commonly used matching variables are age, sex, race, and socioeconomic status.

convection (as applied to air and water motion)
Predominantly vertical motion of air or of water, induced by the expansion of the air or of water heated by the earth's surface, or by human activity, and its resulting buoyancy.
[2]

conversion
See *chemical conversion*, *biotransformation.*

core grade
Quality rating, based on standard evaluation criteria established by the U.S. Office of Pesticide Programs regulatory agencies, given to toxicological studies after submission by registrants.

corrosive
1. adj., Causing a surface-destructive effect on contact; in *toxicology*, this normally means causing visible destruction of the skin, eyes, or the lining of the respiratory tract or the gastrointestinal tract.
2. n., Substance that causes a surface-destructive effect on contact.

count mean diameter
Mean of the diameters of all particles in a population.
See also *mass mean diameter.*

count median diameter
Calculated diameter in a population of particles in a gas or liquid phase above which there are as many particles with larger diameters as there are particles below it with smaller diameters.
[2]
See also *mass median diameter.*

crackles
See *crepitations.*

crepitations
crackles
râles
Abnormal respiratory sounds heard on auscultation of the chest, produced by passage of air through passages which contain secretion or exudate or which are constricted by spasm or a thickening of their walls.
See also *rhonchi*.

Note: Auscultation is the process of listening for sounds within the body by ear unassisted or using a stethoscope.

criteri/on (pl. -a)
Validated set of data used as a basis for judgment.

criterion validity
Extent to which the measurement correlates with an external criterion of the phenomenon under study.

critical concentration (for a cell or an organ)
Concentration of a substance at and above which adverse functional changes, reversible or irreversible, occur in a cell or an organ.
[2]

critical dose
Dose of a substance at and above which adverse functional changes, reversible or irreversible, occur in a cell or an organ.
[2]

critical effect
For *deterministic effects*, the first *adverse effect* that appears when the *threshold* (*critical*) *concentration* or dose is reached in the *critical organ*: Adverse effects with no defined threshold concentration are regarded as critical.
[2]

critical end-point
Toxic effect used by the USEPA as the basis for a *reference dose*.

critical group
Part of a *target* population most in need of protection because it is most *susceptible* to a given *toxicant*.

critical organ (in toxicology)
Organ that first attains the *critical concentration* of a substance and exhibits the *critical effect* under specified circumstances of *exposure* and for a given population.
After [2]

critical organ concentration (of a substance)
Mean *concentration* of a substance in the *critical organ* at the time the substance reaches its *critical concentration* in the most sensitive type of cell in the organ.
[2]

critical period (of development)
Stage of development of an organism (e.g., organogenesis in the fetus) that is of particular importance in the life cycle if the normal full development of some anatomical, physiological, metabolic, or psychological structure or function is to be attained.

critical study
pivotal study
Investigation yielding the *no-observed-adverse-effect-level* that is used by the USEPA as the basis of the *reference dose*.

cross-product ratio
See *odds ratio.*

cross-sectional study (of disease *prevalence* and associations)
disease frequency survey
prevalence study
Study that examines the relationship between diseases (or other *health*-related characteristics) and other variables of interest as they exist in a defined population at one particular time.

Note: Disease *prevalence* rather than *incidence* is normally recorded in a cross-sectional study and the temporal sequence of cause and effect cannot necessarily be determined.

cumulative death rate
Proportion of a defined group that dies within the specified time period (e.g., month, year).

Note: It may refer to all deaths or to deaths from a specific cause or *specific* causes.

cumulative effect
Overall change that occurs after repeated *doses* of a substance or radiation.
[2]

cumulative incidence
incidence proportion
Number or proportion of individuals in a group who experience the onset of a *health*-related event during a specified time interval.

Note: This interval is generally the same for all members of the group, but, as in lifetime *incidence*, it may vary from person to person without reference to age.

cumulative incidence rate
Proportion of the *cumulative incidence* to the total population.
[2]

cumulative incidence ratio
Value obtained by dividing the *cumulative incidence rate* in the *exposed* population by the cumulative incidence rate in the unexposed population.

cumulative median lethal dose
Estimate of the total administered amount of a substance that is associated with the death of half a population of animals when the substance is administered repeatedly in doses which are generally fractions of the *median lethal dose*.

cumulative risk
1. Probability of a common harmful effect associated with concurrent *exposure* by all relevant pathways and routes of exposure to a group of substances that share a common chemical mechanism of toxicity.
2. Total probability of a harmful effect over time.

cutaneous
dermal
Pertaining to the skin.

cyanogenic
Describing any compound able to produce cyanide.

Note: An example is amygdalin, found in peach and apricot stones.

cyanosis
Bluish coloration, especially of the skin and mucous membranes and fingernail beds, caused by abnormally large amounts of reduced *hemoglobin* in the blood vessels as a result of deficient oxygenation.

cyanotoxin
Toxin produced by Cyanobacteria, sometimes called blue–green algae.

Note: Examples are microcystin and cylindrospermin.

cyclooxygenase specific inhibitors
Substances, such as aspirin and ibuprofen, that block the activity of cyclooxygenase (COX), an *enzyme* that is responsible for the formation of prostanoids (including prostaglandins, prostacyclin, and thromboxane); inhibition of COX can provide relief from *inflammation* and pain.

cytochromes
Conjugated proteins containing heme as the *prosthetic group* and associated with electron transport and with redox processes.
[2]

cytochrome P420
Inactive derivative of cytochrome P450 found in microsomal (see *microsome*) preparations.

cytochrome P448
Obsolete term for *cytochrome P450* I, A1, and A2, one of the major families of the cytochromes P450 hemoproteins.

Note: During the monooxygenation of certain substances, often a *detoxification* process, these iso-enzymes may produce intermediates which can initiate *mutations*, *cancer*, *immunotoxic* reactions, and *adverse effects*.

cytochrome P450 (CYP)
Member of a superfamily of heme-containing monooxygenases involved in *xenobiotic metabolism*, cholesterol biosynthesis, and steroidogenesis, in eukaryotic organisms found mainly in the *endoplasmic reticulum* and inner mitochondrial membrane of cells. "P450" refers to the observation that a solution of this enzyme exposed to carbon monoxide strongly absorbs light at a wavelength of 450 nm compared with the unexposed solution (a difference spectrum caused by a thiolate in the axial position of the heme opposite to the carbon monoxide ligand).
After [2]

cytogenetics
Branch of genetics that correlates the structure and number of *chromosome*s as seen in isolated cells with variation in *genotype* and *phenotype*.

cytokine
Any of a group of soluble proteins that are released by a cell causing a change in function or development of the same cell (autocrine), an adjacent cell (paracrine), or a distant cell (endocrine). Cytokines

are involved in reproduction, growth, and development; normal homeostatic regulation; response to injury and repair; blood clotting; and host resistance (immunity and tolerance).

cytoplasm
Fundamental substance or matrix of the cell (within the *plasma* membrane) which surrounds the nucleus, *endoplasmic reticulum*, *mitochondria*, and other *organelles*.

cytotoxic
Causing damage to cell structure or function.

death rate
Estimate of the proportion of a population that dies during a specified period. The numerator is the number of persons dying during the period; the denominator is the size of the population, usually estimated as the mid-year population. The death rate in a population is generally calculated by the formula:

10^n (number of deaths during a specified period)/(number of persons at *risk* of dying during the period)

where n is usually either 3 or 5 giving rates per 1000 or per 100 000 people in the population studied.

Note 1: This rate is an estimate of the person-time death rate, the death rate per 10^n person-years: usually $n = 3$. If the rate is low, it is also a good estimate of the *cumulative death rate*.

Note 2: This term is sometimes described as the crude death rate.

decipol
Unit of perceived air quality: air on mountains or the sea has a decipol = 0.01; city air with moderate air pollution has a decipol = 0.05–0.03; acceptable indoor air quality has decipol = 1.4 (for 80 % satisfaction).

decompensation
Explicit pathophysiological changes following compensation for *adverse effects*.

decontamination
Process of rendering harmless (by neutralization, *elimination*, removal, etc.) a potentially *toxic* substance in the natural environment, laboratory areas, the workplace, other indoor areas, clothes, food, water, sewage, etc.

defoliant
Substance used for removal of leaves by its *toxic* action on living plants.

dehydrogenase
Enzyme that catalyzes oxidation of compounds by removing hydrogen.

delayed effect
latent effect
Consequence occurring after a *latent period* following the end of *exposure* to a *toxic* substance or other harmful environmental factor.

***de minimis* risk**
See *risk de minimis.*

denaturation
1. Addition of methanol, acetone, or other suitable chemical(s) to alcohol to make it unfit for drinking.
2. Change in molecular structure of proteins so that they cannot function normally, often caused by splitting of hydrogen bonds following *exposure* to reactive substances or heat.

denitrification
Reduction of nitrates to nitrites, nitrogen oxides, or dinitrogen (N_2) catalyzed by facultative *aerobic* soil bacteria under *anaerobic* conditions.

dental fluorosis
Tooth enamel malformations due to excessive fluoride *exposure* during dental development.

deoxyribonucleic acid (DNA)
Constituent of *chromosome*s that stores the hereditary information of an organism in the form of a sequence of purine and pyrimidine bases: this information relates to the synthesis of proteins, and hence it is a determinant of all physical and functional activities of the cell, and consequently of the whole organism.

deoxyribonucleic acid (DNA) **cloning**
Replication of *DNA* sequences ligated into a suitable *vector* in an appropriate host organism.
See *deoxyribonucleic acid.*
[9]

deoxyribonucleic acid (DNA) **repair**
Restoration of the molecular structure of *DNA* after it has been damaged by a chemical or physical agent: This may involve direct DNA damage reversal, base excision repair, nucleotide excision repair, mismatch repair, or double-strand break repair

deoxyribonucleic acid (DNA) **sequencing**
Determining the order of base pairs in a *DNA* molecule.
See *deoxyribonucleic acid.*
After [9]

dependence
1. A psychic craving for a *drug* or other substance that may or may not be accompanied by a physical dependency.
2. Reliance on a drug or other substance to maintain *health*.

depilatory
Substance causing loss of hair.

deposition
1. Process by which a substance arrives at a particular organ or tissue site, for example, the deposition of particles on the ciliated epithelium of the bronchial airways.
2. Process by which a substance sediments out of the atmosphere or water and settles in a certain place.

dermal
cutaneous
Pertaining to the skin.

dermal irritation
Skin reaction resulting from a single or multiple *exposure* to a physical or chemical entity at the same site, characterized by the presence of *inflammation*; it may result in cell death.

dermatitis
Inflammation of the skin: contact dermatitis is due to local *exposure* and may be caused by irritation, allergy, or infection.

descriptive epidemiology
Study of the occurrence of disease or other *health*-related characteristics in populations, including general observations concerning the relationship of disease to basic characteristics such as age, sex, race, occupation, and social class; it may also be concerned with geographic location. The major characteristics in descriptive epidemiology can be classified under the headings: individuals, time, and place.

desensitization
Suppression of sensitivity of an organism to an allergen to which the organism has been *exposed* previously.

desiccant
1. Drying agent.
2. In agriculture, a substance used for drying up plants and facilitating their mechanical harvesting.

desorption
Decrease in the amount of adsorbed substance; opposite of *adsorption*.

desquamation
Shedding of an outer layer of skin in scales or shreds.

deterministic
Term applied to *health* effects, the severity of which varies with the dose and for which a *threshold* is believed to exist.

deterministic effect
deterministic process
Phenomenon committed to a particular outcome determined by fundamental physical principles.
See also *stochastic effect.*
[2]

detoxification
detoxication
1. Process, or processes, of chemical modification that make a *toxic* molecule less toxic.
2. Treatment of patients suffering from poisoning in such a way as to promote physiological processes which reduce the probability or severity of *adverse effects*.

detriment
Estimated measure of the expected harm or loss associated with an *adverse event*, usually in a manner chosen to facilitate meaningful addition over different events. It is generally the integrated product of arbitrary values of *risk* and *hazard* and is often expressed in terms such as costs in U.S. dollars, loss in expected years of life or loss in productivity, and is needed for numerical exercises such as cost–benefit analysis.

developmental toxicity
*Adverse effect*s on the developing organism (including structural abnormality, altered growth, or functional deficiency or death) resulting from *exposure* through conception, gestation (including organogenesis), and postnatally up to the time of sexual maturation.

diaphoresis
Profuse perspiration.

diaphoretic
sudorific
Substance that causes sweating.

diarrheal shellfish poisoning (DSP)**, diarrhetic shellfish poisoning** (DSP)
Serious illness that is a consequence of consumption of bivalve shellfish (mollusks) such as mussels, oysters, and clams that have ingested, by filter feeding, large quantities of microalgae containing a group of high-molecular-weight polyethers such as okadaic acid, dinophysis toxins, pectenotoxins, and yessotoxin; *gastroenteritis* develops shortly after ingestion and generally lasts 1–2 days.

diffusion
Spontaneous differential movement of components in a system.

Note: In molecular terms, the driving force for diffusion is random thermal motion. In thermodynamic terms, the driving force is a gradient of chemical potential.

[2]

diffusion coefficient, D
Proportionality constant D, relating the *flux* (flux density) of amount of entities B, $J_{n,\mathrm{B}}$, to their *concentration* gradient

$$J_n = -D \operatorname{grad} c_{\mathrm{B}}$$

After [2]

dimercaprol
2,3-dimercaptopropan-1-ol
See *2,3-bis(sulfanyl)propan-1-ol*.

diploid
Chromosome state in which the chromosomes are present in homologous pairs.

Note: Normal human somatic (nonreproductive) cells are diploid (they have 46 chromosomes), whereas reproductive cells, with 23 chromosomes, are haploid.

discharge
See *emission.*

discharge standard
discharge release limit
effluent standard
emission standard
Maximum amount of a *pollutant* released from a given source to a specified medium which is acceptable under specified circumstances.

discontinuous effect
See *intermittent effect.*

discordance (genetic)
Antonym: *concordance*
Any difference in a character between individuals due to genetic differences such as may occur in dizygotic twins, or between matched pairs in a *case cohort study*.

disease
Literally, dis-ease, lack of ease; pathological condition that presents a group of symptoms peculiar to it and which establishes the condition as an abnormal entity different from other normal or pathological body states.

discontinuous effect
See *intermittent effect.*

dispersion (in environmental chemistry)
Dilution of a *pollutant* by spreading in the atmosphere or water due to diffusion or turbulent action.

disposition
1. Natural tendency shown by an individual or group of individuals, including any tendency to acquisition of specific diseases, often due to hereditary factors.
2. Total of the processes of *absorption* of a chemical into the circulatory systems, *distribution* throughout the body, *biotransformation*, and *excretion*.

[2]

dissipation
Reduction in the amount of a *pesticide* or other compound that has been applied to plants, soil, etc. (used when it is not clear whether this is by mineralization degradation, binding, or leaching).

distributed source
See *area source.*

distribution
1. Apportionment of a solute between two phases. The terms "partition" or "extraction" may also be used in this sense where appropriate.

[2]
2. Dispersal of a substance and its derivatives throughout the natural environment or throughout an organism.

[2]
3. Final location(s) of a substance within an organism after dispersal.

distribution constant
See *partition ratio.*

distribution volume
Theoretical volume of a body *compartment* throughout which a substance is calculated to be distributed.
[2]

2,3-disulfanyl-1-propanol
See *2,3-bis(sulfanyl)propan-1-ol.*

diuresis
Excretion of urine, especially in excess.

diuretic
micturitic
Agent that increases urine production.

DNA
See *deoxyribonucleic acid*.

DNA adduct
See *adduct.*

DNA amplification
See *gene amplification, deoxyribonucleic acid.*

DNA cloning
See *deoxyribonucleic acid cloning.*

DNA repair
See *deoxyribonucleic acid repair.*

DNA sequencing
See *deoxyribonucleic acid sequencing.*

dominant
Allele that expresses its phenotypic effect when present in either the homozygous or the heterozygous state.
After [9]

dominant half life
Half life of a fraction of a substance in a specific organ or *compartment* if it defines approximately the overall *clearance* rate for that substance at a specific time point.
[2]

dominant lethal mutation
Genetic change occurring in a germ cell that does not cause dysfunction of the gamete but which is lethal to the fertilized egg or developing embryo which develops from it.

Note: Induction of a dominant lethal event after *exposure* to a chemical substance (dominant lethal test) indicates that the substance has affected germinal tissue of the test species.

dosage
Dose divided by product of mass of organism and time of dose.

Note: Often expressed as mg (kg body weight)$^{-1}$ day^{-1} and may be used as a synonym for dose.

[2]

dose (of a substance)
Total amount of a substance administered to, taken up, or absorbed by an organism, organ, or tissue.
[2]

dose (of radiation)
Energy or amount of photons absorbed by an irradiated object during a specified *exposure* time divided by area or volume.
[2]

dose–effect
Relation between *dose* and the magnitude of a measured biological change.
[2]

dose–effect curve
Graph of the relation between *dose* and the magnitude of the biological change produced measured in appropriate units.

dose–effect relationship
Association between *dose* and the resulting magnitude of a continuously graded change, either in an individual or in a population.
[2]

dose–response curve
Graph of the relation between *dose* and the proportion of individuals in a population responding with a defined biological effect.
[2]

dose–response relationship
Association between *dose* and the *incidence* of a defined biological effect in an *exposed* population usually expressed as percentage.
[2]

Draize test
Evaluation of materials for their potential to cause dermal or ocular irritation and corrosion following local *exposure*; generally using the rabbit model (almost exclusively the New Zealand White) although other animal species have been used.

drug
medicine
pharmaceutical
Any substance that when absorbed into a living organism may modify one or more of its functions.

Note: The term is generally accepted for a substance taken for a therapeutic purpose, but is also commonly used for abused substances.

duplicate portion sampling method (diet/food)
duplicate diet study
Study in which test persons consume their ordinary diet but, for each meal, they prepare for subsequent analysis a duplicate portion of all food as prepared, served, and consumed.

duplicate samples
Two *sample*s taken under the same or comparable conditions.
See *replicate sampling*.

dysarthria
Imperfect articulation of speech due to neuromuscular damage.

dysfunction
Abnormal, impaired, or incomplete functioning of an organism, organ, tissue, or cell.

dysplasia
Abnormal development of an organ or tissue identified by morphological examination.

dyspnea
Difficult or labored breathing: shortness of breath.

ecogenetics
Study of the influence of hereditary factors on the effects of *xenobiotics* on individual organisms.

ecology
Branch of biology that studies the interactions between living organisms and all factors (including other organisms) in their environment: such interactions encompass environmental factors that determine the distributions of living organisms.

ecosystem
Grouping of organisms (microorganisms, plants, animals) interacting together, with, and through their physical and chemical environments, to form a functional entity within a defined environment.

ecotoxicologically relevant concentration (ERC)
environmentally relevant concentration (ERC)
Concentration of a *pesticide* (active ingredient, formulations, and relevant metabolites) that is likely to affect a determinable ecological characteristic of an exposed system.
After [9]

ecotoxicology
Study of the *toxic* effects of chemical and physical agents on all living organisms, especially on populations and communities within defined *ecosystems*; it includes transfer pathways of these agents and their interactions with the environment.

ectohormone
See *pheromone.*

ectoparasiticide
Substance intended to kill parasites living on the exterior of the host.

eczema
Acute or chronic skin *inflammation* with *erythema*, papules, vesicles, pustules, scales, crusts, or scabs, alone or in combination, of varied *etiology*.

edema
oedema
Presence of abnormally large amounts of fluid in intercellular spaces of body tissues.

effect biomarker
See *biomarker of effect.*

effective concentration (EC)
Concentration of a substance that causes a defined magnitude of *response* in a given system.

Note: EC_{50} is the median concentration that causes 50 % of maximal response.

effective dose (ED)
Dose of a substance that causes a defined magnitude of *response* in a given system.

Note: ED_{50} is the median dose that causes 50 % of maximal response.

effluent
Fluid, solid, or gas discharged from a given source into the external environment.

element (in molecular biology)
Sequence in the promoter region of a *gene* that regulates expression of that *gene* through interaction with a trans-acting factor.

elimination (in toxicology)
Disappearance of a substance from an organism or a part thereof, by processes of *metabolism*, *secretion*, or *excretion*.
[2]
See also *clearance.*

elimination half life or half time
Period taken for the *plasma concentration* of a substance to decrease by half.

Note: May also be applied to other body compartments such as blood, specific organs, or tissues.

elimination rate
Differential with respect to time of the *concentration* or amount of a substance in the body, or a part thereof, resulting from *elimination*.
[2]

eliminator (of a poison)
Substance that contributes to the *elimination* of a poison from an organism.

embryo
1. Stage in the developing mammal at which the characteristic organs and organ systems are being formed: for humans, this involves the stages of development from the second to the eighth week postconception (inclusive).
2. In birds, the stage of development from the fertilization of the ovum up to hatching.
3. In plants, the stage of development within the seed.

embryonic period
Period from fertilization to the end of major organogenesis.
[8]

embryotoxicity
1. Production by a substance of *toxic* effects in progeny in the first period of pregnancy between conception and the fetal stage.
2. Any *toxic* effect on the conceptus as a result of prenatal *exposure* during the embryonic stages of development: These effects may include malformations and variations, malfunctions, altered growth, prenatal death, and altered postnatal function.

embryotropic effect
Change in the *embryo* and the regulation of its development.

emesis
Vomiting.

emission
discharge
effluent
release
Release of a substance from a source, including discharges to the wider environment.

emission and exposure control
Technical and administrative procedures and specifications applied for the monitoring, reduction, or *elimination* of *emissions* from a source or *exposure* to a target.

emission standard
Quantitative limit on the *emission* or discharge of a substance from a source, usually expressed in terms of a time-weighted average *concentration* or a *ceiling value*.

endemic
Present in a community or among a group of people; said of a disease prevailing continually in a region.

endocon
Portion of a conjugated metabolite that is derived from a natural product (such as a sugar, amino acid, or other organic acid) of the metabolizing organism.
See also *exocon*, *phase II reaction*.
After [6]

endocrine
Pertaining to *hormones* or to the glands that secrete hormones directly into the bloodstream.

endocrine disrupter
endocrine modifier
Exogenous chemical that alters function(s) of the endocrine system and consequently causes *adverse* health *effects* in an intact organism, its progeny, or (sub)populations.
[8]

endocrine modifier
See *endocrine disrupter.*

endocytosis
Uptake of material into a cell by invagination of the *plasma* membrane and its internalization in a membrane-bounded vesicle.
[2]
See also *phagocytosis*, *pinocytosis.*

endogenous
Antonym: *exogenous*
Produced within or caused by factors within an organism.
[2]

endoplasmic reticulum
Intracellular complex of membranes in which proteins and lipids, as well as molecules for export, are synthesized and in which the *biotransformation* reactions of the monooxygenase enzyme systems occur.

Note: May be isolated as *microsomes* following cell fractionation procedures.

endothelial
Pertaining to the layer of flat cells lining the inner surface of blood and lymphatic vessels, and the surface lining of serous and synovial membranes.

endothelium
Layer of flattened epithelial cells lining the heart, blood vessels, and lymphatic vessels.
[2]

endotoxin
Toxin that forms an integral part of the cell wall of certain bacteria and is released only upon breakdown of the bacterial cell; endotoxins do not form toxoids.

enteritis
Intestinal *inflammation*.

enterohepatic circulation
Cyclical process involving intestinal re*absorption* of a substance that has been excreted through the bile, followed by transfer back to the liver, making it available for biliary *excretion* again.

environment
Aggregate, at a given moment, of all external conditions and influences to which a system under study is subjected.

environmental damage
*Adverse effect*s to the natural environment.

environmental exposure level (EEL)
Level (*concentration* or amount or a time integral of either) of a substance to which an organism or other component of the environment is *exposed* in its natural surroundings.

environmental fate
Destiny of a chemical or biological *pollutant* after release into the natural environment.

environmental health
Human welfare and its influence by the environment, including technical and administrative measures for improving the human environment from a *health* point of view.

environmental health impact assessment
Estimate of the *adverse effects* to *health* or *risk*s likely to follow from a proposed or expected environmental change or development.

environmental health criteria documents
Critical publications of IPCS containing reviews of methodologies and existing knowledge—expressed, if possible, in quantitative terms—of selected substances (or groups of substances) on identifiable, immediate, and long-term effects on human *health* and welfare.

environmental hygiene
environmental sanitation
Practical control measures used to improve the basic environmental conditions affecting human *health*, for example, clean water supply, human and animal *waste* disposal, protection of food from biological contamination, and housing conditions, all of which are concerned with the quality of the human environment.

environmental impact assessment (EIA)
Appraisal of the possible environmental consequences of a past, ongoing, or planned action, resulting in the production of an environmental impact statement or "finding of no significant impact (FONSI)".

environmental impact statement (EIS)
Report resulting from an *environmental impact assessment*.

environmental medicine
Specialty devoted to the prevention and management of environmentally induced injury, illness, and disability, and the promotion of the health of individuals, families, and communities by ensuring a healthy environment.

environmental monitoring
Continuous or repeated measurement of agents in the environment to evaluate environmental *exposure* and possible damage by comparison with appropriate reference values based on knowledge of the probable relationship between ambient exposure and resultant *adverse effect*s.

environmental protection
1. Actions taken to prevent or minimize *adverse effect*s to the natural environment.
2. Complex of measures including monitoring of environmental *pollution*, development and practice of environmental protection principles (legal, technical, and hygienic), including *risk assessment*, *risk management*, and *risk communication*.

environmental quality objective (EQO)
Overall state to be aimed for in a particular aspect of the natural environment, for example, "water in an estuary such that shellfish populations survive in good *health*".

Note: Unlike an environmental quality standard, the EQO is usually expressed in qualitative and not quantitative terms.

environmental quality standard (EQS)
ambient standard
Amount *concentration* or mass concentration of a substance that should not be exceeded in an environmental system, often expressed as a *time-weighted average* measurement over a defined period.

environmental risk assessment
Estimate of the probability that harm will result from a defined *exposure* to a substance in an environmental medium. The estimate is valid only for a given species and set of conditions.

environmental sanitation
See *environmental hygiene.*

environmental tobacco smoke (ETS)
See *sidestream smoke.*

environmental transformation
Chemical transformation of substances resulting from interactions in the environment.

environmentally relevant concentration
See *ecotoxicologically relevant concentration.*

enzootic
Present in a community or among a group of animals; said of a disease prevailing continually in a region.

enzyme
Biological catalyst: a protein, nucleic acid, or a conjugate of a protein with another compound (coenzyme).

enzyme induction
Process whereby an enzyme is synthesized in response to a specific substance or to other agents such as heat or a metal species.
[2]

epidemiology
Study of the distribution and determinants of *health*-related states or events in specified populations and the application of this study to control of health problems.

epigastric
Pertaining to the upper-middle region of the abdomen.

epigene/sis n., -tic adj.
Phenotypic change in an organism brought about by alteration in the expression of genetic information without any change in the genomic sequence itself.

Note: Common examples include changes in nucleotide base methylation and changes in histone acetylation. Changes of this type may become heritable.

epigenetic
See *epigene/sis, -tic.*

epileptiform
Occurring in severe or sudden spasms, as in convulsion or epilepsy.

epithelioma
Any tumor derived from *epithelium*.

epithelium
Sheet of one or more layers of cells covering the internal and external surfaces of the body and hollow organs.
[2]

epitope
Any part of a molecule that acts as an antigenic determinant: A macromolecule can contain many different epitopes, each capable of stimulating production of a different specific *antibody*.

equilibrium
State of a system in which the defining variables (temperature, pressure, chemical potential) have constant values in time.
[2]

equivalent diameter (of a particle)
Diameter of a spherical particle of the same density as a particle under investigation that, relative to a given phenomenon or property, would behave in the same way as the particle under investigation.

erythema
Redness of the skin produced by congestion of the capillaries.

eschar
Slough or dry scab on an area of skin that has been burnt.

estimated daily intake (EDI)
Prediction of the daily *intake* of a residue of a potentially harmful agent based on the most realistic estimation of the residue levels in food and the best available food consumption data for a specific population: Residue levels are estimated taking into account known uses of the agent, the range of contaminated commodities, the proportion of a commodity treated, and the quantity of home-grown or imported commodities.

Note: The EDI is expressed in mg residue per person.

estimated environmental concentration (EEC)
Predicted *concentration* of a substance, typically a *pesticide*, within an environmental *compartment* based on estimates of quantities released, discharge patterns, and inherent disposition of the substance (fate and distribution) as well as the nature of the specific receiving *ecosystems*.
See also *expected environmental concentration.*
After [9]

estimated exposure concentration (EEC)
Measured or calculated amount or mass *concentration* of a substance to which an organism is likely to be *exposed*, considering *exposure* by all sources and routes.

estimated exposure dose (EED)
Measured or calculated *dose* of a substance to which an organism is likely to be *exposed*, considering *exposure* by all sources and routes.

estimated maximum daily intake (EMDI)
Prediction of the maximum daily intake of a residue of a potentially harmful agent based on assumptions of average food consumption per person and maximum residues in the edible portion of a commodity, corrected for the reduction or increase in residues resulting from preparation, cooking, or commercial processing.

Note: The EMDI is expressed in mg residue per person.

etiology
aetiology
1. Science dealing with the cause or origin of *disease*.
2. In individuals, the cause or origin of disease.

eukaryote
Antonym: *prokaryote*
Cell or organism with the genetic material packed in a membrane-surrounded structurally discrete nucleus and with well-developed cell organelles.

Note: The term includes all organisms except archaebacteria, eubacteria, and cyanobacteria (until recently classified as cyanophyta or blue–green algae).

European Inventory of Existing Chemical Substances (EINECS)
List of all substances supplied either singly or as components in preparations to persons in a Member State of the European Community on any occasion between 1 January 1971 and 18 September 1981.

eutrophic
Describes a body of water with a high *concentration* of nutrient salts and a high or excessive rate of biological production.

eutrophication
Adverse change in the chemical and biological status of a body of water following depletion of the oxygen content caused by decay of organic matter resulting from high primary production as a result of enhanced input of nutrients.

excess lifetime risk
Additional or excess *risk* incurred over the lifetime of an individual by *exposure* to a *toxic* substance.

excess rate
See *rate difference.*

exchange transfusion
Method of active artificial *elimination* of *toxicity* consisting in complete replacement of blood of the patient by donor blood.

excipient
Any largely inert substance added to a *drug* to give suitable consistency or form to the drug.

excitotoxicity
Pathological process by which neurons are damaged and killed by the overactivation of *receptors* for the excitatory neurotransmitter glutamate, such as the *N*-methyl-D-aspartic acid (NMDA) receptor and α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) receptor.

Note: Excitotoxins like NMDA and kainic acid bind to glutamate t receptors, and can cause excitotoxicity by allowing high levels of calcium ions to enter cells, activating enzymes such as phospholipases, endonucleases, and proteases such as calpain which damage cell structures including the cytoskeleton, membranes, and *DNA*.

excretion
Discharge or *elimination* of an absorbed or *endogenous* substance, or of a *waste* product, and (or) its *metabolites*, through some tissue of the body and its appearance in urine, feces, or other products normally leaving the body.

Note: Excretion does not include the passing of a substance through the intestines without *absorption*.

[2]
See also *clearance*, *elimination.*

excretion rate
Amount of substance and (or) its *metabolite*s that is excreted divided by time of excretion.
[2]

exocon
Portion of a conjugated metabolite that is derived from the parent molecule.
[6]

exogenous
Antonym: *endogenous*
Resulting from causes or derived from materials external to an organism.

exogenous substance
See *xenobiotic.*

exon
Coding section of a *gene* that is separated from other coding sequences of the same gene by intervening noncoding sequences.
See *intron.*

exothelium
Layer of flattened epithelial cells external to an organ or tissue.

expected environmental concentration (EEC)
expected exposure concentration (EEC)
Calculated *concentrations* of a substance, typically a *pesticide*, in various environmental compartments based on calculations using maximum-*exposure* scenarios.

Note: EEC models assume a maximum number of applications per growing season at the maximum rate of application according to the application methods stated on the product label.

After [10]

expected exposure concentration (EEC)
See *expected environmental concentration*.

experimental model ecosystem
See *microcosm.*

explant
Living tissue removed from its normal environment and transferred to an artificial medium for growth.

exponential decay
Variation of a quantity according to the law

$$A = A_0 e^{-\lambda t}$$

where A and A_0 are the values of the quantity being considered at time t and zero, respectively, and λ is an appropriate constant.
[2]

exposed
Antonyms: non-exposed, unexposed
Subject to a factor that is under study in the environment, for instance, an environmental *hazard*.

exposed group (sometimes abbreviated to **exposed**) (in epidemiology)
People (or other organisms) who have been *exposed* to a supposed cause of a disease or *health* state of interest, or possess a characteristic that is a determinant of the health outcome of interest.

exposure
1. *Concentration*, amount, or intensity of a particular physical or chemical agent or environmental agent that reaches the *target population*, organism, organ, tissue, or cell, usually expressed in numerical terms of concentration, duration, and frequency (for chemical agents and microorganisms) or intensity (for physical agents).
2. Process by which a substance becomes available for *absorption* by the target population, organism, organ, tissue, or cell, by any route.

3. For X- or gamma radiation in air, the sum of the electrical charges of all the ions of one sign produced when all electrons liberated by photons in a suitably small element of volume of air completely stopped, divided by the mass of the air in the volume element.

[2]

exposure assessment
Process of measuring or estimating *concentration* (or intensity), duration, and frequency of *exposure*s to an agent present in the environment or, if estimating hypothetical exposures, that might arise from the release of a substance, or radionuclide, into the environment.

exposure biomarker
See *biomarker of exposure.*

exposure control
See *emission and exposure control.*

exposure–effect curve
See *concentration–effect curve.*

exposure limit
General term defining an administrative substance *concentration* or intensity of *exposure* that should not be exceeded.

exposure ratio
In a *case control study*, value obtained by dividing the rate at which persons in the case group are *exposed* to a *risk* factor (or to a protective factor) by the *rate* at which persons in the control group are exposed to the risk factor (or to the protective factor) of interest.

exposure–response relationship
See *concentration–response relationship*, *dose–response relationship.*

exposure surface
Surface on a *target* where a substance (e.g., a *pesticide*) is present. With mammals, 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 gastrointestinal tract, the respiratory tract, and the urinary tract lining.

[12]

exposure test
Determination of the level, *concentration*, or *uptake* of a potentially *toxic* compound and (or) its *metabolite*(s) in biological *sample*s from an organism (blood, urine, hair, etc.) and the interpretation of the results to estimate the absorbed *dose* or degree of environmental *pollution*; or the measuring of biochemical effects, usually not direct *adverse effect*s of the substance, and relating them to the quantity of substance absorbed, or to its concentration in the environment.

expressed sequence tag (EST)
Partial or full complementary *DNA* sequence that can serve as a marker for a region of the *genome* which encodes an expressed product.
[9]

expression (in genetics)
Conversion of the genetic information encoded in *DNA* into a final gene product (either a protein or any of the different types of RNA).

Note: Because changes in *RNA* synthesis are often estimated by measuring mRNA levels, the term "gene expression" is often misleadingly used as synonymous with transcription. The term "gene expression" includes transcription, processing, and splicing of mRNA, as well as translation, and post-translational modification of the protein product.

external validity
Generalizability of the results of a particular study, beyond the limits of the population actually studied.

extracellular space
Volume within a tissue, outside cells, and excluding vascular and lymphatic space.
[2]

extracellular volume
Volume of fluid outside the cells but within the outer surface of an organism.
[2]

extraction ratio
Amount of substance extracted from a source divided by the total contained within the source.
[2]

extra risk
Probability that an agent produces an observed *response*, as distinguished from the probability that the response is caused by a spontaneous event unrelated to the agent.

extraneous residue limit (ERL)
Refers to a *pesticide* residue or contaminant arising from environmental sources (including former agricultural uses) other than the use of a pesticide or contaminant substance directly or indirectly on the commodity. It is the maximum *concentration* of a pesticide residue or contaminant that is recommended by the *Codex Alimentarius Commission* to be legally permitted or recognized as acceptable in or on food, agricultural commodity, or animal feed.

Note: The mass content is expressed in milligrams of pesticide residue or contaminant per kilogram of commodity.

extrapolation
Calculation, based on quantitative observations in *exposed* test species or in vitro test systems, of predicted *dose–effect* and *dose–response relationships* for a substance in humans and other biota including interspecies extrapolations and extrapolation to susceptible groups of individuals.

Note: The term may also be used for qualitative information applied to species or conditions that are different from the ones in which the original investigations were carried out.

extrapyramidal movement disorders
Involuntary movement disorders mediated by signaling through neurons outside the pyramidal (corticospinal) tract, often describing side effects of psychiatric medications.

fecundity
1. Ability to produce offspring frequently and in large numbers.
2. In demography, the physiological ability to reproduce.
3. Ability to produce offspring within a given period of time.

[8]

feromone
ectohormone
pheromone
Substance used in olfactory communication between organisms of the same species eliciting a change in sexual or social behavior.

fertility
Ability to conceive and to produce offspring: For litter-bearing species, the number of offspring per litter is used as a measure of fertility.

Note: Reduced fertility is sometimes referred to as subfertility.

fertility toxicant
Produces abnormalities of male or female reproductive functions or impairs reproductive capacity.

fertilizer
Substance applied to soil or hydroponic systems for improving the root nutrition of plants with the aim of increasing crop yields and (or) controlling production.

fetal period
See *fetus.*

fetotoxicity
Toxicity to the *fetus*.

fetus (often incorrectly foetus)
Young mammal within the uterus of the mother from the visible completion of characteristic organogenesis until birth.

Note: In humans, this period is usually defined as from the third month after fertilization until birth (prior to this, the young mammal is referred to as an embryo).

fibrosis
Abnormal formation of fibrous tissue.

fiducial limit
Form of confidence limit given as a stated probability, for example, $P = 0.95$.

Note: In toxicology, the terms "fiducial limits" and "confidence limits" are generally considered to be synonymous.

finding of no significant impact (FONSI)
Statement prepared and issued to the public when the results of an environmental impact assessment identify no harmful effects of concern.
See *environmental impact assessment*.

first-order chemical reaction
first-order reaction
1. Chemical reaction where the initial rate is directly proportional to the *concentration* of one of the reactants.

[2]
2. Any process in which a variable decreases with time at a constant fractional amount.

[2]

first-pass effect
Biotransformation and, in some cases, *elimination* of a substance in the liver after *absorption* from the intestine and before it reaches the *systemic* circulation.
[2]

first-pass metabolism
See *first-pass effect.*

fixed dose procedure
Acute *toxicity* test in which a substance is tested initially at a small number (3 or 4) predefined *dose*s to identify which produces evident toxicity without lethality: The test may be repeated at one or more higher or lower defined discriminating doses to satisfy the criteria.

fluoridosis
See *fluorosis.*

fluorosis
fluoridosis
*Adverse effect*s of fluoride, as in dental or skeletal fluorosis.

flux (of a quantity)
Flow rate of an entity through a cross-section perpendicular to the flow divided by the cross-sectional area.

foci (singular **focus**) **in neoplasia**
Small groups of cells distinguishable, in appearance or histochemically, from the surrounding tissue: indicative of an early stage of a lesion that may lead to the formation of a neoplastic nodule.

foetus
See *fetus.*

follow-up study
See *cohort study.*

food additive
Any substance, not normally consumed as a food by itself and not normally used as a typical ingredient of a given food, whether or not it has nutritive value, that is added intentionally to food for a technological (including organoleptic) purpose in the manufacture, processing, preparation, treatment, packing, packaging, transport, or holding of the food. Addition results, or may be reasonably expected to result (directly or indirectly), in the substance or its byproducts becoming a component of, or otherwise affecting, the characteristics of the food to which it is added.

Note: The term does not include "contaminants" or substances added to food for maintaining or improving nutritional qualities.

food allergy
Hypersensitivity reaction to substances in the diet to which an individual has previously been sensitized.

food chain
Sequence of transfer of matter and energy in the form of food from organism to organism in ascending or descending *trophic levels*.

food intolerance
Physiologically based reproducible, unpleasant (adverse) reaction to a specific food or food ingredient that is not immunologically based.

food web
Network of *food chains*.

forced diuresis
Method of stimulating diuresis based on performing hydrational therapy, sometimes with parallel introduction of diuretics, with the aim of achieving increased clearance of a *toxic* substance in urine.

foreign substance
See *xenobiotic.*

founder effect
Changes in allelic frequencies that occur when a small group is separated from a large population and establishes a colony in a new location.
[9]

fractionation
Process of classification of an analyte or a group of analytes from a *sample* according to physical (e.g., size, solubility) or chemical (e.g., bonding, reactivity) properties.
[2]

frame-shift mutation
Point *mutation* involving either the deletion or insertion of one or two nucleotides in a *gene*: By the frame shift mutation, the normal reading frame used when decoding nucleotide triplets in the gene is altered.

fumigant
Substance that is vaporized in order to kill or repel pests.

functional genomics
Development and implementation of technologies to characterize the mechanisms through which *gene*s and their products function and interact with each other and with the environment.
[9]

fungicide
Substance intended to kill fungi.

fungus preparation
Substance obtained from fungi that has an insecticidal effect reflecting the pathogenicity of the fungi for insects.

gamete
Reproductive cell (either sperm or egg) containing a haploid set of *chromosome*s.

gametocide
Substance intended to kill *gametes*.

gastroenteritis
Inflammation of the stomach and intestine.

gastrointestinal
Pertaining to or communicating with the stomach and intestine.

gavage
Administration of materials directly into the stomach by esophageal intubation.

gene
Length of *DNA* or *RNA* (in viruses) that encodes a functional product, which may be a polypeptide or a ribonucleic acid.

Note: A gene is the fundamental unit of heredity.

After [9]

gene amplification
Occurrence of extra copies of a *gene*; with respect to a plasmid, an increase in the number of plasmid copies per cell, which may be induced by a specific treatment.

Note: Spontaneous gene amplification frequently occurs in tumor cells.

gene expression
Transcriptional activation of a *gene* so that its functional product is produced.

gene therapy
Introduction of genetic material into an individual, or the modification of the individual's genetic material, in order to achieve a therapeutic or prophylactic objective.
After [9]

genetic epidemiology
Study of the correlations between phenotypic trends and genetic variation across population groups and the application of the results of such a study to control of health problems.

gene map
Map showing the positions in the *genome* of *gene*s or other genetic markers, either relative to each other or as a physical map of absolute distances.

generally regarded as safe (GRAS)
Phrase used to describe the USFDA philosophy that justifies approval of food additives that may not meet the usual test criteria for *safety* but have been used extensively and have not demonstrated that they cause any harm to consumers.

genetically modified organism (GMO)
Bacterium, plant, or animal whose *DNA* has been deliberately altered.

genetic polymorphism
Existence of inter-individual differences in *DNA* sequences coding for one specific *gene*, giving rise to different functional and (or) morphological traits.
After [2]

genetic susceptibility
Predisposition to a particular *disease* or sensitivity to a substance due to the presence of a specific allele or combination of *alleles* in an individual's *genome*.
After [9]

genetic toxicology
Study of chemically or physically induced changes to the structure of *DNA*, including *epigenetic* phenomena or *mutations* that may or may not be heritable.

genome
Complete set of chromosomal and extrachromosomal *genes* of an organism, a cell, an organelle, or a virus, i.e., the complete *DNA* component of an organism (or the complete *RNA* component of an RNA virus).

Note: This includes both the DNA present in the chromosomes and that in subcellular organelles (e.g., mitochondria or chloroplasts).

[2]

genomics
1. Science of using *DNA*- and *RNA*-based technologies to demonstrate alterations in *gene* expression.
2. (in toxicology) Method providing information on the consequences for gene expression of interactions of the organism with environmental stress, *xenobiotics*, etc.

[2]

genotoxic
Capable of causing a change to the structure of the *genome.*

genotype
Genetic constitution of an organism as revealed by genetic or molecular analysis; the complete set of *gene*s possessed by a particular organism, cell, organelle, or virus.

germ-free animal
axenic animal
Animal grown under sterile conditions in the period of postnatal development: Such animals are usually obtained by Caesarean operation and kept in special sterile boxes in which there are no viable microorganisms (sterile air, food, and water are supplied).

germ-line cell
Cell with a haploid *chromosome* content.

Note: In animals, the germ-line cells are the sperm or egg (synonym *gamete*); in plants, the pollen cell or the ovum.

After [9]

germinal aplasia
Complete failure of gonad development.

germ warfare
See *biological warfare.*

glomerular
Pertaining to a tuft or cluster, as of a plexus of capillary blood vessels or nerve fibers, especially referring to the capillaries of the glomerular of the kidney.

glomerulus
Tuft or a cluster, as of a plexus of capillary blood vessels or nerve fibers (e.g., capillaries of the filtration apparatus of the kidney).

glomerular filtration
Formation of an ultrafiltrate of the blood occurring in the *glomerulus* of the kidney.
[2]

glomerular filtration rate
Volume of ultrafiltrate formed in the kidney tubules from the blood passing through the glomerular capillaries divided by time of filtration.
[2]

glue-sniffing
Inhalation of solvent vapor from plastic cements or other adhesives in order to become intoxicated.
See also *solvent abuse*.

glycobiology
See *glycomics.*

glycome
Description of the complete set of carbohydrates and their functions in a living organism.

glycomics
glycobiology
Global study of the structure and function of carbohydrates, especially oligosaccharides (short chains of sugars) in a living organism.

gnotobiont
See *gnotobiote.*

gnotobiota
Specifically and entirely known microfauna and microflora of a specially reared laboratory animal.

gnotobiot/e n., **-ic** adj.
gnotobiont
Specially reared laboratory animal whose microflora and microfauna are specifically known in their entirety.

goiter
Noncancerous enlargement of the thyroid gland, visible as a swelling at the front of the neck, that is often associated with iodine deficiency.

goitrogen
Any substance (such as thiouracil) that induces the formation of a goiter.

gonadotropic
Pertaining to effects on sex glands and on the systems that regulate them.

good agricultural practice (GAP) **in the use of pesticides**
Nationally authorized safe uses of *pesticides* under actual conditions necessary for effective and reliable pest control.

Note: It encompasses a range of levels of pesticide applications up to the highest authorized use, applied in a manner that leaves a residue which is the smallest amount practicable. Authorized safe uses include nationally registered or recommended uses, that take into account public and occupational *health* and environmental safety considerations. Actual conditions include any stage in the production, storage, transport, distribution, and processing of food commodities and animal feed.

good laboratory practice (GLP) **principles**
Fundamental rules incorporated in OECD guidelines and national regulations concerned with the process of effective organization and the conditions under which laboratory studies are properly planned, performed, monitored, recorded, and reported.

good manufacturing practice (GMP) **principles**
Fundamental rules incorporated in national regulations concerned with the process of effective organization of production and ensuring standards of defined quality at all stages of production, distribution, and marketing.

Note: Minimization of *waste* and its proper disposal are part of this process.

graded effect
Antonyms: *all-or-none effect*, *quantal effect*, *stochastic effect*
Consequence that can be measured on a graded scale of intensity or severity and its magnitude related directly to the *dose* or *concentration* of the substance producing it.

graminicide
Pesticide (herbicide) used for the control of weedy grasses (*Gramineae*).
[6]

granuloma
Granular growth or *tumor*, usually of lymphoid and epithelial cells.

ground treatment of plants
Dusting or spraying of plants with *pesticides* by hand, by special machines, or by apparatus fixed to tractors or driven by them.

guideline for exposure limits
Scientifically judged quantitative value (a *concentration* or number) of an environmental constituent that ensures aesthetically pleasing air, water, or food and from which no *adverse effect* is expected concerning noncarcinogenic endpoints, or that gives an acceptably low estimate of lifetime *cancer risk* from those substances which are proven human *carcinogens* or carcinogens with at least limited evidence of human *carcinogenicity*.

guideline value
Quantitative measure (a *concentration* or a number) of a constituent of an environmental medium that ensures aesthetically pleasing air, water, or food and does not result in a significant *risk* to the user.

guides to air quality
Sets of atmospheric *concentration*s and *exposure* times that are associated with specific effects of varying degrees of *pollution* on humans, animals, vegetation, and the environment in general.

guides to environmental quality
Sets of *concentration*s, numbers and *exposure* times that are associated with the specific effects of factors in environmental media on humans, animals, vegetation, and the environment in general.

guinea-pig maximization test
Magnusson and Kligman test
Widely used skin test for screening possible contact *allergens*: considered to be a useful method to identify likely moderate and strong *sensitizers* in humans.

haem
See *heme.*

half life, $t_{1/2}$
half time
Time required for the *concentration* of a reactant in a given reaction to reach a value that is the arithmetic mean of its initial and final (equilibrium) values. For a reactant that is entirely consumed, it is the time taken for the reactant concentration to fall to one-half of its initial value.

Note: The half life of a reaction has meaning only in special cases:

1. For a first-order reaction, the half life of the reactant may be called the half life of the reaction.
2. For a reaction involving more than one reactant, with the *concentration*s of the reactants in their stoichiometric ratios, the half life of each reactant is the same, and may be called the half life of the reaction.

If the concentrations of reactants are not in their stoichiometric ratios, there are different half lives for different reactants, and one cannot speak of the half life of the reaction.
See also *biological half life*, *elimination half life.*
[2]

half time, $t_{1/2}$
See *half life.*

haploid
monoploid
State in which a cell contains only one set of *chromosome*s.

haplotype
1. Contraction of the phrase "haploid genotype", the genetic constitution of an individual with respect to one member of a pair of allelic *genes*: Haplotype can refer to only one locus or to an entire genome (a *genome*-wide haplotype would comprise half of a diploid genome, including one allele from each allelic gene pair).
2. Set of *single nucleotide polymorphisms* found to be statistically associated on a single chromatid.

hapten
Low-molecular-mass *species* which is not itself antigenic unless complexed with a carrier, such as a protein. Once bound, it presents an *epitope* that can cause the *sensitization* of *lymphocytes*.
After [1]

harm
adverse effect
Damage or *adverse effect* to a population, species, individual organism, organ, tissue, or cell.

harmful occupational factor
Component of the work environment, the effect of which on a worker under certain conditions leads to ill *health* or reduction of working ability.

harmful substance
noxious substance
Substance that, following contact with an organism, can cause ill *health* or *adverse effect*s either at the time of *exposure* or later in the life of the present and future generations.

hazard
Set of inherent properties of a substance, mixture of substances, or a process involving substances that, under production, usage, or disposal conditions, make it capable of causing *adverse effect*s to organisms or the environment, depending on the degree of *exposure*; in other words, it is a source of danger.
See also *risk.*

hazard assessment
Determination of factors controlling the likely effects of a *hazard* such as the *dose–effect* and *dose–response relationships*, variations in *target* susceptibility, and mechanism of *toxicity*.

hazard communication standard
U.S. OSHA standard requiring all employers to inform employees of the *hazard* of substances in the workplace and the steps necessary to avoid harm.

hazard evaluation
Establishment of a qualitative or quantitative relationship between *hazard* and benefit, involving the complex process of determining the significance of the identified hazard and balancing this against identifiable benefit.

Note: This may subsequently be developed into a *risk* evaluation.

hazard identification
Determination of substances of concern, their *adverse effect*s, *target* populations, and conditions of *exposure*, taking into account *toxicity* data and knowledge of effects on human *health*, other organisms, and their environment.

hazard index (HI)
Sum of the *hazard* quotients for substances that affect the same target organ or organ system.

Note: Ideally, hazard quotients should be combined for pollutants that cause *adverse effects* by the same mechanism. Aggregate exposures below a hazard index of 1.0 were unlikely to result in adverse health effects over a lifetime of *exposure*. A hazard index greater than 1.0 does not necessarily suggest a likelihood of adverse effects. The hazard index cannot be translated to a probability that adverse effects will occur, and is not likely to be proportional to risk.

hazard quotient (HQ)
Ratio of *toxicant exposure* (estimated or measured) to a reference value regarded as corresponding to a threshold of *toxicity*.

Note: If the *hazard* quotient exceeds unity, the toxicant may produce an *adverse effect*, but normally this will require a hazard quotient of several times unity; a hazard quotient of less than 1.0 indicates that no adverse effects are likely over a lifetime of exposure.

hazardous production factor
hazard at work
hazardous occupational factor
Production factor the effect of which on a worker under certain conditions results in injury or some impairment of *health*.

health
1. State of complete physical, mental, and social well-being, and not merely the absence of *disease* or infirmity.
2. State of dynamic balance in which an individual's or a group's capacity to cope with the circumstances of living is at an optimal level.
3. State characterized by anatomical, physiological, and psychological integrity; ability to perform personally valued family, work, and community roles; ability to deal with physical, biological, psychological, and social stress; a feeling of well-being; and freedom from the *risk* of disease and untimely death.
4. In ecology, a sustainable steady state in which humans and other living organisms can coexist indefinitely.

health advisory level (HAL)
In the United States, nonregulatory health-based reference level of chemical traces (usually in ppm, i.e., mg L^{-1}) in drinking water at which there are no adverse health *risks* when ingested over various periods of time.

Note: Such levels are established for 1 day, 10 days, long-term and life-time *exposure* periods. They allow for a wide margin of safety.

health-based exposure limit
Maximum *concentration* or intensity of *exposure* that can be tolerated without significant effect (based on only scientific and not economic evidence concerning exposure levels and associated *health* effects).

health hazard
Any factor or *exposure* that may adversely affect *health*.

health surveillance
Periodic medico-physiological examinations of *exposed* workers with the objective of protecting *health* and preventing occupationally related disease.

healthy worker effect
Epidemiological phenomenon observed initially in studies of occupational *diseases*: Workers usually exhibit lower overall disease and death rates than the general population, due to the fact that the old, severely ill, and disabled are ordinarily excluded from employment. Death rates in the general population may be inappropriate for comparison, if this effect is not taken into account.

heat shock proteins
stress proteins
Group of proteins whose synthesis is increased by increased transcription when cells are exposed to elevated temperatures.

Note: Production of high levels of heat shock proteins can also be triggered by *exposure* to different kinds of environmental stress conditions, for example, infection, *inflammation*, exposure of the cell to chemicals (such as ethanol, arsenicals, or certain metal species), ultraviolet light, starvation, hypoxia (oxygen deprivation), nitrogen deficiency (in plants), or water deprivation. Hence, the alternative name, stress proteins. Their upregulation is sometimes described more generally as part of the stress response.

heavy metal
toxic metal
Erroneous terms used commonly in the toxicological literature but having no generally agreed meaning, sometimes even applied to nonmetals, and therefore a source of confusion and to be avoided. The term "metal" is adequate without the qualifying adjective but may be misleading since it implies a solid material when toxicological concern is mostly for the ionic form or another chemical species.

helminthagogue
See *anthelmint(h)ic.*

helminthic
See *anthelmint(h)ic*.

hematemesis
Vomiting of blood.

hematoma
Localized accumulation of blood, usually clotted, in an organ, space, or tissue, due to a failure of the wall of a blood vessel.

hematotoxicity
Adverse changes in blood caused by *exposure* to chemicals.

hematuria
Presence of blood in the urine.

heme
haem
Complex consisting of an iron ion coordinated to a *porphyrin* acting as a tetradentate ligand, and to one or two axial ligands.
After [3]

hemochromatosis
Hereditary disorder affecting iron metabolism in which excessive amounts of iron accumulate in the body tissues.

Note: The disorder is characterized by diabetes mellitus, liver dysfunction, and a bronze pigmentation of the skin.

hemodialysis
Use of an artificial kidney to remove *toxic* compounds from the blood by passing it through a tube of semipermeable membrane.

Note: The tube is bathed in a dialyzing solution to restore the normal chemical composition of the blood while permitting diffusion of toxic substances from the blood.

hemoglobin
Heme-containing protein in red blood cells with an important function in transporting oxygen from the lungs to body tissues.

hemoglobinuria
Presence of free *hemoglobin* in the urine.

hemolysin
Substance that damages the membrane of erythrocytes causing the release of *hemoglobin*.

hemolysis
Release of *hemoglobin* from erythrocytes, and its appearance in the *plasma*.

hemoperfusion
Passing blood through a column of charcoal or adsorbent resin for the removal of *drug*s or *toxins*.

hemosiderin
Insoluble iron(III) hydroxide-based pigment deposited in cells in conditions of iron overload.

Henderson–Hasselbalch equation
Equation of the form:

$$pH = pK_a - \lg([HA]/[A^-])$$

for the calculation of the pH of solutions where the ratio $[HA]/[A^-]$ is known and HA and A^- are the hydronated and dehydronated forms of an acid, respectively.
Corrected from [3]

hepatic
Pertaining to the liver.

hepatotoxic
Poisonous to liver cells.

Henry's law constant
At constant temperature and pressure, the ratio of the partial pressure of a gas above a liquid to its solubility in the liquid and therefore a measure of its partition between the gas phase and the solute phase.

Note 1: The solubility may be expressed in any convenient units, such as amount fraction, molality, or amount (substance) concentration. The exact definition used should always be given.

Note 2: Rigorously, the Henry's law constant is the limiting value at zero partial pressure.

[13]

herbicide
Substance intended to kill plants.

heterozygote
Organism that has different allelic forms of a specified *gene* on each of a pair of homologous *chromosomes* or describing the *genome* of that organism.
After [9]

Hill plot
Graphical method for analyzing binding of a molecule A to a macromolecule P with n binding sites. A Hill plot of $\lg[\theta/(1-\theta)]$ vs. $\lg[A]$ has a slope of 1 if binding is noncooperative and >1 for cooperative binding, where $\theta = [A]_{bound}/n[P]_{total}$ is the fraction of sites occupied.
[2]

histamine
2-(1H-imidazol-4-yl)ethan-1-amine, an amine derived from histidine by decarboxylation and released from cells in the *immune system* as part of an allergic reaction: It is a powerful stimulant of gastric secretion, constrictor of bronchial smooth muscle, and vasodilator.

histogenic origin
Germ cell layer of the *embryo* from which a given adult tissue develops.

histology
Study (usually microscopic) of the anatomy of tissues and their cellular and subcellular structure.

histopathology
Microscopic pathological study of the anatomy and cell structure of tissues in disease to reveal abnormal or adverse structural changes.

hit-and-run effect
Toxicity that follows a single *exposure* to a substance.

homeostasis
Normal, internal stability in an organism maintained by coordinated responses of the organ systems that automatically compensate for environmental changes.

homology (in biology)
1. Similarity of anatomical structures in different species because of shared ancestry
2. Similarity of *DNA* or *RNA* nucleotide sequences, or of protein amino-acid sequences, supporting the hypothesis that they share a common ancestor.

   Note: Homology among DNA or RNA nucleotide sequences, or among protein amino-acid sequences, is often concluded on the basis of sequence similarity. In general, if there are almost identical sequences, it is likely that they are homologous. However, it is possible that highly similar sequences were not derived from a common ancestor, i.e., they are similar but not homologous.

homozygote
Organism that has the same allelic form of a specified *gene* on each of a pair of homologous chromosomes or describing the genome of that organism.
After [9]

horme/sis n., **-tic** adj.
Benefit at low dose of a substance that is harmful at a higher dose.

hormone
Substance formed in one organ or part of the body and carried in the blood to another organ or part where it selectively alters functional activity.

human ecology
Interrelationship between humans and the entire environment—physical, biological, socioeconomic, and cultural, including the interrelationships between individual humans or groups of humans and other human groups or groups of other species.

human equivalent dose
Human *dose* of an agent that is believed to induce the same magnitude of a *toxic* effect that the known animal dose has induced.

human exposure threshold (of toxicological concern)
Generic value of *exposure* to a substance, or a group of substances falling within a defined structural class, below which there is expected to be no appreciable risk to human health.

hydrolysis
Chemical reaction of a substance with water, usually resulting in the formation of one or more derivatives.

hydrophilic/ adj., **-ity** n.
lipophobic
Antonym: *hydrophobic*
Describing the character of a substance, material, molecular entity, or group of atoms which has an affinity for water.

hydrophobic/ adj., **-ity** n.
lipophilic
Antonym: *hydrophilic*
Describing the character of a substance, material, molecular entity, or group of atoms which is insoluble or confers insolubility in water, or resistance to wetting or hydration.

hygiene
Science of *health* and its preservation.

hyper-
Antonym: *hypo-*
Prefix meaning above or excessive: when used with the suffix "-emia" refers to blood and with the suffix "-uria" refers to urine, for example, "hyperbilirubinemia".

hyperemia
Excessive amount of blood in any part of the body.

hyperalimentation
Ingestion or administration of nutrients in excess of optimal amounts.

hyperbilirubinemia
Excessive *concentration* of bilirubin in the blood.

hypercalcemia
Excessive *concentration* of calcium in the blood.

hyperglycemia
Excessive *concentration* of glucose in the blood.

hyperkalemia
Excessive *concentration* of potassium in the blood.

hypernatremia
Excessive *concentration* of sodium in the blood.

hyperparathyroidism
Abnormally increased parathyroid gland activity that affects, and is affected by, *plasma* calcium *concentration*.

hyperplasia
Abnormal multiplication or increase in the number of normal cells in a tissue or organ.

hyper-reactivity
Term used to describe the responses of (effects on) an individual to (of) an agent when they are qualitatively those expected, but quantitatively increased.

hyper-reflexia
Exaggeration of reflexes.

hypersensitivity
State in which an individual reacts with *allergic* effects following *exposure* to a certain substance (*allergen*) after having been *exposed* previously to the same substance.

Note: Most common chemical-induced allergies are type I (IgE-mediated) and type IV (cell-mediated) hypersensitivity.

hypersusceptibility
Excessive reaction following *exposure* to a given amount or *concentration* of a substance as compared with the large majority of other *exposed* subjects.

hypertension
Persistently high blood pressure in the arteries or in a circuit, for example, pulmonary hypertension or hepatic portal hypertension.

hypertrophy
Excessive growth in bulk of a tissue or organ through increase in size but not in number of the constituent cells.

hypervitaminosis
Condition resulting from the ingestion of an excess of one or more vitamins.

hypo-
Prefix meaning under, deficient: when used with the suffix "-emia" refers to blood and with the suffix "-uria" refers to urine, for example, "hypocalcemia".

hypocalcemia
Abnormally low calcium *concentration* in the blood.

hypokalemia
Abnormally low potassium *concentration* in the blood.

hypomagnesemia
Abnormally low magnesium *concentration* in the blood.

hyponatremia
Abnormally low sodium *concentration* in the blood.

hypovolemic
Pertaining to an abnormally decreased volume of circulating fluid (*plasma*) in the body.

hypoxemia
Deficient oxygenation of the blood.

hypoxia
1. Abnormally low dioxygen content or tension.
2. Deficiency of dioxygen in the inspired air, in blood, or in tissues, short of anoxia.

hypoxic
Dioxygen-deficient.

iatrogenic
Any adverse condition resulting from medical treatment.

icterus
Excess of bile pigment in the blood and consequent deposition and retention of bile pigment in the skin and the sclera.

idiopathic environmental intolerance
See *multiple chemical sensitivity.*

idiosyncrasy
Genetically based unusually high sensitivity of an organism to the effect of certain substances.

immediately-dangerous-to-life-or-health-concentration (IDLHC)
According to the U.S. NIOSH, the maximum *exposure concentration* from which one could escape within 30 min without any escape-impairing symptoms or any irreversible *health* effects.

immission
Environmental *concentration* of a *pollutant* resulting from a combination of *emission*s and dispersals (often synonymous with *exposure*).

immune complex
Product of an *antigen–antibody* reaction that may also contain components of the complement system.

immune response
Selective reaction of the body to substances that are foreign to it, or that the *immune system* identifies as foreign, shown by the production of antibodies and *antibody*-bearing cells or by a cell-mediated *hypersensitivity* reaction.

immune system
Integrated network of organs, glands, and tissues that has evolved to protect the body from foreign substances, including bacteria, viruses, and other infection-causing parasites and pathogens.

Note: The immune system may produce hypersensitivity reactions reactions which, in the extreme, can be fatal. If the immune system misidentifies normal body components as foreign, this leads to autoimmune disorders, such as lupus, in which the body destroys its own constituents.

immunoassay
Ligand-binding assay that uses a specific antigen or antibody, capable of binding to the analyte, to identify and quantify substances. The antibody can be linked to a radioisotope (radioimmunoassay, RIA) or to an enzyme which catalyzes an easily monitored reaction (enzyme-linked immunosorbent assay, ELISA), or to a highly fluorescent compound by which the location of an antigen can be visualized (immunofluorescence).
[3]

immunochemistry
Study of biochemical and molecular aspects of immunology, especially the nature of *antibodies*, *antigens*, and their interactions.

immunogen
See *antigen.*

immunoglobulin
Family of closely related glycoproteins capable of acting as antibodies and present in *plasma* and tissue fluids; immunoglobulin E (IgE) is the source of *antibody* in type I *hypersensitivity* (*allergic*) reactions.

immunoglobulin E-mediated hypersensitivity
State in which an individual reacts with allergic effects caused fundamentally by the reaction of *antigen*-specific *immunoglobulin* E following *exposure* to a certain substance (*allergen*) after having been *exposed* previously to the same substance.

immunomodulation
Modification of the functioning of the *immune system* by the action of a substance that increases or reduces the ability to produce *antibodies*.

immunopotentiation
Enhancement of the capacity of the *immune system* to produce an effective response.

immunosuppression
Reduction in the functional capacity of the *immune response*; may be due to:
1. Inhibition of the normal response of the *immune system* to an *antigen*.
2. Prevention, by chemical or biological means, of the production of an *antibody* to an antigen by inhibition of the processes of transcription, translation, or formation of tertiary structure.

immunosurveillance
Mechanisms by which the *immune system* is able to recognize and destroy *malignant* cells before the formation of an overt *tumor*.

immunotoxic
Harmful to the *immune system*.

impermeable
Of a membrane, not allowing a given substance to pass through. When applied to nonbiological membranes with no qualification, the term normally refers to water.

implantation
Attachment of the fertilized ovum (blastocyst) to the endometrium and its subsequent embedding in the compact layer, occurring 6 or 7 days after fertilization of the ovum.
[8]

in silico
Phrase applied to data generated and analyzed using computer modeling and information technology.

in vitro
Antonym: *in vivo*
In glass, referring to a study in the laboratory usually involving isolated organ, tissue, cell, or biochemical systems.

in vivo
Antonym: *in vitro*
In the living body, referring to a study performed on a living organism.

incidence
Number of occurrences of illness commencing, or of persons falling ill, during a given period in a specific population: usually expressed as a rate.

Note: When expressed as a rate, it is the number of ill persons divided by the average number of persons in the specified population during a defined period, or alternatively divided by the estimated number of persons at the mid-point of that period.

[2]

incidence rate (epidemiology)
Measure of the frequency at which new events occur in a population.

Note: This is the value obtained by dividing the number of new events that occur in a defined period by the population at *risk* of experiencing the event during this period, sometimes expressed as person-time.

incremental unit risk estimate
For an air pollutant, this is the additional lifetime *cancer risk* occurring in a hypothetical population in which all individuals are *exposed* continuously from birth throughout their lifetimes to a *concentration* of 1 microgram per cubic meter ($\mu g\ m^{-3}$) of the pollutant in the air they breathe.

indication
Quantity value provided by a measuring instrument or a measuring system.
[7]

indirect exposure
1. *Exposure* to a substance in a medium or vehicle other than the one originally receiving the substance.
2. Exposure of people to a substance by contact with a person directly *exposed*.

individual monitor
See *personal sampler.*

individual protective device (IPD)
personal protective device (PPD)
personal protective equipment (PPE)
Device for individual use for protection of the whole body, eyes, respiratory pathways, or skin of workers against hazardous and harmful production factors.

individual risk
Probability that an individual person will experience an *adverse effect*.

inducer
Substance that causes *induction*.

induction
Increase in the rate of synthesis of an *enzyme* in response to the action of an *inducer* or environmental conditions.

Note: Often the inducer is the substrate of the induced enzyme or a structurally similar substance (gratuitous inducer) that is not metabolized.

induction period
latent period
Time from the onset of *exposure* to the appearance of signs of *disease*.

industrial hygiene
See *occupational hygiene.*

inert chemical
Substance that is not generally reactive.

inert ingredient
Any intentionally added ingredient of a mixture that does not contribute to the desired biological effect: This definition does not include impurities and does not imply that the inert ingredient has no biological effects.
Related term: *active ingredient*

infertility (in human medicine)
Inability to become pregnant within 1 year of unprotected intercourse.
[8]

inflammation
Reaction of the body to injury or to infectious, allergic, or chemical irritation; characterized by redness, swelling, heat, and pain resulting from dilation of the blood vessels accompanied by loss of *plasma* and leucocytes (white blood cells) into the tissues.

infusion (in physiology)
Therapeutic introduction of a fluid other than blood, as a (usually saline) solution, into a vein. [2]

ingestion
1. Process of taking food and drink into the body by mouth.
2. Process of taking in particles by a phagocytic cell.

inhalation
Act of drawing in of air, vapor, or gas and any suspended *particulates* into the lung.

inherently biodegradable
Class of compounds for which there is unequivocal evidence of *biodegradation* (primary or ultimate) in any test of biodegradability.

inhibitory concentration (IC)
Concentration of a substance that causes a defined inhibition of a given system.

Note: IC_{50} is the median concentration that causes 50 % inhibition.

inhibitory dose (ID)
Dose of a substance that causes a defined inhibition of a given system.

Note: ID_{50} is the median dose that causes 50 % inhibition.

initiator
1. Agent that induces a change in a *chromosome* or *gene* that leads to the induction of *tumors* after a second agent, called a *promoter*, is administered to the tissue.
2. Substance that starts a chain reaction

Note: An initiator is consumed in a chain reaction, in contrast to a catalyst.

insecticide
Substance intended to kill insects.

intake
Amount of a substance that is taken into the body, regardless of whether or not it is absorbed: The total daily intake is the sum of the daily intake by an individual from food, drinking-water, and inhaled air.

integral indicator of toxic effect
Parameter (such as body weight or temperature) characterizing the overall changes in the general state of the organism *exposed* to a *toxic* substance.

interactome
Large-scale protein–protein interaction map.

interfacial layer
Inhomogeneous space region intermediate between two bulk phases in contact, and where properties are significantly different from, but related to, the properties of the bulk phases.
[2]

intermittent effect
discontinuous effect
Biological change that comes and goes at intervals.

internal dose
See *absorbed dose.*

internal validity
Selection and comparison of index and comparison groups in such a manner that, apart from *sampling error*, the observed differences between these groups with respect to dependent variables under study may be attributed only to the hypothesized effect under investigation.

interpolation
Estimation of a value between two known data points.

interpretation (of data or findings)
Evaluation of the observations from an investigation or study in order to determine their significance for human *health*, for the environment or for both.

interspecies dose conversion
Process of extrapolating from the doses of one animal species to another, for example, from rodent dose to human equivalent.

interstitial fluid
Aqueous solution filling the narrow spaces between cells.
[2]

interstitial pneumonia
Chronic form of pneumonia involving increase of the interstitial tissue and decrease of the functional lung tissue.

intervention study
Epidemiological investigation designed to test a hypothesized cause–effect relationship by intentional change of a supposed causal factor in a population.

intestinal reabsorption
Absorption further down the intestinal tract of a substance or substances that have been absorbed before and subsequently excreted into the intestinal tract, usually through the bile.

intoxication

1. Poisoning: pathological process with clinical signs and symptoms caused by a substance of *exogenous* or *endogenous* origin.
2. Drunkenness following consumption of beverages containing ethanol or other compounds affecting the central nervous system.

intrinsic activity

Maximal stimulatory effect induced by a compound in relation to that of a given reference compound.
[2]

intrinsic clearance

Volume of *plasma* or blood from which a substance is completely removed in a period of time under unstressed conditions.
[2]

intrinsic factor (in biochemistry)

Specific protein required for the absorption of vitamin B_{12} and secreted by cells in the gastric glands of the stomach.
[2]

intron

Noncoding sequence within *gene*s that separates the exons (coding regions).

Note: Introns are spliced out of the m*RNA* molecule created from a *gene* after transcription and prior to translation.

After [9]

ionizing radiation

Any radiation consisting of directly or indirectly ionizing particles or a mixture of both or photons with energy higher than the energy of photons of ultraviolet light or a mixture of both such particles and photons.

irreversible alteration

Change from normal structure or function that persists or progresses after cessation of *exposure* of the organism.

irritant

1. n., Substance that causes *inflammation* following immediate, prolonged, or repeated contact with skin, mucous membrane, or other biological material.

   Note: A substance capable of causing inflammation on first contact is called a primary irritant.

2. adj., Causing inflammation following immediate, prolonged, or repeated contact with skin, mucous membrane, or other tissues.

ischemia
Local deficiency of blood supply and hence oxygen to an organ or tissue owing to constriction of the blood vessels or to obstruction.

isotonic
Denoting a liquid exerting the same osmotic pressure or chemical potential of water (*water potential*) as another liquid with which it is being compared.

itai-itai disease
Illness (renal osteomalacia) observed in the Toyama prefecture of Japan, resulting from the ingestion of cadmium-contaminated rice.

Note: Damage occurred to the *renal* and skeleto-articular systems, the latter being very painful ("itai" means "ouch" in Japanese and refers to the intense pain caused by the condition).

jaundice
Pathological condition characterized by deposition of bile pigment in the skin and mucous membranes, including the conjunctivae, resulting in yellow appearance of the patient or animal.

joint effect
Simultaneous or successive effect of factors of diverse types (chemical, physical, biological) on an organism.

kairomone
Semiochemical that is produced by one organism inducing a response in an organism of another species that is unfavorable to the emitter.
Related terms: *allomone*, *synomone*

kinetics (in chemistry)
Branch of chemistry concerned with measuring and studying rates of chemical reactions.
[2]

ketone bodies
Acetoacetate, beta-hydroxybutyrate, and acetone, produced from acetyl-CoA, mainly in the mitochondria of liver cells when carbohydrates are so scarce that energy must be obtained from breaking down fatty acids; beta-hydroxybutyrate is not itself a ketone, but is called a ketone body because, like the other compounds, it is produced from ketones.

ketosis
Pathological increase in the production of *ketone bodies*, for example, following blockage or failure of carbohydrate metabolism.

kinetics (in toxicology)
See *toxicokinetics.*

knock-down
Technique used to decrease the expression of a particular *gene* in a cell or living organism in order to define its function.

knock-in
Technique used to express an *exogenous gene* or to overexpress an *endogenous* gene in a living organism in order to define its function.

Note: In mammalian toxicology, this technique is most readily applied to the mouse.

knock-out (in biology)
Technique used to inactivate a particular *gene* in a living organism in order to define its function.

Note: In mammalian toxicology, this technique is most readily applied to the mouse.

After [9]

lachrymation
See *lacrimation.*

lacrimation
Secretion and discharge of tears.

lachrymator
See *lacrimator.*

lacrimator
Substance that irritates the eyes and causes the production of tears or increases the flow of tears.

larvicide
Substance intended to kill larvae.

laryngospasm
Reflex spasmodic closure of the sphincter of the *larynx*, particularly the glottic sphincter.

larynx
Main organ of voice production, the part of the respiratory tract between the *pharynx* and the trachea.

lassitude
Weakness; exhaustion.

latency
See *latent period.*

latent effect
See *delayed effect.*

latent period
1. Delay between *exposure* to a harmful substance and the manifestations of a *disease* or other *adverse effect*s.
2. Period from disease initiation to disease detection.

[2]

lavage
Irrigation or washing out of a hollow organ or cavity such as the stomach, intestines, or lungs.

laxative
cathartic
purgative
Substance that causes evacuation of the intestinal contents.

lead colic (painters' colic)
Chronic intestinal pains and constipation caused by lead poisoning.

lesion
1. Area of pathologically altered tissue.
2. Injury or wound.
3. Infected patch of skin.

lethal
Deadly; fatal; causing death.

lethal concentration (LC)
Concentration of a substance in an environmental medium that causes death following a certain period of *exposure*.

lethal dose (LD)
Amount of a substance or physical agent (e.g., radiation) that causes death when taken into the body.

lethal synthesis
Metabolic formation of a highly *toxic* compound often leading to death of affected cells.

leukemia
Progressive, *malignant* disease of the blood-forming organs, characterized by distorted proliferation and development of leucocytes and their precursors in the bone marrow and blood.

leukopenia
Reduced *concentration* of leukocytes in the blood.

lgP_{ow}
lgK_{ow}
Logarithm to the base 10 of the partition coefficient of a substance between octan-1-ol and water.

Note: This is used as an empirical measure for lipophilicity in calculating *bioaccumulation*, fish *toxicity*, membrane *adsorption*, and penetration, etc.

library (in DNA bioinformatics)
Collection of *DNA* sequences in a searchable electronic form.

library (in molecular biology)
Collection of genomic or complementary *DNA* sequences that have been cloned in a *vector* and grown in an appropriate host organism (e.g., bacteria, yeast).
After [9]

life-long exposure
Subjection to a potentially *toxic* substance during the whole lifetime.

ligand
Ion, molecule, or molecular group that binds to another chemical entity to form a larger complex.

limacide
Substance intended to kill mollusks including the gastropod mollusk, *Limax*.

limit recommended
See *recommended exposure limit.*

limit test
Acute *toxicity* test in which, if no ill-effects occur at a preselected maximum dose, no further testing at greater *exposure* levels is required.

limit value (LV)
Limit *concentration* at or below which Member States of the European Community must set their *environmental quality standard* and *emission standard* for a particular substance according to Community Directives.

limited evidence
According to the USEPA's Guidelines for Carcinogen *Risk* Assessment [17], "limited evidence" is a collection of facts and accepted scientific inferences that suggests that an agent may be causing an effect, but this suggestion is not strong enough to be considered established fact.

linearized multistage model
Sequence of steps in which (a) a *multistage model* is fitted to *tumor incidence* data; (b) the maximum linear term consistent with the data is calculated; (c) the low-*dose* slope of the *dose–response* function

is equated to the coefficient of the maximum linear term; and (d) the resulting slope is then equated to the upper bound of *potency*.

lipophilic/ adj., **-ity** n.
hydrophobic/ adj., -ty n.
Antonyms: *hydrophilic/ -ity*, *lipophobic/ -ity*
Having an affinity for fat and high lipid solubility.

Note: This is a physicochemical property which describes a partitioning equilibrium of solute molecules between water and an immiscible organic solvent, favoring the latter, and which correlates with *bioaccumulation*.

lipophobic/ adj., **-ity** n.
hydrophilic/ adj., -ity n.
Antonyms: *hydrophobic/* adj. *ity n., lipophilic/* adj. *ity n.*
Having a low affinity for fat and a high affinity for water.

liposome
1. Artificially formed lipid droplet, small enough to form a relatively stable suspension in aqueous media, useful in membrane transport studies and in *drug* delivery.
2. Lipid droplet in the *endoplasmic reticulum* of a fatty liver.

After [1]

local effect
Change occurring at the site of contact between an organism and a *toxicant*.

logit
In competitive binding assays, the *logit*-log *dose* relationship, in which the *response* is defined by:

$$R = \text{logit}\,(y) = \lg\,[y/(1 - y)]$$

where $y = b/b_0$ with b = fraction of tracer bound and b_0 = value of b with no unlabelled ligand in the system.

Note: Logit-transformed assay data frequently yield straight-line dose–response data, amenable to statistical analysis. More generally in toxicology, the transformation is applied to dose–response data where b_0 denotes the maximum response in the absence of a toxic substance.

[2]

log-normal distribution
Distribution function $F(y)$, in which the logarithm of a quantity is normally distributed, i.e.,

$$F(y) = f\text{gauss}(\ln y)$$

where $f\text{gauss}(x)$ is a Gaussian (or normal) *distribution*.
[3]

log-normal transformation
Transformation of data with a logarithmic function that results in a normal *distribution*.
[2]

long-term effect
See *chronic effect.*

long-term exposure
See *chronic exposure.*

long-term toxicity
See *chronic toxicity.*

lowest-effective dose (LED)
Lowest *dose* of a chemical inducing a specified effect in a specified fraction of *exposed* individuals.
[2]

lowest lethal concentration found
See *minimum lethal concentration.*

lowest-observed-adverse-effect level (LOAEL)
Lowest *concentration* or amount of a substance (*dose*), found by experiment or observation, that causes an *adverse effect* on morphology, functional capacity, growth, development, or life span of a *target* organism distinguishable from normal (control) organisms of the same species and strain under defined conditions of *exposure*.

lowest-observed-effect level (LOEL)
Lowest *concentration* or amount of a substance (*dose*), found by experiment or observation, that causes any alteration in morphology, functional capacity, growth, development, or life span of *target* organisms distinguishable from normal (control) organisms of the same species and strain under the same defined conditions of *exposure*.

lymphocyte
Animal cell that interacts with a foreign substance or organism, or one which it identifies as foreign, and initiates an immune response against the substance or organism.

Note: There are two main groups of lymphocytes, B lymphocytes and T lymphocytes.

lymphoma
General term comprising *tumors* and conditions allied to tumors arising from some or all of the cells of lymphoid tissue.

lysimeter
Laboratory column of selected representative soil or a protected monolith of undisturbed field soil with which it is possible to *sample* and monitor the movement of water and other substances.

lysosome
Membrane-bound cytoplasmic organelle containing hydrolytic enzymes.

Note: Release of these enzymes from lysosomes damaged by xenobiotics can cause autolysis of the cell.

macrophage
Large (10–20 μm diameter) amoeboid and phagocytic cell found in many tissues, especially in areas of *inflammation*, derived from blood monocytes and playing an important role in host defense mechanisms.

macroscopic (gross) **pathology**
Study of changes associated with disease that are visible to the naked eye without the need for a microscope.

Mad Hatter syndrome
See *mercurialism.*

Magnusson and Kligman test
See *guinea-pig maximization test.*

mainstream smoke (tobacco smoking)
Smoke that is inhaled by the smoker.

malaise
Vague feeling of bodily discomfort.

malignancy
Population of cells showing both uncontrolled growth and a tendency to invade and destroy other tissues.

Note: A malignancy is life-threatening.

malignant
Antonym: *benign*
1. Tending to become progressively worse and to result in death if not treated.
2. In *cancer*, cells showing both uncontrolled growth and a tendency to invade and destroy other tissues.

mania
Emotional disorder (mental illness) characterized by an expansive and elated state (euphoria), rapid speech, flight of ideas, decreased need for sleep, distractibility, grandiosity, poor judgment, and increased motor activity.

margin of exposure (MOE)
Ratio of the *no-observed-adverse-effect level* (NOAEL) to the theoretical or *estimated exposure dose* (EED) or *concentration* (EEC).

margin of safety (MOS)
See *margin of exposure.*

mass mean diameter
Diameter of a spherical particle with a mass equal to the mean mass of all the particles in a population.

mass median diameter
Diameter of a spherical particle with the median mass of all the particles in a population.

material safety data sheet (MSDS)
Compilation of information required under the U.S. OSHA *Hazard* Communication Standard on the identity of hazardous substances, *health* and physical *hazard*s, *exposure* limits, and precautions.

maximum allowable (admissible, acceptable) concentration (MAC)
Regulatory value defining the *concentration* that if inhaled daily (in the case of work people for 8 h with a working week of 40 h; in the case of the general population, 24 h) does not, in the present state of knowledge, appear capable of causing appreciable harm, however long delayed during the working life or during subsequent life or in subsequent generations.

maximum average daily concentration of an atmospheric pollutant
peak daily average concentration of an air pollutant
Highest of the average daily *concentration*s recorded at a definite point of measurement during a certain period of observation.

maximum contaminant level (MCL)
Under the Safe Drinking Water Act (USA), primary MCL is a regulatory *concentration* for drinking water which takes into account both *adverse effect*s (including sensitive populations) and technological feasibility (including natural background levels): Secondary MCL is a regulatory concentration based on "welfare", such as taste and staining, rather than *health*, but also takes into account technical feasibility.

Note: MCL Goals (MCLG) under the Safe Drinking Water Act do not consider feasibility and are zero for all human and animal *carcinogens*.

maximum exposure limit (MEL)
Occupational *exposure* limit legally defined in the United Kingdom under COSHH as the maximum *concentration* of an airborne substance, averaged over a reference period, to which employees may be *exposed* by inhalation under any circumstances, and set on the advice of the HSC Advisory Committee on *Toxic* Substances.

maximum permissible concentration (MPC)
See *maximum allowable concentration.*

maximum permissible daily dose
Maximum daily dose of substance whose penetration into a human body during a lifetime will not cause diseases or *health hazard*s that can be detected by current investigation methods and will not adversely affect future generations.

maximum permissible level (MPL)
Level, usually a combination of time and *concentration*, beyond which any *exposure* of humans to a chemical or physical agent in their immediate environment is unsafe.

maximum residue limit (MRL) **for pesticide residues**
Maximum contents of a *pesticide* residue (expressed as mg kg^{-1} fresh weight) recommended by the *Codex Alimentarius Commission* to be legally permitted in or on food commodities and animal feeds.

Note: MRLs are based on data obtained following *good agricultural practice* and foods derived from commodities that comply with the respective MRLs are intended to be toxicologically acceptable.

maximum residue limit (MRL) **for veterinary drugs**
Maximum contents of a *drug* residue (expressed as mg kg^{-1} or μg kg^{-1} fresh weight) recommended by the *Codex Alimentarius Commission* to be legally permitted or recognized as acceptable in or on food commodities and animal feeds.

Note: The MRL is based on the type and amount of residue considered to be without any toxicological *hazard* for human *health* as expressed by the acceptable daily intake (ADI) or on the basis of a temporary ADI that uses an additional uncertainty factor. It also takes into account other relevant public health *risks* as well as food technological aspects.

maximum tolerable concentration (MTC)
Highest *concentration* of a substance in an environmental medium that does not cause death of test organisms or species (denoted by LC_0).

maximum tolerable dose (MTD)
Highest amount of a substance that, when introduced into the body, does not kill test animals (denoted by LD_0).

maximum tolerable exposure level (MTEL)
Maximum amount (*dose*) or *concentration* of a substance to which an organism can be *exposed* without leading to an *adverse effect* after prolonged *exposure* time.

maximum tolerated dose (MTD)
High *dose* used in *chronic toxicity* testing that is expected on the basis of an adequate *subchronic* study to produce limited *toxicity* when administered for the duration of the test period.

Note 1: It should not induce
(a) overt toxicity, for example appreciable death of cells or organ dysfunction, or
(b) *toxic* manifestations that are predicted materially to reduce the life span of the animals except as the result of neoplastic development, or
(c) 10 % or greater retardation of body weight gain as compared with control animals.

Note 2: In some studies, toxicity that could interfere with a carcinogenic effect is specifically excluded from consideration.

maximum velocity, V_{max}
maximum rate
In *Michaelis–Menten kinetics*, the maximum rate of *conversion* of a substrate when its *concentration* is not rate-limiting.
[2]

mean life
mean time
Average lifetime of a molecular, atomic, or nuclear system in a specified state.

Note: For an exponentially decaying system, it is the average time for the number of molecules, atoms, or nuclei in a specified state to decrease by a factor of e, the base of natural logarithms.

mean residence time (in pharmacokinetics) (MRT)
Average time a *drug* molecule remains in the body or an organ after rapid intravenous injection.

Note 1: Like clearance, its value is independent of dose.

Note 2: After an intravenous bolus:

$$t_r = A_m / A$$

where t_r is the MRT, A is the area under the plasma concentration–time curve, and A_m is the area under the moment curve.

Note 3: For a drug with one-compartment distribution characteristics, MRT equals the reciprocal of the elimination rate constant.

After [2]

measurement uncertainty
See *uncertainty.*

median effective concentration (EC_{50})
Statistically derived median *concentration* of a substance in an environmental medium expected to produce a certain effect in 50 % of test organisms in a given population under a defined set of conditions.

Note: EC_n refers to the median concentration that is effective in n % of the test population.

median effective dose (ED_{50})
Statistically derived median *dose* of a chemical or physical agent (radiation) expected to produce a certain effect in 50 % of test organisms in a given population or to produce a half-maximal effect in a biological system under a defined set of conditions.

Note: ED_n refers to the median dose that is effective in n % of the test population.

median lethal concentration (LC_{50})
Statistically derived median *concentration* of a substance in an environmental medium expected to kill 50 % of organisms in a given population under a defined set of conditions.

median lethal dose (LD_{50})
Statistically derived median *dose* of a chemical or physical agent (radiation) expected to kill 50 % of organisms in a given population under a defined set of conditions.

median lethal time (TL_{50})
Statistically derived median time interval during which 50 % of a given population may be expected to die following *acute* administration of a chemical or physical agent (radiation) at a given *concentration* under a defined set of conditions.

median narcotic concentration (NC_{50})
Statistically derived median *concentration* of a substance in an environmental medium expected to cause *narcotic* conditions in 50 % of a given population under a defined set of conditions.

median narcotic dose (ND_{50})
Statistically derived dose of a substance expected to cause *narcotic* conditions in 50 % of test animals under a defined set of conditions.

medicine
1. Science and practice of diagnosing, treating, or preventing disease and other damage to the body or mind.
2. Any drug or therapy used to treat disease or injury.

   Note: Any substance may be used as a drug or a remedy; the end effect will depend on the dose.

meiosis
Process of "reductive" cell division, occurring in the production of *gametes*, by means of which each daughter nucleus receives half the number of *chromosome*s characteristic of the somatic cells of the species.
See also *miosis*.

mercurialism
Mad Hatter syndrome
Chronic poisoning caused by *exposure* to mercury, often by breathing its vapor but also by skin absorption and, less commonly, by ingestion.

Note: Central nervous system damage usually predominates.

mesocosm
See *microcosm.*

mesothelioma
Malignant *tumor* of the mesothelium of the pleura, pericardium, or peritoneum, that may be caused by *exposure* to asbestos fibers and some other fibers.

metabolic activation
bioactivation
Biotransformation of a substance to a more biologically active derivative.
[2]

metabolic enzymes
Proteins that catalyze chemical transformations of body constituents and, in more common usage, of *xenobiotics*.
[2]

metabolic half life
metabolic half time
Time required for one-half of the quantity of a substance in the body to be metabolized.

Note: This definition assumes that the final quantity in the body is zero. See *half life*.

metabolic model
Analysis and theoretical reconstruction of the way in which the body deals with a specific substance, showing the proportion of the intake that is absorbed, the proportion that is stored and in what tissues, the rate of breakdown in the body and the subsequent fate of the metabolic products, and the rate at which it is eliminated (see *elimination*) by different organs as unchanged substance or *metabolites*.

metabolic transformation
Biotransformation of a substance that takes place within a living organism.

metabolism
1. Sum total of all physical and chemical processes that take place within an organism from uptake to elimination.
2. In a narrower sense, the physical and chemical changes that take place in a substance within an organism, including *biotransformation* to *metabolites*.

metabolite
Intermediate or product resulting from *metabolism*.

metabolomics
See *metabonomics.*

metabonomics
metabolomics
Evaluation of cells, tissues, or biological fluids for changes in *metabolite* levels that follow *exposure* to a given substance, in order to determine the metabolic processes involved, to evaluate the disruption in

intermediary metabolic processes that results from *exposure* to that substance, or to determine the part of the genome that is responsible for the changes.

Note: Although "metabolomics" and "metabonomics" are frequently used as synonyms, there is a growing consensus that there is a difference in that "metabolomics" places a greater emphasis on comprehensive metabolic profiling, while "metabonomics" is used to describe multiple (but not necessarily comprehensive) metabolic changes caused by a biological perturbation.

After [2]

metaplasia
Abnormal transformation of an adult, fully differentiated tissue of one kind into a differentiated tissue of another kind.

metastasis
1. Movement of bacteria or body cells, especially *cancer* cells, from one part of the body to another, resulting in change in location of a disease or of its symptoms from one part of the body to another.
2. Growth of pathogenic microorganisms or of abnormal cells distant from the site of their origin in the body.

methaemoglobin
See *methemoglobin.*

methemoglobin
methaemoglobin
Derivative of *hemoglobin* that is formed when the iron(II) in the *heme* porphyrin is oxidized to iron(III); this derivative cannot transport dioxygen.

methemoglobinaemia
methaemoglobinaemia
Presence of methaemoglobin in the blood in greater than normal proportion.

methemoglobin-forming substance
methaemoglobin-forming substance
Substance capable of oxidizing directly or indirectly the iron(II) in *hemoglobin* to iron(III) to form methemoglobin.

Michaelis constant, K_M
Substance *concentration* of *substrate* at which the rate of reaction is equal to one-half of the limiting rate (maximum rate).

Note: Also called the *Michaelis concentration*. The Michaelis constant (Michaelis concentration) may be used only when *Michaelis–Menten kinetics* is obeyed.

[2]

Michaelis–Menten kinetics
Description of the dependence of an initial rate of reaction upon the *concentration* of a substrate S that is present in large excess over the concentration of an *enzyme* or other catalyst (or reagent) E with the appearance of saturation behavior following the Michaelis–Menten equation:

$$v = V[S]_o/(K_M + [S])$$

where v is the observed initial rate, V is its limiting value at substrate saturation (i.e., $[S] >> K_M$), and K_M the substrate concentration when $v = V/2$. The definition is experimental, i.e., it applies to any reaction that follows an equation of this general form. The symbols V_{max} or v_{max} are sometimes used for V.

Note 1: The parameters V and K_M (the "*Michaelis constant*") of the equation can be evaluated from the slope and intercept of a linear plot of $1/v$ vs. $1/[S]$ ("Lineweaver–Burk plot") or from slope and intercept of a linear plot of v vs. $v/[S]$ ("Eadie–Hofstee plot").

Note 2: A Michaelis–Menten equation is also applicable to the condition where E is present in large excess, in which case the total *concentration* $[E]_o$ appears in the equation instead of $[S]_o$.

Note 3: The term has sometimes been used to describe reactions that proceed according to the scheme:

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_{cat}} \text{Products}$$

in which case $K_M = (k_{-1} + k_{cat})/k_1$ (Briggs–Haldane conditions). It has more usually been applied only to the special case in which $k_{-1} >> k_{cat}$ and $K_M = k_{-1}/k_1 = K_S$, the dissociation constant of the complex. In this case, K_M is a true dissociation constant (Michaelis–Menten conditions).

See also *rate-controlling step*.
[3]

Michaelis–Menten mechanism
Simplest mechanism that explains *Michaelis–Menten kinetics*.

Note 1: According to the mechanism, a substrate S first combines with a molecule of enzyme E, and this process is followed by a step in which the *enzyme*-substrate complex ES breaks down (sometimes with the participation of the solvent) into enzyme and reaction products:

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES$$

$$ES \xrightarrow{k_2} E + \text{Products}$$

If, as is usual, the substrate S is present in great excess of the enzyme it can be shown that steady-state conditions apply, and that the rate equation is:

$$v = \frac{k_2 \left[E\right]_o \left[S\right]_o}{\left(k_{-1} + k_1\right)/k_1 + \left[S\right]_o}$$

where $[E]_o$, $[S]_o$ are the total *concentrations* of enzyme and substrate. This equation is of the required general form of the Michaelis–Menten equation.

Note 2: Other, more complicated, mechanisms lead to the *Michaelis–Menten equation*, adherence to which therefore does not require that the Michaelis–Menten mechanism applies.

[2]

microalbuminuria
Chronic presence of albumin in slight excess in urine.

microarray
Grid of nucleic acid molecules of known sequence linked to a solid substrate, which can be probed with a sample containing either m*RNA* or *complementary DNA* from a cell or tissue to reveal changes in *gene* expression relative to a control sample.

Note: Microarray technology, which is also known as "DNA gene chip" technology, allows the expression of many thousands of *genes* to be assessed in a single experiment.

After [8]

microcosm
experimental model ecosystem
Artificial test system that simulates major characteristics of the natural environment for the purposes of ecotoxicological assessment.

Note: Such a system would commonly have a terrestrial phase, with substrate, plants, and herbivores, and an aquatic phase, with vertebrates, invertebrates, and plankton. The term "*mesocosm*" implies a more complex and larger system than the term "*microcosm*", but the distinction is not clearly defined.

micromercurialism
Early or subclinical effects of *exposure* to elemental mercury detected at the low *exposure* levels.

micronucleus test
Test for *mutagenicity* in which animals are treated with a test agent after which time the frequency of micronucleated cells is determined; if a test group shows significantly increased levels of micronucleated cells compared to a control group, the chemical is considered capable of inducing chromosomal damage.

microproteinaemia
Chronic presence of microprotein (alpha-1 and beta-2 microglobulin) in blood, indicating proximal renal tubule damage.

microsome
Artefactual spherical particle, not present in the living cell, derived from pieces of the *endoplasmic reticulum* present in homogenates of tissues or cells.

Note: Microsomes sediment from such homogenates (usually the *S*9 fraction) when centrifuged at 100 000 g for 60 min: The microsomal fraction obtained in this way is often used as a source of *monooxygenase enzymes*.

micturitic
See *diuretic.*

midstream sampling
Taking an *aliquot* of a flowing liquid, such as urine, avoiding initial and terminal flow periods which are likely to be unrepresentative.
[2]

Minamata disease
Neurological *disease* caused by methylmercury, first seen in subjects ingesting contaminated fish from Minamata Bay in Japan.

mineralization
Complete conversion of organic substances to inorganic derivatives, often visible as microscopic deposits which may be associated with damage to soft tissue (e.g., in the kidney).

minimal risk level (MRL)
Estimate of the daily human *exposure* to a hazardous substance that is likely to be without appreciable risk of adverse noncancer *health* effects over a specified duration of exposure: This substance-specific estimate is used by ATSDR health assessors to identify contaminants and potential health effects that may be of concern at hazardous waste sites.

minimum lethal concentration (LC_{min})
Lowest *concentration* of a *toxic* substance in an environmental medium that kills individual organisms or test species under a defined set of conditions.

minimum lethal dose (LD_{min})
Lowest amount of a substance that, when introduced into the body, may cause death to individual species of test animals under a defined set of conditions.

miosis
meiosis (obsolete)
myosis
Abnormal contraction of the pupil of the eye to less than 2 mm.

miscible
Liquid substances capable of mixing without separation into two phases; refers to liquid mixtures.

miticide
Substance intended to kill mites.

mitochondri/on sing., **/a** pl.
Eukaryote cytoplasmic organelle that is bounded by an outer membrane and an inner membrane; the inner membrane has folds called cristae that are the center of ATP synthesis in oxidative phosphorylation in the animal cell and supplement ATP synthesis by the chloroplasts in photosynthetic cells.

Note: The mitochondrial matrix within the inner membrane contains ribosomes, many oxidative *enzymes*, and a circular *DNA* molecule that carries the genetic information for a number of these enzymes.

mitogen
Substance that induces *lymphocyte* transformation or, more generally, *mitosis* and cell proliferation.

mitosis
Process by which a cell *nucleus* divides into two daughter nuclei, each having the same genetic complement as the parent cell: Nuclear division is usually followed by cell division.

mixed-function oxidase (MFO)
See *monooxygenase.*

modifying factor (MF)
See *safety factor, uncertainty factor.*

molluskicide
limacide
molluscicide
Substance intended to kill mollusks.

monitoring
Continuous or repeated observation, measurement, and evaluation of *health* and (or) environmental or technical data for defined purposes, according to prearranged schedules in space and time, using comparable methods for sensing and data collection.

Note: Evaluation requires comparison with appropriate reference values based on knowledge of the probable relationship between ambient *exposure* and *adverse effects*.

monoclonal
Pertaining to a specific protein from a single clone of cells, all molecules of this protein being the same.

monoclonal antibody
Antibody produced by cloned cells derived from a single *lymphocyte*.

monooxygenase
mixed-function oxidase
Enzyme that catalyzes reactions between an organic compound and molecular oxygen in which one atom of the oxygen molecule is incorporated into the organic compound and one atom is reduced to

water; involved in the *metabolism* of many natural and foreign compounds giving both unreactive products and products of different or increased *toxicity* from that of the parent compound.

Note: Such enzymes are the main catalysts of phase 1 reactions in the metabolism of *xenobiotics* by the *endoplasmic reticulum* or by preparations of *microsomes*.

Monte Carlo simulation
Analysis of a sequence of events using random numbers to generate possible outcomes in an iterative process.
After [2]

morbidity
Any departure, subjective or objective, from a state of physiological or psychological well-being: In this sense, "sickness", "illness", and "morbid condition" are similarly defined and synonymous.

morbidity rate
Term (to be avoided) used loosely to refer to *incidence* or *prevalence* rates of *disease*.

morbidity survey
Method for the estimation of the *prevalence* and (or) *incidence* of a *disease* or diseases in a population.

mordant
Substance that fixes a dyestuff in or on a material by combining with the dye to form an insoluble compound, used to fix or intensify stains in a tissue or cell preparation.

mortality
Death as studied in a given population or subpopulation.

Note: The term "mortality" is often used incorrectly instead of "mortality rate".

mortality rate
See *death rate.*

mortality study
Investigation dealing with death rates or proportion of deaths attributed to specific causes as a measure of response.

mucociliary transport
Process of removal of particles from the bronchi of the lungs in a mucus stream moved by cilia, thus contributing to *uptake* from the gastrointestinal tract.
[2]

Mulliken population analysis
Partitioning scheme based on the use of density and overlap matrices, at one time used for allocating the electrons of a molecular entity in some fractional manner among its various parts (atoms, bonds, orbitals).
[2]

multicompartment model
Product of a *compartmental analysis* requiring more than two *compartments*.
[2]

multifactorial disease
Illness with pathogenesis dependent on complex interplay of genetic and (or) environmental factors.
After [9]

multigeneration study
1. *Toxicity* test in which two to three generations of the test organism are *exposed* to the substance being assessed.
2. Toxicity test in which only one generation is exposed and effects on subsequent generations are assessed.

multiple chemical sensitivity (MCS)
idiopathic environmental intolerance
Intolerance condition attributed to extreme sensitivity to various environmental chemicals, found in air, food, water, building materials, or fabrics.

Note: This syndrome is characterized by the patient's belief that his or her symptoms are caused by very low-level *exposure* to environmental chemicals. The term "chemical" is used to refer broadly to many natural and man-made chemical agents, some of which have several chemical constituents. Several theories have been advanced to explain the cause of multiple chemical sensitivity, including allergy, toxic effects, and neurobiologic sensitization. There is insufficient scientific evidence to confirm a relationship between any of these possible causes and symptoms.

multiple (or multiphasic) screening
Procedure that has evolved by combining single screening tests, and is the logical corollary of mass screening.

Note 1: Where much time and effort have been spent by a population in attending for a single test such as mass radiography, it is natural to consider the economy of offering other tests at the same time.

Note 2: Multiple (or multiphasic) screening implies the administration of a number of tests, in combination, to large groups of people.

multipotent
Of a cell, capable of giving rise to several different kinds of structure or types of cell.
[2]

multistage cluster sampling
Cluster sampling with more than two stages, each sampling being made on aggregates (or clusters) in which the clusters already obtained by the preceding sampling have been divided.

multistage model
Dose–response model for *cancer* death estimation of the form

$$P = 1 - \exp[-(q_o + q_1 d_1 + q_2 d_2 + \ldots + q_k d_k)]$$

where P is the probability of cancer death from a continuous *dose* rate, d_i, of group (or stage) $i = 0, 1, 2...$, the q's are constants, and k is the number of dose groups (or, if less than the number of dose groups, k is the number of biological stages believed to be required in the *carcinogen*esis process). With the *multistage model*, it is assumed that cancer is initiated by cell *mutations* in a finite series of steps. [2]

multistage sampling
Type of sampling in which the *sample* is selected by stages, the sampling units at each stage being subsampled from the larger units chosen at the previous stage.

multivariate statistics
Set of statistical tools to analyze data matrices using regression and (or) pattern recognition techniques. [2]

murine
Of or belonging to the family of rats and mice (Muridae).

mutagen
Agent that can induce heritable changes (*mutation*s) of the *genotype* in a cell as a consequence of alterations in or loss of genetic material.

mutagenesis
Induction (or generation) of heritable changes (*mutation*s) of the *genotype* in a cell as a consequence of alterations or loss of *genes* or *chromosome*s (or parts thereof).

mutagenicity
Ability of a physical, chemical, or biological agent to induce (or generate) heritable changes (*mutation*s) in the *genotype* in a cell as a consequence of alterations or loss of *genes* or *chromosome*s (or parts thereof).

mutation
Any relatively stable heritable change in genetic material that may be a chemical transformation of an individual *gene* (*gene* or point *mutation*), altering its function, or a rearrangement, gain, or loss of part of a *chromosome*, that may be microscopically visible (chromosomal mutation).

Note: Mutation can be either germinal, and inherited by subsequent generations, or somatic and passed through cell lineage by cell division.

myalgia
Pain or tenderness in a muscle or group of muscles.

myasthenia
Muscular weakness.

mycotoxin
Toxin produced by a fungus.

Note: Examples are aflatoxins, tricothecenes, ochratoxin, and patulin.

mydriasis
Extreme dilation of the pupil of the eye, either as a result of normal physiological response or in response to a chemical *exposure*.

myelosuppression
Reduction of bone marrow activity leading to a lower *concentration* of platelets, red cells, and white cells in the blood.

nanoparticle
Microscopic particle whose size is measured in nanometers, often restricted to so-called nanosized particles (NSPs; <100 nm in aerodynamic diameter), also called *ultrafine particles*.

nanotoxicology
Scientific discipline involving the study of the actual or potential danger presented by the harmful effects of nanoparticles on living organisms and *ecosystems*, of the relationship of such harmful effects to *exposure*, and of the mechanisms of action, diagnosis, prevention, and treatment of intoxications.

narcotic
1. Nonspecific usage—an agent that produces insensibility or stupor.
2. Specific usage—an opioid, any natural or synthetic *drug* that has morphine-like actions.

natriuretic
Substance increasing the rate of excretion of sodium ion in the urine.

natural occurrence
Presence of a substance in nature, as distinct from presence resulting from inputs from human activities.

Note: The contamination of the natural environment by some man-made compounds may be so widespread that it is practically impossible to get access to biota with a truly natural level; only "normal" levels can be measured, those which are usually prevalent in places where there is no obvious local contamination.

necropsy
See *autopsy.*

necro/sis n., **/tic** adj.
Sum of morphological changes resulting from cell death by lysis and (or) enzymatic degradation, usually accompanied by *inflammation* and affecting groups of cells in a tissue.

Note: Not to be confused with *apoptosis*.

[2]

negligible risk
1. Probability of *adverse effects* occurring that can reasonably be described as trivial.
2. Probability of adverse effects occurring that is so low that it cannot be reduced appreciably by increased regulation or investment of resources.

nematicide
nematocide
Substance intended to kill nematodes.

neonat/e n., **/al** adj.
Infant during the first 4 weeks of postnatal life.

Note: For statistical purposes, some scientists have defined the period as the first 7 days of postnatal life. The precise definition varies from species to species.

neoplas/ia, -m
New and abnormal formation of tissue as a *tumor* or growth by cell proliferation that is faster than normal and continues after the initial stimulus that initiated the proliferation has ceased.

nephritis
Inflammation of the kidney, leading to kidney failure, usually accompanied by *proteinuria*, *hematuria*, *edema*, and *hypertension*.

nephropathy
renopathy
Any *disease* or abnormality of the kidney.

nephrosis
Disease of the kidneys marked by degeneration of renal tubular epithelium.

nephrotoxic
Chemically harmful to the cells of the kidney.

neural
Pertaining to a nerve or to the nerves.

neurologic shellfish poisoning (NSP)
Serious illness that is a consequence of consumption of toxic bivalve shellfish (mollusks) such as mussels, oysters, and clams that have ingested, by filter feeding, large quantities of microalgae containing brevetoxin: Symptoms include *gastroenteritis*; rectal burning; *paresthesias* of the face, trunk, and limbs; *myalgias*; *ataxia*; *vertigo*; and reversal of hot/cold sensation.
See also *amnesic shellfish poisoning*, *diarrheal shellfish poisoning.*

neuron(e)
Nerve cell, the morphological and functional unit of the central and peripheral nervous systems.

neuropathy
Any *disease* of the central or peripheral nervous system.

neurotoxic/ adj., **/ity** n.
Able to produce chemically an *adverse effect* on the nervous system: such effects may be subdivided into two types.

1. Central nervous system effects (including transient effects on mood or performance and pre-senile dementia such as Alzheimer's disease).
2. Peripheral nervous system effects (such as the inhibitory effects of organophosphorus compounds on synaptic transmission).

nitrification
Sequential oxidation of ammonium salts to nitrite and nitrate by microorganisms.

nitrosative stress
Adverse effects occurring when the generation of reactive nitrogen species in a system exceeds the system's ability to neutralize and eliminate them; nitrosative stress may lead to nitrosylation reactions that can alter protein structure, thus inhibiting normal function.

no-acceptable-daily-intake-allocated
This expression is applicable to a substance for which the available information is not sufficient to establish its safety, or when the specifications for identity and purity are not adequate, or when the available data show that the substance is hazardous and should not be used.

Note: The basis for the use of the expression should be determined before action is taken; in the first two cases above, not being able to allocate an ADI does not mean that the substance is unsafe.

***n*-octanol-water partition coefficient**
Obsolete for *octan-1-ol-water partition coefficient.*
See *octan-1-ol-water partition coefficient.*

nodule
Small node or boss that is solid and can be detected by touch.

no-effect dose (NED)
subthreshold dose
Amount of a substance that has no effect on the organism.

Note: It is lower than the *threshold* of harmful effect and is estimated while establishing the threshold of harmful effect.

no-effect level (NEL)
Maximum dose (of a substance) that produces no detectable changes under defined conditions of *exposure*.

Note: This term tends to be substituted by *no-observed-adverse-effect level* (NOAEL) or *no-observed-effect level* (NOEL).

non-bioenvironmental transformation
Change in the chemical or physical nature of a substance occurring as a result of physicochemical conditions and independent of any biological system.

nonionizing radiation
Electromagnetic radiation of low energy that is not capable of causing ionization.

nonoccupational exposure
Environmental *exposure* outside the workplace to substances that are otherwise associated with particular work environments and (or) activities and processes that occur there.

nonstochastic
See *deterministic*.

non-target organism
Organism affected by a *pesticide* although not the intended object of its use.

no-observed-adverse-effect level (NOAEL)
Greatest *concentration* or amount of a substance, found by experiment or observation, which causes no detectable adverse alteration of morphology, functional capacity, growth, development, or life span of the *target* organism under defined conditions of *exposure*.

no-observed-effect level (NOEL)
Greatest *concentration* or amount of a substance, found by experiment or observation, that causes no alterations of morphology, functional capacity, growth, development, or life span of *target* organisms distinguishable from those observed in normal (control) organisms of the same species and strain under the same defined conditions of *exposure*.

no-response level (NRL)
Maximum *dose* of a substance at which no specified response is observed in a defined population and under defined conditions of *exposure*.

nosocomial
Associated with a hospital or infirmary, especially used of *diseases* that may result from treatment in such an institution.

noxious substance
See *harmful substance.*

nucle/us (in cell biology) sing., **/i** pl.
Compartment in the interphase eukaryotic cell bounded by a double membrane and containing the genomic *DNA*, with the associated functions of transcription and processing.

nuisance threshold
Lowest *concentration* of an air pollutant that can be considered objectionable.

nutritional table method
Procedure for evaluating the dietary intake of a large number of people.

Note 1: The accuracy of the method depends on the accuracy with which records of the food consumption can be established and the accuracy of the nutritional tables specifying the *concentration* of various nutrients, vitamins, essential, and non-essential substances including pesticide residues.

Note 2: For each record of quantity of food consumed during a certain time period, the daily intake of the substance in question is calculated by multiplying the substance concentration in the food item (as obtained from the nutritional table) by the quantity of food consumed and dividing by the time of observation.

nychthemeral
circadian
Relating to or exhibiting a nychthemeron or 24-h period.

nystagmus
Involuntary, rapid, rhythmic movement (horizontal, vertical, rotary, mixed) of the eyeball, usually caused by a disorder of the labyrinth of the inner ear or a malfunction of the central nervous system.

objective environment
Actual physical, chemical, and social environment as described by objective measurements, such as noise levels in decibels and *concentration*s of air *pollutants*.

occupational environment
Surrounding conditions at a workplace.

occupational exposure
Experience of substances, intensities of radiation, etc., or other conditions while at work.

occupational exposure limit (OEL)
Regulatory level of *exposure* to substances, intensities of radiation, etc., or other conditions, specified appropriately in relevant government legislation or related codes of practice.

occupational exposure standard (OES)
1. Level of *exposure* to substances, intensities of radiation, etc., or other conditions considered to represent specified good practice and a realistic criterion for the control of exposure by appropriate plant design, engineering controls, and, if necessary, the addition and use of personal protective clothing.
2. In UK, *health*-based exposure limit defined under COSHH Regulations as the *concentration* of any airborne substance, averaged over a reference period, at which, according to current knowledge, there is no evidence that it is likely to be injurious to employees, if they are *exposed* by inhalation, day after day, to that concentration, and set on the advice of the HSE Advisory Committee on *Toxic* Substances.

occupational hygiene
Identification, assessment, and control of physicochemical and biological factors in the workplace that may affect the *health* or well-being of those at work and in the surrounding community.

occupational medicine
Specialty devoted to the prevention and management of occupational injury, illness, and disability, and the promotion of the *health* of workers, their families, and their communities.

occupational safety and health
See *occupational hygiene.*

octan-1-ol–water partition coefficient, P_{ow}, K_{ow}
Ratio of the solubility of a chemical in octan-1-ol divided by its solubility in water.

Note: Measure of *lipophilicity*, used in the assessment of both the uptake and physiological distribution of organic chemicals and prediction of their environmental fate.

ocular
Pertaining to the eye.

odds
Ratio of the probability of occurrence of an event to that of non-occurrence, or the ratio of the probability that something is so, to the probability that it is not so.

odds ratio (OR), θ
cross-product ratio
relative odds
Quotient obtained by dividing one set of odds by another. The terms "odds" or "odds ratio" are defined differently according to the situation under discussion. Consider the following notation for the distribution of a binary *exposure* and a disease in a population or a *sample*.

	Exposed	Nonexposed
Disease	*a*	*b*
No disease	*c*	*d*

The odds ratio (cross-product ratio) is *ad*/*bc*.

Note 1: The *exposure*-odds ratio for a set of case control data is the ratio of the odds in favor of exposure among the cases (*a*/*b*) to the odds in favor of exposure among non-cases (*c*/*d*), which is equal to *ad*/(*bc*). With incident cases, unbiased subject selection, and a "rare" disease (say, under 2 % cumulative *incidence* rate over the study period), *ad*/*bc* is an approximate estimate of the *risk* ratio. With incident cases, unbiased subject selection, and density sampling of controls, *ad*/*bc* is an estimate of the ratio of the person-time incidence rates (force of morbidity) in the *exposed* and unexposed. No rarity assumption is required for this.

Note 2: The disease-odds (rate-odds) ratio for a cohort or cross-section is the ratio of the odds in favor of disease among the exposed population (*a*/*c*) to the odds in favor of disease among the unexposed (*b*/*d*), which is equal to *ad*/*bc* and hence is equal to the exposure-odds ratio for the cohort or cross-section.

Note 3: The *prevalence*-odds ratio refers to an odds ratio derived cross-sectionally, as, for example, an odds ratio derived from studies of prevalent (rather than incident) cases.

Note 4: The *risk*-odds ratio is the ratio of the odds in favor of getting disease, if exposed, to the odds in favor of getting disease if not *exposed*. The odds ratio derived from a cohort study is an estimate of this.

odor threshold
odour threshold
odor detection threshold
In principle, the lowest *concentration* of an odorant in the air that can be detected by a human being.

Note: In practice, a panel of "sniffers" is often used, and the *threshold* taken as the concentration at which 50 % of the panel can detect the odorant (although some workers have also used 100 % thresholds). The odor concentration at the detection threshold may be defined as one odor unit.

oedema
See *edema.*

olf
Unit used to measure scent emission of people and objects; one olf is defined as the scent emission of an "average person", a sitting adult who takes an average of 0.7 baths per day and whose skin has a total area of 1.8 m^2; the scent emission of an object or person is measured by specially trained personnel comparing it to normed scents.

Note: The olf should not be confused with the of unit of scent immission (as opposed to emission), the *decipol*, which also takes into account the ventilation system's air volume flow.

olfactometer
Apparatus for testing the power of the sense of smell.

oligozoospermia
Sperm *concentration* less than a reference value.
[8]

oliguria
Excretion of a diminished amount of urine in relation to fluid intake.

-omics, -omes
Neologism referring to the fields of study in biology ending in the suffix -omics, such as *genomics* or *proteomics*: The related neologism -omes are the objects of study of the field such as the *genome* or *proteome*, respectively.

oncogene
Gene that can cause neoplastic (see *neoplasia*) transformation of a cell; oncogenes are slightly changed equivalents of normal genes known as proto-oncogenes.

oncogenesis
Production or causation of *tumors*.

oncogenic
Capable of producing *tumors* in animals, either *benign* (noncancerous) or *malignant* (cancerous).
[9]

one-compartment model
Kinetic model, where the whole body is thought of as a single *compartment* in which the substance distributes rapidly, achieving an *equilibrium* between blood and tissue immediately.
[2]

one-hit model
Dose–response model of the form

$$P = 1 - e^{-bd}$$

where P is the probability of *cancer* death from a continuous *dose* rate, d, and b is a constant.

onycholysis
Loosening or detachment of the nail from the nail bed following some destructive process.

oogenesis
Process of formation of the ovum (plural ova), the female *gamete*.

operon
Complete unit of *gene* expression and regulation, including structural genes, regulator gene(s), and control elements in *DNA* recognized by regulator gene product(s).

ophthalmic
Pertaining to the eye.

organ dose
Amount of a substance or physical agent (radiation) absorbed by an organ.

organelle
Microstructure or separated compartment within a cell that has a specialized function, for example, ribosome, peroxisome, lysosome, Golgi apparatus, mitochondrion, nucleolus, nucleus.

organic carbon partition coefficient, K_{oc}
Measure of the tendency for organic substances to be adsorbed by soil or sediment, expressed as:

$$K_{oc} = \frac{\text{(mass adsorbed substance)/(mass organic carbon)}}{\text{(mass concentration of absorbed substance)}}$$

The K_{oc} is substance-specific and is largely independent of soil properties.

organoleptic
1. Relating to perception by a sensory organ.
2. Involving the use of sensory organs, e.g., organoleptic tests.

osteo-
Prefix meaning pertaining to bone.

osteodystrophy
Abnormal development of bone.

osteogenesis
Formation or development of bone.

osteomalacia
Condition marked by softening of the bones (due to impaired mineralization, with excess accumulation of osteoid), with pain, tenderness, muscular weakness, anorexia, and loss of weight, resulting from deficiency of vitamin D and calcium.

osteoporosis
Significant decrease in bone mass with increased porosity and increased tendency to fracture.

ovicide
Substance intended to kill eggs.

oxidative stress
Adverse effects occurring when the generation of *reactive oxygen species* (ROS) in a system exceeds the system's ability to neutralize and eliminate them; excess ROS can damage a cell's lipids, protein, or *DNA*.

palpitation
1. Unduly rapid or throbbing heartbeat that is noted by a patient; it may be regular or irregular.
2. Undue awareness by a patient of a heartbeat that is otherwise normal.

paralysis
Loss or impairment of motor function.

paralytic shellfish poisoning (PSP)
Serious illness that is a consequence of consumption of toxic bivalve shellfish (mollusks) such as mussels, oysters, and clams that have ingested, by filter feeding, large quantities of microalgae containing saxitoxin or its derivatives.

Note: Initially there is tingling, numbness, and burning of the tongue and lips, which spreads to the face, neck, arms, fingertips, legs, and toes; this is followed by weakness of the upper and lower limbs, loss of motor coordination, and, in severe cases, paralysis.

para-occupational exposure
1. *Exposure* of a worker's family to substances carried from the workplace to the home.
2. Exposure of visitors to substances in the workplace.

parasympathetic
Of, relating to, or affecting the parasympathetic nervous system which stimulates digestive secretions, slows the heart, constricts the pupils of the eyes, and dilates blood vessels.
See *sympathetic nervous system*.

parasympatholytic
Producing effects resembling those caused by interruption of the parasympathetic nerve; also called anticholinergic.

parasympathomimetic
cholinomimetic
Producing effects resembling those caused by stimulation of the parasympathetic nervous system.

parenteral dosage
Method of introducing substances into an organism avoiding the gastrointestinal tract (subcutaneously, intravenously, intramuscularly, etc.).

paresis
Slight or incomplete paralysis.

paresthesia
paraesthesia
Abnormal or unexplained tingling, pricking, or burning sensation on the skin.

particulate matter (in atmospheric chemistry)
1. General term used to describe airborne solid or liquid particles of all sizes.

   Note: The term *aerosol* is recommended to describe airborne particulate matter.

2. Particles in air, usually of a defined size and specified as PM_n where n is the maximum *aerodynamic diameter* (usually expressed in μm) of at least 50 % of the particles.

[2]

partition coefficient
Concentration of a substance in one phase divided by the concentration of the substance in the other phase when the heterogeneous system of two phases is in *equilibrium*.

Note 1: The ratio of concentrations (or, strictly speaking, activities) of the same molecular species in the two phases is constant at constant temperature.

Note 2: The *octan-1-ol–water partition coefficient* is often used as a measure of the *bioconcentration* factor for modeling purposes.

[2]

Note 3: This term is in common usage in toxicology but is not recommended by IUPAC for use in chemistry and should not be used as a synonym for partition constant, partition ratio, or distribution ratio.

partition ratio, K_D
Ratio of the *concentration* of a substance in a single definite form, A, in the extract to its *concentration* in the same form in the other phase at equilibrium, for example, for an aqueous/organic system:

$$K_D(A) = [A]^{org}/[A]^{aq}$$

[2]

passive sampler
Device for taking samples of environmental media following diffusional contact with a suitable collecting material.
See *personal sampler.*

passive smoking
Inhalation of sidestream smoke by people who do not smoke themselves.
See also *sidestream smoke.*

patch test
Test for allergic sensitivity in which a suspected *allergen* is applied to the skin on a small surgical pad.

Note: Patch tests may be used to detect *exposure* to *pesticides*.

peak daily average concentration of an air pollutant
See *maximum average daily concentration of an atmospheric pollutant.*

penetration (in cell biology)
1. Action of entering or passing through a cell membrane.
2. Ability or power to enter or pass through a cell membrane.

perceived environment
perceived risk
See *subjective environment.*

percutaneous
Through the skin following application on the skin.

perfusion (in physiology)
1. Act of pouring over or through, especially the passage of a fluid through the vessels of a specific organ.
2. Liquid poured over or through an organ or tissue.

[2]

perinatal
Relating to the period shortly before and after birth, usually from the 20^{th} to the 29^{th} week of gestation to 1 to 4 weeks after birth.

peritoneal dialysis
Method of artificial *detoxication* in which a *toxic* substance from the body is transferred into liquid that is instilled into the peritoneum.

Note: Effectively, this represents the employment of the peritoneum surrounding the abdominal cavity as a dialyzing membrane for the purpose of removing *waste* products or toxins accumulated as a result of *renal* failure.

permeability
Ability or power to enter or pass through a cell membrane.

permeability coefficient, P
Quantity defining the permeability of molecules across a cell membrane and expressed as

$$P = \frac{KD}{\Delta x}$$

where K is the partition coefficient, D is the diffusion coefficient, and Δx is the thickness of the cell membrane.

Note: SI units m s^{-1}; frequently used units cm s^{-1}, with units cm^2 s^{-1} for D, cm for Δx.

permeable
Of a membrane, allowing a given substance to pass through.

Note: When applied to nonbiological membranes with no qualification, the term normally refers to water.

permeation
Action of entering or passing through a cell membrane.

permissible exposure limit (PEL)
Recommendation by U.S. OSHA for a *time-weighted average concentration* that must not be exceeded during any 8-h work shift of a 40-h working week.

peroxisome
Organelle, similar to a *lysosome*, characterized by its content of catalase (EC 1.11.1.6), peroxidase (EC 1.11.1.7), and other oxidative *enzymes*.

persistence
Attribute of a substance that describes the length of time that the substance remains in a particular environment before it is physically removed or chemically or biologically transformed.

persistent inorganic pollutant (PIP)
Inorganic substance that is stable in the environment, is liable to long-range transport, may bioaccumulate in human and animal tissue, and may have significant impacts on human health and the environment.

Note 1: Examples are arsenides, fluorides, cadmium salts, and lead salts.

Note 2: Some inorganic chemicals, like crocidolite asbestos, are persistent in almost all circumstances, but others, like metal sulfides, are persistent only in unreactive environments; sulfides can generate hydrogen sulfide in a reducing environment or sulfates and sulfuric acid in oxidizing environments. As with organic substances, persistence is often a function of environmental properties.

persistent organic pollutant (POP)
Organic chemical that is stable in the environment, is liable to long-range transport, may bioaccumulate in human and animal tissue, and may have significant impacts on human health and the environment.

Examples: dioxin, PCBs, DDT, tributyltin oxide (TBTO).

Note: The Stockholm Convention on Persistent Organic Pollutants was adopted at a Conference of Plenipotentiaries held from 22 to 23 May 2001 in Stockholm, Sweden; by signing this convention, governments have agreed to take measures to eliminate or reduce the release of POPs into the environment.

personal monitoring
Type of environmental monitoring in which an individual's *exposure* to a substance is measured and evaluated.

Note: This is normally carried out using a personal *sampler*.

personal protective device (PPD)
individual protective device (IPD)
personal protective equipment (PPE)
Equipment (clothing, gloves, hard hat, respirator, etc.) worn by an individual to prevent *exposure* to a potentially *toxic* substance.

personal sampler
individual sampler
Compact, portable instrument for individual air sampling, measuring, or both, the content of a harmful substance in the respiration zone of a working person.
See also *passive sampler.*

pest
Organism that may harm public *health*, attacks food and other materials essential to mankind, or otherwise affects human beings adversely.

pesticide
A substance intended to kill pests.

Note: In common usage, any substance used for controlling, preventing, or destroying animal, microbiological, or plant pests.

pesticide residue
Any substance or mixture of substances found in humans or animals or in food and water following use of a pesticide: the term includes any specified derivatives, such as degradation and conversion products, metabolites, reaction products, and impurities considered to be of toxicological significance.

phagocytosis
Process by which particulate material is endocytosed by a cell.
[2]
See also *endocytosis*, *pinocytosis.*

pharmaceutical
Medicinal *drug*.

pharmacodynamics
Process of interaction of pharmacologically active substances with *target* sites in living systems, and the biochemical and physiological consequences leading to therapeutic or *adverse effect*s.
[2]

pharmacogenetics
Study of the influence of genetic factors on the effects of *drug*s on individual organisms.
[2]

pharmacogenomics
Methods and science permitting identification of the *gene*s which influence individual variation in the efficacy or toxicity of therapeutic agents, and the application of this information in clinical practice.
[2]

pharmacokinetics
1. Process of the *uptake* of *drug*s by the body, the *biotransformation* they undergo, the *distribution* of the *drug*s and their metabolites in the tissues, and the *elimination* of the drugs and their metabolites from the body.
2. Study of such processes.

[2]

pharmacology
Science of the use and effects of *drug*s: may be subdivided into *pharmacokinetics* and *pharmacodynamics* defined above.
[2]

pharynx
Throat, the part of the digestive tract between the esophagus below and the mouth and nasal cavities above and in front.

phase I reaction of *biotransformation*
Enzymic modification of a substance by oxidation, reduction, hydrolysis, hydration, dehydrochlorination, or other reactions catalyzed by *enzymes* of the cytosol, of the *endoplasmic reticulum* (microsomal enzymes), or of other cell *organelles*.
See also *cytochrome P450.*

phase II reaction of *biotransformation*
Binding of a substance, or its *metabolites* from a phase I reaction, with *endogenous* molecules (*conjugation*), making more water-soluble derivatives that may be excreted in the urine or bile.

Note: Phase II reactions include glucuronidation, sulfation, acetylation, amino acid (e.g., glycine), and glutathione conjugation.

phase III reaction of *biotransformation*
Further *metabolism of conjugated metabolites* produced by *phase II reactions*.
[2]

phenome
Complete phenotypic description of an organism (by analogy with *genome*).

phenotype
Observable structural and functional characteristics of an organism determined by its *genotype* and modulated by its environment.

pheromone
See *feromone.*

photo-irritation
Inflammation of the skin caused by *exposure* to light, especially that due to *metabolites* formed in the skin by *photolysis*.

photolysis
Cleavage of one or more covalent bonds in a molecular entity resulting from absorption of light, or a photochemical process in which such cleavage is an essential part.

Note: Term often used incorrectly to describe irradiation of a sample, although in the combination *flash photolysis* this usage is accepted.

[3]

photooxidation
Oxidation reactions induced by light. Common processes are:

1. Loss of one or more electrons from a chemical species as a result of photoexcitation of that species.
2. Reaction of a substance with oxygen under the influence of ultraviolet, visible, or infrared light. When oxygen remains in the product, this latter process is also called photooxygenation. Reactions in which neither the substrate nor the oxygen are electronically excited (i.e., photosensitized oxidations) are sometimes called photoinitiated oxidations.

[3]

photophobia
Abnormal visual intolerance of light.

photosensitization of skin
Allergic reaction (see *allergy*) due to a metabolite formed by the influence of light.

phototoxicity
*Adverse effect*s produced by *exposure* to light energy, especially those produced in the skin.

physical map (in genetics)
Map showing how much *DNA*, measured in base pairs, separates two genes.

Note: Not to be confused with a genetic map which shows the position of genes in relation to each other, based on the frequency of crossing overs.

physiological availability
See *bioavailability.*

physiological pharmacokinetic model
See *physiologically based pharmacokinetic modeling.*

physiologically based pharmacokinetic modeling (PBPK)
toxicologically based pharmacokinetic modeling
Mathematical modeling of kinetic behavior of a substance, based on measured physiological parameters.
[2]

pinocytosis
Type of *endocytosis* in which soluble materials are taken up by the cell and incorporated into vesicles for digestion.
[2]

piscicide
Substance intended to kill fish.

pivotal study
See *critical study.*

placentation
1. Formation of a placenta in the uterus.
2. Type or structure of a placenta.
3. In botany, arrangement of placentas within the plant ovary.

plasma (in biology)
1. Fluid component of blood in which the blood cells and platelets are suspended.
2. Fluid component of semen produced by the accessory glands, the seminal vesicles, the prostate, and the bulbo-urethral glands.
3. Cell substance outside the nucleus (i.e., the cytoplasm).

plasma half life
See *elimination half life.*

plasmapheresis
Removal of blood from the body and centrifuging it to obtain *plasma* and packed red blood cells: The blood cells are resuspended in a physiologically compatible solution (usually type-specific fresh frozen plasma or albumin) and returned to the donor or injected into a patient who requires blood cells rather than whole blood.

plasmid
Autonomous self-replicating extra-chromosomal circular *DNA* molecule present in bacteria and yeast.

Note 1: Plasmids replicate autonomously each time a bacterium divides and are transmitted to the daughter cells.

Note 2: DNA segments are commonly cloned using plasmid *vectors*.

After [9]

pleura
Lining of the lung.

ploidy
Term indicating the number of sets of *chromosome*s present in an organism.

plumbism
saturnism
Chronic poisoning caused by absorption of lead or lead salts.

pneumoconiosis
Usually fibrosis of the lungs that develops owing to (prolonged) inhalation of inorganic or organic dusts.

Note: Cause-specific types of pneumoconiosis are:
1. anthracosis: from coal dust
2. asbestosis: from asbestos dust
3. byssinosis: from cotton dust
4. siderosis: from iron dust
5. silicosis: from silica dust
6. stannosis: from tin dust

pneumonitis
Inflammation of the lung.

point mutation
Change in a single base pair in *DNA*.

point source
Single *emission* source in a defined location.

poison (in toxicology)
Substance that, taken into or formed within the organism, impairs the *health* of the organism and may kill it.

poison-bearing
Containing a *poison*.

poisoning
intoxication
Morbid condition produced by a *poison*.

pollutant
Any undesirable solid, liquid, or gaseous matter in a solid, liquid, or gaseous environmental medium.

Note 1: "Undesirability" is often *concentration*-dependent, low concentrations of most substances being tolerable or even essential in many cases.

Note 2: A primary pollutant is one emitted into the atmosphere, water, sediments, or soil from an identifiable source.

Note 3: A secondary pollutant is a pollutant formed by chemical reaction in the atmosphere, water, sediments, or soil.

pollution
Introduction of *pollutants* into a solid, liquid, or gaseous environmental medium, the presence of pollutants in a solid, liquid, or gaseous environmental medium, or any undesirable modification of the composition of a solid, liquid, or gaseous environmental medium.

polyclonal antibody
Antibody produced by a number of different cell types.

polydipsia
Chronic excessive thirst.

polymerase chain reaction (PCR)
Technique by which specific *DNA* segments are amplified selectively using cycles of annealing, chain extension, and thermal dissociation.
After [9]

polymorphism in metabolism
polymorphia (in metabolism)
Interindividual variations in *metabolism* of endogenous and *exogenous* compounds due to genetic influences, leading to enhanced side effects or *toxicity* of *drug*s (e.g., poor vs. fast metabolizers) or to different clinical effects (metabolism of steroid hormones).

polyuria
Excessive production and discharge of urine.

population (in statistics)
Totality of related items under consideration.

Note 1: A clearly defined part of a population is called a subpopulation. The term "population segment" is sometimes used as a synonym for subpopulation.

Note 2: In the case of a random variable, the probability distribution is considered as defining the population of that variable.

population (in epidemiology)
Assemblage of individuals with defined characteristics.

population at risk
Persons who can and may develop an adverse *health* effect and who are potentially *exposed* to a substance under study. People already having chronic disease are excluded from the population at *risk* in studies of the *incidence* of the *adverse effect*.
[2]

population critical concentration (PCC)
Concentration of a substance in the critical organ at which a specified percentage of the *exposed* population has reached the individual critical organ concentration.

Note: The percentage is indicated by PCC-10 for 10 %, PCC-50 for 50 %, etc. (similar to the use of the term LD_{50}).

population effect
Absolute number or *incidence* rate of cases occurring in a group of people.

population risk
See *societal risk.*

porphin(e)
See *porphyrin*.

porphyria
Disturbance of porphyrin *metabolism* characterized by increased formation, accumulation, and excretion of porphyrins and their precursors.

porphyrin
porphin(e)
Natural pigment containing a fundamental skeleton of four pyrrole nuclei united through the α-positions by four methine groups to form a macrocyclic structure.

posology
Pharmacological study of the choice of appropriate *dose* of a drug in relation to the physiological factors, such as age, that may influence its effect.

post-translational modification
Processes by which proteins are biochemically modified within a cell following their synthesis on the ribosomes.

potency (in toxicology)
Expression of relative *toxicity* of an agent as compared to a given or implied standard or reference.

potentiation
Dependent action in which a substance or physical agent at a *concentration* or *dose* that does not itself have an *adverse effect* enhances the harm done by another substance or physical agent.
See also *synergism.*

practical certainty (of safety)
Numerically specified low *risk* of *exposure* to a potentially *toxic* substance (e.g., 1 in 1000) or socially acceptable low risk of *adverse effect*s from such an exposure applied to decision making in regard to chemical safety.

precautionary principle
Approach to risk management that can be applied in circumstances of scientific uncertainty, reflecting a perceived need to take action in the face of a potentially serious risk without waiting for definitive results of scientific research.

Note: The 1992 Rio Declaration on Environment and Development says: "In order to protect the environment, the precautionary approach shall be widely applied by states according to their capabilities. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation."

precision (in metrology)
Closeness of agreement between *indications* obtained by replicate measurements on the same or similar objects under specified conditions.

Note: Measurement precision is usually expressed numerically by measures of imprecision, such as standard deviation, variance, or coefficient of variation under the specified conditions of measurement.

[7]

precordial
Pertaining to the region over the heart and lower thorax.

precursor
Substance from which another, usually more biologically active, substance is formed.

predicted environmental concentration (PEC)
predicted exposure concentration (PEC)
See *estimated environmental concentration.*

predicted exposure concentration (PEC)
See *estimated environmental concentration*.

predicted no-effect concentration (PNEC)
Concentration that is expected to cause no adverse effect to any naturally occurring population in an environment at risk from *exposure* to a given substance.

predictive validity
Reliability of a measurement expressed in terms of its ability to predict the criterion: An example would be an academic aptitude test that was validated against subsequent academic performance.

predictive value
Percentage of positive results that are true positives or of negative results that are true negatives.

premature ovarian failure
Follicular depletion by the age of 35 years.
[8]

preneoplastic
Before the formation of a *tumor*.

prevalence
Number of instances of existing cases of a given disease or other condition in a given population at a designated time; sometimes used to mean *prevalence rate*.

Note: When used without qualification, refers usually to the situation at a specified time (point prevalence).

prevalence rate (ratio)
Total number of individuals who have an attribute or disease at a particular time (or during a particular period) divided by the population at *risk* of having the attribute or disease at this point in time or midway through the period.

primary pollutant
See *pollutant.*

prior informed consent (PIC)
Concept in law and medicine that states that before one is subjected to a risk, especially a risk of bodily harm, one is entitled to be fully informed well in advance of the nature of that *risk* in order to make an informed decision about whether to accept it or not.

primary protection standard
Accepted maximum level of a *pollutant* (or its indicator) in the *target* organism, or some part thereof, or an accepted maximum intake of a pollutant or nuisance into the target under specified circumstances.

probability sample
See *random sample*.

probit
Probability unit obtained by adding 5 to the normal deviates of a standardized normal distribution of results from a dose response study.

Note 1: Addition of 5 removes the complication of handling negative values.

Note 2: A plot of probit against the logarithm of *dose* or *concentration* gives a linear plot if the response follows a logarithmic normal distribution. Estimates of the LD_{50} and ED_{50} (or LC_{50} and EC_{50}) can be obtained from this plot.

procarcinogen
Substance that has to be metabolized before it becomes a *carcinogen*.
[2]

prodrug
Precursor converted to an active form of a *drug* within the body.
[2]

progression (in oncology)
Increase in the size of a *tumor* or spread of *cancer* in the body.

prokaryote
Unicellular organism, characterized by the absence of a membrane-enclosed nucleus.

Note: Prokaryotes include bacteria, blue–green algae, and mycoplasmas.

promoter (in molecular genetics)
Sequence of nucleotides in a *DNA* molecule to which *RNA* polymerase binds so as to start transcription.

promoter (in oncology)
Agent that induces *cancer* when administered to an animal or human being who has been *exposed* to a cancer *initiator*.

promotor
Erroneous spelling of *promoter* (in molecular genetics), found in some literature.

pro-pesticide
Substance applied in a form that is not active as a *pesticide* and which becomes active once it enters an organism and undergoes chemical modification.

prophage
Latent state of a phage *genome* in a lysogenic bacterium.

proportional mortality rate (ratio)
Proportion of observed deaths from a specified condition in a defined population divided by the proportion of deaths expected from this condition in a standard population, expressed either on an age-specific basis or after age adjustment.

prospective cohort study
See *cohort study.*

prosthetic group
Nonprotein entity essential for an *enzyme's* activity and tightly bound to the enzyme molecule in its active form.
[2]

proteinuria
Excretion of excessive amounts of protein (derived from blood *plasma* or kidney tubules) in the urine.

proteome
Description of the complete set of proteins encoded by the *genome*.
[2]

proteomics
Global analysis of *gene* expression using a variety of techniques to identify and characterize proteins.

Note: It can be used to study changes caused by *exposure* to chemicals and to determine if changes in m*RNA* expression correlate with changes in protein expression: the analysis may also show changes in post-translational modification, which cannot be distinguished by mRNA analysis alone.

[2]

provisional tolerable weekly intake (PTWI)
See *tolerable weekly intake.*

pseudo-acceptable daily intake (PADI)
Intake for a substance derived by applying a thousandfold uncertainty factor to the lowest low-effect level for noncarcinogenic endpoints.

pseudoadaptation
Apparent adaptation of an organism to changing conditions of the environment (especially chemical) associated with stresses in biochemical systems that exceed the limits of normal (homeostatic) mechanisms.

Note: Essentially, there is a temporary concealed pathology that later on can be manifested in the form of explicit pathological changes sometimes referred to as "decompensation".

psychosis
Any major mental disorder characterized by derangement of the personality and loss of contact with reality.

psychotropic
Exerting an effect upon the mind and capable of modifying mental activity.

public health impact assessment
Applying *risk* assessment to a specific target population of known size, giving as the end product a quantitative statement about the number of people likely to be affected in a particular population.

pulmonary
Pertaining to the lung(s).
[2]

purgative
See *laxative.*

pyrexia
Condition in which the temperature of a human being or mammal is above normal.

pyrogen
Any substance that produces fever.

quality assurance
All those planned and systematic actions necessary to provide adequate confidence that a product or service will satisfy given requirements for quality.

quality control
1. Operational techniques and activities that are used to fulfill requirements for quality.
2. In toxicology, procedures incorporated in experimental protocols to reduce the possibility of error, especially human error.

   Note: This is a requirement of *good laboratory practice*.

quantal
Describing a condition that can be expressed only as "occurring" or "not occurring", such as death.
[2]

quantal effect
all-or-none effect
Antonym: *graded effect*
Condition that can be expressed only as "occurring" or "not occurring", such as death or occurrence of a *tumor*.

quantitative structure–activity relationship (QSAR)
Quantitative structure–biological activity model derived using *regression analysis* and containing as parameters physicochemical constants, indicator variables, or theoretically calculated values.

Note: The term is extended by some authors to include chemical reactivity, i.e., activity and reactivity are regarded as synonyms. This extension is discouraged.

[2]

quantitative structure–metabolism relationship (QSMR)
Quantitative association between the physicochemical and (or) the structural properties of a substance and its metabolic behavior.
[2]

radiant power
Power emitted, transferred, or received as radiation.

radiation toxicology
Scientific study involving research, education, prevention, and treatment of diseases caused by ionizing or nonionizing radiation.

râles
See *crepitations.*

random sample
probability sample
Antonym: *biased sample*
Subset of units of a population that is arrived at by selecting units such that each possible unit has a fixed and known probability of selection.

rate (in epidemiology)
Measure of the frequency with which an event occurs in a defined population in a specified period of time.

Note 1: Most such rates are ratios, calculated by dividing a numerator (e.g., the number of deaths) or newly occurring cases of a disease in a given period, by a denominator, (e.g., the average population during that period).

Note 2: Some rates are proportions, i.e., the numerator is contained within the denominator (as when a number of patients with a given disease is divided by the total population from which they come).

[2]

rate constant, k
rate coefficient
Numerical constant in a rate-of-reaction (v) equation; for example, $v = k\,[A]^{\alpha}[B]^{\beta}$.....where [A], [B] etc. are reactant concentrations, k is the rate constant, and α, β, etc. are corresponding empirical constants.

Note: For further consideration of the relevant mathematics, see [3].

rate-controlling step
rate-determining step
rate-limiting step
In a reaction occurring by a composite reaction sequence, an elementary reaction, the rate constant for which exerts a strong effect—stronger than that of any other rate constant—on the overall rate.

Note 1: It is recommended that the expressions *rate-controlling*, *rate-determining*, and *rate-limiting* be regarded as synonymous, but some special meanings sometimes given to the last two expressions are considered under a separate heading.

Note 2: For further consideration of this term, see [3].

After [3]

rate-determining step
See *rate-controlling step.*

rate difference (RD)
Absolute difference between two *rates*.

Note 1: For example, the difference in *incidence* rate between a population group *exposed* to a causal factor and a population group not exposed to the factor.

Note 2: In comparisons of exposed and unexposed groups, the term *excess rate* may be used as a synonym for rate difference.

rate-limiting step
See *rate-controlling step.*

rate ratio (in epidemiology) (RR)
Value obtained by dividing the *rate* in an *exposed* population by the rate in an unexposed population.

ratticide
Substance intended to kill rats.

reabsorption (in biology)
Absorption by a living organism of a substance which it has previously absorbed and then released (e.g., the uptake of a substance from the proximal renal tubule following glomerular filtration).

reactive nitrogen species (RNS)
Radical nitrogen-based molecules that can act to facilitate nitrosylation reactions; reactive nitrogen species include dioxidonitrogen(•) (nitrogen dioxide, nitryl radical) NO_2•, oxidonitrogen(•) (nitrogen monoxide, nitrosyl radical) NO• oxidonitrogen(1+) (nitrosyl cation) NO^+, hydroxyoxidonitrogen (nitrous acid) HNO_2, and oxidonitrate(1−) NO^-.

reactive oxygen species (ROS)
Intermediates in the reduction of molecular dioxygen O_2 to water.

Note: Examples are superoxide O_2^{-}•, hydrogen peroxide H_2O_2, and hydroxyl HO•.

[2]

readily biodegradable
Arbitrary classification of substances that have passed certain specified screening tests for ultimate biodegradability; these tests are so stringent that such compounds will be rapidly and completely biodegraded in a wide variety of *aerobic* environments.
See also *biodegradation.*

reasonable maximum exposure (RME)
Highest *exposure* that is reasonably expected to occur.

Note: Typically, the 95 % upper confidence limit of the *toxicant* distribution is used: If only a few data points (6–10) are available, the maximum detected *concentration* is used.

recalcitrance
Ability of a substance to remain in a particular environment in an unchanged form.

receptor
Molecular structure in or on a cell which specifically recognizes and binds to a compound and acts as a physiological signal transducer or mediator of an effect.
[2]

receptor-mediated endocytosis
Endocytosis of a substance and its *receptor* following receptor binding.
[2]

recessive gene
Allele which in the heterozygous state is expected to have no effect on the *phenotype* of the organism which carries it.
After [9]

recombinant DNA
DNA made by transplanting or splicing DNA into the DNA of host cells in such a way that the modified DNA can be replicated in the host cells in a normal fashion.

recombinant DNA technology
Methods involving the use of *restriction enzymes* to cleave *DNA* at specific sites, allowing sections of DNA molecules to be inserted into *plasmid* or other vectors and cloned in an appropriate host organism (e.g., a bacterial or yeast cell).
After [9]

recommended exposure level (REL) (in toxicology)
Highest allowable regulatory airborne concentration.

Note: This exposure concentration is not expected to injure workers. It may be expressed as a ceiling limit or as a time-weighted average (TWA).

reconstitution
Restoration to original form of a substance previously altered for preservation and storage.
[2]

recovery
1. Process leading to partial or complete restoration of a cell, tissue, organ, or organism following its damage from *exposure* to a harmful substance or agent.
2. Term used in analytical and preparative chemistry to denote the fraction of the total quantity of a substance recoverable following a chemical procedure.

recovery factor
Fraction or percentage of the total quantity of a substance extracted under specified conditions.

recycling (of waste)
Process or method allowing for the recovery of some value from a *waste*, either as reusable material or as energy.

reference concentration (RfC)
An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation *exposure* to the human population (including sensitive subgroups which include children, asthmatics, and the elderly) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

Note: It can be derived from various types of human or animal data such as NOAEL, LOAEL, or benchmark concentration, with uncertainty factors generally applied to reflect limitations of the data used. It is generally used in USEPA's noncancer health assessments.

reference distribution
Statistical distribution of reference values.

reference dose (RfD)
An estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral *exposure* to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

Note: It can be derived from a NOAEL, LOAEL, or benchmark dose, with uncertainty factors generally applied to reflect limitations of the data used. It is generally used in USEPA's noncancer health assessments.

reference group
See *reference sample group.*

reference individual
Person selected with the use of defined criteria for comparative purposes in a clinical study.

reference interval
Area between and including two reference limits, for example, the percentiles 2.5 and 97.5.

reference limit
Boundary value defined so that a stated fraction of the reference values is less than or exceeds that boundary value with a stated probability.

reference material (RM)
calibration material
standard material
standard
Material, sufficiently homogeneous and stable regarding one or more properties, used in *calibration*, in assignment of a value to another material, or in quality assurance.
[7]

reference population
Group of all reference individuals used to establish criteria against which a population that is being studied can be compared.

reference sample group
Selected reference individuals, statistically adequate numerically to represent the reference population.

reference value
Quantity value, generally accepted as having a suitably small measurement uncertainty, to be used as a basis for comparison with values of quantities of the same kind.
[14]

regioselectiv/ity n., **-e** adj.
Terms referring to a reaction in which one direction of bond making or breaking occurs preferentially over all other possible directions.

Note: Reactions are termed completely (100 %) regioselective if the discrimination is complete, or partially (*x* %), if the product of reaction at one site predominates over the product of reaction at other sites.

[2]

regression analysis
Statistical methods for modeling a set of dependent variables, *Y*, in terms of combinations of predictors, *X*.
[2]

regulatory dose
Term used by the USEPA to describe the expected dose resulting from human *exposure* to a substance at the level at which it is regulated in the environment.

regulatory sequence
DNA sequence to which specific proteins bind to activate or repress the expression of a *gene*.

relative excess risk (RER)
Measure that can be used in comparison of adverse reactions to *drugs*, or other *exposures*, based solely on the component of *risk* due to the exposure or drug under investigation, removing the risk due to background exposure experienced by all in the population. The *relative excess risk*, R, is given by

$$R = (R_1 - R_0)/(R_2 - R_0)$$

where R_1 is the *rate* in the population, R_2 is the rate in the comparison population, and R_0 is the rate in the general population.

Note: Rate is used here as in epidemiology.

[2]

relative odds
See *odds ratio.*

relative risk (RR)
risk ratio
rate ratio
1. Ratio of the *risk* of disease or death among the *exposed* to the risk among the unexposed.
2. Ratio of the *cumulative incidence rate* in the exposed to the cumulative incidence rate in the unexposed.

relative systemic availability
Quantity of metabolizable substance divided by product of quantity of absorbed substance and *exposure*.
[2]

remediation
1. Giving a remedy.
2. Removal of pollution or contaminants from environmental media such as soil, groundwater, sediment, or surface water for the general protection of human health and the environment.

remedy
Anything, such as a medicine or therapy, that relieves pain, cures disease, or corrects a disorder.

renal
Pertaining to the kidneys.
[2]

renal plasma flow
Volume of *plasma* passing through the kidneys in unit time.
[2]

renopathy
See *nephropathy.*

repeatability
measurement repeatability
Measurement precision under *repeatability* conditions of measurement.
[14]

repeatability condition
repeatability condition of measurement
Condition of measurement in a set of conditions including the same measurement procedure, operator, measuring system, operating conditions, and location, and replicated measurements over a short period of time.
[14]

repellent
Substance used mainly to repel blood-sucking insects in order to protect humans and animals.

Note: This term may also be used for substances used to repel mammals, birds, rodents, mites, plant pests, etc.

replicate sampling
Act of taking multiple *sample*s concurrently under comparable conditions.

Note: Replicate sampling may be accomplished by taking samples adjacent in time or space.

replication
1. Duplicated or repeated performance of an experiment under similar (controlled) conditions to reduce to a minimum the error, and to estimate the variations and thus obtain a more precise result: Each determination, including the first, is called a replicate.
2. Process whereby the genetic material is duplicated.

reproducibility
measurement reproducibility
Measurement precision under reproducibility conditions of measurement.
[14]

reproducibility condition
reproducibility condition of measurement
Condition of measurement in a set of conditions including different locations, operators, and measuring systems.

Note 1: The different measuring systems may use different measurement procedures.

Note 2: A specification should give the conditions changed and unchanged, to the extent practical.

[14]

reproductive toxicant
Substance or preparation that produces nonheritable *adverse effects* on male and female reproductive function or capacity and on resultant progeny.

reproductive toxicology
Study of the nonheritable *adverse effect*s of substances on male and female reproductive function or capacity and on resultant progeny.

reserve capacity
Physiological or biochemical capacity that may be available to maintain homeostasis when the body or an organism is *exposed* to an environmental change.

reservoir (in biology)
Storage *compartment* from which a substance may be released with subsequent biological effects.
[2]

residence time
See *mean residence time.*

residual risk
Health risk remaining after risk reduction actions are implemented.
[2]

residual time
See *mean residence time.*

residue
Contaminant remaining in an organism or in other material such as food or packaging, following *exposure*.

resistance (in toxicology)
Ability to withstand the effect of various factors, including potentially *toxic* substances.

resorption (in biology)
Process in which the components of some differentiated structure that has been produced by the body undergo lysis and assimilation.

Note: Specifically in developmental toxicology, term applied to the lysis and assimilation of the fetus caused by chemical or biological stress of the pregnant mother.

resorptive effect
Action of a substance after its reabsorption from the gut into the blood.

respirable dust
respirable particles
Mass fraction of dust (particles) that penetrates to the unciliated airways of the lung (the alveolar region).

Note: This fraction is represented by a cumulative log-normal curve having a median aerodynamic diameter of 4 μm, standard deviation 2 μm (values for humans).

[2]

response
Proportion of an *exposed* population with a defined effect or the proportion of a group of individuals that demonstrates a defined effect in a given time at a given *dose rate*.

restriction enzymes
Endonucleases that recognize specific base sequences within a *DNA* helix, creating a double-strand break of DNA.

Note: Type I restriction *enzymes* bind to these recognition sites but subsequently cut the DNA at different sites. Type II restriction enzymes both bind and cut within their recognition or *target* sites.

[3]

retention
1. Amount of a substance that is left from the total absorbed after a certain time following *exposure*.
2. Holding back within the body or within an organ, tissue, or cell of matter that is normally eliminated.

retrospective study
Research design used to test etiological hypotheses in which inferences about *exposure* to the putative causal factor(s) are derived from data relating to characteristics of the persons or organisms under study or to events or experiences in their past.

Note: The essential feature is that some of the persons under study have the *disease* or other outcome condition of interest, and their characteristics and past experiences are compared with those of other, unaffected persons. Persons who differ in the severity of the disease may also be compared.

returned effect of poisons
Enhancement of the *dose–effect* relationship for a poison following repeated *exposure* to decreasing doses.

reverse mutation (back mutation)
Mutation in a mutant *allele* which makes it capable of producing the nonmutant *phenotype*; this may result from restoration of the original *DNA* sequence of the *gene* or from production of a new DNA sequence which has the same effect.

reverse transcription
Process by which an *RNA* molecule is used as a template to make a single-stranded *DNA* copy.

reversible alteration
Change from normal structure or function, induced by a substance or other agent(s), that returns to normal status or within normal limits after cessation of *exposure*.

rhabdomyolysis
Acute, fulminating, potentially lethal disease of skeletal muscle that causes disintegration of striated muscle fibers as evidenced by myoglobin in the blood and urine.

rhinitis
Inflammation of the nasal mucosa.

rhonch/us sing., **/i** pl.
Harsh *crepitation* in the throat, often resembling snoring.

ribonucleic acid (RNA)
Linear, usually single-stranded, polymer of ribonucleotides, each containing the sugar ribose in association with a phosphate group and one of four nitrogenous bases: adenine, guanine, cytosine, or uracil.

Note: RNA encodes the information for the sequence of amino acids in proteins synthesized using it as a template.

risk
1. Probability of *adverse effects* caused under specified circumstances by an agent in an organism, a population, or an ecological system.
2. Probability of a hazard causing an adverse effect.
3. Expected frequency of occurrence of a harmful event arising from such an *exposure.*

After [2]

risk assessment
Identification and quantification of the *risk* resulting from a specific use or occurrence of a chemical or physical agent, taking into account possible harmful effects on individuals or populations *exposed* to the agent in the amount and manner proposed and all the possible routes of *exposure*.

Note: Quantification ideally requires the establishment of *dose–effect* and *dose–response* relationships in likely *target* individuals and populations.

risk assessment management process
Global term for the whole process from *hazard* identification to *risk* management.

risk associated with a lifetime exposure
Probability of the occurrence of a specified undesirable event following *exposure* of an individual person from a given population to a specified substance at a defined level for the expected lifetime of the average member of that population.

risk aversion
Tendency of an individual person to avoid *risk*.

risk characterization
Outcome of *hazard* identification and *risk* estimation applied to a specific use of a substance or occurrence of an environmental *health* hazard.

Note: Risk characterization requires quantitative data on the *exposure* of organisms or people at risk in the specific situation. The end product is a quantitative statement about the proportion of organisms or people affected in a target population.

risk communication
Interpretation and communication of *risk* assessments in terms that are comprehensible to the general public or to others without specialist knowledge.

risk *de minimis*
negligible risk
Risk that is negligible and too small to be of societal concern (usually assumed to be a probability below 10^{-5} or 10^{-6}).

Note 1: This term can also mean "virtually safe".

Note 2: In the United States, this is a legal term used to mean "negligible risk to the individual".

risk estimation
Assessment, with or without mathematical modeling, of the probability and nature of effects of *exposure* to a substance based on quantification of *dose–effect* and *dose–response* relationships for that substance and the population(s) and environmental components likely to be *exposed* and on assessment of the levels of potential exposure of people, organisms, and environment at *risk*.

risk evaluation
Establishment of a qualitative or quantitative relationship between *risk*s and benefits, involving the complex process of determining the significance of the identified *hazard*s and estimated risks to those organisms or people concerned with or affected by them.

risk identification
Recognition of a potential *hazard* and definition of the factors required to assess the probability of *exposure* of organisms or people to that hazard and of harm resulting from such exposure.

risk indicator
See *risk marker.*

risk management
Decision-making process involving considerations of political, social, economic, and engineering factors with relevant *risk* assessments relating to a potential *hazard* so as to develop, analyze, and compare regulatory options and to select the optimal regulatory response for safety from that hazard.

Note: Essentially risk management is the combination of three steps: *risk evaluation*; *emission* and *exposure* control; *risk monitoring*.

risk marker
risk indicator
Attribute that is associated with an increased probability of occurrence of a disease or other specified outcome and that can be used as an indicator of this increased *risk*.

Note: A risk marker is not necessarily a causal factor.

risk monitoring
Process of following up the decisions and actions within *risk management* in order to check whether the aims of reduced *exposure* and risk are achieved.

risk perception
Subjective perception of the gravity or importance of the *risk* based on a person's knowledge of different risks and the moral, economic, and political judgment of their implications.

risk phrases
Word groups identifying potential *health* or environmental *hazard*s required under CPL Directives (European Community); may be incorporated into *Safety* Data Sheets.

risk quotient
Ratio of *predicted environmental concentration* to *predicted no-effect concentration*.

Note: The higher this value above 1, the greater the risk. If the value is below 1, there should be no risk as a result of the predicted *exposure*.

risk ratio
Value obtained by dividing the probability of occurrence of a specific effect in one group by the probability of occurrence of the same effect in another group, or the value obtained by dividing the probability of occurrence of one potentially hazardous event by the probability of occurrence of another.

Note: Calculation of such ratios is used in choosing between options in *risk management*.

risk-specific dose
Amount of *exposure* corresponding to a specified level of *risk*.

RNA
See *ribonucleic acid.*

rodenticide
Substance intended to kill rodents.

route of *exposure*
Means by which a *toxic* agent gains access to an organism by administration through the gastrointestinal tract (ingestion), lungs (inhalation), skin (topical), or by other routes such as intravenous, subcutaneous, intramuscular, or intraperitoneal routes.

S9 fraction
Supernatant fraction obtained from an organ (usually liver) homogenate by centrifuging at 9000 *g* for 20 min in a suitable medium; this fraction contains cytosol and microsomes.

safety
Reciprocal of *risk*: practical certainty that injury will not result from a *hazard* under defined conditions.

Note 1: Safety of a *drug* or other substance in the context of human *health*: the extent to which a substance may be used in the amount necessary for the intended therapeutic purpose with a minimum risk of *adverse* health *effects*.

Note 2: Safety (toxicological): The high probability that injury will not result from *exposure* to a substance under defined conditions of quantity and manner of use, ideally controlled to minimize exposure.

safety data sheet
Single page giving toxicological and other *safety* advice, usually associated with a particular preparation, substance, or process.

safety factor (SF)
See *uncertainty factor.*

safety pharmacology
Science directed to the discovery, development, and safe therapeutic use of biologically active substances as a result of the identification, monitoring, and characterization of potentially undesirable pharmacodynamic activities of these substances in nonclinical studies.

saluretic
See *natriuretic.*

sample (in statistics)
1. Group of individuals often taken at random from a population for research purposes.
2. One or more items taken from a population or a process and intended to provide information on the population or process.
3. Portion of material selected from a larger quantity so as to be representative of the whole.

sampling error
That part of the total error (the estimate from a *sample* minus the population value) associated with using only a fraction of the population and extrapolating to the whole, as distinct from analytical or test error.

Note: Sampling error arises from a lack of homogeneity in the parent population.

[2]

sarcoma
Malignant tumor arising in a connective tissue and composed primarily of *anaplastic* cells resembling supportive tissue (see *anaplasia*).

saturable elimination
Elimination that becomes *concentration*-independent at a concentration at which the elimination process is functioning maximally.
[2]

saturnia
Pain in a joint resulting from lead poisoning.

saturnism
plumbism
Intoxication caused by lead.

Scatchard plot
Method for analyzing data for freely reversible ligand/*receptor* binding interactions.

Note: The graphical plot is [bound ligand]/[free ligand] against [bound ligand], with slope the negative reciprocal of the binding affinity and intercept on the x-axis the number of receptors.

[2]

scotoma
Area of diminished or lost vision within the visual field, surrounded by an area of less affected or normal vision.

sclerosis
Hardening of an organ or tissue, especially that due to excessive growth of fibrous tissue.

screening
1. Carrying out of a test(s), examination(s), or procedure(s) in order to expose undetected abnormalities, unrecognized (incipient) diseases, or defects: Examples are mass X-rays and cervical smears.
2. Pharmacological or toxicological screening consists of a specified set of procedures to which a series of compounds is subjected to characterize pharmacological and toxicological properties and to establish *dose–effect* and *dose–response* relationships.

screening level
Decision limit or cut-off point at which a *screening* test is regarded as positive.

secondary metabolite
Product of biochemical processes other than the normal metabolic pathways, mostly produced in microorganisms or plants after the phase of active growth and under conditions of nutrient deficiency.

secondhand smoke
See *sidestream smoke.*

second messenger
Intracellular effector substance increasing or decreasing as a result of the stimulation of a *receptor* by an *agonist*, considered as the "first messenger".
[2]

secretion
1. Process by which a substance such as a hormone or *enzyme* produced in a cell is passed through a *plasma membrane* to the outside, for example, the intestinal lumen or the blood (internal secretion).
2. Solid, liquid, or gaseous material passed from the inside of a cell through a plasma membrane to the outside as a result of cell activity.

sedative
Substance that exerts a soothing or tranquillizing effect.

self-cleaning of water (in a reservoir)
Water purification by natural biological and physicochemical processes.

self-purification of the atmosphere
Purification of the atmosphere from contaminants by natural biological and physicochemical processes.

semichronic
See *subchronic.*

semiochemical
Substance produced by plants or animals, or a synthetic analogue thereof, that evokes a behavioral response in individuals of the producing species or other species (e.g., *allomones*, *kairomones*, *pheromones*, and *synomones*).

semipermeable (selectively or differentially permeable) **membrane**
Membrane that will preferentially allow certain molecules or ions to pass through it while preventing the passage of others.

sensibilization
See *sensitization.*

sensitivity (in metrology and analytical chemistry), *A*
1. Quotient of the change in the *indication* and the corresponding change in the value of the quantity being measured.

[7]

2. Slope of the calibration curve. If the curve is in fact a "curve", rather than a straight line, then of course sensitivity will be a function of analyte concentration or amount. If sensitivity is to be a unique performance characteristic, it must depend only on the chemical measurement process, not upon scale factors.

[3]

sensitivity (of a screening test)
Extent (usually expressed as a percentage) to which a method gives results that are free from false negatives.

Note 1: The fewer the false negatives, the greater the sensitivity.

Note 2: Quantitatively, sensitivity is the proportion of truly diseased persons in the screened population who are identified as diseased by the screening test.

sensitization
Immune response whereby individuals become *hypersensitive* to substances, pollen, dandruff, or other agents that make them develop a potentially harmful *allergy* when they are subsequently *exposed* to the sensitizing material (*allergen*).

sensitizer
Substance causing *sensitization*.

sensory effect level
1. Intensity, where the detection *threshold* level is defined as the lower limit of the perceived intensity range (by convention, the lowest *concentration* that can be detected in 50 % of the cases in which it is present).
2. Quality, where the recognition threshold level is defined as the lowest concentration at which the sensory effect can be recognized correctly in 50 % of the cases.
3. Acceptability and annoyance, where the nuisance threshold level is defined as the concentration at which not more than a small proportion of the population, less than 5 %, experiences annoyance for a small part of the time, less than 2 %.

Note: Since annoyance will be influenced by a number of factors, a nuisance threshold level cannot be set on the basis of concentration alone.

serum
Clear watery fluid especially that moistens the surface of serous membranes or that exudes through *inflammation* of any of these membranes.
[2]

serum
blood serum
Watery proteinaceous portion of the blood that remains after clotting.
[2]

shellfish poisoning
Serious illness which is a consequence of consumption of bivalve shellfish (mollusks) such as mussels, oysters, and clams that have ingested, by filter feeding, large quantities of microalgae.
See *amnesic shellfish poisoning*, *diarrheal shellfish poisoning*, *neurologic shellfish poisoning*, *paralytic shellfish poisoning.*

short-term effect
See *acute effect.*

short-term exposure limit (STEL)
Fifteen-minute *time-weighted average* (TWA) *exposure* recommended by ACGIH which should not be exceeded at any time during a workday, even if the 8-h TWA is within the *threshold limit value: time-weighted average*, TLV-TWA.

Note: Workers can be exposed to a maximum of four STEL periods per 8-h shift, with at least 60 min between exposure periods.

[2]

short-term toxicity
See *acute toxicity.*

side-effect
Action of a *drug* other than that desired for beneficial pharmacological effect.

siderosis
1. *Pneumoconiosis* resulting from the inhalation of iron dust.
2. Excess of iron in the urine, blood, or tissues, characterized by hemosiderin granules in urine and iron deposits in tissues.

sidestream smoke
environmental tobacco smoke (ETS)
secondhand smoke
Cloud of small particles and gases that is given off from the end of a burning tobacco product (cigarette, pipe, cigar) between puffs and is not directly inhaled by the smoker.

Note: This is the smoke that gives rise to passive inhalation on the part of bystanders.

sign
Objective evidence of a disease, deformity, or an effect induced by an agent, perceptible to an examining physician.

signal transduction
Molecular pathways through which a cell senses changes in its external or internal environment and changes its pattern of *gene* expression or *enzyme* activity in response.
After [9]

silicosis
Pneumoconiosis resulting from inhalation of silica dust.

simulation test
Procedure designed to predict the rate of *biodegradation* of a compound under relevant environmental conditions.

single nucleotide polymorphism (SNP)
Single base variation at a chromosomal locus which exists stably within populations (typically defined as each variant form being present in at least 1–2 % of individuals).
After [8]

sink
In environmental chemistry, an area or part of the environment in which, or a process by which, one or more *pollutants* is removed from the medium in which it is dispersed.

Note: For example, moist ground acts as a sink for sulfur dioxide in the air.

sister chromatid exchange (SCE)
Reciprocal exchange of *chromatin* between two replicated *chromosome*s that remain attached to each other until anaphase of *mitosis*; used as a measure of *mutagenicity* of substances that produce this effect.

skeletal fluorosis
Osteosclerosis due to fluoride.

slimicide
Substance intended to kill slime-producing organisms.

Note: Used on paper stock, water cooling systems, paving stones, etc.

slope factor
Value, in inverse *concentration* or *dose* units, derived from the slope of a *dose–response* curve; in practice, limited to *carcinogenic* effects with the curve assumed to be linear at low concentrations or doses.

Note: The product of the slope factor and the *exposure* is taken to reflect the probability of producing the related effect.

societal risk
Total probability of harm to a human population including the probability of *adverse effects* to *health* of descendants and the probability of disruption resulting from loss of services such as industrial plant or loss of material goods and electricity.

soil partition coefficient (soil K_d)
Experimental ratio of a substance's concentration in the soil to that in the aqueous (dissolved) soil phase at equilibrium: It is valid only for the specific concentration and solid/solution ratio of the test.
See also *organic carbon partition coefficient.*
[6]

solvent abuse
solvent sniffing
Deliberate inhalation (or drinking) of volatile solvents, in order to become intoxicated.

solvent-sniffing
See *solvent abuse.*

somatic
1. Pertaining to the body as opposed to the mind.
2. Pertaining to nonreproductive cells or tissues.
3. Pertaining to the framework of the body as opposed to the viscera.

soporific
Substance producing sleep.

sorption
Noncommittal term used instead of *adsorption* or *absorption* when it is difficult to discriminate experimentally between these two processes.

speciation (in chemistry)
Distribution of an element among defined *chemical species* in a system.
[3]

speciation analysis (in chemistry)
Analytical activities of identifying and (or) measuring the quantities of one or more individual *chemical species* in a *sample*.
[3]

species
1. In biological systematics, group of organisms of common ancestry that are able to reproduce only among themselves and that are usually geographically distinct.
2. See *chemical species.*

species differences in sensitivity
Quantitative or qualitative differences of response to the action(s) of a potentially *toxic* substance on various species of living organisms.

species-specific sensitivity
Quantitative and qualitative features of response to the action(s) of a potentially *toxic* substance that are characteristic for a particular species of living organism.

specific death rate
Death rate computed for a subpopulation of individual organisms or people having a specified characteristic or attribute, and named accordingly.

Example: Age-specific death rate, the number of deaths of persons of a specified age during a given period of time, divided by the total number of persons of that age in the population during that time.

specificity (of a screening test)
Proportion of truly nondiseased persons who are identified by the screening test.

specific pathogen free (SPF)
Describing an animal removed from its mother under sterile conditions just prior to term and subsequently reared and kept under sterile conditions.

specimen
Specifically selected portion of any substance, material, organism (specifically tissue, blood, urine, or feces) or environmental medium assumed to be representative of the parent substance, etc. at the time it is taken for the purpose of diagnosis, identification, study, or demonstration.

spectral radiant power
The radiant power at wavelength lambda (λ) per unit wavelength interval.

splicing
Processes through which *introns* are removed from a m*RNA* prior to translation and the *exons* joined. [9]

spreader
Agent used in some *pesticide* formulations to extend the even disposition of the active ingredient.

stability half life (half time)
Time required for the amount of a substance in a formulation to decrease, for any reason, by one-half (50 %).
See also *half life*, *half time.*

standard
That which is established as a measure or model to which others of a similar nature should conform.

standard (in law or regulation)
technical directive
Technical specification, usually in the form of a document available to the public, drawn up with the consensus or general approval of all interests affected by it, based on the consolidated results of science, technology, and experience, aimed at the promotion of optimum community benefits and approved by a body recognized on the national, regional, or international level.

standard (in analytical chemistry)
See *reference material*, *standard material.*

standardization
1. Making any substance, *drug*, or other preparation conform to type or precisely defined characteristics.
2. Establishment of precisely defined characteristics, or precisely defined methods, for future reference.
3. Definition of precise procedures for administering, scoring, and evaluating the results of a new method that is under development.

standard material (in analytical chemistry)
standard
See *reference material.*

standard(ized) morbidity ratio (SMR)
Ratio of the number of patients with a particular *disease* observed in a study group or population to the total number of people in the group or population multiplied by 100.

Note: This ratio is usually expressed as a percentage.

standard(ized) mortality ratio (SMR)
Ratio of the number of deaths observed in the study group or population to the number of deaths that would be expected if the study population had the same specific rates as the standard population, multiplied by 100.

Note: This ratio is usually expressed as a percentage.

stannosis
Pneumoconiosis resulting from inhalation of tin dust.

steady state (in chemistry and toxicology)
State of a system in which the conditions do not change in time.

Note: For further information, see [3].

[2]

stem cell
Multipotent cell with mitotic potential that may serve as a precursor for many kinds of differentiated cells.
[2]

stereoselective synthesis
Chemical reaction (or reaction sequence) in which one or more new elements of chirality are formed in a substrate molecule and which produces the stereoisomeric (enantiomeric or diastereoisomeric) products in unequal amounts.

Note: Traditionally called asymmetric synthesis.

[2]

stereoselectivity
Specificity of chemical reactivity of stereoisomers based on their three-dimensional molecular structure.
[2]

stochastic
Pertaining to or arising from chance and hence obeying the laws of probability.

stochastic effect
stochastic process
Phenomenon pertaining to or arising from chance, and hence obeying the laws of probability.

stochastic process
See *stochastic effect.*

stratification (in epidemiology)
Process of or result of separating a *sample* into several subsamples according to specified criteria such as age groups, socioeconomic status, etc.

stratified sample
Subset of a population selected according to some important characteristic.

stress proteins
See *heat shock proteins.*

structural alert
Chemical grouping which is known to be associated with a particular type of toxic effect (e.g., mutagenicity).

structure–activity relationship (SAR)
Association between specific aspects of molecular structure and defined biological action.
See also *quantitative structure–activity relationship.*

structure–metabolism relationship (SMR)
Association between the physicochemical and (or) the structural properties of a substance and its metabolic behavior.
[2]

subacute
See *subchronic.*

subchronic
Repeated over a short period, usually about 10 % of the life span; an imprecise term used to describe *exposure*s of intermediate duration.

subchronic effect
Biological change resulting from an environmental alteration lasting about 10 % of the lifetime of the test organism.

Note: In practice with experimental animals, such an effect is usually identified as resulting from multiple or continuous *exposures* occurring over 3 months (90 days). Sometimes a subchronic effect is distinguished from a *subacute* effect on the basis of its lasting for a much longer time.

subchronic toxicity test
Animal experiment serving to study the effects produced by the test substance when administered in repeated *doses* (or continually in food, drinking water, air) over a period of up to about 90 days.

subclinical effect
Biological change with detectable symptoms following *exposure* to an agent known to cause *disease* either before symptoms of the disease occur or when they are absent.

subfertility
Fertility below the normal range for a given species.
[8]

subjective environment
perceived environment
Surrounding conditions as perceived by persons living in these conditions.

substrate (in biology)
1. Substance material on which an *enzyme* acts.
2. Surface on which an organism grows or to which is attached.

subthreshold dose
See *no-effect dose.*

sudorific
See *diaphoretic.*

sufficient evidence
According to the USEPA's Guidelines for *Carcinogen Risk Assessment*, sufficient evidence is a collection of facts and scientific references that is definite enough to establish that an *adverse effect* is caused by the agent in question.

suggested no-adverse-response level (SNARL)
Maximum *dose* or *concentration* that on current understanding is likely to be tolerated by an *exposed* organism without producing any harm.

suicide reaction
Formation of irreversible cleavage complexes (also referred to as "suicide complexes") leading to cell death.

summary sheet
Two-to-four page summary of a *risk assessment*.

summation (in neurophysiology)
Process of addition of separate postsynaptic responses caused by stimuli that are adjacent in time and space.

Note: Excitation of a synapse evokes a graded potential change in the postsynaptic membrane that may be below the threshold required to trigger an impulse. If two or more such potentials are caused either nearly simultaneously, at different synapses on the same neuron (spatial summation), or in rapid succession at the same synapse (temporal summation), the summed response may be sufficient to trigger a postsynaptic impulse. Summation may occur between excitatory potentials, inhibitory potentials, or between an excitatory and an inhibitory potential.

Superfund
Federal authority, established by the U.S. Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) in 1980, to respond directly to releases or threatened releases (such as from landfills or waste disposal areas) of hazardous substances that may endanger *health* or welfare.

superoxide dismutase
Enzymatic antioxidant that removes the potentially toxic superoxide ion (O^{2-}) by disproportionating it to O_2 and hydrogen peroxide (H_2O_2).

superthreshold dose
See *toxic dose.*

surface layer
Region of space comprising and adjoining the phase boundary between a solid and liquid phase, between a solid and gas phase, or between a liquid and gas phase within which properties of matter are significantly different from the values in the adjoining bulk phases.

surrogate
Relatively well studied *toxicant* whose properties are assumed to apply to an entire chemically and toxicologically related class; for example, benzo(a)pyrene data may be used as toxicologically equivalent to that for all *carcinogenic* polynuclear aromatic hydrocarbons.

surveillance
Systematic ongoing collection, collation, and analysis of data and the timely dissemination of information to those who need to know in order that action can be taken to initiate investigative or control measures.

susceptible
vulnerable
Describing a group of organisms more vulnerable to a given *exposure* than the majority of the population to which they belong.

Note: Susceptibility may reflect gender, age, physiological status, or genetic constitution of the organisms at risk.

[2]

susceptibility biomarker
See *biomarker of susceptibility.*

susceptibility
Condition of lacking the power to resist a particular *disease* or infection; thus, in susceptible people, "normal expected" results occur, but with a lower *exposure* (or *dose*) than in the rest of the population.

sympathetic nervous system
Part of the autonomic nervous system originating in the thoracic and lumbar regions of the spinal cord that tends to inhibit or oppose the physiological effects of the *parasympathetic* nervous system, as in tending to reduce digestive secretions, speed up the heart, and contract blood vessels.
See *parasympathetic*.

sympatholytic
anti-adrenergic
1. adj., Blocking transmission of impulses from the adrenergic (sympathetic) postganglionic fibers to effector organs or tissues.
2. n., Agent that blocks transmission of impulses from the adrenergic (sympathetic) postganglionic fibers to effector organs or tissues.

sympathomimetic
adrenergic
1. adj., Producing effects resembling those of impulses transmitted by the postganglionic fibers of the *sympathetic nervous system*.
2. n., Agent that produces effects resembling those of impulses transmitted by the postganglionic fibers of the sympathetic nervous system.

symptom
Any subjective evidence of a disease or an effect induced by a substance as perceived by the affected subject.

symptomatology
General description of all of the signs and symptoms of *exposure* to a *toxicant*.

Note: Signs are the overt (observable) responses associated with exposure (such as convulsions, death, etc.), whereas symptoms are covert (subjective) responses (such as nausea, headache, etc.).

synapse
Functional junction between two neurons, where a nerve impulse is transmitted from one neuron to another.

synaptic transmission
See *synapse.*

syndrome
Set of *signs* and *symptoms* occurring together and often characterizing a particular *disease*-like state.

synergism (in toxicology)
synergistic effect
synergy (in toxicology)
Pharmacological or toxicological interaction in which the combined biological effect of *exposure* to two or more substances is greater than expected on the basis of the simple summation of the effects of each of the individual substances.

synergist (in toxicology)
Substance that contributes more than additively to a mutual effect with another substance.

synergistic effect
See *synergism.*

synergy
See *synergism.*

synomone
Semiochemical that is produced by one organism inducing a response in an organism of another species that is favorable to both the emitter and the responding organism.
See *allomone*, *kairomone.*

synteny
Property of *gene*s which reside on the same *chromosome*.

systematic sample
Subset selected according to some simple rule such as specified date or alphabetic classification.

systemic
1. Relating to the body as a whole.
2. Occurring at a site in the body remote from the point of contact with a substance.
After [1]

systemic effect
Consequence that is either of a generalized nature or that occurs at a site distant from the point of entry of a substance.

Note: A systemic effect requires *absorption* and distribution of the substance in the body.

systems biology
Study of the mechanisms underlying complex biological processes as integrated systems of many diverse, interacting components.

Note: It involves (1) collection of large sets of experimental data (by high-throughput technologies and/or by mining the literature of reductionist molecular biology and biochemistry), (2) proposal of mathematical models that might account for at least some significant aspects of this data set, (3) accurate computer solution of the mathematical equations to obtain numerical predictions, and (4) assessment of the quality of the model by comparing numerical simulations with the experimental data.

tachy-
Prefix meaning rapid as in *tachycardia* and *tachypnoea*.

tachycardia
Antonym: *bradycardia*
Abnormally fast heartbeat.

tachypnoea
Antonym: *bradypnoea*
Abnormally fast breathing.

taeniacide
Substance intended to kill tapeworms.

target (in biology)
Any organism, organ, tissue, cell, or cell constituent that is subject to the action of an agent.

target population (in epidemiology)
1. Collection of individuals, items, measurements, etc. about which inferences are required: The term is sometimes used to indicate the population from which a *sample* is drawn and sometimes to denote any reference population about which inferences are needed.
2. Group of persons for whom an intervention is planned.

T cell
See *T lymphocyte*.

technical directive
See *standard*.

telomere
Structure which terminates the arm of a *chromosome*.

Note: A similar term "telomer", with a different meaning is found in the IUPAC "Gold Book" [3].

temporary acceptable daily intake
Value for the *acceptable daily intake* (ADI) proposed for guidance when data are sufficient to conclude that use of the substance is safe over the relatively short period of time required to generate and evaluate further safety data, but are insufficient to conclude that use of the substance is safe over a lifetime.

Note: A higher-than-normal *safety* factor is used when establishing a temporary ADI, and an expiration date is established by which time appropriate data to resolve the safety issue should be available.

temporary maximum residue limit
Regulatory value established for a specified, limited time when only a temporary *acceptable daily intake* has been established for the *pesticide* concerned or, with the existence of an agreed acceptable daily intake, the available residue data are inadequate for firm maximum residue recommendations.

teratogen
Substance that, when administered prenatally (to the mother), induces permanent structural malformations or defects in the offspring.

teratogenicity
1. Potential to cause the production of nonheritable structural malformations or defects in offspring.
2. Production of nonheritable structural malformations or defects in offspring.

teratology
Study of malformations, monstrosities, or serious deviations from normal development in organisms.

testing of chemicals
1. In *toxicology*, evaluation of the therapeutic and potentially *toxic* effects of substances by their application through relevant routes of *exposure* with appropriate organisms or biological systems so as to relate effects to *dose* following application.
2. In chemistry, qualitative or quantitative analysis by the application of one or more fixed methods and comparison of the results with established standards.

tetanic
Pertaining to tetanus, characterized by tonic muscle spasm.

theoretical maximum daily intake (TMDI)
Predicted maximum daily intake of a residue, assuming that it is present at the *maximum residue level* and that average daily consumption of foods per person is represented by assessed regional diets: It is expressed in milligrams of residue per person per day.
After [14]

therapeutic cloning
Generation and manipulation of stem cells with the objective of deriving cells of a particular organ or tissue to treat a disease.

therapeutic index
Ratio between *toxic* and therapeutic doses (the higher the ratio, the greater the safety of the therapeutic dose).

three-dimensional quantitative structure–activity relationship (3D-QSAR)
Quantitative association between the three-dimensional structural properties of a substance and its biological properties.
[2]
See *quantitative structure–activity relationship.*

threshold
Dose or *exposure concentration* below which a defined effect will not occur.
See also *critical effect.*

threshold concentration
See *threshold.*

threshold dose
See *threshold.*

threshold limit value–ceiling (TLV–C)
As defined by ACGIH, *concentration* of a potentially *toxic* substance that should not be exceeded during any part of the working *exposure*.
[2]

threshold limit value–short-term exposure limit (TLV–STEL)
As defined by ACGIH, *concentration* to which it is believed that workers can be *exposed* continuously for a short period of time without suffering from (1) irritation, (2) *chronic* or irreversible tissue damage, or (3) *narcosis* of sufficient degree to increase the likelihood of accidental injury, impair self-rescue or materially reduce work efficiency, and provided that the daily TLV-TWA is not exceeded.

Note: It is not a separate independent *exposure* guideline; rather, it supplements the TLV-TWA limit where there are recognized *acute* effects from a substance whose *toxic* effects are primarily of a chronic nature. TLV-STELs are recommended only where *toxic* effects have been reported from high short-term exposures in either humans or animals.

[2]

threshold limit value–time-weighted average (TLV–TWA)
As defined by ACGIH, *time-weighted average concentration* for a conventional 8-h workday and a 40-h workweek, to which it is believed nearly all workers may be repeatedly *exposed*, day after day, without *adverse effect*.
[2]

threshold of toxicological concern (TTC)
Human *exposure* threshold value for a group of chemicals below which there should be no appreciable risk to human health.

thrombocytopenia
Decrease in the number of blood platelets (thrombocytes).

thyrotoxicosis
Condition resulting from excessive concentrations of thyroid hormones, as in hyperthyroidism, characterized by bulging eyes and rapid heart rate.

tidal volume
Quantity of air or test gas that is inhaled and exhaled during one respiratory cycle.

time-weighted-average-exposure (TWAE)
time-weighted-average concentration (TWAC)
Concentration in the *exposure* medium at each measured time interval multiplied by that time interval and divided by the total time of observation.

Note: For occupational exposure, a working shift of 8 h is commonly used as the averaging time.

tinnitus
Continual noise in the ears, such as ringing, buzzing, roaring, or clicking.

tissue dose
Amount of a substance or physical agent (radiation) absorbed by a tissue.

tissue/plasma partition coefficient
See *partition ratio.*

T lymphocyte
Animal cell that possesses specific cell surface *receptor*s through which it binds to foreign substances or organisms, or those which it identifies as foreign, and which initiates *immune responses*.

tolerable daily intake (TDI)
Estimate of the amount of a potentially harmful substance (e.g., contaminant) in food or drinking water that can be ingested daily over a lifetime without appreciable *health risk*.

Note 1: For regulation of substances that cannot be easily avoided, a provisionally *tolerable weekly intake* (PTWI) may be applied as a temporary limit.

Note 2: *Acceptable daily intake* is normally used for substances not known to be harmful, such as food additives.

[2]

tolerable risk
Probability of suffering disease or injury that can, for the time being, be tolerated, taking into account the associated benefits, and assuming that the *risk* is minimized by appropriate control procedures.

tolerable weekly intake (TWI)
Estimate of the amount of a potentially harmful substance (e.g., a contaminant) in food or drinking water that can be ingested weekly over a lifetime without appreciable *health risk*.
[2]

tolerance
1. Adaptive state characterized by diminished effects of a particular *dose* of a substance: The process leading to tolerance is called "adaptation".
2. In food *toxicology*, dose that an individual can tolerate without showing an effect.
3. Ability to experience *exposure* to potentially harmful amounts of a substance without showing an *adverse effect*.
4. Ability of an organism to survive in the presence of a *toxic* substance: Increased tolerance may be acquired by adaptation to constant *exposure*.
5. In immunology, state of specific immunological unresponsiveness.

tonic
1. Characterized by tension, especially muscular tension.
2. Medical preparation that increases or restores normal muscular tension.

topical (in medicine)
Applied directly to the surface of the body.
[2]

topical effect
Consequence of application of a substance to the surface of the body which occurs at the point of application.
[2]

torsade de pointes
Potentially lethal form of ventricular *tachycardia* following chronic abuse of alcohol and mainly due to hypomagnesemia.

total diet study
1. Study designed to establish the pattern of *pesticide* residue intake by a person consuming a defined diet.
2. Study undertaken to show the range and amount of various foodstuffs in a typical diet or to estimate the total amount of a specific substance in a typical diet.

total terminal residue (of a pesticide)
Summation of levels of all the residues of a defined *pesticide* in a food.
See also *residue.*
After [6]

toxemia (blood poisoning)
1. Condition in which the blood contains *toxins* produced by body cells at a local source of infection or derived from the growth of microorganisms.
2. Pregnancy-related condition characterized by high blood pressure, swelling, and fluid retention, and proteins in the urine.

toxic
Able to cause injury to living organisms as a result of physicochemical interaction.

toxicant
See *toxic substance.*

toxic chemical
See *toxic substance.*

toxic dose
superthreshold dose
Amount of a substance that produces intoxication without lethal outcome.

toxicity
1. Capacity to cause injury to a living organism defined with reference to the quantity of substance administered or absorbed, the way in which the substance is administered and distributed in time (single or repeated *doses*), the type and severity of injury, the time needed to produce the injury, the nature of the organism(s) affected, and other relevant conditions.
2. *Adverse effect*s of a substance on a living organism defined as in 1.

3. Measure of incompatibility of a substance with life: This quantity may be expressed as the reciprocal of the absolute value of *median lethal dose* ($1/LD_{50}$) or *concentration* ($1/LC_{50}$).

toxicity equivalency factor (TEF), f
Ratio of the toxicity of a chemical to that of another structurally related chemical (or index compound) chosen as a reference.
[6]

toxicity equivalency factor (in *risk assessment*) (TEF), f
Ratio of the toxicity of a chemical to that of another structurally related chemical (or index compound) chosen as a reference. Factor used to estimate the *toxicity* of a complex mixture, commonly a mixture of chlorinated dibenzo-*p*-dioxins [oxanthrenes], furans, and biphenyls: In this case, TEF is based on relative toxicity to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin [2,3,7,8-tetrachlorooxanthrene] for which the $f = 1$.

toxicity equivalent (TEQ), T_{xe}
Contribution of a specified component (or components) to the *toxicity* of a mixture of related substances.

Note 1: The amount-of-substance (or substance) *concentration* of total toxicity equivalent is the sum of that for the components B, C … N.

Note 2: Toxicity equivalent is most commonly used in relation to the reference *toxicant* 2,3,7,8-tetrachlorodibenzo-p-dioxin [2,3,7,8-tetrachlorooxanthrene] by means of the *toxicity equivalency factor* (TEF, *f*) which is 1 for the reference substance. Hence, where c is the amount-of-substance concentration:

$$T_{xe} = \sum_{i=B}^{N} f_1 c_i$$

toxic substance
Substance causing injury to living organisms as a result of physicochemical interactions.
[2]

$t_{1/2}$
See *half life*, *half time.*

toxicity exposure ratio (TER)
Ratio of the measure of the effects (e.g., LD_{50}, LC_{50}, NOEC) to the estimated *exposure*.

Note: It is the reciprocal of a *risk quotient* or *hazard quotient*.
[6]

toxicity test
Experimental study of the *adverse effect*s of *exposure* of a living organism to a substance for a defined duration under defined conditions.

toxic material
See *toxic substance.*

toxicodynamics
Process of interaction of potentially *toxic substance*s with *target* sites, and the biochemical and physiological consequences leading to *adverse effect*s.

toxicogenomics
Scientific subdiscipline that combines *toxicology* with *genomics* to determine how an organism's genetic make-up influences its response to a toxic substance.

toxicogenetics
Study of the influence of hereditary factors on the effects of potentially *toxic* substances on individual organisms.

toxicokinetics
1. Generally, the overall process of the *absorption* in biology (*uptake*) of potentially *toxic* substances by the body, the distribution of the substances and their metabolites in tissues and organs, their *metabolism* (*biotransformation*), and the *elimination* of the substances and their metabolites from the body.
2. In validating a toxicological study, the collection of toxicokinetic data, either as an integral component in the conduct of nonclinical toxicity studies or in specially designed supportive studies, in order to assess systemic *exposure*.

toxicological data sheet
Document that gives in a uniform manner data relating to the *toxicology* of a substance, its production and application, properties and methods of identification.

Note: The data sheet may also include recommendations on protective measures.

toxicologically based pharmacokinetic modeling (TBPK)
See *physiologically based pharmacokinetic modeling.*

toxicology
Scientific discipline involving the study of the actual or potential danger presented by the harmful effects of substances on living organisms and ecosystems, of the relationship of such harmful effects to *exposure*, and of the mechanisms of action, diagnosis, prevention, and treatment of intoxications.

toxicometry
Term sometimes used to indicate a combination of investigative methods and techniques for making a quantitative assessment of *toxicity* and the *hazard*s of potentially *toxic* substances.

toxicophobia
Morbid dread of *poisons*.

toxicophoric group
toxogenic group
toxophoric group
Structural moiety that upon metabolic activation exerts *toxic* effects: The presence of a toxicophoric group indicates only potential and not necessarily actual *toxicity* of a *drug* or other substances.

toxicovigilance
Active process of identification, investigation, and evaluation of various *toxic* effects in the community with a view to taking measures to reduce or control *exposure*(s) involving the substance(s) which produces these effects.

toxic substance
chemical etiologic agent
poison
toxicant
toxic chemical
toxic material
Material causing injury to living organisms as a result of physicochemical interactions.

toxification
Metabolic conversion of a potentially *toxic* substance to a product that is more toxic.

toxin
Poisonous substance produced by a biological organism such as a microbe, animal, plant, or fungus.

Note: Examples are botulinum toxin, tetrodotoxin, pyrrolizidine alkaloids, and amanitin.

toxinology
Scientific discipline involving the study of the chemistry, biochemistry, pharmacology, and *toxicology* of *toxins*.

toxogenic group
See *toxicophoric group.*

toxophoric group
See *toxicophoric group.*

traceability (in metrology)
Property of a measurement result whereby the result can be related to a stated reference through a documented unbroken chain of calibrations, each contributing to the measurement uncertainty.
[7]

tracer
1. Means by which something may be followed; for example, a radioactive isotope may replace a stable chemical element in a *toxic* compound enabling the toxicokinetics to be followed.
2. Labeled member of a population used to measure certain properties of that population.

tracer substance
Substance that can be tracked through one or more reactions or systems, often by detecting an incorporated isotope.
[2]

transcription
Process by which the genetic information encoded in a linear sequence of nucleotides in one strand of *DNA* is copied into an exactly complementary sequence of *RNA*.

transcriptome
Total m*RNA* expressed in a cell or tissue at a given point in time.

transcriptomics
Global analysis of *gene* expression to identify and evaluate changes in synthesis of m*RNA* after chemical *exposure*.
[2]

transformation
1. Alteration of a cell by incorporation of foreign genetic material and its subsequent expression in a new *phenotype*.
2. Conversion of cells growing normally to a state of rapid division in culture resembling that of a *tumor*.
3. Chemical modification of substances in the environment.

transformed cell
Cell that has become genetically altered spontaneously or by incorporation of foreign *DNA* to produce a cell with an extended lifetime in culture.
[2]

transformed cell line
See *cell line*, *transformed cell.*

transgene
Gene from one source that has been incorporated into the genome of another organism.

transgenic
Adjective used to describe animals carrying a *gene* introduced by micro-injecting *DNA* into the nucleus of the fertilized egg.

translation
Process through which a polypeptide chain of amino acid molecules is generated as directed by the sequence of a particular m*RNA* sequence.

transposon
Mobile nucleic acid element.

treatability
In relation to *waste* water, the amenability of substances to removal without adversely affecting the normal operation of biological treatment processes (such as a sewage treatment plant).

triage
1. Process for sorting people into groups based on their need for or likely benefit from immediate medical treatment.

   Note: Triage is used in hospital emergency rooms, on battlefields, and at disaster sites when limited medical resources must be allocated.

2. System used to allocate a scarce commodity, such as food, to those most likely to benefit from it.
3. Process in which things are ranked in terms of importance or priority.

trophic level
Amount of energy in terms of food that an organism needs.

Note: Organisms not needing organic food, such as plants, are said to be on a low trophic level, whereas predator species needing food of high energy content are said to be on a high trophic level. The trophic level indicates the level of the organism in the food chain.

trueness
Closeness of agreement between the average of a theoretically infinite number of replicate measured quantity values and a reference quantity value.

tubular reabsorption
Transfer of solutes from the *renal* tubule lumen to the tubular epithelial cell and normally from there to the peritubular fluid.
[2]

tumorigenic
Able to cause *tumors*.

tumor
tumour
neoplasm
1. Any abnormal swelling or growth of tissue, whether *benign* or *malignant*.
2. An abnormal growth, in rate and structure, that arises from normal tissue, but serves no physiological function.

tumor necrosis factor (TNF)
cachectin
cachexin
Protein produced by several of the body's cell types, such as white blood cells, red blood cells, and other cells that line the blood vessels; it promotes the destruction of some types of *cancer* cells and is a *cytokine* involved in systemic *inflammation*.

tumor progression
Sequence of changes by which a *benign tumor* develops from the initial lesion to a *malignant* stage.

tumor suppressor gene
Gene that serves to protect cells from entering a cancerous state.

Note: According to Knudson's "two-hit" hypothesis, both alleles of a particular *tumor* suppressor *gene* must acquire a mutation before the cell will enter a transformed state.

turnover time
See *mean life.*

two-compartment model
Product of *compartmental analysis* requiring two *compartments*.
[2]
See *compartmental modeling*, *multicompartment model.*

ulcer
Defect, often associated with *inflammation*, occurring locally or at the surface of an organ or tissue owing to sloughing of necrotic (see *necrosis*) tissue.

ultrafine particle
Particle in air of *aerodynamic diameters* 100 nm.

Note: As a group, ultrafine particles are referred to as PM0.1 (100 nm is 0.1 μm).

[2]

uncertainty (in metrology)
Parameter characterizing the dispersion of the quantity values being attributed to a measurand, based on the information used.

Note: The parameter may be, for example, a standard deviation or the half width of an interval, having a stated coverage probability.

[7]

uncertainty factor (UF)
1. In assay methodology, confidence interval or fiducial limit used to assess the probable precision of an estimate.
2. In *toxicology*, value used in extrapolation from experimental animals to man (assuming that man may be more sensitive) or from selected individuals to the general population. For example, a value applied to the *no-observed-effect-level* (NOEL) or *no-observed-adverse-effect-level* (NOAEL) to derive an *acceptable daily intake* (ADI) or *tolerable daily intake* (TDI).

   Note: The NOEL or NOAEL is divided by the value to calculate the ADI or TDI.

See also *modifying factor*, *safety factor.*

unit risk
Upper-bound excess lifetime *cancer risk* estimated to result from continuous *exposure* to an agent at a *concentration* of 1 μg L^{-1} in water, or 1 μg m^{-3} in air.

Note: The interpretation of unit risk is as follows: if unit risk = 1.5×10^{-6} μg L^{-1}, 1.5 excess tumors are expected to develop per 1 000 000 or 10^6 people if exposed daily for a lifetime to 1 μg of the chemical in 1 litre of drinking water.

upper boundary
Estimate of the plausible upper limit to the true value of a quantity.

Note: This is usually not a statistical confidence limit.

uptake
Entry of a substance into the body, an organ, a tissue, a cell, or the body fluids by passage through a membrane or by other means.

urticaria
Vascular reaction of the skin marked by the transient appearance of smooth, slightly elevated patches (wheals, hives) that are redder or paler than the surrounding skin and often attended by severe itching.

vacuole
Membrane-bound cavity within a cell.

validity of a measurement
Expression of the degree to which a measurement measures what it purports to measure.

validity of a study
Degree to which the inferences drawn, especially generalizations extending beyond the study *sample*, are warranted when account is taken of the study methods, the representativeness of the study sample, and the nature of the population from which it is drawn.

vasoconstriction
Antonym: *vasodilation*
Decrease of the caliber of the blood vessels leading to a decreased blood flow.

vasodilation
Antonym: *vasoconstriction*
Increase in the caliber of the blood vessels, leading to an increased blood flow.

vector
See *cloning vector.*

vehicle
Substance(s) used to formulate active ingredients for administration or use.

Note: In this context, it is a general term for solvents, suspending agents, etc.

venom
Animal *toxin* generally used for self-defense or predation and usually delivered by a bite or sting.

ventilation
1. Process of supplying a building or room with fresh air.
2. Process of exchange of air between the ambient atmosphere and the lungs.
3. In physiology, the amount of air inhaled per day.
4. Oxygenation of blood.

ventricular fibrillation
Irregular heartbeat characterized by uncoordinated contractions of the ventricle.

vermicide
Substance intended to kill intestinal worms.

vermifuge
See *anthelmint(h)ic.*

vertigo
Dizziness; an illusion of movement as if the external world were revolving around one's self or as if one's self were revolving in space.

vesicant
1. adj., Producing blisters on the skin.
2. n., Substance that causes blisters on the skin.

vesicle
1. In cell biology, small bladder-like, membrane-bound sac containing aqueous solution or fat.
2. In pathology, blisterlike elevation on the skin containing serous fluid.

virtually safe dose (VSD)
Human *exposure* over a lifetime to a carcinogen which has been estimated, using mathematical modeling, to result in a very low incidence of *cancer*, somewhere between zero and a specified incidence (e.g., 1 cancer in 1 000 000 exposed people).

virucide
antiviral
Substance used to control viruses.
[6]

volume of distribution
Apparent (hypothetical) volume of fluid required to contain the total amount of a substance in the body at the same *concentration* as that present in the *plasma* assuming equilibrium has been attained.

volatile organic chemical (VOC)
Any organic compound having, at 293.15 K, a vapor pressure of 0.01 kPa or more, or having a corresponding volatility under the particular condition of use.
[15]

waste
Anything that is discarded deliberately or otherwise disposed of on the assumption that it is of no further use to the primary user.

wasting syndrome
Disease marked by weight loss and atrophy of muscular and other connective tissues that is not directly related to a decrease in food and water consumption.

water potential (in physiology)
Difference in free energy or chemical potential (per unit molal volume) between pure water and water in cells and solutions.

Weibull model
Dose–response model of the form

$$P(d) = \gamma + (1 - \gamma)(1 - e^{-\beta d\alpha})$$

where $P(d)$ is the probability of a tumor (or other response) from lifetime, continuous *exposure* at dose d until age t (when tumor is fatal), α is a fitted dose parameter (sometimes called the Weibull parameter), β is a fitted dose parameter, and γ is the background response rate.

weight-of-evidence for toxicity
Extent to which the available biomedical data support the hypothesis that a substance causes a defined *toxic* effect such as cancer in humans.

withdrawal effect
Adverse event following withdrawal from a person or animal of a *drug* to which they have been chronically *exposed* or on which they have become dependent.

working zone
Space measuring up to 2 m over the level of the floor or platform that contains a worker's permanent or temporary station.

x-disease
Hyperkeratotic disease in cattle following *exposure* to chlorinated dibenzo-*p*-dioxins, naphthalenes, and related compounds.

xenobiotic
Compound with a chemical structure foreign to a given organism.

Note: Frequently restricted to man-made compounds.

yeast two-hybrid system
Genetic method for analyzing the interactions of proteins.

zero-order kinetics
Kinetics of a reaction in which the *rate* is independent of the *concentration*(s) of the reactants.
[2]

zoocide
Substance intended to kill animals.

zygote
1. Cell such as a fertilized egg resulting from the fusion of two *gametes*.
2. Cell obtained as a result of complete or partial fusion of cells produced by *meiosis*.

ANNEX 1: ABBREVIATIONS AND ACRONYMS USED IN TOXICOLOGY LITERATURE

ADI	acceptable daily intake
ADME	absorption, distribution, metabolism, excretion
ADMET	absorption, distribution, metabolism, excretion, toxicokinetics
AF	assessment factor
AIC	Akaike Information Criterion, C: a measure of the goodness of fit of an estimated statistical model calculated in the general case from the equation $C = 2k - 2 \ln L$
ALARA(P)	as low as reasonably achievable (practicable) In UK, regulations relating to worker exposure In USA, goal of risk management (USNRC regulations)
ASP	amnesic shellfish poisoning
ATP	adenosine triphosphate
AUC	area under the concentration–time curve
AUMC	area under the moment curve
BAC	bacterial artificial chromosome
BAL	British anti-Lewisite
BCF	bioconcentration factor
BEI	biological exposure indices (ACGIH)
BEM	biological effect monitoring
BMC	benchmark concentration
BMCL	confidence limit for BMC
BMD	benchmark dose
BMDL	confidence limit for BMD
BMDS	benchmark dose at a given standard deviation
BMR	benchmark rate
BOD	biochemical oxygen demand; biological oxygen demand
b.w., b.wt.	body weight
cDNA	complementary DNA

CMR	carcinogenic, mutagenic, and reproductive (toxicant)
COD	chemical oxygen demand
CoMFA	comparative molecular field analysis
COPC	compound of probable concern
CRM	certified reference material
CSAF	chemical specific adjustment factor
CTD	common technical document (drug registration)
CYP	cytochrome P450
Cyt	cytochrome
CV	ceiling value
D	absorbed dose of radiation
DDT	dichloro diphenyl trichloroethane
DNA	deoxyribonucleic acid
DNEL	derived no-effect level
DSP	diarrheal shellfish poisoning; diarrheic shellfish poisoning
EC	effective concentration, Enzyme Commission, European Community
EC_{50}	median effective concentration to 50 % of a population
EC_n	median effective concentration to n % of a population
eCTD	electronic common technical document (drug registration)
ED	effective dose
EDC	endocrine-disrupting compound
EDI	estimated daily intake
ED_{50}	median effective dose to 50 % of a population
ED_n	median effective dose to n % of a population
EEC	estimated environmental exposure concentration; estimated exposure concentration; expected environmental exposure concentration
EED	estimated exposure dose
EEL	environmental exposure level
EIA	environmental impact assessment
EIS	environmental impact statement
ELISA	enzyme-linked immunosorbent assay
EMDI	estimated maximum daily intake
EQO	environmental quality objective
EQS	environmental quality standard
ERL	extraneous residue limit
EST	expressed sequence tag
ETS	environmental tobacco smoke
f	toxicity equivalency factor
F	fraction of dose absorbed; bioavailability
FONSI	finding of no significant impact
GAP	good agricultural practice
GCP	good clinical practice
GHS	global harmonization system for classification of hazardous substances
GLP	good laboratory practice
GFR	glomerular filtration rate
GMO	genetically modified organism
GMP	good manufacturing practice
GRAS	generally regarded as safe
HAL	health advisory level
HAZOP	hazard and operability study

HEQ	human equivalent dose
HSG	Health and Safety Guide (IPCS)
HQ	hazard quotient
i.c.	intracutaneous
IC	inhibitory concentration
IC_n	inhibitory concentration to *n* % of a population
i.d.	intradermal
ID	inhibitory dose
ID_n	inhibitory dose to *n* % of a population
IDLHC	immediately dangerous to life and health concentration
i.m.	intramuscular
inhl	by inhalation
i.p.	intraperitoneal
IPD	individual protective device
I-TEF	international toxicity equivalency factor
i.v.	intravenous
K_d	soil partition coefficient
K_M	Michaelis constant
K_{oc}	organic carbon partition coefficient
K_{ow}	octan-1-ol–water partition coefficient
K_D	partition ratio
LADD	lifetime average daily dose
LC_{min}	minimum lethal concentration
LC_n	median concentration lethal to *n* % of a test population
LC_{50}	see LCn
LD	lethal dose
LD_{min}	minimum lethal dose
LD_n	median dose lethal to *n* % of a test population
LD_{50}	see LDn
LED	lowest effective dose
LEDx	lowest effective dose for a biological effect in x % of the individuals in the test population
LEL	lowest-effect level, same as LOEL
LOEL	lowest-observed-effect level
LOAEL	lowest-observed-adverse-effect level
LT_n	median time for death of *n* % of a test population
LV	limit value
MAC	maximum allowable concentration
MAK	maximal arbeitsplatz konzentration (German)
MCL	maximum contaminant level
MCLG	maximum contaminant level goal
MCS	multiple chemical sensitivity
MEL	maximum exposure limit
MF	modifying factor
MFO	mixed-function oxidase
MN	micronucleus
MOE	margin of exposure
MOS	margin of safety
MPC	maximum permissible concentration
MPL	maximum permissible level

MRL	maximum residue limit; minimal risk level (ATSDR)
MRT	mean residence time
mRNA	messenger ribonucleic acid
MSDS	material safety data sheet
MTC	maximum tolerable concentration
MTD	maximum tolerable dose; maximum tolerated dose
MTEL	maximum tolerable exposure level
NADP(H)	nicotinamide adenine dinucleotide phosphate (reduced)
NAG	*N*-acetyl-D-glycosaminidase
NC_n	median concentration narcotic to *n* % of a population
ND_n	median dose narcotic to *n* % of a population
NED	no-effect dose
NEL	no-effect level, same as NOEL
NOAEL	no-observed-adverse-effect level
NOEL	no-observed-effect level
NRL	no-response level
NSAID	nonsteroidal anti-inflammatory drug
NSC	normalized sensitivity coefficient
NSP	nanosized particle; nanoparticle (ultrafine)
OEL	occupational exposure level
OES	occupational exposure standard
OR	odds ratio
PADI	pseudo-acceptable daily intake
PAH	polycyclic aromatic hydrocarbon
PBPK	physiologically based pharmacokinetic modeling
PBPD	physiologically based pharmacodynamic modeling
PBTK	physiologically based toxicokinetic modeling
PBB	polybrominated biphenyl
PCB	polychlorinated biphenyl
PCC	population critical concentration
PCDF	polychlorinated dibenzofuran
PCR	polymerase chain reaction
PEC	predicted environmental concentration; predicted exposure concentration
PEL	permissible exposure limit
PBT	persistent, bioaccumulative, and toxic
p.c.	per cutim (Latin) = through the skin
PEL	permissible exposure limit
PIC	prior informed consent
PIP	persistent inorganic pollutant
$PM_{0.1}$	ultrafine particles in air with a maximum aerodynamic diameter <0.1 μm
$PM_{2.5}$	particles in air with a maximum aerodynamic diameter of 2.5 μm
PM_{10}	particles in air with a maximum aerodynamic diameter of 10 μm
PMR	proportionate mortality rate, ratio
PNEC	predicted no-effect concentration
p.o.	per os (Latin) = by mouth
POP	persistent organic pollutant
P_{OW}	octan-1-ol–water partition coefficient
Q	quality factor (radiation)
PPAR	peroxisome proliferator-activated receptor
PPD	personal protective device

PPE	personal protective equipment
PSP	paralytic shellfish poisoning
PTWI	provisional tolerable weekly intake
QSAR	quantitative structure–activity relationship
3D-QSAR	three-dimensional quantitative structure–activity relationship
QSMR	quantitative structure–metabolism relationship
RD	rate difference
REL	recommended exposure limit (NIOSH)
RER	relative excess risk
RfC	reference concentration
RfD	reference dose
RIA	radio-immunoassay
RME	reasonable maximum exposure
RNA	ribonucleic acid
RNS	reactive nitrogen species
RR	rate ratio; relative risk
ROS	reactive oxygen species
S-9	rat liver microsome preparation
SAR	structure–activity relationship; standard absorption rate
s.c.	subcutaneous
SCE	sister chromatid exchange
SD	standard deviation
SE	standard error
SF	safety factor
SMR	standard morbidity ratio; standard mortality ratio; structure–metabolism relationship
SNARL	suggested no-adverse-response level
SNP	single nucleotide polymorphism
SPF	specific pathogen free
STEL	short-term exposure limit
$t_{1/2}$	half life; half time
T_{eq}	toxicity equivalent
TBPK	toxicologically based pharmacokinetic modeling
TCDD	2,3,7,8-tetrachlorodibenzo-*p*-dioxin [2,3,7,8-tetrachlorooxanthrene]
TDI	tolerable daily intake
TEF	toxicity equivalency factor
TEQ	toxicity equivalent
TER	toxicity exposure ratio
TL_n	see LT_n
TLV	threshold limit value (ACGIH)
TLV-C	threshold limit value (ACGIH)–ceiling
TLV–STEL	threshold limit value (ACGIH)–short-term exposure limit
TLV–TWA	threshold limit value (ACGIH)–time-weighted average
TMDI	theoretical maximum daily intake
TTC	threshold of toxicological concern
TWA	time-weighted average
TWAC	time-weighted average concentration
TWAE	time-weighted average exposure
TWI	tolerable weekly intake
UDP	uridine diphosphate
UF	uncertainty factor

V_{max}	maximum velocity
VOC	volatile organic compound
vPvB	very persistent and very bioaccumulative
VSD	virtually safe dose

ANNEX 2: ABBREVIATIONS AND ACRONYMS OF NAMES OF INTERNATIONAL BODIES AND LEGISLATION

ABT	American Board of Toxicology
ACGIH	American Conference of Governmental Industrial Hygienists
ATS	Academy of Toxicological Science
ATSDR	Agency for Toxic Substances and Diseases Registry
BCR	Bureau Communautaire de Référence (Bruxelles)
BIBRA	British Industrial Biological Research Association
CCFA	Codex Committee on Food Additives
CCPR	Codex Committee on Pesticide Residues
CDC	Centers for Disease Control and Prevention
CEC	Commission of the European Communities
CEN	Committee Européen de Normalisation
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act (USA)
CHIP	Classification, Hazard Information, and Packaging (UK)
COSHH	Control of Substances Hazardous to Health Regulations (UK)
CPL	Classification, Packaging, and Labeling
CTD	Common Technical Document for the Registration of Pharmaceuticals for Human Use for submission to the FDA and ICH
DFG	Deutsche Forschungsgemeinschaft (German Research Council)
EC	European Community; European Commission
ECB	European Chemicals Bureau
ECHA	European CHemicals Agency
EEA	European Environmental Agency
EEC	European Economic Community
EINECS	European Inventory of Existing Chemical Substances
ELINCS	European List of New Chemical Substances
EMEA	European Medicines Agency
EPA	Environmental Protection Agency (USA), same as USEPA
EU	European Union
EUROTOX	European Society of Toxicology
EUSES	European Uniform System for Evaluation of Substances
FAO	Food and Agricultural Organization
FDA	Food and Drug Administration (USA), same as USFDA
FIOH	Finnish Institute of Occupational Health
HSE	Health and Safety Executive (UK)
IAEA	International Atomic Energy Agency
IARC	International Agency for Research on Cancer
ICCA	International Council of Chemical Associations
ICH	International Conference for Harmonization
ICRP	International Commission on Radiological Protection
ICSU	International Council of Scientific Unions (since 1998, International Council of Science)
IFCC	International Federation of Clinical Chemists

ILO	International Labor Organization
IoB	Institute of Biology
IPCS	International Program on Chemical Safety, UNEP, ILO, WHO
IRIS	Integrated Risk Information System (USA)
IRPTC	International Register of Potentially Toxic Chemicals, now UNEP Chemicals
ISEAAA	International Society for Exposure Assessment and Analysis
ISO	International Organization for Standardization
IUCLID	International Uniform Chemical Information Database, containing unvalidated property and hazard information for 2 604 EU high production volume chemicals, submitted under the Existing Substances Regulation, EC 793/93
IUPAC	International Union of Pure and Applied Chemistry
IUTOX	International Union of Toxicology
JECFA	Joint FAO/WHO Expert Committee on Food Additives
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
NAS	National Academy of Sciences (USA)
NBS	National Bureau of Standards (USA), now NIST
NIH	National Institutes of Health (USA)
NIOSH	National Institute of Occupational Safety and Health (USA)
NIST	National Institute of Standards and Technology (USA), formerly NBS
NRC	National Research Council (USA)
OECD	Organization for Economic Cooperation and Development
OEHHA	Organization of Environmental Health Hazard Assessment (USA)
OMS	Organisation Mondiale de la Santé, same as WHO
OSHA	Occupational Safety and Health Administration (USA)
RCPath	Royal College of Pathologists
REACH	Registration, Evaluation, and Authorisation of CHemicals
RIVM	Rijksinstituut voor Volksgezondheid en Milieu
RSC	Royal Society of Chemistry
SCOPE	Scientific Committee on Problems of the Environment (ICSU)
SOT	Society of Toxicology (USA)
TSCA	Toxic Substances Control Act (USA)
UNEP	United Nations Environment Program
USEPA	United States Environmental Protection Agency, same as EPA
USFDA	United States Food and Drug Administration, same as FDA
WHO	World Health Organization, same as OMS

ANNEX 3: CLASSIFICATION OF CARCINOGENICITY

1. Classification according to IARC [16]

Classification based on the weight of the evidence and not on *potency* as follows.

1. Sufficient evidence. Causal relationship has been established between *exposure* to the agent and human cancer: a positive relationship has been observed between exposure to the agent and cancer in studies in which chance, bias, and confounding could be ruled out with reasonable confidence.
2. Limited evidence. Positive association has been observed between exposure to the agent and cancer for which a causal interpretation is considered to be credible, but chance, bias, or confounding could not be ruled out with reasonable confidence.
3. Inadequate evidence. Available studies are of insufficient quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of a causal association.

4. Evidence suggesting lack of carcinogenicity. There are several adequate studies covering the full range of doses to which human beings are known to be *exposed*, which are mutually consistent in not showing a positive association between exposure to the agent and any studied cancer at any observed level of exposure. A conclusion of "evidence suggesting lack of *carcinogenicity*" is inevitably limited to the cancer sites, circumstances, and doses of exposure and length of observation covered by the available studies. In addition, the possibility of a very small *risk* at the levels of exposure studied can never be excluded.
5. Overall evaluation. Total body of evidence is taken into account; the agent is described according to the wording of one of the following categories, and the designated group is given. The categorization of an agent is a matter of scientific judgement, reflecting the strength of the evidence derived from studies in humans and in experimental animals and from other relevant data.

Group 1 The agent (mixture) is carcinogenic to humans. The exposure circumstance entails exposures that are carcinogenic to humans.

This category is used only when there is sufficient evidence of carcinogenicity in humans.

Exceptionally, an agent (mixture) may be placed in this category when evidence of carcinogenicity in humans is less than sufficient, but there is sufficient evidence of carcinogenicity in experimental animals and strong evidence in exposed humans that the agent (mixture) acts through a relevant mechanism of carcinogenicity.

Group 2 This category includes agents, mixtures, and exposure circumstances for which, at one extreme, the degree of evidence of carcinogenicity in humans is almost sufficient, as well as those for which, at the other extreme, there are no human data but for which there is evidence of carcinogenicity in experimental animals. Agents, mixtures, and exposure circumstances are assigned to either 2A (probably carcinogenic to humans) or 2B (possibly carcinogenic to humans) on the basis of epidemiological and experimental evidence of carcinogenicity and other relevant data.

Group 2A The agent (mixture) is probably carcinogenic to humans. The exposure circumstance entails exposures that are probably carcinogenic to humans.

This category is used when there is limited evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals. In some cases, an agent (mixture) may be classified in this category when there is inadequate evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals and strong evidence that the carcinogenesis is mediated by a mechanism that operates in humans. Exceptionally, an agent, mixture, or exposure circumstance may be classified in this category solely on the basis of limited evidence of carcinogenicity in humans.

Group 2B The agent (mixture) is possibly carcinogenic to humans. The exposure circumstance entails exposures that are probably carcinogenic to humans

This category is generally used for agents, mixtures, and exposure circumstances for which there is limited evidence of carcinogenicity in humans and less than sufficient evidence of carcinogenicity in experimental animals. It may also be used when there is inadequate evidence of carcinogenicity in humans but there is sufficient evidence of carcinogenicity in experimental animals. In some instances, an agent, mixture, or exposure circumstance for which there is inadequate evidence of carcinogenicity in humans but limited evidence of carcinogenicity in experimental animals together with supporting evidence from other relevant data may be placed in this group.

Group 3 The agent (mixture or exposure circumstance) is not classifiable as to its carcinogenicity to humans.

This category is used most commonly for agents, mixtures, and exposure circumstances for which the *evidence of carcinogenicity is inadequate* in humans and *inadequate or limited* in experimental animals.

Exceptionally, agents (mixtures) for which the *evidence of carcinogenicity is inadequate* in humans but *sufficient* in experimental animals may be placed in this category when there is strong evidence that the mechanism of carcinogenicity in experimental animals does not operate in humans.

Agents, mixtures, and exposure circumstances that do not fall into any other group are also placed in this category.

Group 4 The agent (mixture) is probably not carcinogenic to humans.

This category is used for agents or mixtures for which there is evidence suggesting lack of carcinogenicity in humans and in experimental animals. In some circumstances, agents or mixtures for which there is inadequate evidence of carcinogenicity in humans but evidence suggesting lack of carcinogenicity in experimental animals, consistently and strongly supported by a broad range of other relevant data, may be classified in this group.

2. Classification according to the USEPA [17,18]

Group A: "Human Carcinogen"

"This group is used only when there is sufficient evidence from epidemiologic studies to support a causal association between exposure to the agents and cancer."

Group B (1 and 2): "Probable Human Carcinogen"

"This group includes agents for which the weight of evidence of human carcinogenicity based on epidemiologic studies is 'limited' and also includes agents for which the weight of evidence of carcinogenicity based on animal studies is 'sufficient'. The group is divided into two subgroups. Usually, Group B1 is reserved for agents for which there is limited evidence of carcinogenicity from epidemiological studies. It is reasonable, for practical purposes, to regard an agent for which there is 'sufficient evidence of carcinogenicity' in animals as if it presented a carcinogenic risk to humans. Therefore, agents for which there is 'sufficient' evidence from animal studies and for which there is 'inadequate evidence' or 'no data' from epidemiologic studies would usually be categorized under Group B2."

Group C: "Possible Human Carcinogen"

"This group is used for agents with limited evidence of carcinogenicity in animals in the absence of human data. It includes a wide variety of evidence, e.g., (a) a malignant tumor response in a single well-conducted experiment that does not meet conditions for sufficient evidence, (b) tumor responses of marginal statistical significance in studies having inadequate design or reporting, (c) benign but not malignant tumors with an agent showing no response in a variety of short-term tests for mutagenicity, and (d) responses of marginal statistical significance in a tissue known to have a high or variable background rate."

Group D: "Not Classifiable as to Human Carcinogenicity"

"This group is generally used for agents with inadequate human and animal evidence of carcinogenicity or for which no data are available."

Group E: "Evidence of Non-Carcinogenicity for Humans"

"This group is used for agents that show no evidence for carcinogenicity in at least two adequate animal tests in different species or in both adequate epidemiologic and animal studies.

The designation of an agent as being in Group E is based on the available evidence and should not be interpreted as a definitive conclusion that the agent will not be a carcinogen under any circumstances."

3. Classification according to the European Union [19]

For the purpose of classification and labeling and having regard to the current state of knowledge, such substances are divided into three categories:

Category 1
Substances known to be carcinogenic to man. There is sufficient evidence to establish a casual association between human exposure to a substance and the development of cancer.

Category 2
Substances which should be regarded as if they are carcinogenic to man. There is sufficient evidence to provide a strong presumption that human exposure to a substance may result in the development of cancer, generally on the basis of

- appropriate long-term animal studies and
- other relevant information.

Category 3
Substances which cause concern for humans owing to possible carcinogenic effects but in respect of which the available information is not adequate for making a satisfactory assessment. There is some evidence from appropriate animal studies, but this is insufficient to place the substance in category 2.

4. Classification according to the American Conference of Governmental Industrial Hygienists, Inc. (ACGIH) [5]

A1: Chemical substances that are confirmed to be carcinogenic for humans
A2: Chemical substances that are suspected to be carcinogenic for humans
A3: Chemical substances that are carcinogenic for animals
A4: Substances that are not classified as carcinogenic
A5: Substances that are not suspected to be carcinogenic for humans

REFERENCES

1. J. H. Duffus. *Pure Appl. Chem.* **65**, 2003 (1993).
2. M. Nordberg, J. H. Duffus, D. M. Templeton. *Pure Appl. Chem.* **76**, 1033 (2004).
3. IUPAC. *Compendium of Chemical Terminology*, 2nd ed. (the "Gold Book"), compiled by A. D. McNaught and A. Wilkinson, Blackwell Science, Oxford (1997). XML on-line corrected version: <http://goldbook.iupac.org> (2006–) created by M. Nic, J. Jirat, B. Kosata; updates compiled by A. Jenkins.
4. IUPAC. *Compendium of Analytical Nomenclature: Definitive Rules 1997*, 3rd ed., prepared for publication by J. Inczédy, T. Lengyel, A. M. Ure, Blackwell Science, Oxford (1997). On-line version: <http://www.iupac.org/publications/analytical_compendium/>.
5. ACGIH. *2005 TLVs® and BEIs®*. American Conference of Governmental Industrial Hygienists, Cincinnati, OH (2005).
6. G. R. Stephenson, I. G. Ferris, P. T. Holland, M. Nordberg. *Pure Appl. Chem.* **78**, 2075 (2006).
7. Joint Committee for Guides in Metrology (JCGM). *International Vocabulary of Metrology - Basic and General Concepts and Associated Terms (VIM),* 3rd edition (Final draft 2006-08-01). On-line version: <http://www.ncsli.org/vim/wg2_doc_N318_VIM_3rd_edition_2006-08-01%20(3).pdf>.
8. IPCS. *Principles for Evaluating Health Risks to Reproduction Associated with Exposure to Chemicals*, Environmental Health Criteria 225, World Health Organization, Geneva (2001).
9. WHO. *Genomics and World Health*, World Health Organization, Geneva (2002).

10. Extoxnet Glossary of Terms, EXTOXNET - The EXtension TOXicology NETwork, a cooperative effort of University of California-Davis, Oregon State University, Michigan State University, Cornell University, and the University of Idaho. Primary files are maintained and archived at Oregon State University (2007). On-line version: <http://extoxnet.orst.edu/faqs/glossary.htm>.
11. WSSA. *Herbicide Handbook*, 8th ed., Weed Science Society of America, Lawrence, KS (2002).
12. IPCS. IPCS Risk Assessment Terminology, Part 2: IPCS Glossary of Key Exposure Assessment Terminology, International Program on Chemical Safety, World Health Organization, Geneva (2002). On-line version: <http://www.who.int/ipcs/methods/harmonization/areas/ipcsterminologyparts1and2.pdf>.
13. IUPAC. *Quantities, Units and Symbols in Physical Chemistry*, 2nd ed., prepared for publication by I. Mills, T. Cvitaš, K. Homann, N. Kallay, K. Kuchitsu. Blackwell Scientific, Oxford (1993).
14. WHO. *Guidelines for Predicting Dietary Intake of Pesticide Residues* (revised), WHO/FSF/FOS/97.7, World Health Organization, Geneva (1997).
15. Commission of the European Communities. *Proposal for a Council Directive on limitation of emissions of volatile organic compounds due to the use of organic solvents in certain industrial activities*. 96/0276 (SYN) Article 2.
16. IARC. *Preamble to the IARC Monographs*, 2005 International Agency for Research on Cancer, Lyon (2005). <http://monographs.iarc.fr/ENG/Preamble/>.
17. USEPA. *Guidelines for Carcinogen Risk Assessment*, U.S. Environmental Protection Agency, Washington, DC (1986). <http://www.epa.gov/iris/backgr-d.htm>.
18. USEPA. *Guidelines for Carcinogen Risk Assessment*, U.S. Environmental Protection Agency, Washington, DC (2005). <http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=116283>.
19. Health and Safety Commission. *Approved Guide to the Classification and Labelling of Substances and Preparations Dangerous for Supply*, 4th ed., L 100, HSE Books, Sudbury (1999).