

*This report contains the collective views of an international group of experts and does not necessarily represent the decisions or the stated policy of the World Health Organization*

**WHO Technical Report Series**

**808**

---

# **WHO EXPERT COMMITTEE ON DRUG DEPENDENCE**

---

Twenty-seventh Report



---

**World Health Organization**

**Geneva 1991**

WHO Library Cataloguing in Publication Data

WHO Expert Committee on Drug Dependence  
WHO Expert Committee on Drug Dependence: twenty-seventh report.

(WHO technical report series ; 808)

1. Substance dependence 2. Substance abuse 3. Drug and narcotic control  
4. Benzodiazepines 5. Propylhexedrine 5. Tetrahydrocannabinol  
I. Series

ISBN 92 4 120808 2  
ISSN 0512-3054

(NLM Classification: WM 270)

**© World Health Organization 1991**

Publications of the World Health Organization enjoy copyright protection in accordance with the provisions of Protocol 2 of the Universal Copyright Convention. For rights of reproduction or translation of WHO publications, in part or *in toto*, application should be made to the Office of Publications, World Health Organization, Geneva, Switzerland. The World Health Organization welcomes such applications.

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the Secretariat of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

**Printed in Switzerland**

91/8744 – Benteli – 6500

# Contents

1. Introduction	1
2. Benzodiazepines	2
2.1 Scheduling differentiation	2
2.2 Benzodiazepines under international control	3
2.3 Benzodiazepines not at present under international control	4
2.3.1 Brotizolam	4
2.3.2 Etizolam	5
2.3.3 Quazepam	6
3. Propylhexedrine	7
3.1 Substance identification	8
3.2 Similarity to already known compounds and effects on the central nervous system	8
3.3 Dependence potential	8
3.4 Actual abuse and/or evidence for likelihood of abuse	8
3.5 Therapeutic usefulness	9
3.6 Recommendation	9
4. Dronabinol	10
4.1 Therapeutic usefulness	10
4.2 Abuse liability and public health and social consequences of abuse of dronabinol	11
4.3 Assessment of the possibility of dronabinol's transfer to Schedule II leading to an increase in its abuse	11
4.4 Assessment of the possibility of dronabinol's transfer to Schedule II leading to an increase in the abuse of cannabis	12
4.5 Scope of recommendation	12
4.6 Recommendation	12
5. Exempted preparations	13
5.1 Outline of exempted preparations notified by the United States of America	13
5.2 Assessment and recommendation	14
6. General recommendations	15
6.1 Training with regard to psychoactive substances	15
6.2 Education of health professionals in the rational use of psychotropic drugs	15
6.3 Treatment of drug dependence	15
6.4 Drug abuse surveillance systems	16
6.5 Collection of drug-abuse-related data in developing countries	16
6.6 Study on the impact of scheduling	16
6.7 Information on exemption-terminated preparations	16
Acknowledgements	17
References	17

# WHO Expert Committee on Drug Dependence

Geneva, 24–28 September 1990

## Members\*

- Professor N. Cortes-Maramba, Department of Pharmacology, College of Medicine, University of the Philippines, Manila, Philippines (*Vice-Chairman*)
- Professor A. H. Ghodse, Director, Addictive Behaviour Services and Research Unit, St George's Hospital Medical School, London, England
- Dr G. W. Hanks, Consultant Physician, Continuing Care Unit, Royal Marsden Hospital, London, England
- Professor L. Harris, Chairman, Department of Pharmacology, Virginia Commonwealth University, Richmond, VA, USA (*Rapporteur*)
- Mr Liew Kee-Hooi, Jalan 17/17, Petaling Jaya, Malaysia
- Dr D. Mohan, Professor, National Drug and Alcohol Dependence Treatment Centre, All India Institute of Medical Sciences, New Delhi, India
- Professor O. Ogunremi, Department of Behavioural Sciences, University of Ilorin, Ilorin, Nigeria
- Dr H. Petursson, Medical Director, Department of Psychiatry, Borgarspitalinn, Reykjavik, Iceland
- Professor T. Yanagita, Director, Preclinical Research Laboratories, Central Institute of Experimental Animals, Kawasaki, Japan (*Chairman*)

## Representatives of other Organizations†

- International Criminal Police Organization (INTERPOL)*  
Mr P. Morgese, Drug Subdivision, INTERPOL, Lyon, France
- International Federation of Pharmaceutical Manufacturers Associations (IFPMA)*  
Ms M. Cone, Vice-President of Scientific Affairs, Geneva, Switzerland
- International Narcotics Control Board (INCB)*  
Professor S. O. Kayaalp, Member, INCB, Vienna International Centre, Vienna, Austria
- United Nations Division of Narcotic Drugs*  
Professor K. Szendrei, Chief, Applied Scientific Research and Technical Advisory Section, United Nations Division of Narcotic Drugs, Vienna International Centre, Vienna, Austria
- World Federation of Proprietary Medicine Manufacturers (WFPMM)*  
Represented by Ms M. Cone, International Federation of Pharmaceutical Manufacturers Associations

## Secretariat

- Mr H. Emblad, Director, Programme on Substance Abuse, WHO, Geneva, Switzerland
- Dr R. Griffiths, Department of Psychiatry, Johns Hopkins University School of Medicine, Baltimore, MD, USA (*Temporary Adviser*)
- Dr M. Klein, Food and Drug Administration, Rockville, MD, USA (*Temporary Adviser*)
- Mr T. Yoshida, Programme on Substance Abuse, WHO, Geneva, Switzerland (*Secretary*)

\* Unable to attend: Dr R. Welz, Assistant Professor of Medical Psychology, University of Göttingen, Göttingen, Federal Republic of Germany.

† Unable to attend: Mr M. van Hulst, Director-General, International Organization of Consumers Unions, Central Office, The Hague, Netherlands.

## 1. **Introduction**

The WHO Expert Committee on Drug Dependence met in Geneva from 24 to 28 September 1990. The meeting was opened on behalf of the Director-General by Dr Hu Ching-Li, Assistant Director-General, who stressed the practical implications of the Committee's recommendations – which should be comprehensive and balanced – for international control of drugs of abuse under the existing international conventions. Referring to the emphasis now being placed by WHO on the reduction of demand for illicit drugs, Dr Hu informed the Committee of recent changes in the Organization's structure, as a result of which a new Programme on Substance Abuse had been established, which would focus on prevention and control of alcohol and drug abuse.

The assessment by WHO of a psychoactive substance and its recommendation on international control measures to be applied under the Single Convention on Narcotic Drugs, 1961 (as amended by the 1972 protocol), or the Convention on Psychotropic Substances, 1971, have in recent years been carried out in accordance with guidelines adopted by the Executive Board of WHO in 1986. By decision of the Executive Board in January 1990, these guidelines have been revised to take account of the experience gained, to streamline the assessment procedure, and to specify clearly the criteria for the selection of substances for a critical review. Under the *Revised Guidelines for the WHO Review of Dependence-producing Psychoactive Substances for International Control (1)*, WHO will not undertake a critical review of a substance unless it has received a notice from a Party to the international conventions or a request from the United Nations Commission on Narcotic Drugs to do so, or has information that the substance in question may fulfil the criteria for inclusion in one of the schedules of the conventions. Selection of substances for a critical review, formerly undertaken by the Programme Planning Working Group of WHO under the previous guidelines, has become part of the function of the Expert Committee, which will continue to conduct the critical review. The same principle will apply to a "re-review" (a second or further review) of substances already under control in one of the schedules.

Mr H. Emblad, Director of the Programme on Substance Abuse, briefly explained the priority areas of the programme and informed the Committee of a plan to expand the scope of its activity from reviewing psychoactive substances for recommendations on scheduling to a broader range of technical issues related to reduction of demand.

## 2. **Benzodiazepines**

### 2.1 **Scheduling differentiation**

In 1984, 33 benzodiazepines were placed in Schedule IV of the Convention on Psychotropic Substances, 1971, by the United Nations Commission on Narcotic Drugs upon the recommendation of WHO. At that time, it was pointed out that there were differences among them, but further studies were needed to determine whether those differences would be of sufficient magnitude and significance to warrant differential scheduling. In 1988, the Programme Planning Working Group of WHO, which previously selected substances for a critical review by the Expert Committee, recommended that all the benzodiazepines be reviewed, including those already under international control. In 1989, the Expert Committee reviewed 4 benzodiazepines and recommended in its twenty-sixth report (2) that midazolam, of which the salts are soluble in water and for which there was evidence of actual abuse, be included in Schedule IV of the Convention on Psychotropic Substances, 1971. In view of the plan to review all the benzodiazepines at the twenty-seventh meeting of the Expert Committee, the Committee in 1989 deferred its recommendations on the other three substances (brotizolam, etizolam, and quazepam) for which there was at that time little evidence of their occasioning public health and social problems.

At its present meeting the Committee had a general discussion on the questions whether differential scheduling of individual benzodiazepines would be feasible from the technical point of view and whether it were needed for public health and social reasons. In order to justify differential scheduling, it is necessary to consider the significance of public health and social problems associated with the abuse of a substance. Systematic epidemiological studies will provide some data to determine the extent of public health and social consequences. It is also desirable to know the impact of scheduling a substance on the extent of its abuse and on its availability for legitimate purposes. Of all the types of data included in the evaluation of individual benzodiazepines, the Committee felt the following items to be the most important in determining possible differential scheduling, although it was noted that none of them can be used alone as an independent criterion for differentiation.

#### **Human pharmacokinetic studies:**

Onset of action, elimination time, and duration of effect after both single and repeated administrations may be important determinants of the dependence potential of individual substances. Active metabolites may contribute to the overall effects of a substance.

#### **Preclinical studies:**

1. Drug discrimination.
2. Physical dependence.
3. Self-administration.

**Clinical studies:**

1. Categorization of subjective effects in persons with histories of drug abuse.
2. Determination of euphoriant, liking, and reinforcing effects in persons with histories of drug abuse.
3. Assessment of physical dependence.

**Epidemiological data and information on illicit activities:**

1. Utilization data.
2. Reports of extent and nature of actual abuse.
3. Survey data.
4. Drug seizures.
5. Reports of clandestine manufacturing.
6. Diversion from licit sources.

**Clinical usefulness and breadth of therapeutic indications**

**2.2 Benzodiazepines under international control**

The Committee examined the available data on the 34 currently controlled benzodiazepines with the aim of determining whether or not they are appropriately scheduled under the Convention on Psychotropic Substances, 1971, conducting its review according to the recently revised guidelines (1). The Committee paid particular attention to trends in the pattern of abuse and reports of illicit traffic that might reflect the degree of seriousness of public health and social problems produced by individual substances.

The following benzodiazepines were found to be appropriately controlled at their present level in Schedule IV of the Convention on Psychotropic Substances, 1971:

alprazolam	halazepam	nimetazepam
bromazepam	ketazolam	nitrazepam
chlordiazepoxide	lorazepam	oxazepam
clobazam	lormetazepam	prazepam
clonazepam	medazepam	temazepam
clorazepate	midazolam	triazolam.
flurazepam		

The Committee decided that, for the present, they require no action.

For the following benzodiazepines, which have been controlled since 1984, and were found to have moderate to high therapeutic usefulness, there are few or no reports of abuse or illicit activity:

camazepam	ethyl loflazepate	nordazepam
clotiazepam	fludiazepam	oxazolam
cloxazolam	haloxazolam	pinazepam
delorazepam	loprazolam	tetrazepam.
estazolam		

The Committee recommends that WHO continues to monitor these compounds to amass enough data to determine whether or not they should be placed under critical review to consider descheduling.

In comparison with all other benzodiazepines reviewed, diazepam and flunitrazepam showed a continuing higher incidence of abuse and association with illicit activities. The higher abuse potential of diazepam than that of several other benzodiazepine anxiolytics has also been demonstrated in human experimental studies and survey studies of drug abusers, supported by information received from health professionals engaged in the treatment of drug dependence.

The Committee recommends that WHO continues to keep diazepam and flunitrazepam under surveillance in order to determine whether or not they merit being placed under critical review to consider appropriate scheduling.

### 2.3 **Benzodiazepines not at present under international control**

At its twenty-sixth meeting, the Expert Committee deferred scheduling decisions on 3 benzodiazepines (brotizolam, etizolam, and quazepam) to the present meeting (2). Following the recently revised guidelines (1), the Committee at its present meeting reviewed information on these substances that had been collected by WHO, its Member States, various international organizations, and the pharmaceutical industry, and that had been provided by members of the Committee. The results of the Committee's deliberations on the individual substances are detailed below.

#### 2.3.1 ***Brotizolam***

##### *Substance identification*

Brotizolam (INN; CAS 57801-81-7), chemically 2-bromo-4-(*o*-chlorophenyl)-9-methyl-6*H*-thieno[3,2-*f*]triazolo[4,3-*a*][1,4]diazepine, is also known as Lendormin, Lindormin, Ladormin, and Lendorm. No stereoisomers are possible.

##### *Similarity to already known substances and effects on the central nervous system (CNS)*

Brotizolam is a benzodiazepine possessing the full range of group-specific CNS-depressant effects of these compounds, so that it is an anxiolytic, anticonvulsant, sedative-hypnotic, muscle relaxant, etc. In animal experiments, brotizolam is as efficacious as diazepam in most of its pharmacological effects. Clinical studies of the hypnotic effects suggest that brotizolam is approximately 20–40 times as potent as diazepam. Brotizolam is freely soluble in chloroform and slightly soluble in water. It is rapidly absorbed and has an elimination half-life of approximately 5–10 hours in humans.

##### *Dependence potential*

Brotizolam has been demonstrated to have some reinforcing effects in monkeys. Drug-discrimination studies in monkeys indicated that it had pentobarbital-like effects. The subjective effects of brotizolam in humans have been found to be similar to those of nitrazepam and flurazepam. In



physical-dependence studies in animals, brotizolam substituted for barbital and produced withdrawal signs typical of the sedative-hypnotic class.

In human studies in insomniac patients, brotizolam has been reported to cause rebound-insomnia (i.e., transient worsening of sleep) after termination of repeated dosing as a hypnotic. Other than this mild sign of withdrawal, human studies on physical dependence are not available. Furthermore, only a few cases of dependence/withdrawal syndrome have been reported.

#### *Actual abuse and/or evidence of likelihood of abuse*

There is, at present, very little direct evidence of actual abuse of brotizolam. There are currently no reports of illicit trafficking, production or diversion of brotizolam. The Committee noted the relatively low level of production reported and the short period of time since it was introduced into the market.

#### *Therapeutic usefulness*

Brotizolam is currently available in 15 countries and marketed in tablet strengths of 0.125 and 0.25 mg for the treatment of sleep disturbances.

#### *Recommendation*

On the basis of the available data concerning its pharmacological profile, dependence potential, and possible abuse, the Committee rated the abuse liability of brotizolam as low to moderate and the therapeutic usefulness as moderate to high. Few public health and social problems are currently associated with the use of brotizolam. The Committee considered that the degree of seriousness of the public health and social problems associated with the abuse of this substance was not great enough to warrant international control. The Committee did not recommend scheduling of brotizolam.

### **2.3.2 Etizolam**

#### *Substance identification*

Etizolam (INN; CAS 40054-69-1), chemically 4-(*o*-chlorophenyl)-2-ethyl-9-methyl-6*H*-thieno[3,2-*f*]-*s*-triazolo[4,3-*a*][1,4]diazepine, is also known as Depas, Pasaden, Y-7131 and AHR-3219. No stereoisomers are possible.

#### *Similarity to already known substances and effects on the central nervous system*

Etizolam is a benzodiazepine possessing the full range of group-specific CNS-depressant effects of these compounds, so that it is an anxiolytic, anticonvulsant, sedative-hypnotic, muscle relaxant, etc. Unlike diazepam, it has some imipramine-like neuropharmacological and behavioural effects in preclinical studies. In animal experiments, etizolam is 6–10 times more potent than diazepam in most of its pharmacological effects. Clinical

studies of the hypnotic effects suggest that etizolam is approximately 10 times as potent as diazepam. It is practically insoluble in water, but soluble in dilute acid, and has an elimination half-life of approximately 6–16 hours in humans.

#### *Dependence potential*

Etizolam has been demonstrated to have some reinforcing effects in monkeys. In physical-dependence studies in animals, it substituted for barbital and produced withdrawal signs typical of the sedative-hypnotic class. Drug-discrimination studies in monkeys indicated that it had pentobarbital-like effects.

In clinical observations of physical dependence, one case of mild withdrawal manifestations was reported.

#### *Actual abuse and/or evidence of likelihood of abuse*

There is, at present, very little direct evidence of actual abuse of etizolam. There are currently no reports of illicit trafficking, production or diversion of etizolam. The Committee noted the relatively limited distribution of the drug and the short period of time since it was introduced into the market.

#### *Therapeutic usefulness*

Etizolam is currently in use in Japan, where it is marketed in tablet strengths of 0.5 and 1.0 mg for the treatment of anxiety disorders and some forms of sleep disturbance.

#### *Recommendation*

On the basis of the available data concerning its pharmacological profile, dependence potential, and possible abuse, the Committee rated the abuse liability of etizolam as low to moderate and the therapeutic usefulness as moderate to high. Few public health and social problems are currently associated with the use of etizolam. The Committee considered that the degree of seriousness of the public health and social problems associated with the abuse of this substance was not great enough to warrant international control. The Committee did not recommend scheduling of etizolam.

### **2.3.3 Quazepam**

#### *Substance identification*

Quazepam (INN; CAS 36735-22-5), chemically 7-chloro-5-(*o*-fluorophenyl)-1,3-dihydro-1-(2,2,2-trifluoroethyl)-2*H*-1,4-benzodiazepine-2-thione, is also known as Oniria, Quazium, Selepam, Prosedar, Dormalin, and Temodol. No stereoisomers are possible.

#### *Similarity to already known substances and effects on the central nervous system*

Quazepam is a benzodiazepine possessing the full range of group-specific,

CNS-depressant effects of these compounds, so that it is an anxiolytic, anticonvulsant, sedative-hypnotic, muscle relaxant, etc. In animal experiments, quazepam is as efficacious as diazepam in most of its pharmacological effects. Clinical studies suggest that the hypnotic effects of quazepam are approximately equivalent to those of flurazepam. Quazepam is soluble in methylene chloride and hexane, but insoluble in water. It has an elimination half-life of approximately 40 hours in humans.

#### *Dependence potential*

Quazepam has been demonstrated to have some reinforcing effects in monkeys. In physical-dependence studies in animals, it substituted for barbital and produced withdrawal signs typical of the sedative-hypnotic class. Drug-discrimination studies in monkeys indicated pentobarbital-like effects with quazepam. Human studies on dependence potential are not available.

#### *Actual abuse and/or evidence of likelihood of abuse*

There is at present no direct evidence of actual abuse or illicit trafficking, production or diversion of quazepam. The Committee noted the relatively short period of time since the drug was introduced into the market.

#### *Therapeutic usefulness*

Quazepam is currently available in 9 countries in 15-mg tablets for the treatment of sleep disturbances.

#### *Recommendation*

On the basis of the available data concerning its pharmacological profile and dependence potential, the Committee rated the abuse liability of quazepam as low to moderate and the therapeutic usefulness as moderate to high. No public health and social problems are currently associated with the use of quazepam. The Committee considered that the degree of seriousness of the public health and social problems associated with the abuse of this substance was not great enough to warrant international control. The Committee did not recommend scheduling of quazepam.

### 3. **Propylhexedrine**

A notification from the Government of the United States of America concerning the descheduling of propylhexedrine has been transmitted to WHO. Propylhexedrine is, at present, controlled under Schedule IV of the Convention on Psychotropic Substances, 1971. The first critical review of propylhexedrine that resulted in its scheduling was initiated by WHO, and was conducted at the twenty-second meeting of the WHO Expert Committee on Drug Dependence in 1985 (3), as part of a group of 28 stimulant phenethylamines. Propylhexedrine was subsequently reviewed at the twenty-fifth meeting of the Expert Committee (4), which examined

the available information and noted little evidence of significant public health or social problems associated with propylhexedrine, especially in the USA, where it is readily available as an over-the-counter nasal inhaler preparation. It recommended, however, that no change be made in the scheduling of propylhexedrine but that the substance should be reviewed again in two years. At its present meeting, the Committee reviewed the past assessment of propylhexedrine as well as new information collected by the Secretariat and provided by the Government of the United States of America. Considering the revised WHO guidelines (1), the Committee focused especially on recent data on actual abuse and illicit activity. An updated review of propylhexedrine is presented below.

### 3.1 **Substance identification**

Propylhexedrine (INN; CAS 101-40-6) is chemically ( $\pm$ )-*N*, $\alpha$ -dimethylcyclohexaneethylamine. It has one chiral carbon atom in the molecule, so that two stereoisomeric forms and one racemate are possible.

### 3.2 **Similarity to already known compounds and effects on the central nervous system**

Animal pharmacological studies indicate that propylhexedrine has some stimulant actions, for example on locomotor activity, and pressor effects in common with amphetamine.

In humans, propylhexedrine produces pressor and stimulant effects similar to those of dexamphetamine but is significantly less potent. Administered by inhalation, propylhexedrine has local vasoconstrictor activity similar to that of ephedrine, but the duration of the activity is longer. Mucosal rebound congestion and chronic rhinitis may occur following excessive use of propylhexedrine in nasal inhalers. Amphetamine-like intoxication symptoms have been observed after oral or intravenous abuse.

### 3.3 **Dependence potential**

Studies in rats infused with propylhexedrine indicate that it acts as a typical stimulant of the central nervous system to which some tolerance develops. In drug-discrimination studies, propylhexedrine produced complete generalization to amphetamine in monkeys but only partial generalization in pigeons. It was self-administered by monkeys trained to self-administer cocaine, but at much lower response rates.

There have been no controlled laboratory studies of the dependence potential of propylhexedrine in human subjects.

### 3.4 **Actual abuse and/or evidence for likelihood of abuse**

Oral and intravenous abuse of propylhexedrine has been documented over a period of about 30 years, usually in the form of single case reports.

Some of these reports mention severe adverse reactions after intravenous use, including myocardial infarction, “shock lung” syndrome, and death. Since 1988, when the Committee last reviewed propylhexedrine, more information has become available on the incidence of abuse. People who abuse a variety of drugs on a chronic basis do not find the subjective effects of propylhexedrine very appealing and rarely bother to use it despite its easy availability. The Drug Abuse Warning Network in the USA reported two emergency-room and one medical-examiner mentions for propylhexedrine from 1988 to 1989. Earlier data from the Drug Abuse Warning Network were also considered by the Committee. This network has not detected a significant amount of propylhexedrine abuse over the past 7 years. The threshold for inclusion in the list of “most frequently mentioned drugs” (which recently contained 256 drugs) is 10 reported episodes of abuse in any one year. Propylhexedrine did not exceed this threshold in 1983, 1984, 1986, 1987, 1988, or 1989. Since 1982, there have been only 50 mentions of propylhexedrine abuse out of a total of a million reported episodes of drug abuse. The Committee considered these mentions in relation to production within the USA and Canada of about 2 500 000 inhalers (approximately equivalent to 100 kg) annually, all of which were readily available over the counter. Since 1988, illicit traffic has been reported in only two countries. In the Federal Republic of Germany, only one prescription forgery was reported. In the USA, 4 cases involving propylhexedrine were reported: 3 cases primarily involving seizures of small amounts (a total of 8.8 g) of propylhexedrine from facilities described as “clandestine laboratories”, and another involving 2 nasal inhalers.

Based on these recent trends and the length of time that propylhexedrine has been available, the Committee concluded that propylhexedrine is not likely to be abused so as to constitute significant public health and social problems. However, the Committee considered it desirable not to make propylhexedrine available in over-the-counter forms other than inhalers.

### 3.5 Therapeutic usefulness

Propylhexedrine is used in an inhalant form for nasal decongestion. An oral formulation of the hydrochloride has been used as an anorectic agent in the treatment of obesity. A number of alternative drugs are available for both these indications. The Committee rated the therapeutic usefulness of propylhexedrine as low to moderate.

### 3.6 Recommendation

The Committee reviewed new documentary data indicating that the incidence of abuse and illicit trafficking was still very low and confirming the absence of any significant public health problems. Considering the revised WHO guidelines (1), the Committee recommended that propylhexedrine should be removed from international control under the Convention on Psychotropic Substances, 1971.

## 4. **Dronabinol**

Dronabinol (INN; CAS 1972-08-3), chemically (6a*R*,10a*R*)-6a,7,8,10a-tetrahydro-6,6,9-trimethyl-3-pentyl-6*H*-dibenzo[*b,d*]pyran-1-ol, is one of the stereochemical variants of *delta*-9-tetrahydrocannabinol, the active principle of cannabis. Dronabinol is included in Schedule I of the Convention on Psychotropic Substances, 1971. Dronabinol was reviewed by the twenty-sixth meeting of the WHO Expert Committee on Drug Dependence (2) in response to a notification by the Government of the United States of America, requesting the transfer of *delta*-9-tetrahydrocannabinols (*delta*-9-THC) from Schedule I to Schedule II of the Convention. At that time the Committee rated the abuse liability of dronabinol as high, although few public health and social problems were associated with its therapeutic use, and rated its therapeutic usefulness as moderate to high as an antiemetic adjunct to cancer chemotherapy in selected cases. Based on the above assessment, the Committee recommended rescheduling of dronabinol from Schedule I to Schedule II.

The United Nations Commission on Narcotic Drugs did not endorse this recommendation. Some delegations pointed out that the value of dronabinol in therapy did not seem to counterbalance its high potential for abuse, which would constitute a serious disadvantage if dronabinol were moved to Schedule II. It was suggested, however, that WHO should continue collecting data on its therapeutic usefulness for another review.

The Committee reviewed additional data compiled on therapeutic usefulness, and reconsidered the abuse potential and the possible implications of rescheduling, bearing in mind the concerns expressed by the Commission on Narcotic Drugs.

### 4.1 **Therapeutic usefulness**

Dronabinol is an effective antiemetic in the management of nausea and vomiting induced by cancer chemotherapy, with efficacy similar to that of oral phenothiazines. There is evidence that, when used in combination with phenothiazines, its efficacy is enhanced and its side-effects are reduced. There are limited data comparing dronabinol with the most effective antiemetic regimens used today to manage chemotherapy-induced nausea and vomiting. Some data indicate that dronabinol is less effective than intravenous metoclopramide when used to treat nausea and vomiting caused by highly emetic cancer-chemotherapy drugs. There are no adequate comparative data on dexamethasone or 5-HT<sub>3</sub>-receptor blockers; it should be noted, however, that the 5-HT<sub>3</sub> blockers are not yet generally available.

Dronabinol causes various adverse reactions owing to its effects on the central nervous system. Although the frequent occurrence of these side-effects lessens its value as a therapeutic agent, dronabinol currently has a real but limited place in the management of chemotherapy-induced

nausea and vomiting and may be useful in patients refractory to other antiemetics.

It is nevertheless obvious, in the assessment of the Committee, that dronabinol has therapeutic usefulness that is definitely greater than that of the other substances in Schedule I, which have “very limited, if any” therapeutic usefulness, and that is comparable to that of a number of drugs in Schedule II.

The therapeutic usefulness of dronabinol, which is based on the balance between its therapeutic benefits and adverse consequences, may vary from country to country depending on a number of factors such as the prevalence of cancer and the extent of use of cancer chemotherapy as well as the supply of pharmaceutical products in general.

#### **4.2 Abuse liability and public health and social consequences of abuse of dronabinol**

The pharmacology of synthetic (-)-*trans-delta-9*-tetrahydrocannabinol (dronabinol) is regarded as identical to that of cannabis since the psychoactive pharmacological effects of cannabis are attributable to the effects of this substance. However, the Committee assessed the likelihood of actual abuse and adverse public health and social consequences of dronabinol and synthetic THC as being substantially lower than those of cannabis. The Committee came to this conclusion since the determinants of the abuse liability of a dependence-producing substance involve factors such as popularity, availability, and price, as well as the pharmacology of the substance.

There are no reports on actual abuse of dronabinol or its public health and social consequences. Introduction of pure *delta-9*-THC into the illicit market-place through illicit production, either by synthesis or by extraction from plant materials, is not economically viable. No case of clandestine manufacture of dronabinol has been reported in the USA and there is only one report in the world as a whole. Diversion of dronabinol preparations is also extremely rare; only one case of diversion and some cases of theft have been reported in the USA since the drug was marketed in 1986.

Thus, the Committee assessed the extent of the risk that might be caused by abuse of licit and illicit synthetic THC as not being especially serious, particularly in the light of the massive volume and relatively low cost of cannabis in the illicit market-place.

#### **4.3 Assessment of the possibility of dronabinol's transfer to Schedule II leading to an increase in its abuse**

Substances in Schedule II of the Convention on Psychotropic Substances, 1971, are subject to strict control measures similar to those applicable to narcotic drugs in Schedule I of the Single Convention on Narcotic Drugs,

such as morphine. Although it is likely that the licit supply and use of dronabinol will increase, it is reasonable to predict, from the experience in the countries in which it is already marketed, that its abuse or diversion into illicit traffic will remain insignificant. This may also be inferred from the absence of evidence of significant abuse of nabilone, a synthetic homologue of dronabinol with a similar pharmacological profile, which is not controlled at the international level, in spite of its marketing in several countries since 1983.

With regard to the possibility of increasing the abuse of illicit dronabinol or clandestinely manufactured *delta*-9-THC, it is unlikely that a change in the scheduling status of dronabinol would enhance the economic viability of its clandestine manufacture in view of the massive availability of cannabis, a strong competitor of natural origin, at relatively low cost.

#### 4.4 **Assessment of the possibility of dronabinol's transfer to Schedule II leading to an increase in the abuse of cannabis**

Since cannabis is controlled under the Single Convention on Narcotic Drugs, a change in the scheduling of dronabinol under the Convention on Psychotropic Substances would not entail any change in the control status of cannabis. Nevertheless, there might be a concern about the possibility that the official recognition of therapeutic usefulness of dronabinol might encourage the “medicinal” use of cannabis and thus its abuse. However, cannabis is already the most widely abused illicit drug in the world, with an annual seizure figure of 30 000 to 40 000 tonnes. It is unlikely that such recognition will make a significant difference to the current level of massive cannabis abuse.

#### 4.5 **Scope of recommendation**

Although the data on the therapeutic usefulness and dependence liability relate only to one stereochemical variant of *delta*-9-THC (namely, dronabinol), it was noted that making a distinction between this single isomer and the others contained in the group may create legal and forensic analytical problems in some countries. For this reason, it is recommended that *delta*-9-THC and its stereochemical variants be rescheduled together.

#### 4.6 **Recommendation**

It is recommended that *delta*-9-tetrahydrocannabinol and its stereochemical variants be rescheduled from Schedule I to Schedule II of the Convention on Psychotropic Substances, 1971.



## 5. Exempted preparations

In December 1989, WHO was informed by the United Nations (DND 411/1(2), DND 421/12(2) USA)<sup>1</sup> that the Government of the United States of America had exempted the 111 preparations summarized below from certain control measures.

Under the Convention on Psychotropic Substances, 1971, governments are allowed to exempt preparations containing psychotropic substances, other than those in Schedule I, from certain control measures when the preparation is compounded in such a way that it presents no, or a negligible, risk of abuse and the psychotropic substance cannot be recovered by readily applicable means in a quantity liable to abuse. No exemption is possible from several mandatory control measures, including the licensing requirement for manufacture, the obligation for record-keeping concerning manufacturing and initial disposal, and prohibition of export to a country on specific notification by that country.

The revised guidelines (1) provide that WHO should carry out an assessment of notifications of exempted preparations in all cases in which the preparation is not limited to domestic consumption. Since the licit exportation of exempted preparations cannot be ruled out under the current regulatory system of the United States of America, the Committee assessed these preparations taking into account the exemption guidelines adopted in 1984 by the United Nations Commission on Narcotic Drugs in resolution 1(S-VIII) (5).

### 5.1 Outline of exempted preparations notified by the United States of America

The exempted preparations are as follows:

- 55 preparations containing up to 50 mg of butalbital (Schedule III) per capsule or tablet,
- 10 preparations containing 5 mg of chlordiazepoxide hydrochloride (Schedule IV) per capsule,
- 3 preparations containing 5–10 mg of chlordiazepoxide per tablet,
- 37 preparations containing 3–50 mg of phenobarbital (Schedule IV) per tablet or 0.5–3.24 mg/ml in elixir,
- 6 preparations containing secbutabarbital (Schedule IV) or its sodium salt in quantities ranging from 8 to 20 mg per capsule or tablet, or 1–3 mg/ml in elixir.

---

<sup>1</sup> A copy of this notification can be obtained by writing to: United Nations Division of Narcotic Drugs, Vienna International Centre, P.O. Box 500, A-1400, Vienna, Austria.

These preparations have been exempted from the following control measures:

- Article 8, paragraphs 1, 2, and 4, referring to licensing except as it applies to manufacture.
- Article 10, paragraph 2, regarding prohibition of advertisement to the general public.
- Article 11, referring to records except for paragraphs 6 and 7, which apply to the quantities of psychotropic substances used in the manufacture of exempt preparations and to the preservation of records for reporting under Article 16.
- Article 15, referring to inspection except as it applies to manufacture.
- Article 16, paragraphs 4(b) and 5, referring to reporting to the International Narcotics Control Board.
- Article 12, paragraph 2, regarding export declarations with respect to the 55 preparations containing butalbital.

The preparations containing barbiturates are compounded with such drugs as antipyretic analgesics, anticholinergics, ephedrine, anticonvulsants, and xanthenes in varying quantities. Those of chlordiazepoxide or its salt are compounded with either sodium estrogen sulfate or clidinium bromide. The rationale applied by the exempting authorities of the United States of America is based on the concept of combining with the controlled substance an amount of counteractive drug sufficient to cause early subjective deterrent side-effects.

According to the exempting authorities, only minor incidents of abuse have been reported, although these preparations have been available in the USA for many years. However, there is no legal mechanism to control the export of the preparations.

## 5.2 **Assessment and recommendation**

There is some concern about the possibility that some of these preparations or substances extracted from them will be abused in such a way as to constitute significant public health and social problems if they are exported to another country. Although they are reported to have caused no significant abuse problems in the exempting country, their possible export requires a more careful review in the future in order to determine whether termination of the exemption of some of these preparations is needed.

It is also noted that the guidelines adopted by the Commission on Narcotic Drugs in 1984 (5) state that there should be no exemption from the requirements of Article 12, on export declarations, and of Article 10, paragraph 2, on the prohibition of advertisement to the general public. In this regard, the exemptions with respect to the 55 preparations containing butalbital are inconsistent with the 1984 guidelines, although it would appear that the requirement of Article 10, paragraph 2, is in any case met by the national requirement applicable to products sold only on prescription.

The Committee therefore recommends that the exemption of the 55 preparations containing butalbital from the requirement of Article 12, paragraph 2, be terminated.

It would also be desirable that appropriate provisional measures be taken by the Government of the United States of America to ensure that none of the 111 preparations will be exported without appropriate notice to the authorities of any importing country until such time as WHO can conduct a systematic review of the exemptions.

## **6. General recommendations**

### **6.1 Training with regard to psychoactive substances**

The Committee, recalling previous recommendations (2, 6-8) on the need to develop and upgrade the expertise of personnel at national level through training with regard to psychoactive substances, commended the efforts that have been made by WHO. The Committee reaffirmed the importance of and need for such training and urged WHO, in collaboration with the United Nations Division of Narcotic Drugs, other relevant United Nations bodies, and governments, to continue, support and expand training programmes nationally and internationally. Particularly needed are training in data collection and processing and in assessment of public health and social problems, and education of health-care personnel with regard to rational prescribing and use of psychoactive substances, as well as the encouragement of institutions to expand their training curricula with respect to psychoactive substances.

### **6.2 Education of health professionals in the rational use of psychotropic drugs**

In pursuit of its educational programme to expose different groups of health professionals to concepts of the rational use of drugs, WHO has conducted separate workshops for medical, nursing, and pharmacy groups. These workshops have been highly beneficial in reducing abuse-related problems. There is a need to promote the principle of the health-care team, based on interdisciplinary collaboration, and the Committee therefore recommends, for consideration by WHO, the holding of workshops that would bring together these three professional groups.

### **6.3 Treatment of drug dependence**

The Committee recognized that improved treatment of drug dependence is vital to the reduction of drug abuse and its public health and social consequences and noted that, in the USA for example, national interest is actively focusing on a new programme involving the development of medications to treat addictive disorders. International progress in treatment may be further promoted by participation of the World Health

Organization. Therefore, WHO should consider developing a role for the international community in this area through its collaborating centres and its broad programmes and expertise at the international level.

#### **6.4 Drug abuse surveillance systems**

WHO should encourage the development of surveillance systems as early monitoring systems for detecting abuse of drugs in medical use. Such systems could be directed to drugs which, because of their dependence potential, are capable of producing abuse but have not yet produced actual abuse and public health and social problems. For developing a surveillance system for unscheduled or descheduled dependence-producing drugs, WHO should consult with scientific experts and epidemiologists and encourage the input of the relevant United Nations bodies (e.g., the Division of Narcotic Drugs and the International Narcotics Control Board), WHO collaborating centres, the pharmaceutical industry, and law-enforcement agencies.

#### **6.5 Collection of drug-abuse-related data in developing countries**

The Committee noted that the data for evaluating overdose or abuse come predominantly from North America and Europe. No comparable data emanate regularly from developing countries, though “emergency rooms” or equivalent settings do exist within their health services. It is therefore recommended that WHO along with other bodies in the United Nations system, including their regional offices, should collaborate with selected countries or institutions (e.g., major public hospitals in large cities) to make the recording of such information more systematic, as described in a previous WHO Expert Committee report (7). Such information would be of assistance to the WHO Expert Committee on Drug Dependence and to national authorities in their future deliberations.

#### **6.6 Study on the impact of scheduling**

The importance of knowledge about the impact of scheduling psychoactive substances on the practice of medicine and pharmacy was recognized by various WHO Expert Committees and Working Groups during the 1980s. Although the totality of the effects of control has never been the subject of systematic inquiry, WHO has started looking at some of these issues. Thus, a preliminary study, which involves a more detailed scrutiny in four countries of the impact of scheduling and of the development of the appropriate methodology, has been initiated. The Committee acknowledged the importance of this study and believed that it would be important to continue with it. The Committee recommends that efforts be made to facilitate the completion of the study.

#### **6.7 Information on exemption-terminated preparations**

The Committee recommended that WHO in cooperation with the United

Nations Division of Narcotic Drugs continue to inform Member States about the preparations for export that contain psychotropic substances whose exemptions have been terminated. The information should state not only the brand name but also the composition, quantity of each active ingredient, and the reasons for such termination.

## Acknowledgements

The Expert Committee wishes to acknowledge the contribution to its discussions of the following members of staff of WHO, Geneva: Dr J. Bertolote, Division of Mental Health; Mr M. Grant, Programme on Substance Abuse; Dr M. ten Ham, Pharmaceuticals; Dr J. Idänpään-Heikkilä, Division of Drug Management and Policies; Ms N. Teoh, Cancer and Palliative Care; Mr T.S.R. Topping, Office of the Legal Counsel; and Dr G.M. Weiss, Programme on Substance Abuse; and of Dr N. MacDonald, Professor of Palliative Care, University of Alberta, Edmonton, Canada.

The Committee also wishes to acknowledge the generous contributions of Dr E. M. Sellers, Addiction Research Foundation, Toronto, Canada; Dr Yng-Shiuh Sheu, National Institute on Drug Abuse, Rockville, MD, USA; Dr J. Tolliver, Drug Enforcement Administration, Washington, DC, USA; and Dr H. de Wit, University of Chicago, Chicago, IL, USA, in preparing working documents for the meeting.

## References

1. Revised Guidelines for the WHO Review of Dependence-producing Psychoactive Substances for International Control. In: *Executive Board, eighty-fifth session, Geneva, 15–24 January 1990: resolutions and decisions; annexes*. Geneva, World Health Organization, 1990, Annex 7 (document EB85/1990/REC/1; available on request from Distribution and Sales, World Health Organization, 1211 Geneva 27, Switzerland).
2. WHO Technical Report Series, No. 787, 1989 (*WHO Expert Committee on Drug Dependence: twenty-sixth report*).
3. WHO Technical Report Series, No. 729, 1985 (*WHO Expert Committee on Drug Dependence: twenty-second report*).
4. WHO Technical Report Series, No. 775, 1989 (*WHO Expert Committee on Drug Dependence: twenty-fifth report*).
5. United Nations, Commission on Narcotic Drugs. Report on the Eighth Special Session, 6–10 February 1984. *Economic and Social Council, Official Records, 1984, Supplement No. 3*. New York, 1984, pp. 43–44 (document E/CN.7/1984/13).
6. WHO Technical Report Series, No. 618, 1978 (*WHO Expert Committee on Drug Dependence: twenty-first report*).
7. WHO Technical Report Series, No. 656, 1981 (*Assessment of public health and social problems associated with the use of psychotropic drugs: report of the WHO Expert Committee on Implementation of the Convention on Psychotropic Drugs*).
8. WHO Technical Report Series, No. 761, 1988 (*WHO Expert Committee on Drug Dependence: twenty-fourth report*).

## World Health Organization Technical Report Series

### *Recent reports:*

No.		Sw.fr.*
737	(1986) <b>Resistance of vectors and reservoirs of disease to pesticides</b> Tenth report of the WHO Expert Committee on Vector Biology and Control (87 pages)	12.-
738	(1986) <b>Regulatory mechanisms for nursing training and practice: meeting primary health care needs</b> Report of a WHO Study Group (71 pages)	10.-
739	(1986) <b>Epidemiology and control of African trypanosomiasis</b> Report of a WHO Expert Committee (127 pages)	16.-
740	(1986) <b>Joint FAO/WHO Expert Committee on Brucellosis</b> Sixth report (132 pages)	18.-
741	(1987) <b>WHO Expert Committee on Drug Dependence</b> Twenty-third report (64 pages)	9.-
742	(1987) <b>Technology for water supply and sanitation in developing countries</b> Report of a WHO Study Group (38 pages)	7.-
743	(1987) <b>The biology of malaria parasites</b> Report of a WHO Scientific Group (229 pages)	32.-
744	(1987) <b>Hospitals and health for all</b> Report of a WHO Expert Committee on the Role of Hospitals at the First Referral Level (82 pages)	12.-
745	(1987) <b>WHO Expert Committee on Biological Standardization</b> Thirty-sixth report (149 pages)	20.-
746	(1987) <b>Community-based education for health personnel</b> Report of a WHO Study Group (89 pages)	12.-
747	(1987) <b>Acceptability of cell substrates for production of biologicals</b> Report of a WHO Study Group (29 pages)	5.-
748	(1987) <b>WHO Expert Committee on Specifications for Pharmaceutical Preparations</b> Thirtieth report (50 pages)	9.-
749	(1987) <b>Prevention and control of intestinal parasitic infections</b> Report of a WHO Expert Committee (86 pages)	12.-
750	(1987) <b>Alternative systems of oral care delivery</b> Report of a WHO Expert Committee (58 pages)	9.-
751	(1987) <b>Evaluation of certain food additives and contaminants</b> Thirtieth report of the Joint FAO/WHO Expert Committee on Food Additives (57 pages)	9.-
752	(1987) <b>WHO Expert Committee on Onchocerciasis</b> Third report (167 pages)	24.-
753	(1987) <b>Mechanism of action, safety and efficacy of intrauterine devices</b> Report of a WHO Scientific Group (91 pages)	12.-
754	(1987) <b>Progress in the development and use of antiviral drugs and interferon</b> Report of a WHO Scientific Group (25 pages)	5.-
755	(1987) <b>Vector control in primary health care</b> Report of a WHO Scientific Group (61 pages)	9.-
756	(1987) <b>Children at work: special health risks</b> Report of a WHO Study Group (49 pages)	9.-
757	(1987) <b>Rational use of diagnostic imaging in paediatrics</b> Report of a WHO Study Group (101 pages)	14.-
758	(1987) <b>The hypertensive disorders of pregnancy</b> Report of a WHO Study Group (114 pages)	16.-

\* Prices in developing countries are 70% of those listed here.

759	<b>(1987) Evaluation of certain food additives and contaminants</b> Thirty-first report of the Joint FAO/WHO Expert Committee on Food Additives (53 pages)	9.-
760	<b>(1987) WHO Expert Committee on Biological Standardization</b> Thirty-seventh report (203 pages)	28.-
761	<b>(1988) WHO Expert Committee on Drug Dependence</b> Twenty-fourth report (34 pages)	6.-
762	<b>(1988) Training and education in occupational health</b> Report of a WHO Study Group (47 pages)	6.-
763	<b>(1988) Evaluation of certain veterinary drug residues in food</b> Thirty-second report of the Joint FAO/WHO Expert Committee on Food Additives (40 pages)	6.-
764	<b>(1988) Rheumatic fever and rheumatic heart disease</b> Report of a WHO Study Group (58 pages)	8.-
765	<b>(1988) Health promotion for working populations</b> Report of a WHO Expert Committee (49 pages)	8.-
766	<b>(1988) Strengthening ministries of health for primary health care</b> Report of a WHO Expert Committee (110 pages)	12.-
767	<b>(1988) Urban vector and pest control</b> Eleventh report of the WHO Expert Committee on Vector Biology and Control (77 pages)	9.-
768	<b>(1988) WHO Expert Committee on Leprosy</b> Sixth report (51 pages)	8.-
769	<b>(1988) Learning together to work together for health</b> Report of a WHO Study Group (72 pages)	9.-
770	<b>(1988) The use of essential drugs</b> Third report of the WHO Expert Committee (63 pages)	8.-
771	<b>(1988) WHO Expert Committee on Biological Standardization</b> Thirty-eighth report (221 pages)	26.-
772	<b>(1988) Appropriate diagnostic technology in the management of cardiovascular diseases</b> Report of a WHO Expert Committee (41 pages)	6.-
773	<b>(1988) Smokeless tobacco control</b> Report of a WHO Study Group (81 pages)	11.-
774	<b>(1988) Salmonellosis control: the role of animal and product hygiene</b> Report of a WHO Expert Committee (83 pages)	11.-
775	<b>(1989) WHO Expert Committee on Drug Dependence</b> Twenty-fifth report (48 pages)	6.-
776	<b>(1989) Evaluation of certain food additives and contaminants</b> Thirty-third report of the Joint FAO/WHO Expert Committee on Food Additives (64 pages)	8.-
777	<b>(1989) Epidemiology of work-related diseases and accidents</b> Tenth report of the Joint ILO/WHO Committee on Occupational Health (71 pages)	9.-
778	<b>(1989) Health guidelines for the use of wastewater in agriculture and aquaculture</b> Report of a WHO Scientific Group (74 pages)	9.-
779	<b>(1989) Health of the elderly</b> Report of a WHO Expert Committee (98 pages)	12.-
780	<b>(1989) Strengthening the performance of community health workers in primary health care</b> Report of a WHO Study Group (46 pages)	6.-
781	<b>(1989) New approaches to improve road safety</b> Report of a WHO Study Group (62 pages)	8.-
782	<b>(1989) Monitoring and evaluation of oral health</b> Report of a WHO Expert Committee (69 pages)	9.-
783	<b>(1989) Management of human resources for health</b> Report of a WHO Expert Committee (61 pages)	8.-

784	(1989) <b>The use of synthetic antigens for diagnosis of infectious diseases</b> Report of a WHO Scientific Group (73 pages)	9.-
785	(1989) <b>Health surveillance and management procedures for food-handling personnel</b> Report of a WHO Consultation (47 pages)	6.-
786	(1989) <b>WHO Expert Committee on Biological Standardization</b> Thirty-ninth report (184 pages)	22.-
787	(1989) <b>WHO Expert Committee on Drug Dependence</b> Twenty-sixth report (32 pages)	4.-
788	(1989) <b>Evaluation of certain veterinary drug residues in food</b> Thirty-fourth report of the Joint FAO/WHO Expert Committee on Food Additives (66 pages)	9.-
789	(1990) <b>Evaluation of certain food additives and contaminants</b> Thirty-fifth report of the Joint FAO/WHO Expert Committee on Food Additives (48 pages)	6.-
790	(1990) <b>WHO Expert Committee on Specifications for Pharmaceutical Preparations</b> Thirty-first report (79 pages)	9.-
791	(1990) <b>Pesticide application equipment for vector control</b> Twelfth report of the WHO Expert Committee on Vector Biology and Control (58 pages)	8.-
792	(1990) <b>Prevention in childhood and youth of adult cardiovascular diseases: time for action</b> Report of a WHO Expert Committee (105 pages)	12.-
793	(1990) <b>Control of the leishmaniases</b> Report of a WHO Expert Committee (158 pages)	18.-
794	(1990) <b>Educational imperatives for oral health personnel: change or decay?</b> Report of a WHO Expert Committee (43 pages)	6.-
795	(1990) <b>Effective choices for diagnostic imaging in clinical practice</b> Report of a WHO Scientific Group (131 pages)	16.-
796	(1990) <b>The use of essential drugs</b> Fourth report of the WHO Expert Committee (57 pages)	8.-
797	(1990) <b>Diet, nutrition, and the prevention of chronic diseases</b> Report of a WHO Study Group (203 pages)	26.-
798	(1990) <b>Chemistry and specifications of pesticides</b> Thirteenth report of the WHO Expert Committee on Vector Biology and Control (77 pages)	9.-
799	(1990) <b>Evaluation of certain veterinary drug residues in food</b> Thirty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives (68 pages)	9.-
800	(1990) <b>WHO Expert Committee on Biological Standardization</b> Fortieth report (221 pages)	26.-
801	(1990) <b>Coordinated health and human resources development</b> Report of a WHO Study Group (53 pages)	8.-
802	(1990) <b>The role of research and information systems in decision-making for the development of human resources for health</b> Report of a WHO Study Group (54 pages)	8.-
803	(1990) <b>Systems of continuing education: priority to district health personnel</b> Report of a WHO Expert Committee (50 pages)	8.-
804	(1990) <b>Cancer pain relief and palliative care</b> Report of a WHO Expert Committee (75 pages)	9.-
805	(1990) <b>Practical chemotherapy of malaria</b> Report of a WHO Scientific Group (141 pages)	16.-
806	(1991) <b>Evaluation of certain food additives and contaminants</b> Thirty-seventh report of the Joint FAO/WHO Expert Committee on Food Additives (49 pages)	10.-
807	(1991) <b>Environmental health in urban development</b> Report of a WHO Expert Committee (65 pages)	11.-