### WORLD HEALTH ORGANIZATION TECHNICAL REPORT SERIES

No. 437

# WHO EXPERT COMMITTEE ON DRUG DEPENDENCE

Seventeenth Report

WORLD HEALTH ORGANIZATION

GENEVA

1970

### © World Health Organization 1970

Publications of the World Health Organization enjoy copyright protection in accordance with the provisions of Protocol 2 of the Universal Copyright Convention. Nevertheless governmental agencies or learned and professional societies may reproduce data or excerpts or illustrations from them without requesting an authorization from the World Health Organization.

For rights of reproduction or translation of WHO publications in toto, application should be made to the Division of Editorial and Reference Services, 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 Director-General of the World Health Organization concerning the legal status of any country or territory or of its authorities, or concerning the delimitation of its frontiers.

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 which are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

PRINTED IN SWITZERLAND

### WORLD HEALTH ORGANIZATION TECHNICAL REPORT SERIES

No. 437

### WHO EXPERT COMMITTEE ON DRUG DEPENDENCE

Seventeenth Report

### CORRIGENDUM

Page 13, paragraph 4.4, Group (a), item 2:

Delete SKF 5301

es que la persona de la companya de

. . .

### CONTENTS

		Page
1.	Introduction	5
2.	Work of international bodies concerned with drug dependence	5
3.	Draft Protocol on Psychotropic Substances	9
4.	Classification of drugs by level of control required	10
5.	Notifications	21
6.	Review of drugs previously considered	24
7.	Treatment and rehabilitation	24
8.	Methadone maintenance	25
9.	Specific opiate antagonists in therapy	26
An	nex. List of drugs under international narcotics control .	27

#### WHO EXPERT COMMITTEE ON DRUG DEPENDENCE

Geneva, 25-30 August 1969

#### Members:

- Dr M. A. Attisso, Professor, Faculty of Medicine and Pharmacy, University of Dakar, Senegal
- Dr H. Brill, Director, Pilgrim State Hospital, West Brentwood, N.Y., USA (Rapporteur)
- Dr N. B. Eddy, Consultant on Narcotics, National Institutes of Health, Bethesda, Md., USA
- Dr L. Goldberg, Professor of Research on Alcohol and Analgesics, Department of Alcohol Research, Karolinska Institute, Stockholm, Sweden (Chairman)
- Dr E. Hosoya, Professor and Head of Department of Pharmacology, School of Medicine, Keio University, Tokyo, Japan
- Dr J. Jacob, Head, Department of Pharmacology and Toxicology, Pasteur Institute, Paris, France
- Dr P. Kielholz, Professor of Psychiatry, University of Basle, Switzerland
- Dr K. Pengsritong, Deputy Under Secretary of State for Public Health Affairs, Ministry of Public Health, Bangkok, Thailand
- Dr M. Shepherd, Professor of Epidemiological Psychiatry, Institute of Psychiatry, London, England
- Dr V. V. Vasil'eva, Professor and Consultant, Moscow, USSR (Vice-Chairman)
- Dr O. Vinar, Chief, Department of Psychopharmacology, Psychiatric Research Institute, Prague, Czechoslovakia

#### Representatives of other organizations:

#### United Nations:

- Mr Ansar Khan, Chief, Commission Secretariat and Information, Division of Narcotic Drugs, United Nations, Geneva
- Mr O. J. Braenden, Ph. D., Chief, Scientific and Technical Section, Division of Narcotic Drugs, United Nations, Geneva
- Mr V. Kúsević, Ph. D., Director, Division of Narcotic Drugs, United Nations, Geneva

### International Narcotics Control Board:

- Mr J. Dittert, Secretary
- Mr L. Manueco-Jenkins, Social Affairs Officer

### International Council on Alcohol and Addictions:

Mr A. Tongue, Executive Director

### Secretariat:

- Dr D. C. Cameron, Chief Medical Officer, Drug Dependence, WHO (Secretary)
- Dr H. Halbach, Director, Division of Pharmacology and Toxicology, WHO
- Dr H. Isbell, Professor of Medicine, Department of Medicine, University of Kentucky, Lexington, USA (Consultant)

## WHO EXPERT COMMITTEE ON DRUG DEPENDENCE

### **Seventeenth Report**

#### I. INTRODUCTION

The WHO Expert Committee on Drug Dependence met in Geneva from 25 to 30 August 1969.

Dr P. Dorolle, Deputy Director-General, opened the meeting on behalf of the Director-General and welcomed the members of the Committee, the representatives of the Secretary-General of the United Nations, the representatives of the International Narcotics Control Board and of the International Council on Alcohol and Addictions. He noted that the Committee was invited to consider a number of items of special relevance to the public health problems resulting from the increasingly widespread use of dependence-producing drugs, particularly those not now under international control. Several WHO expert committees had drawn attention to the dangers involved in the abuse of central nervous system stimulants, depressants and hallucinogens. At the present time, experimentation with these and other dependence-producing drugs was becoming increasingly widespread, especially among young persons. The development of drug dependence was the result of a complex interrelation between the drug, the drug-taker, and his environment, and it was necessary to adopt a balanced approach to these three facets of the problem.

### 2. WORK OF INTERNATIONAL BODIES CONCERNED WITH DRUG DEPENDENCE

### 2.1 World Health Organization

The Committee noted with satisfaction (a) that WHO and the countries and agencies collaborating with it in the development of techniques for the international monitoring of adverse drug reactions <sup>1</sup> have given special attention to reporting drug dependence during the last year, even though the level of reporting still remains low, and (b) that WHO, on the request

<sup>&</sup>lt;sup>1</sup> Wld Hlth Org. techn. Rep. Ser., 1969, No. 407, p. 14 (section 2.1.1).

of governmental agencies, disseminates early information on all types of adverse drug reactions to the governmental health services of all Member States of the Organization.

Also noted was the attention being given by WHO to finding ways of contributing effectively to programmes aimed at achieving a reduction of drug-taking behaviour, especially among youth. Additionally, the Committee learned of the development of plans for a series of travelling seminars on national responses to problems of alcoholism and drug dependence. Such seminars would enable participants from a variety of fields to observe operating programmes and to exchange information on the practical aspects of developing suitable local and national programmes.

### 2.2 United Nations

The Committee noted the report of the twenty-third session of the Commission on Narcotic Drugs of the United Nations Economic and Social Council which contained evidence of the very substantial efforts devoted to the development of a Draft Protocol on Psychotropic Substances (See section 3). In addition to this major activity, the Commission had adopted, among others, a resolution, later also adopted by the Council, relative to the urgent application of control measures to certain stimulant drugs.<sup>2</sup>

In addition to requesting that urgent attention be given to "the problem of abuse of psychotropic substances not yet under international control, including the possibility of placing such substances under international control", the General Assembly also requested the Secretary-General, in co-operation with the International Narcotics Control Board, to develop "plans for putting an end to the illegal or uncontrolled production of narcotic raw materials" and invited specialized agencies to participate. The Committee learned that WHO had participated in an Inter-Agency ad hoc meeting devoted to this subject.

The Committee noted with appreciation the publication in late 1968 of the third edition of the *Multilingual List of Narcotic Drugs under International Control*.<sup>5</sup> The current edition, written in English, French, Russian

<sup>&</sup>lt;sup>1</sup> United Nations, Commission on Narcotic Drugs (1969) Document E/4606/Rev. 1 (Economic and Social Council: Official Records).

<sup>&</sup>lt;sup>2</sup> United Nations, Commission on Narcotic Drugs (1969) Document E/4606/Rev. 1 (Economic and Social Council: Official Records, p. 95, resolution D).

<sup>&</sup>lt;sup>3</sup> United Nations General Assembly. Resolution 2433 (XXIII). In: Official Records of the General Assembly, Twenty-Third Session, Supplement No. 18 (A/7218), pp. 43-44.

<sup>&</sup>lt;sup>4</sup> United Nations General Assembly. Resolution 2434 (XXIII). In: Official Records of the General Assembly, Twenty-Third Session, Supplement No. 18 (A/7218), p. 44.

<sup>&</sup>lt;sup>5</sup> United Nations (1968) Narcotic drugs under international control. Multilingual list, 3rd ed. (Document E/CN.7/513)

and Spanish, contains additional listings in Arabic, Chinese, Greek, Hebrew, Japanese, Korean and Thai. It is designed as a reference work, not only for research workers but also for enforcement officers and others concerned with problems relating to narcotic drugs.

Arrangements have been made for a travelling team to visit French-speaking countries in Africa in 1969 to assist narcotic and other enforcement officers with the development of increasingly effective methods for the control of the illicit traffic in narcotics. It is expected that a comparable mission to English-speaking countries in Africa will be undertaken in 1970 and a seminar for law enforcement officers in Latin America is to be held in the latter part of 1969.

Work on the *Draft Protocol on Psychotropic Substances* is reviewed in section 3.

### 2.3 International Narcotics Control Board

The Committee reviewed the First Report of the International Narcotics Control Board <sup>1</sup> and was informed that, in addition to the regular work of carrying out obligations imposed upon it by existing international instruments, the Board had also given extensive consideration to the formulation of the Draft Protocol on Psychotropic Substances (see section 3). Further, it had assisted the governments of several countries with regard to improving their methods for supervising legitimate trade in narcotics.

### 2.4 Economic Commission for Europe

The Committee was advised of the activities of the Working Party on Road Traffic Safety of the Economic Commission for Europe which had developed a preliminary draft for a resolution on the "fitness of drivers". A Joint Meeting of the Working Party and of members of the WHO Secretariat concerned with drug dependence, mental health and occupational health was held early in the year to discuss means of reducing the frequency and severity of road accidents. Among other things, attention was given to the abuse of alcohol and other drugs in relation to driver fitness.

### 2.5 Council of Europe

The Committee was pleased to learn that the Committee on Public Health of the Council of Europe was devoting considerable attention to the collection of information from European countries concerning medical aspects and social consequences of drug dependence and resources available

<sup>&</sup>lt;sup>1</sup> United Nations, International Narcotics Control Board (1968) First Report, Document E/INCB/1 (Economic and Social Council: Official Records).

for the prevention of such dependence and the treatment of drug-dependent persons. It also learned with interest that a Sub-Committee on Penal Aspects of Narcotic and Drug Dependence of the Council was undertaking a three-year study in European countries of their laws relating to these questions, the effectiveness of these laws, and the assumptions underlying them.

### 2.6 The International Council on Alcohol and Addictions

The Committee was pleased to learn that this Organization, which was originally concerned primarily with alcohol and alcoholism, had been finding it very useful to employ a "combined approach" to the problems of abuse of alcohol and other dependence-producing drugs, as suggested in the fourteenth report of the WHO Expert Committee on Mental Health <sup>1</sup> and in the sixteenth report of the WHO Expert Committee on Drug Dependence. <sup>2</sup> A combined approach was also being adopted by numerous other organizations throughout the world that had formerly been concerned exclusively with one type of dependence.

The Council believed that there was an important need to inform the general public in all countries of the policies and activities of the various agencies within the United Nations family that were concerned with drug dependence and considered that non-governmental organizations, such as the Council, could make a significant contribution to spreading such information. The Committee supported this view.

### 2.7 International Police Association

The Committee was gratified to learn that the International Police Association was organizing a course on "The Management of Young Drug Addicts". This programme, being developed for the benefit of police officers from several European countries, was to be held in Copenhagen in late 1969 and was expected to concentrate primarily on non-penal methods.

### 2.8 Need for unified international approach

The Committee observed that, while many international organizations had an important interest in the problems associated with drug dependence, those principally concerned were:

(a) the United Nations Commission on Narcotic Drugs, which has major responsibilities relative to the formulation and review of policies and procedures for the control of certain dependence-producing drugs;

<sup>&</sup>lt;sup>1</sup> Wld Hlth Org. techn. Rep. Ser., 1967, No. 363, p. 8 (section 1).

<sup>&</sup>lt;sup>2</sup> Wld Hlth Org. techn. Rep. Ser., 1969, No. 407, p. 14 (section 2.1).

- (b) the International Narcotics Control Board, which supervises the national implementation of the international treaties; and
- (c) the World Health Organization, which is the medical body concerned with this important medical problem and its social ramifications.

The Committee considered it important that the trend toward ever closer co-operation between these bodies be fostered in every way possible. The complex inter-relations between man, his environment and dependence-producing drugs demanded the closest possible co-ordination of all feasible approaches and the utilization of all available resources.

### 3. DRAFT PROTOCOL ON PSYCHOTROPIC SUBSTANCES

The Committee noted that, at its twenty-third session, the United Nations Commission on Narcotic Drugs had given detailed consideration to a draft entitled Protocol on the control of psychotropic drugs outside the scope of the Single Convention on Narcotic Drugs, 1961. At the end of the session, the Office of Legal Affairs of the United Nations, in collaboration within the Division of Narcotic Drugs, prepared a Draft Protocol on Psychotropic Substances 2 based on the actions taken by the Commission. The Draft Protocol was forwarded for comment to governments and to appropriate international organizations.

The Committee reviewed, in broad outline, the main provisions for controlling the manufacture and distribution of substances to be listed in the several Schedules of the Protocol. Noting that the term "psychotropic substance", as used in the Protocol, applied only to substances specifically listed in one of the first four Schedules, the Committee observed that (a) since the term "psychotropic" has come to be widely applied to a large class of drugs used extensively in medical therapy, and (b) since many of these drugs do not produce drug dependence, there was considerable likelihood that the use of the unqualified, broad term "psychotropic" to designate only the dependence-producing members of that larger class would lead to confusion and misunderstanding on the part of persons not familiar with the details of the Protocol. The Committee suggested that consideration be given to the addition of a qualifying term, such as "dependence-producing", when speaking of psychotropic substances to be controlled under the Draft Protocol.

Commenting on Article 6, paragraph 3 of the Draft Protocol, the Committee suggested that it would be desirable to word the paragraph in such

<sup>&</sup>lt;sup>1</sup> United Nations, Commission on Narcotic Drugs (1969) Document E/4606/Rev. 1, p. 71 (Economic and Social Council: Official Records).

<sup>&</sup>lt;sup>2</sup> United Nations, Commission on Narcotic Drugs (1969) Document E/4606/Rev. 1 p. 106 (Annex IV) (Economic and Social Council: Official Records).

a way as to make it quite clear that the approval of research projects would be concerned only with their objectives, the safety of persons involved, and protection against diversion of dependence-producing substances, and that it would have no reference to the details of the research protocol.

The Committee expressed its agreement with the comments earlier forwarded by the Director-General of WHO to the Secretary-General of the United Nations.

### 4. CLASSIFICATION OF DRUGS BY LEVEL OF CONTROL REQUIRED

### 4.1 General considerations

The Committee noted the previous recommendations of WHO Expert Committees, of the World Health Assembly and of other international organizations concerning the abuse and control of drugs not now under international control and reaffirmed the opinions expressed by these bodies that international control of some of these substances is urgently necessary.

In reviewing the report of the WHO Expert Committee on Drug Dependence that met in 1968, the Committee noted particularly the following points and indicated its agreement with them:

- (1) the criteria for determining the need for drug control; 4
- (2) the conclusion that "the need, type and degree of international (and other) control must be based on two considerations: (a) the degree of risk to public health and (b) the usefulness of the drug in medical therapy";  $^5$
- (3) the recommendations concerning the need for control provisions that would be flexible enough to accommodate new substances as they might be discovered and the need to assure that drugs under control would be readily available "for scientific research, when justified, but only under appropriate safeguards"; <sup>5</sup>

<sup>&</sup>lt;sup>1</sup> Wld Hlth Org. techn. Rep. Ser., 1952, No. 57, p. 11 (section 8); 1954, No. 76, p. 11 (section 8); 1957, No. 116, p. 10 (section 10); 1964, No. 273, p. 11 (section 7); 1965, No. 312, p. 9 (section 7); 1966, No. 343, p. 11 (section 8); 1969, No. 407, p. 17 (section 3).

<sup>&</sup>lt;sup>2</sup> Off. Rec. Wld Hlth Org., 1965, 143, 31 (Resolution WHA 18.47); 1967, 160, 26 (Resolutions WHA 20.42 and WHA 20.43); 1968, 168, 20 (Resolution WHA 21.42).

<sup>&</sup>lt;sup>3</sup> United Nations, Commission on Narcotic Drugs (1956) Document 2891, p. 38 (para. 328); (1957) Document E/3010/Rev. 1, p. 40 (para. 388); (1962) Document E/3648, p. 31 (para. 205); (1966) Document E/4294, p. 38 (para. 305); (1968) Document E/4455, p. 34 (para. 325); p. 36 (para. 335) (1969) Document E/4606/Rev. 1, p. 62 (chapter VI); p. 95 (resolution D) (Economic and Social Council: Official Records).

<sup>4</sup> Wld Hlth Org. techn. Rep. Ser., 1969, No. 407, p. 11 (section 1.4).

<sup>&</sup>lt;sup>5</sup> Wld Hlth Org. techn. Rep. Ser., 1969, No. 407, p. 18 (section 3).

(4) the concept that drugs not now under international control could be classified according to the level of control of which they were in need.

On the basis of these principles, five groups of drugs, designated (a) to (e), were defined in the sixteenth report. Although agreeing for the most part with the proposed five groups, the Committee was of the opinion that it would be desirable to subdivide group (b) into two subgroups (defined below), in order to give greater recognition to the criteria "the degree of risk to public health" and "the usefulness of the drugs in medical therapy". The Committee furthermore concluded that the purposes for which group (e) had been suggested—namely, "to alert governments to a potential but low degree of hazard and to encourage them to monitor the use of such drugs" —could be achieved in other ways than by the creation of a special group. There were a number of possible alternatives, including linkage with the programme of reports on adverse drug reactions referred to in section 2.1, and the Committee recommended that this question be given further consideration.

In the belief that a suitable alternative mechanism would be found, the Committee omitted group (e) from its classification. In deciding on this action, the Committee took into account the desirability of keeping the number of control groups as small as possible and also the probability that group (e) would have consisted largely of drugs that, for reasons other than any dependence-producing properties, would have already required a medical prescription in most countries.

The total number of groups proposed by the Committee thus remains at five, and these are defined as follows:  $^2$ 

- (a) drugs having a liability to abuse constituting an especially serious risk to public health and having very limited, if any, therapeutic usefulness;
- (b.1) drugs whose liability to abuse constitutes a substantial risk to public health and having little to moderate therapeutic usefulness;
- (b.2) drugs whose liability to abuse constitutes a substantial risk to public health but having moderate to great therapeutic usefulness;
- (c) drugs whose liability to abuse constitutes a smaller but still significant risk to public health and having a therapeutic usefulness ranging from little to great; and
- (d) preparations of drugs contained in groups (b.1), (b.2) or (c) "compounded with non-dependence-producing ingredients in such low concen-

<sup>&</sup>lt;sup>1</sup> Wld Hlth Org. techn. Rep. Ser., 1969, No. 407, p. 18 (section 3).

 $<sup>^2</sup>$  In order to facilitate comparisons with the groups suggested in the sixteenth report of the WHO Expert Committee on Drug Dependence, corresponding groups are here identified by the same letter and the two groups created by subdivision of group (b) are referred to as group (b.1) and group (b.2); as noted above, group (e) has been eliminated.

trations or in such other manner as to render their abuse unlikely and to make recovery of the ... [controlled] ingredient very difficult ".1"

#### 4.2 Consideration of specific drugs

The Committee considered an extensive list of drugs in the course of developing the criteria for definition of the preceding groups. In so doing, the Committee also gave consideration to the broad natue of the controls deemed appropriate to each group, but stressed that its primary concern was with classifying drugs into different groups on the basis of "hazard" and "usefulness". Only when the broad principles of such a classification had been established was it possible to develop suggestions for the types of control appropriate to each group. The suggestions made by the Committee for control measures applicable to the first four groups of drugs are shown in section 4.5. Group (d) preparations are discussed in section 4.6 and some precursors in section 4.7.

In assigning specific selected drugs to one or another of the first four groups, the Committee was faced with the difficulty that there were considerable variations in the quantity and quality of the data available to it on the degree of risk to public health, depending upon how much work had been done on a particular drug and how much experience had been gained with it. The Committee had before it an extensive compilation of technical data on 226 psychoactive drugs and herbs. Included in the compilation were 13 chemical and other categories of central nervous system depressants, 4 such categories of central nervous system stimulants, and 6 categories of hallucinogens, as well as some precursors of a few of the hallucinogens. The data assembled on each of the drugs included information on the following: (a) name, (b) structural chemical formula, (c) symptoms of intoxication, (d) tolerance, (e) psychic dependence, (f) physical dependence, (g) certain pharmacological characteristics, (h) major dangers of abuse, and (i) a tentative abuse-potential rating, together with appropriate references in several languages.2

### 4.3 Distinction between "drugs recommended for control" and "analogous drugs"

Because of the substantial variation in the quality and quantity of the data available on the drugs considered, the Committee decided to

<sup>&</sup>lt;sup>1</sup> Wld Hlth Org. techn. Rep. Ser., 1969, No. 407, p. 19 (section 3).

<sup>&</sup>lt;sup>2</sup> Noting that the compilation would be of great use to those concerned with the control of selected dependence-producing psychotropic substances, as well as to professional persons regularly working in the field, the Committee expressed its hope that the information would be made available in published form. Pending such publication, this compilation is available on request from Drug Dependence, World Health Organization, 1211 Geneva, Switzerland.

divide the lists of drugs in groups (b.2) and (c) into two parts: (i) those drugs about which the evidence supporting a recommendation for control was judged to be clear and unequivocal; and (ii) drugs for which there was insufficient evidence to permit a firm recommendation to be made but whose inclusion in the group was believed to be justified "by analogy". The expression "by analogy" implies that, with respect to chemical structure, pharmacodynamic properties, therapeutic indications, or routes of administration, these drugs showed such close similarities to the "drugs recommended for control" that they were believed to be likely to present a comparable combination of risk to public health and therapeutic usefulness. It must be emphasized, however, that direct evidence of the dependence liability of "analogous drugs" is to some extent deficient because certain relevant studies have not been undertaken or are not yet complete. Consequently, further research and observations are needed on these drugs.

As indicated above, lists of analogous drugs are given only for groups (b.2) and (c); no analogous drugs are listed for groups (a) and (b.1).

### 4.4 Classification of drugs recommended for control and lists of "analogous drugs" $^{\rm 1}$

# Group (a) Drugs recommended for control because their liability to abuse constitutes an especially serious risk to public health and because they have very limited, if any, therapeutic usefulness

	INN	Other nonproprietary or trivial names	Chemical name
1.		DET	N,N-diethyltryptamine
2.		DMHP, SKF 5301	3-(1,2-dimethylheptyl)-7,8,9,10-tetrahydro-6,6,9-trimethyl-6 $H$ -dibenzo[ $b$ , $d$ ]pyran-1-ol
3.		DMT	N,N-dimethyltryptamine
4.	LYSERGIDE	LSD, LSD-25	(+)-N,N-diethyllysergamide (d-lysergic acid diethylamide)
5.		mescaline	3,4,5-trimethoxyphenethylamine
6.		parahexyl	3-hexyl-7,8,9,10-tetrahydro-6,6,9-trimethyl-6 $H$ -dibenzo-[ $b$ , $d$ ]pyran-1-ol
7.		psilocine, psilotsin	3-(2-dimethylaminoethyl)-indol-4-ol

<sup>&</sup>lt;sup>1</sup> The names printed in small capitals in the left-hand column are the International Nonproprietary Names (INN). With one exception (LYSERGIDE), other nonproprietary or trivial names are given only where no INN has yet been proposed.

### DRUG DEPENDENCE

	INN	Other nonproprietary or trivial names	Chemical name
8.	PSILOCYBINE	. •	3-(2-dimethylaminoethyl)- indol-4-yl dihydrogen phosphate
9.		STP, DOM	2,5-dimethoxy-4,α-dimethyl-phenethylamine
10.		tetrahydrocannabinols, all isomers	3-pentyl-6a,7,10,10a-tetrahydro-6,6,9-trimethyl-6 $H$ -dibenzo-[ $b$ , $d$ ]pyran-1-ol

### Group (b.1)

Drugs recommended for control because their liability to abuse constitutes a substantial risk to public health and because they have little to moderate therapeutic usefulness

1.	AMPHETAMINE	$(\pm)$ - $\alpha$ -methylphenethylamine
2.	DEXAMPHETAMINE	(+)-α-methylphenethylamine
3.	METHAMPHETAMINE	$(+)$ - $N$ - $\alpha$ -dimethylphenethylamine
4.	METHYLPHENIDATE	α-phenyl-2-piperidineacetic acid methyl ester
5.	PHENMETRAZINE	3-methyl-2-phenylmorpholine

### Group (b.2)

Drugs recommended for control because their liability to abuse constitutes a substantial risk to public health, although having moderate to great therapeutic usefulness

1. Amobarbit.	AL .	5-ethyl-5-isopentylbarbituric acid
2. CYCLOBARB	ITAL	5-(1-cyclohexen-1-yl)-5-ethyl- barbituric acid
3. GLUTETHIM	IDE	2-ethyl-2-phenylglutarimide
4. PENTOBARBI	ITAL	5-ethyl-5-(1-methylbutyl)- barbituric acid
5. SECOBARBIT	<b>AL</b>	5-allyl-5-(1-methylbutyl)- barbituric acid

### Drugs Analogous To Those in Group (b.2) 1

1.	ALLOBARBITAL		5,5-diallylbarbituric acid
2.		alphenal	5-allyl-5-phenylbarbituric acid
3.	APROBARBITAL	1	5-allyl-5-isopropylbarbituric acid
4.	V	barotalum	5-(2-butenyl)-5-ethylbarbituric acid

<sup>&</sup>lt;sup>1</sup> See section 4.3 for the meaning of the word "analogous" as used in this context. These "analogous drugs" were not formally recommended for control.

### SEVENTEENTH REPORT

	INN	Other nonproprietary or trivial names	Chemical name
5.		brallobarbital	5-allyl-5-(2-bromoallyl)- barbituric acid
6.	BUTALBITAL		5-allyl-5-isobutylbarbituric acid
7.		butobarbital	5-n-butyl-5-ethylbarbituric acid
8.		butylallonal	5-(2-bromoallyl)-5-sec- butylbarbituric acid
9.		cyclopentobarbital	5-allyl-5-(2-cyclopenten-1-yl)- barbituric acid
10.		diberal	5-(1,3-dimethylbutyl)-5- ethylbarbituric acid
11.		dormovit	5-furfuryl-5-isopropyl- barbituric acid
12.		dormupax	5-allyl-5-n-butylbarbituric acid
13.		eldoral	5-ethyl-5-(1-piperidyl)- barbituric acid
14.	-	enallylpropymal	5-allyl-5-isopropyl-1- methylbarbituric acid
15.		ethallobarbital	5-allyl-5-ethylbarbituric acid
16.	HEPTABARB		5-(1-cyclohepten-1-yl)-5- ethylbarbituric acid
17.		hexethal	5-ethyl-5-n-hexylbarbituric acid
18.	NEALBARBITAL		5-allyl-5-neopentylbarbituric acid
19.		pentenal	5-(cyclopenten-1-yl)-5- ethylbarbituric acid
20.	PROBARBITAL		5-ethyl-5-isopropylbarbituric acid
21.		propallylonal	5-(2-bromoallyl)-5-isopropylbarbituric acid
22.		propylbarbital	5,5-dipropylbarbituric acid
23.		rectidon	5-(2-bromoallyl)-5-(1-methyl- butyl)barbituric acid
24.		reposal	5-(bicyclo[3.2.1]octen-2-yl)-5-ethylbarbituric acid
25.	SECBUTABARBITAL		5-sec-butyl-5-ethylbarbituric acid
26.		spirobarbital	5-spiro-(2'-ethyl-3',5'-dimethyl-cyclopentyl)barbituric acid
27.	TALBUTAL		5-allyl-5-sec-butylbarbituric acid
28.	TETRABARBITAL		5-ethyl-5-(1-ethylbutyl)barbi- turic acid

### DRUG DEPENDENCE

	INN	Other nonproprietary or trivial names	Chemical name
29.	VINBARBITAL		5-ethyl-5-(1-methyl-1-butenyl)- barbituric acid
30.	VINYLBITAL		5-(1-methylbutyl)-5-vinyl- barbituric acid

### Group (c)

Drugs recommended for control whose liability to abuse constitutes a smaller but still significant risk to public health, and having a therapeutic usefulness ranging from little to great

1.	AMINOREX		2-amino-5-phenyl-2-oxazoline
2.	AMFEPRAMONE		2-(diethylamino)propiophenone
3.	BARBITAL		5,5-diethylbarbituric acid
4.		chloral hydrate	trichloro-2,2,2-ethanediol-1,1
5.	CHLORDIAZEPOXIDE		7-chloro-2-methylamino-5- phenyl-3 <i>H</i> -1,4-benzodia- zepine-4-oxide
6.	DIAZEPAM		7-chloro-1,3-dihydro-1-methyl-5-phenyl-2 $H$ -1,4-benzodiazepin-2-one
7.		ethchlorvynol	ethyl- $\beta$ -chlorovinylethinyl-carbinol
8.	ETHINAMATE		1-ethynylcyclohexanol carba- mate
9.	MEPROBAMATE		2-methyl-2-propyl-1,3-propanediol dicarbamate
10.	METHAQUALONE		2-methyl-3- <i>o</i> -tolyl-4(3 <i>H</i> )-quinazolinone
11.	METHOHEXITAL		(±)-5-allyl-1-methyl-5- (1-methyl-2-pentynyl)- barbituric acid
12.	METHYLPHENOBARBITAL		5-ethyl- <i>N</i> -methyl-5-phenyl-barbituric acid
13.	METHYPRYLON		3,3-diethyl-5-methyl-2,4- piperidinedione
14.		paraldehyde	cyclic ether of acetaldehyde
15.	PHENCYCLIDINE		1-(1-phenylcyclohexyl)- piperidine
16.	PHENOBARBITAL		5-ethyl-5-phenylbarbituric acid
17.	PIPRADROL		$\alpha, \alpha$ -diphenyl-2-piperidinemethanol
18.		SPA	()-1-dimethylamino-1,2-diphenylethane

### SEVENTEENTH REPORT

INN

Other nonproprietary or trivial names

Chemical name

### Drugs Analogous To Those in Group $(c)^{1}$

1.	AMFECLORAL		$\alpha$ -methyl- $N$ -(2,2,2-trichloro-ethylidene)phenethylamine
2.	AMINOGLUTETHIMIDE		2-(p-aminophenyl)-2-ethylglu- tarimide
3.	BARBEXACLONE		(—)-N,α-dimethylcyclohexane- ethylamine compound with 5-ethyl-5-phenylbarbituric acid
4.	BENZPHETAMINE		$N$ -benzyl- $N$ , $\alpha$ -dimethyl-phenethylamine
5.		bromal	tribromoacetaldehyde
6.		bromal hydrate	tribromoacetaldehyde hydrate
7.		butylchloral hydrate	butylchloral hydrate
8.	CARBUBARB		5-butyl-5-(2-carbamoyloxy- ethyl)barbituric acid
9.		chloralformamide	chloralformamide
10.		chloralimide	chloralimide
11.	CHLORALODOL		2-methyl-4-(2,2,2-trichloro-1-hydroxyethoxy)-2-pentanol
12.	CHLORPHENTERMINE		$p$ -chloro- $\alpha$ , $\alpha$ -dimethylphen- ethylamine
13.	CINPERENE		2-(1-cinnamyl-4-piperidyl)-2- phenylglutarimide
14.	CLOBENZOREX		$(\frac{1}{r})$ -N-(o-chlorobenzyl)- $\alpha$ -methylphenethylamine
15.	CLORACETADOL		$\beta,\beta,\beta$ -trichloro- $\alpha$ -hydroxy- $p$ -acetophenetidide
16.	CLORAL BETAINE		chloral hydrate compound with betaine
17.	CLORETATE		bis(2,2,2-trichlorethyl)-carbonate
18.	FENFLURAMINE		3-(trifluoromethyl)- $N$ -ethyl- $\alpha$ -methylphenethylamine
19.	FLUDOREX		$\beta$ -methoxy- $N$ -methyl- $m$ -(trifluoromethyl)phenethyl-amine
20.		heptobarbital	5-methyl-5-phenylbarbituric acid
21.	HEXOBARBITAL		5-(1-cyclohexen-1-yl)-1,5- dimethylbarbituric acid

<sup>&</sup>lt;sup>1</sup> See section 4.3 for the meaning of the word "analogous" as used in this context. These "analogous" drugs were not formally recommended for control.

	INN	Other nonproprietary or trivial names	Chemical name
22.	MEFENOREX		N-(3-chloropropyl)-α-methyl-phenethylamine
23.	MEPHENTERMINE		$N$ - $\alpha$ , $\alpha$ -trimethylphenethylamine
24.	METHARBITAL		5,5-diethyl-1-methylbarbituric acid
25.	METHYLPENTYNOL		3-methyl-1-pentyn-3-ol
26.		narcobarbital	1-methyl-5-(2-bromoallyl)-5- isopropylbarbituric acid
27.		nicotinylamphetamine	1-phenyl-2-nicotinylamino- propane
28.	NITRAZEPAM		1,3-dihydro-7-nitro-5-phenyl- 2 <i>H</i> -1,4-benzodiazepin-2-one
29.	ORTETAMINE		$o$ - $\alpha$ -dimethylphenethylamine
30.	OXAZEPAM	•	7-chloro-1,3-dihydro-3-hydroxy-5-phenyl-2 <i>H</i> -1,4-benzo-diazepin-2-one
31.	OXIFENTOREX		$N$ -benzyl- $N$ - $\alpha$ -dimethylphenethylamine $N$ -oxide
32.	PEMOLINE		2-imino-5-phenyl-4-oxazoli- dinone
33.	PENTOREX		$\alpha, \alpha, \beta$ -trimethylphenethylamine
34.	PETRICHLORAL		1,1',1'',1'''-(neopentanetetryl- tetraoxy)tetrakis(2,2,2-tri- chloroethanol) <i>or</i> pentaery- thritol chloral
35.	PHENDIMETRAZINE		(+)-3,4-dimethyl-2-phenyl-morpholine
36.	PHENTERMINE		$\alpha, \alpha$ -dimethylphenethylamine
37.	PHETHARBITAL		5,5-diethyl-1-phenyl- barbituric acid
38. 39.	TRICLOFOS	trichlorethanol	1,1,1-trichlorethanol 2,2,2-trichloroethyl dihydrogen phosphate

### 4.5 Suggested types of control for drugs, by groups

Types of control	Proposed groups			
	(a)	(b.1)	(b.2)	(c)
Licensing of manufacture and trade	X	X	X	x
Keeping of records of all transactions from manufacture up to and including retail distribution	X	x		

	-	Proposed groups					
Types of control	(a)	(b-1)	(b-2)	(c)			
Keeping of records of all transactions from manufacture to acquisition by the retailer but excluding retail distribution			х	x			
Prior agreement on individual imports and exports between the governments concerned	х	Х	х				
Reporting (except on estimates) to existing international organs along the lines now required for narcotic drugs under the Single Convention	х	х	X				
An undertaking to prohibit or limit exports to a country whose government so requests	х	Х	X	X			
Availability only on limited medical prescription <sup>1</sup>	Not on prescription	X	x	Х			
Availability only through a non- refillable order and in accordance with a project that has received appropriate prior approval as to objectives and safety	X		-				

### 4.6 Preparations containing controlled drugs

The Committee was of the opinion that a preparation containing one or more controlled drugs should, in general, be subject to the same controls as applicable to the "most controlled" drug in that preparation,<sup>2</sup>

<sup>&</sup>lt;sup>1</sup> "Limited medical prescription" is intended here to mean limitations on the amount, duration of validity, and number of refills. The details of these limitations would be left to governments; it is expected that the limitations would vary according to the nature of the drug involved and local conditions.

<sup>&</sup>lt;sup>2</sup> This would not preclude a greater degree of control being applied to a preparation of a drug listed in group (b.1), (b.2), or (c) than to the basic drug itself if the manner of compounding greatly increased its liability to abuse and thus its risk to public health.

unless the controlled drugs involved were "compounded with non-dependence-producing ingredients in such low concentrations, or in such other manner, as to render their abuse unlikely and to make recovery of the controlled ingredient very difficult". In the latter case, the resulting preparations would be included in group (d) and subject only to the controls suggested in the last paragraph of this section.

The Committee considered that the controls suggested for group (a) drugs should be applied to all preparations of these drugs.

Identification of the preparations that might be included in group (d) is very complex because of the hundreds of preparations involved, the rapidity with which new preparations are being developed and marketed, and the wide variety of non-dependence-producing ingredients with which the drugs listed in groups (b.1), (b.2) and (c) are compounded.

As an approach to one aspect of this complex problem, the Committee suggested that it might be possible to consider all preparations of group (c) drugs, when compounded in designated ways, as a general category or class to be automatically included in group (d), unless particular preparations were shown to be subject to actual abuse. In the latter case, such preparations would be specifically excluded from any general category or class included in group (d).

The Committee suggested further that, when systems of control were being established for dependence-producing psychoactive drugs not previously under control, consideration might be given to the allowance of a period of grace, fixed at 3 or 4 years, during which time preparations containing group (b.1) or (b.2) drugs, when compounded in designated ways, might continue to be subject to a pre-existing, lower level of control (including no control) than that to be applied under the new system to the basic drug itself. If it were desired to continue to apply a lower level of control to a particular preparation beyond the period of grace, an application to that effect would be required, supported by balanced, objective evidence. If the application were granted, the preparation would be included in group (d).

As to the nature of the broad controls to be applied to group (d) preparations, the Committee suggested that manufacturers be licensed, and that complete records be kept as to (1) the amount of basic drug used in their manufacture, (2) the nature of the preparations, and (3) the initial disposal of such preparations. It further suggested that the amount of group (b.1) and (b.2) drugs utilized in making group (d) preparations be reported to existing international organs.

<sup>&</sup>lt;sup>1</sup> See section 4.1, group (d).

### 4.7 Precursors

In 1968, the WHO Expert Committee on Drug Dependence gave attention to the possibility of defining an additional group of controlled substances to comprise "chemical precursors capable of relatively simple transformation into dependence-producing drugs". In view of the difficulties of defining the criteria for inclusion of substances in such a group, however, the 1968 Committee doubted the practicability of developing a list of precursors at that time; it concluded that, in general, each substance required individual evaluation. The present Committee agreed with this position and considered the situation in relation to the following 3 substances:

- (1) cannabidiol, a precursor of the tetrahydrocannabinols used only in their preparation;
- (2) lysergic acid amide, a precursor of lysergide used only in its preparation; and
- (3) lysergic acid, a precursor of lysergide used not only in its preparation but also in the preparation of certain non-dependence-producing drugs having substantial usefulness.

The Committee recommended that these three precursors be controlled and suggested that the broad controls be the same as those suggested for drugs in group (a), except that (1) they should be available to licensed persons only on the basis of a non-refillable order, and (2) records should be kept of all transactions from the production or manufacture of the precursors up to and including the initial disposal of any non-controlled products resulting from their transformation.

### 5. NOTIFICATIONS

### 5.1 Diprenorphine <sup>3</sup>

The Committee considered the notification by the Government of the United Kingdom of Great Britain and Northern Ireland, under Article 3, paragraph 3, subparagraph (iii) of the Single Convention on Narcotic Drugs, 1961, concerning diprenorphine.

Diprenorphine is the dihydroderivative of cyprenorphine. Cyprenorphine was discussed during the fifteenth meeting of the WHO Expert Com-

<sup>&</sup>lt;sup>1</sup> Wld Hlth Org. techn. Rep. Ser., 1969, No. 407, p. 19 (section 3).

<sup>&</sup>lt;sup>2</sup> See section 4.5 of this report.

<sup>&</sup>lt;sup>8</sup> Proposed INN for 21-cyclopropylmethyl-6,7,8,14-tetrahydro- $7\alpha$ -(1-hydroxy-1-methylethyl)-6,14-*endo*-ethenooripavine.

mittee on Dependence-Producing Drugs in 1966.¹ The data available indicate that diprenorphine is a morphine antagonist closely related in chemical and pharmacological properties to cyprenorphine. In the rat, it is approximately 40 times more potent than nalorphine as an antagonist when administered parenterally. It appears to be only weakly effective by mouth. In the morphine-dependent monkey, diprenorphine has been found to be about 16 times as potent as nalorphine in precipitating abstinence phenomena.

It was reported that diprenorphine was likely to be used only as an antagonist and that its application would probably be limited to veterinary medicine. The Committee was of the opinion that knowledge of the relative agonist-antagonist properties of a particular compound did not, at present, permit predictions as to how these properties would relate to its dependence liability. Since direct evidence of the dependence liability of diprenorphine was not available, the Committee was therefore unable to reach a decision as to its need for control.

### 5.2 Amphetamine, dexamphetamine, methamphetamine, methylphenidate, phenmetrazine and pipradrol <sup>2</sup>

The Committee considered the notification of the Government of Sweden and concluded that the substances referred to fell into two groups. Pipradrol cannot be assimilated to the substances in any of the Schedules of the Single Convention on Narcotic Drugs, 1961. The other substances—amphetamine, dexamphetamine, methamphetamine, methylphenidate and phenmetrazine—are pharmacologically similar among themselves and their pattern of abuse and consequent ill effects are sufficiently similar to those of cocaine, especially in so far as their intravenous use is concerned, as to make them assimilable to the drugs in Schedule I of the Single Convention. The Committee believed, therefore, that on purely technical grounds it would be obliged to recommend that amphetamine, dexamphetamine, methylphenidate and phenmetrazine be added to Schedule I of the Single Convention.

On the other hand, there were strong reasons for considering that such a recommendation would be inappropriate. The plenipotentiary conference that had drafted the Single Convention had rejected inclusion of the amphetamines in that Convention; for this and other reasons subsequent efforts had been undertaken to draft a more appropriate protocol for the international control of amphetamines and other dependence-producing substances in urgent need of such control. The Committee was informed that

<sup>&</sup>lt;sup>1</sup> Wld Hlth Org. techn. Rep. Ser., 1966, No. 343, p. 4 (section 1.2).

 $<sup>^2</sup>$  INN names for (±)- $\alpha$ -methylphenethylamine, (+)- $\alpha$ -methylphenethylamine, (+)- $N,\alpha$ -dimethylphenethylamine,  $\alpha$ -phenyl-2-piperadineacetic acid methyl ester, 3-methyl-2-phenylmorpholine, and  $\alpha,\alpha$ -diphenyl-2-piperidinemethanol respectively.

progress had been made in the drafting of such a protocol, but that some years would still have to elapse before it could be completed and become fully effective.

The Committee was of the opinion that the situation with respect to the abuse of amphetamine, dexamphetamine, methamphetamine, methylphenidate, and phenmetrazine was very serious and that there was an important need for urgent action to secure international control. Accordingly, as an emergency measure, immediate consideration should be given to the drafting and implementation of a temporary international instrument to ensure the prompt control of these substances until such time as a more comprehensive agreement for the appropriate control of all dependence-producing psychotropic substances comes into effect. For the above reasons, the Committee

#### RECOMMENDS

- that pending the coming into force of an international protocol for the control of dependence-producing psychotropic substances and to meet the immediate emergency, urgent attention be given to the elaboration of a special temporary international instrument that will provide for speedy international control of the undermentioned dependenceproducing drugs, and that the Director-General of the World Health Organization consult to this effect the Secretary-General of the United Nations;
- 2. that amphetamine, dexamphetamine, methamphetamine, methylphenidate and phenmetrazine, which meet the criteria for control outlined in the sixteenth report of the WHO Expert Committee on Drug Dependence, be subject to control by means of the aforementioned special temporary international instrument; and
- 3. that the special temporary instrument contain provisions for the following types of control: 2
  - (a) licensing of the manufacture of and trade in these substances;
  - (b) keeping of records of all transactions from manufacture up to and including retail distribution;
  - (c) individual imports and exports to be subject to prior agreement between the governments concerned;
  - (d) reporting (except on estimates) to existing international organs along the lines now required for narcotic drugs under the Single Convention;

<sup>&</sup>lt;sup>1</sup> Wld Hlth Org. techn. Rep. Ser., 1969, No. 407, p. 11 (section 1.4).

<sup>&</sup>lt;sup>2</sup> The first recommendation for comparable control provisions are contained in Wld Hlth Org. techn. Rep. Ser., 1965, No. 312, p. 10 (section 7).

- (e) an undertaking to prohibit or limit exports to a country whose government so requests; and
- (f) availability only on limited medical prescription.

#### 6. REVIEW OF DRUGS PREVIOUSLY CONSIDERED

The Committee reviewed the data available on the abuse of pentazocine, dextropropoxyphene and dextromethorphan. Pentazocine is considered capable of producing mild physical and somewhat greater psychic dependence, but does not appear to be creating a public health problem. Dextropropoxyphene appears to be capable of producing similar degrees of physical and psychic dependence. Cases of abuse continue to appear, but the number is small, both in absolute terms and in comparison with the total number of persons treated with the drug.

The Committee took note of the agreement to improve the promotional material issued by the manufacturers of pentazocine and dextropropoxyphene in so far as their statements about the "non-narcotic" character of these drugs and the possibilities of abuse were concerned.

Dextromethorphan appears to be capable of producing only very slight psychic dependence and no physical dependence of the morphine type in man. There has been some abuse, but the number of cases is small.

The Committee reaffirmed the opinion expressed last year <sup>1</sup> that the evidence at present available on the abuse of pentazocine, dextropropoxyphene and dextromethorphan still does not warrant a recommendation for their international control and concluded that a careful scrutiny of the use of these three drugs and other comparable drugs should be maintained.

The Committee also had available to it information about several additional drugs with various combinations of agonist and antagonist properties. Continued scrutiny of these drugs should also be maintained.

The Committee took note of the very complex problems associated with evaluating the dependence liability of drugs possessing both agonist and antagonist properties. Additional research on these problems is needed, especially as some of these compounds are of considerable interest or potential interest as therapeutic agents.

### 7. TREATMENT AND REHABILITATION

The Committee was informed of current trends in treatment with regard primarily to drug dependence of the morphine type in one country.<sup>2</sup> Of particular interest were (1) the increasing availability of specialized treatment and rehabilitation programmes for narcotic-dependent persons in various

<sup>&</sup>lt;sup>1</sup> Wld Hlth Org. techn. Rep. Ser., 1969, No. 407, p. 23 (section 11).

<sup>&</sup>lt;sup>2</sup> Eddy, N. B. (1970) Bull. Narcot., in press.

parts of that country, (2) the development of various types of "self-help" programmes, and (3) the attention being given to evaluating the effectiveness of methadone maintenance as a management method.

General principles of treatment for narcotic-dependent persons were elaborated in 1957 by a WHO Study Group.¹ In the opinion of the Committee, these remain basically sound. Complete abstinence from the use of dependence-producing drugs continues to be the most desirable objective, but such abstinence is not, in the Committee's opinion, the only criterion by which to evaluate the effectiveness of therapy. It must be assessed also in terms of the patient's mental state and his social and economic adjustment.

The Committee stressed the importance of utilizing treatment approaches and methods appropriate to the needs of each patient. It has to be remembered that each type of drug dependence has many characteristics that are unique to it, as well as some others that are common to several types of such dependence,<sup>2</sup> and also that drug dependence of all types involves a complex interaction between the dependent person, his environment and the pharmacodynamics of the drug or drugs involved.<sup>3</sup> Comprehensive treatment and rehabilitation of drug-dependent persons required (1) resources and skills from the fields of medicine, psychology, sociology, and, not infrequently, the law; (2) the full collaboration of each patient's family and other persons significantly related to his daily living; and (3) very often, long-term follow-up and supportive services.

The Committee stressed that, to permit the development of increasingly effective methods for the treatment and rehabilitation of a wide variety of persons, living in different socio-cultural settings and using different types of dependence-producing drugs, intensive studies are needed to clarify (1) the natural history of various types of drug dependence, (2) the factors that influence various persons and groups with respect to their drug-taking behaviour, both before and after some experience with dependence-producing drugs, and (3) the relative effectiveness of different treatment approaches. It is necessary that treatment and rehabilitation programmes and methods be studied in relation to other efforts designed to prevent, reduce and/or "contain" drug dependence and related abuse.

### 8. METHADONE MAINTENANCE

The Committee reviewed recent experiences with methadone maintenance.<sup>4</sup> This method for the management of persons having dependence

<sup>&</sup>lt;sup>1</sup> Wld Hlth Org. techn. Rep. Ser., 1957, No. 131, p. 7 (section 4).

<sup>&</sup>lt;sup>2</sup> Eddy, N. B., Halbach, H., Isbell H., & Seevers, M. H. (1965) Bull. Wld Hlth Org., 32, 721.

<sup>&</sup>lt;sup>3</sup> Halbach, H. (1959) Brit. J. Addict., 56, 27.

<sup>&</sup>lt;sup>4</sup> Eddy, N. B. (1970) Bull. Narcot., 22, 1.

of the morphine type has been considered in previous reports.<sup>1, 2</sup> It was noted that there has been increased emphasis on the use of ambulatory induction. A high-dose technique continues to predominate. It appears that by no means all, or even the majority of, opioid-dependent persons will accept this management method and that the proportion of persons that can be reached through its use is influenced by many factors. Although encouraging results continue to be reported, the Committee believes that methadone maintenance remains experimental and is not suitable for application by individual physicians; it should be used only under the conditions outlined in the sixteenth report.<sup>2</sup>

### 9. SPECIFIC OPIATE ANTAGONISTS IN THERAPY

The use of cyclazocine and naloxone in the therapy of drug-dependent persons was reviewed in the sixteenth report of the Committee.<sup>3</sup> No significant changes have meanwhile been reported in this interesting and promising approach. The number of cases treated with these opiate antagonists remains small, and further testing is required. The Committee expressed the hope that continued efforts would be made to develop a long-acting oral opiate antagonist with no psychomimetic or other adverse side effects.

<sup>&</sup>lt;sup>1</sup> Wld Hlth Org. techn. Rep. Ser., 1966, No. 343, p. 9 (section 6).

<sup>&</sup>lt;sup>2</sup> Wld Hlth Org. techn. Rep. Ser., 1969, No. 407, p. 20 (section 6).

<sup>&</sup>lt;sup>3</sup> Wld Hlth Org. techn. Rep. Ser., 1969, No. 407, p. 21 (section 7).

#### Annex

### LIST OF DRUGS UNDER INTERNATIONAL NARCOTICS CONTROL<sup>1</sup>

Common name or INN *	Chemical designation	mitt	Expert Com- ee on Drug pendence 2.	Control regime	
		Report number	Reference	1931 Conven- tion Group	1961 Conven- tion Sche- dule <sup>3</sup>
acetorphine *	6,7,8,14-tetrahydro-7\(\alpha\)- (1-hydroxy-1-methylbutyl)-6,14-endo-ethenooripavine 3-acetate	15	1966, <b>343</b> , 3	I	I/IV
acetyldihydrocodeine	acetyldihydrocodeine	1	1949, <b>19</b> , 30	II	II
acetylmethadol *	3-acetoxy-6-dimethylamino- 4,4-diphenyl-3-heptane	1	1949, <b>19</b> , 31	I	I
allylprodine *	3-allyl-1-methyl-4-phenyl- 4-propionoxypiperidine	10	1960, <b>188</b> , 3	I	I
alphacetylmethadol *	α-3-acetoxy-6-dimethylamino- 4,4-diphenylheptane	· 4	1954, <b>76</b> , 7	I	I
alphameprodine *	α-3-ethyl-1-methyl-4-phenyl- 4-propionoxypiperidine	7	1957 <b>, 116,</b> 8	I	I
alphamethadol *	α-6-dimethylamino- 4,4-diphenyl-3-heptanol	4	195 <b>4, 76,</b> 7	I	I
alphaprodine'*	α-1,3-dimethyl-4-phenyl- 4-propionoxypiperidine	1	1949 <b>, 19,</b> 30	I	I
anileridine *	1-(p-aminophenethyl)- 4-phenylpiperidine-4-carboxy- lic acid ethyl ester	7	1957 <b>, 116</b> , 7	Ι	I
benzethidine *	1-(2-benzyloxyethyl)- 4-phenylpiperidine-4-carboxy- lic acid ethyl ester	10	1960, <b>188</b> , 4	I	I

<sup>\*</sup> Proposed international non-proprietary name (INN).

The isomers, unless specifically excepted, of the drugs in this Schedule whenever the existence

The esters and ethers, unless appearing in another Schedule, of the drugs in this Schedule whenever the existence of such isomers as possible within the specific chemical designation;

The esters and ethers, unless appearing in another Schedule, of the drugs in this Schedule whenever the existence of such esters and ethers is possible;

The salts of the drugs listed in this Schedule, including the salts of esters, ethers, and isomers as provided above whenever the existence of such salts is possible.

### In Schedule II of the 1961 Convention are included:

The isomers, unless specifically excepted, of the drugs in this Schedule whenever the existence of such isomers is possible within the specific chemical designation;

The salts of the drugs listed in this Schedule, including the salts of the isomers as provided above whenever the existence of such salts is possible.

In Schedule IV of the 1961 Convention are included the salts of the drugs listed in this Schedule henever the formation of such salts is possible.

<sup>&</sup>lt;sup>1</sup> For details such as synonyms and the date of coming into force of international control, see *Multingual List of Narcotic Drugs under International Control* (UN document E/CN.7/513) and also *Annex the statistical forms "Yellow List"* published annually by the International Narcotics Control Board.

<sup>&</sup>lt;sup>2</sup> The references given in this column are to World Health Organization Technical Report Series, 7th the exception of the report published in 1949 which appeared in Official Records of the World Health Organization, No. 19. For the names of earlier Committees, see footnote on page 5.

<sup>&</sup>lt;sup>3</sup> In Schedule I of the 1961 Convention are included:

		WHO Expert Com- mittee on Drug Dependence <sup>2</sup>		Control regime	
Common name or INN *	Chemical designation	Report number	Reference	1931 Conven- tion Group	1961 Conven- tion Sche- dule <sup>3</sup>
benzylmorphine	3-benzylmorphine			I	ı
betacetylmethadol *	β-3-acetoxy-6-dimethylamino- 4,4-diphenylheptane	4	1954, <b>76</b> , 7	Î	Î
betameprodine *	β-3-ethyl-1-methyl-4-phenyl-4-propionoxypiperidine	3	1952, 57, 7	I	1
betamethadol *	β-6-dimethylamino- 4,4-diphenyl-3-heptanol	5	1955, <b>95</b> , 8	I	I
betaprodine *	β-1,3-dimethyl-4-phenyl-4-propionoxypiperidine	1	1949 <b>, 19</b> , 30	I	I
bezitramide *	1-(3-cyano-3,3-diphenyl- propyl)-4-(2-oxo-3-propionyl- 1-benzimidazolyl)-piperidine	16	1969 <b>, 407,</b> 22	. I	I
cannabis and cannabis resin	Cannabis sativa L.			I	I/IV
clonitazene *	2-p-chlorbenzyl-1-(2-diethyl- aminoethyl)-5-nitrobenz- imidazole	11	1961, <b>211</b> , 4	I	1
coca leaf	Erythroxylon coca L.	1		I,	1
cocaine	methyl ester of benzoylecgonine			I	II
codeine	3-methylmorphine			II	II
codoxime *	dihydrocodeinone- O-(carboxymethyl)oxime		•	I	·I
concentrate of poppy straw					I
desomorphine *	dihydrodeoxymorphine	1		I	I/IV
dextromoramide *	(+)-4-[2-methyl-4-oxo- 3,3-diphenyl-4-(1-pyrro- lidinyl)butyl] morpholine	8	1958 <b>, 142</b> , 8	I	I
diampromide *	N-[2-(methylphenethylamino)- propyl]-propionanilide	11	1961, <b>211</b> , 5	I	I
diethylthiambutene *	3-diethylamino-1,1-di- (2'-thienyl)-1-butene	6	1956, <b>102</b> , 10	I	. I
dihydrocodeine	7,8-dihydrocodeine	1	1949, <b>19,</b> 30	· II	II
dihydromorphine	7,8-dihydromorphine	1		I	I,
dimenoxadol *	2-dimethylaminoethyl- 1-ethoxy-1,1-diphenylacetate	9	1959, <b>160</b> , 9	I	I
dimepheptanol *	6-dimethylamino- 4,4-diphenyl-3-heptanol	1	1949, <b>19</b> , 31	I	I
dimethylthiambutene *	3-dimethylamino-1,1-di- (2'-thienyl)-1-butene	4	1954, <b>76</b> , 9	I	1
dioxaphetyl butyrate *	ethyl 4-morpholino- 2,2-diphenylbutyrate	6	1956, 102, 9	I	I
diphenoxylate *	1-(3-cyano-3,3-diphenyl- propyl)-4-phenylpiperidine- 4-carboxylic acid ethyl ester	11	1961, <b>211</b> , 5	1	I
dipipanone *	4,4-diphenyl-6-piperidino- 3-heptanone	5	1955 <b>, 95</b> , 8	I	I
ecgonine	(—)-3-hydroxytropane- 2-carboxylate			I	I
ethylmethylthiambutene *	3-ethylmethylamino-1,1-di- (2'-thienyl)-1-butene	4	1954, 76, 9	I	I
	l .	I			l

### SEVENTEENTH REPORT

	Chemical designation	WHO Expert Com- mittee on Drug Dependence <sup>1</sup>		Control regime	
Common name or INN *		Report number	Reference	1931 Conven- tion Group	1961 Conven- tion Sche- dule <sup>3</sup>
ethylmorphine	3-ethylmorphine			п	
etonitazene *	1-diethylaminoethyl-2-p- ethoxybenzyl-5-nitro- benzimidazole	11	1961, <b>211,</b> 7	. I	I
etorphine *	6,7,8,14-tetrahydro-7α- (1-hydroxy-1-methylbutyl)- 6,14-endo-ethenooripayine	15	1966, <b>343</b> , 5	I	I/IV
etoxeridine *	1-[2-(2-hydroxyethoxy)ethyl]- 4-phenylpiperidine- 4-carboxylic acid ethyl ester	8	1958, <b>142</b> , 9	I	I
fentanyl *	1-phenethyl-4-N-propionyl- anilinopiperidine	13	1964, <b>273</b> , 4	I	I
furethidine *	1-(2-tetrahydrofurfuryl- oxyethyl)-4-phenylpiperidine- 4-carboxylic acid ethyl ester	10	1960, <b>188</b> , 5	I	I
heroin	diacetylmorphine			I	I/IV
hydrocodone *	dihydrocodeinone			I	I
hydromorphinol *	14-hydroxy-7,8-dihydro- morphine	11	1961, <b>211</b> , 7	1	I
hydromorphone *	dihydromorphinone			1	I
hydroxypethidine *	4-(m-hydroxyphenyl)- 1-methylpiperidine- 4-carboxylic acid ethyl ester	1	19 <b>4</b> 9, <b>19</b> , 30	I	I
isomethadone *	6-dimethylamino-5-methyl- 4,4-diphenyl-3-hexanone	1	1949, <b>19</b> , 31	1	I
ketobemidone *	4-(m-hydroxyphenyl)- 1-methyl-4-propionyl- piperidine	1	1949, <b>19</b> , 30	I	I/IV
levomethorphan *	(—)-3-methoxy-N-methyl- morphinan	3	1952, <b>57</b> , 6	I .	I
levomoramide *	(-)-4-[2-methyl-4-oxo- 3,3-diphenyl-4-(1-pyrro- lidinyl)-butyl]morpholine	8	1958 <b>, 142</b> , 8	I	I
levophenacylmorphan *	(-)-3-hydroxy-N-phenacyl- morphinan	10	1960, 188, 5	I	I
levorphanol *	(—)-3-hydroxy-N-methyl- morphinan	3	1952, <b>57</b> , 6	I	I
metazocine *	2'-hydroxy-2,5,9-trimethyl- 6,7-benzomorphan	10	1960 <b>, 188,</b> 6	I	I
methadone *	6-dimethylamino- 4,4-diphenyl-3-heptanone	1	1949, <b>19</b> , 30	I	I
methadone-intermediate	4-cyano-2-dimethylamino- 4,4-diphenylbutane	12	1962, <b>229</b> , 7	I	I
methyldesorphine *	6-methyl-\(\Delta^6\)-deoxymorphine	4	1954, 76, 6	I	I
methyldihydromorphine *	6-methyldihydromorphine	5	1955, 95, 5	Ī	Ī
metopon *	5-methyldihydromorphinone	1	1949, <b>19</b> , 30	I	I
moramide-intermediate	2-methyl-3-morpholino-1,1-diphenylpropane carboxylic acid	12	1962, <b>229</b> , 7	Ι	I
morpheridine *	1-(2-morpholinoethyl)- 4-phenylpiperidine- 4-carboxylic acid ethyl ester	8	1958 <b>, 142</b> , 8	Ι	I

Common name or INN *		mitte	Expert Com- ee on Drug pendence <sup>2</sup>	Control regime	
	Chemical designation	Report number	Reference	1931 Conven- tion Group	1961 Conve tion Sche dule
				I	п
morphine morphine-N-oxide	:			I	I
morphine pentavalent nitrogen derivatives		,		Ī	I
myrophine *	myristylbenzylmorphine	5	1955, <b>95</b> , 6	1	I
nicocodine *	6-nicotinoylcodeine	12	1962, <b>229</b> , 6	n	П
nicodicodine *	6-nicotinoyldihydrocodeine	15	1966, <b>343</b> , 5	1	I
nicomorphine *	3,6-dinicotinoylmorphine	9	19 <b>59, 160,</b> 4	I	I
noracymethadol *	(±)-α-3-acetoxy-6-methylamino-4,4-diphenylheptane	12	1962, <b>229</b> , 5	I	I.
norcodeine *	N-demethylcodeine	9	1959 <b>, 160,</b> 5	II	II
norlevorphanol *	(—)-3-hydroxymorphinan	10	1960 <b>, 188,</b> 6	I	I
normethadone *	6-dimethylamino-4,4- diphenyl-3-hexanone	5	1955, <b>95</b> , 7	I	I
normorphine *	demethylmorphine	9	1959, <b>160</b> , 5	I	I
norpipanone *	4,4-diphenyl-6-piperidino- 3-hexanone	13	1964, 273, 4	Ι.	I
opium				I	II
oxycodone	14-hydroxydihydrocodeinone			I	I
oxymorphone *	14-hydroxydihydro- morphinone	5	1955 <b>, 95</b> , 6	I	I
pethidine *	1-methyl-4-phenylpiperidine- 4-carboxylic acid ethyl ester	1	1949, 19, 30	I	r
pethidine- intermediate A	4-cyano-1-methyl-4-phenyl-piperidine	12	1962, <b>229</b> , 7	I	I
pethidine- intermediate B	4-phenylpiperidine- 4-carboxylic acid ethyl ester	12	1962, <b>229</b> , 7	,I	I
pethidine- intermediate C	1-methyl-4-phenylpiperidine- 4-carboxylic acid	_	19 <b>55, 95,</b> 9	I	I
pethidine- intermediate C, esters of		5	1933, 93, 9	1	1
phenadoxone *	6-N-morpholino-4,4-diphenyl- 3-heptanone	1	1949, <b>19</b> , 31	I	1
phenampromide *	N-(1-methyl-2-piperidino- ethyl)propionanilide	11 -	1961, <b>211</b> , 7	1	I
phenazocine *	2'-hydroxy-5,9-dimethyl- 2-phenethyl-6,7-benzo- morphan	10	1960 <b>, 188,</b> 6	I	I
phenomorphan *	3-hydroxy-N-phenethyl- morphinan	6	1956 <b>, 102</b> , 8	·I	· I
phenoperidine *	1-(3-hydroxy-3-phenyl- propyl)-4-phenylpiperidine- 4-carboxylic acid ethyl ester	11	1961, <b>211</b> , 8	ı	I
pholcodine *	morpholinylethylmorphine	3	1952, <b>57</b> , 5	II	П
piminodine *	4-phenyl-1-(3-phenylamino- propyl)piperidine- 4-carboxylic acid ethyl ester	10	1960, 188, 7	I	I

### SEVENTEENTH REPORT

Common name or INN *	Chemical designation	WHO Expert Com- mittee on Drug Dependence <sup>2</sup>		Control regime	
		Report number	Reference	1931 Conven- tion Group	1961 Conve <b>n-</b> tion Sche- dule <sup>3</sup>
piritramide *	1-(3-cyano-3,3-diphenyl- propyl)-4-(1-piperidino)- piperidine-4-carboxylic acid amide	14	1965, <b>312</b> , 3	I	I
proheptazine *	1,3-dimethyl-4-phenyl-4- propionoxyazacycloheptane	6	1956, <b>102</b> , 11	I	I
properidine *	1-methyl-4-phenylpiperidine- 4-carboxylic acid isopropyl ester	5	1955 <b>, 95,</b> 9	I	I
racemethorphan *	(±)-3-methoxy-N-methyl- morphinan	3	1952, <b>57</b> , 7	I	I
racemoramide *	(±)-4-[2-methyl-4-oxo- 3,3-diphenyl-4-(1-pyrro- lidinyl)butyl]morpholine	8	1958, 142, 8	I	I
racemorphan *	(±)-3-hydroxy-N-methyl- morphinan	3	1952, <b>57</b> , 6	I	I
thebacon *	acetyldihydrocodeinone			I	I
thebaine	3,6-dimethyl-8-dehydro- morphine			I	I
trimeperidine *	1,2,5-trimethyl-4-phenyl-4- propionoxypiperidine	8	1958 <b>, 142</b> , 9	I	I