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# WHO EXPERT COMMITTEE ON ADDICTION-PRODUCING DRUGS

## Thirteenth Report



WORLD HEALTH ORGANIZATION
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1964

## WHO EXPERT COMMITTEE ON ADDICTION-PRODUCING DRUGS

*Geneva, 25-30 November 1963*

*Members :* *

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Dr L. Goldberg, Professor of Research on Alcohol and Analgesics, Karolinska Institutet, Stockholm, Sweden (*Rapporteur*)

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Dr V. V. Vasil'eva, Professor of Pharmacology, Second Moscow Institute of Medicine, Moscow, USSR (*Vice-Chairman*)

*Representatives of the United Nations :*

Mr W. J. Duke, Chief of Section, Division of Narcotic Drugs, United Nations, Geneva

Mr O. J. Braenden, Ph.D., Division of Narcotic Drugs, United Nations, Geneva

*Representative of the Permanent Central Opium Board and the Drug Supervisory Body :*

Mr A. Lande, Dr jur., Secretary of these two bodies, Geneva

*Secretariat :*

Dr H. Halbach, Dr med., Dr Ing., Chief Medical Officer, Addiction-Producing Drugs, WHO (*Secretary*)

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* Unable to attend :

Dr G. Joachimoglu, Professor Emeritus of Pharmacology; formerly Chairman, Superior Health Council, Ministry of Social Welfare, Athens, Greece

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# WHO EXPERT COMMITTEE ON ADDICTION-PRODUCING DRUGS

## Thirteenth Report

The WHO Expert Committee on Addiction-Producing Drugs met in Geneva from 25-30 November 1963.

Dr P. Dorolle, Deputy Director-General, on behalf of the Director-General, opened the session and welcomed the members of the Committee, the representatives of the Secretary-General of the United Nations, and the representative of the Permanent Central Opium Board and the Drug Supervisory Body. Dr N. B. Eddy was elected Chairman, Dr V. V. Vasil'eva Vice-Chairman, and Dr L. Goldberg Rapporteur.

### 1. Notifications

#### 1.1 *1-Dimethylamino-3-phenylindane* [1]

Referring to the notification of the Government of Canada, the Committee considered the accompanying reports, which included data on tests for physical dependence carried out with 1-dimethylamino-3-phenylindane in the monkey and in man. In view of the negative character of the evidence submitted and in the absence of any indication of the convertibility of 1-dimethylamino-3-phenylindane into a product capable of producing addiction, the Committee was of the opinion that 1-dimethylamino-3-phenylindane should not now be regarded either as an addiction-producing drug or as one capable of conversion into an addiction-producing drug. Therefore,

The WHO Expert Committee on Addiction-Producing Drugs

RECOMMENDS that its opinion with respect to 1-dimethylamino-3-phenylindane be communicated to the Secretary-General of the United Nations.

#### 1.2 *Droxypropine* [2]

In its twelfth report,[3] the Committee considered that the information at its disposal was insufficient for it to reach a definite conclusion with respect

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[1] Also designated as *N,N*-dimethyl-3-phenyl-1-indanamine.

[2] International non-proprietary name proposed for 1-[2-(2-hydroxyethoxy)ethyl]-4-phenyl-4-propionylpiperidine.

[3] *Wld Hlth Org. techn. Rep. Ser.*, 1962, **229**, 4 (section 1.2).

to the addiction liability of droxypropine and decided to defer its opinion. Data on tests for physical dependence in the monkey have now been supplemented by clinical tests. In the light of the negative character of the evidence presented and in the absence of any indication of the convertibility of droxypropine into a product capable of producing addiction, the Committee concluded that droxypropine should not now be regarded as an addiction-producing drug or as one capable of conversion into an addiction-producing drug. Therefore,

The WHO Expert Committee on Addiction-Producing Drugs

RECOMMENDS that its opinion with respect to droxypropine be communicated to the Secretary General of the United Nations.

### 1.3 *Fentanyl* [1]

Referring to the notification of the Government of Belgium, the Committee considered that fentanyl (1) produced morphine-like effects, and (2) can be substituted for morphine in a known addiction. Evidence on these points was derived in part from experiments in monkeys. Experience has shown that results obtained in the monkey correlate with those in man, so that, when the former are unequivocal, they may be accepted as evidence of what is to be expected in man. Consequently, the Committee was of the opinion that fentanyl must be considered to be an addiction-producing drug comparable to morphine and that fentanyl and its salts should fall under the regime laid down in the 1931 Convention for the drugs specified in Article 1, paragraph 2, Group I. Therefore,

The WHO Expert Committee on Addiction-Producing Drugs

RECOMMENDS that its opinion with respect to fentanyl and its salts be communicated to the Secretary General of the United Nations.

### 1.4 *Norpipanone* [2]

Referring to the notification of the Government of Hungary, the Committee considered that norpipanone (1) produced morphine-like effects, and (2) can be substituted for morphine in a known addiction. Evidence on these points was derived in part from experiments in monkeys. Experience has shown that results obtained in the monkey correlate with those in man, so that, when the former are unequivocal, they may be accepted as evidence of what is to be expected in man. In addition, the chemical

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[1] International non-proprietary name proposed for 1-phenethyl-4-*N*-propionylanilinopiperidine.

[2] International non-proprietary name proposed for 4,4-diphenyl-6-piperidino-3-hexanone.

structure of norpipanone bears an extremely close relationship to that of other drugs known to be addiction producing.[1] Consequently the Committee was of the opinion that norpipanone must be considered to be an addiction-producing drug comparable to morphine and that norpipanone and its salts should fall under the regime laid down in the 1931 Convention for the drugs specified in Article 1, paragraph 2, Group I. Therefore,

The WHO Expert Committee on Addiction-Producing Drugs

RECOMMENDS that its opinion with respect to norpipanone and its salts be communicated to the Secretary-General of the United Nations.

### 1.5 *Dextropropoxyphene* [2]

The Committee considered again the evidence with respect to the abuse liability of dextropropoxyphene.[3] It concluded that on the basis of five years of marketing experience and repeated observations at the Addiction Research Center, Lexington, Ky., USA, in comparison with other substances, the risk of dextropropoxyphene to public health appeared to be sufficiently low as not now to require international narcotics control.

## 2. Work of International Bodies concerned with Narcotic Drugs

2.1 The reports of the seventeenth [4] and eighteenth [5] sessions of the Commission on Narcotic Drugs of the Economic and Social Council, the relevant resolutions of the Economic and Social Council,[6] and the reports of the Permanent Central Opium Board [7, 8] and Drug Supervisory Body [9] were

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[1] *Wld Hlth Org. techn. Rep. Ser.*, 1956, **102**, 10 (section 5.2.3).

[2] International non-proprietary name for (−)-4-dimethylamino-3-methyl-1,2-diphenyl-2-propionoxybutane.

[3] *Wld Hlth Org. techn. Rep. Ser.*, 1958, **142**, 7 (section 5.1.3).

[4] United Nations, Commission on Narcotic Drugs (1962) *Report of the Seventeenth Session (May-June 1962)—(Economic and Social Council. Official Records : thirty-fourth session. Supplement No. 9)*, Geneva (Document E/3648).

[5] United Nations, Commission on Narcotic Drugs (1963) *Report of the Eighteenth Session (April-May 1963)—(Economic and Social Council. Official Records : thirty-sixth session. Supplement No. 9)*, Geneva (Document E/3775).

[6] United Nations, Economic and Social Council (1963) *Official Records : thirty-sixth session, 2 July - 2 August 1963. Supplement No. 1 : Resolutions*, Geneva, p. 21 (Document E/3816).

[7] United Nations, Permanent Central Opium Board (1961) *Report to the Economic and Social Council on the Work of the Board in 1961*, Geneva (Document E/OB/17).

[8] United Nations, Permanent Central Opium Board (1962) *Report to the Economic and Social Council on the Work of the Board in 1962*, Geneva (Document E/OB/18).

[9] United Nations, Drug Supervisory Body (1961, 1962) *Estimated World Requirements for Narcotic Drugs in 1962 and 1963*, Geneva (Documents E/DSB/19 & 20).

summarized by the Secretary. Several items referred to in these reports were relevant to the Committee's present agenda.

2.2 With reference to the recent regional conference on coca leaf problems and the relevant resolution of the Economic and Social Council,[1] the Committee noted with satisfaction that there is now general agreement on the harmfulness of coca leaf chewing and that the problems connected therewith are to be regarded as a concomitant of unfavourable socio-economic circumstances, with detrimental effects on the individual as well as the society. The general acceptance of this point of view should help in directing efforts towards the betterment of the underlying environmental conditions, wherever possible as part of the general social and economic development of the areas concerned, and towards the eventual solution of the coca leaf problem.

2.3 With reference to the economic significance of coca leaves arising out of a possible increase in the legal production of cocaine for medical purposes, the Committee wished to draw attention to the fact that the medical needs for cocaine have decreased considerably in the past few decades, as a consequence of the continuing development of synthetic local anaesthetics which can replace cocaine in the majority of its therapeutic indications. Therefore, further reduction in the legal manufacture of cocaine is likely and desirable, and this should diminish opportunity for diversion to illicit uses. The Committee was disturbed by the fact that in spite of this there is an upward trend in the abuse of cocaine, particularly in combination with other drugs.

2.4 The Committee was glad to note that the Commission on Narcotic Drugs and the Permanent Central Opium Board [2] were now placing increased emphasis on the sociological and economic aspects of drug abuse. It expressed the hope that the Commission's resolution [3] requesting member states of the United Nations or of the specialized agencies to encourage research on these aspects of the problem would contribute to the elucidation of the epidemiology of drug abuse already called for both by the WHO Expert Committee on Addiction-Producing Drugs [4] and by the WHO Study Group on the Treatment and Care of Drug Addicts.[5]

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[1] United Nations, Economic and Social Council (1963) *Official Records : thirty-sixth session, 2 July - 2 August 1963. Supplement No. 1 : Resolutions*, Geneva, p. 21 (Document E/3816).

[2] United Nations, Permanent Central Opium Board (1963) *Report to the Economic and Social Council on the Work of the Board in 1963*, Geneva (Document E/OB/19).

[3] United Nations Commission on Narcotic Drugs (1962) *Report of the Seventeenth Session, Resolution 2 (XVII)* (Document E/3648, p. 22).

[4] *Wld Hlth Org. techn. Rep. Ser.*, 1960, **188**, 11.

[5] *Wld Hlth Org. techn. Rep. Ser.*, 1957, **131**, 11.

2.5 In connexion with the Commission's resolution on the control of barbiturates [1] the Committee wished to point out that there were a number of non-barbiturate sedatives, hypnotics and other drugs with sedative effect which had been shown to be abused and to produce ill-effects similar to those of the barbiturates. This was of particular significance where the sedative effect was not the one for which the drug was primarily used in medicine, but could be made use of properly under some circumstances, and might also lead to abuse. This may be illustrated by certain of the anti-histamines developed as anti-allergic agents, but exhibiting sufficient sedative action to be used, and abused, as sedatives. Another pertinent case is the recent observation of an epidemic-like outbreak of abuse of hypnotic drugs in a particular region. Methaqualone originally developed as an anti-malarial is currently advertised as a sedative and although introduced into that region only a year ago is now reported to constitute about four-fifths of the total amount of hypnotic drugs abused in the group studied.

2.6 Sudden changes in the drug of choice for abuse amongst groups within a population or in circumscribed areas such as referred to above tend to show, in the Committee's view, the relevance of sociological and environmental factors, as distinct from individual motives, in the etiology of drug abuse. Such fluctuations thus indicate the need for immediate national control measures, as repeatedly recommended by the Committee, for drugs of abuse not under international control (barbiturates [2] or other sedatives [3] and amphetamines [4]).

2.7 With regard to the proposal made in the Commission on Narcotic Drugs for an investigation into the causative role of psychoactive substances in accidents, especially road accidents, the Committee believed that such investigations could profitably be combined with similar studies on the role of alcohol.

2.8 The Committee took cognizance of the 1963 edition of the *Multilingual list of narcotic drugs under international control*.[5] The list has been greatly expanded, partly by the inclusion of names of new drugs, but more particularly by additional names for drugs already known. The list is a helpful tool for anybody working in this field. The Committee hopes that this document will be kept up to date.

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[1] United Nations Commission on Narcotic Drugs (1962) *Report of the Seventeenth Session, Resolution 4 (XVII)* (Document E/3648, p. 31).

[2] *Wld Hlth Org. techn. Rep. Ser.*, 1957, **116**, 10 (sections 9 & 10).

[3] *Wld Hlth Org. techn. Rep. Ser.*, 1958, **142**, 10 (section 6).

[4] *Wld Hlth Org. techn. Rep. Ser.*, 1961, **211**, 9 (section 2.2).

[5] United Nations (1963) *Narcotic drugs under international control. Multilingual list* (Document E/CN.7/436).

## 3. Single Convention on Narcotic Drugs, 1961

3.1 In the course of the preparations for the coming into force of the Single Convention, WHO was invited [1] to make recommendations regarding amendments to the schedules annexed to that treaty instrument. The Committee considered the following changes necessary.

### 3.2 *Schedule I*

The following items should be added :

Fentanyl (1-phenethyl-4-*N*-propionylanilinopiperidine)
Methadone-Intermediate (4-cyano-2-dimethylamino-4,4-diphenylbutane)
Moramide-Intermediate (2-methyl-3-morpholino-1,1-diphenylpropane carboxylic acid)
Noracymethadol ((±)-α-3-acetoxy-6-methylamino-4,4-diphenylheptane)
Norpipanone (4,4-diphenyl-6-piperidine-3-hexanone)
Pethidine-Intermediate-A (4-cyano-1-methyl-4-phenylpiperidine)
Pethidine-Intermediate-B (4-phenylpiperidine-4-carboxylic acid ethyl ester)
Pethidine-Intermediate-C (1-methyl-4-phenylpiperidine-4-carboxylic acid)

The following text should be added (after the entry " Trimeperidine ") :

" Any other product obtained from any of the phenanthrene alkaloids of opium or ecgonine alkaloids of the coca leaf, not listed in Schedule I or II, and neither made nor utilized exclusively for authorized domestic research, unless the government concerned finds that the product in question does not have morphine-like or cocaine-like effects. "

In the entry " Concentrate of Poppy Straw " the words " when such material is made available in trade " should be deleted.

### 3.3 *Schedule II*

Nicocodine (6-nicotinylcodeine) should be added.

Dextropropoxyphene ((+)-4-dimethylamino-3-methyl-1,2-diphenyl-2-propionoxybutane) should be deleted.

### 3.4 *Schedule III*

Of the substances listed in section (1), dextropropoxyphene should be deleted.

The rest of section (1) should read as follows :

" When compounded with one or more other ingredients and containing not more than 100 milligrams of the drug per dosage unit and with a concentration of not more than 2.5 per cent in individual preparations. "

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[1] United Nations, Commission on Narcotic Drugs (1962) *Report of the Seventeenth Session (May-June 1962)—Economic and Social Council, Official Records, thirty-fourth session, Supplement No. 9*, Geneva (Document E/3648, p. 36).

In section (2) the following words should be deleted :

" in such a way that the preparation has no, or a negligible, risk of abuse, and in such a way that the drug cannot be recovered by readily applicable means in a yield which would constitute a risk to public health. "

In section (3) the words " Solid dose " should be deleted.

## 4. Terminology in Regard to Drug Abuse

### " Drug dependence " to replace the terms " drug addiction " and " drug habituation "

The WHO Expert Committee on Addiction-Producing Drugs in 1952 [1] attempted to formulate a definition of addiction applicable to drugs under international control, which it later (1957) [2] revised. The Expert Committee sought also to differentiate addiction from habituation and wrote a definition of the latter which, however, failed in practice to make a clear distinction. The definition of addiction gained some acceptance, but confusion in the use of the terms addiction and habituation and misuse of the former continued. Further, the list of drugs abused increased in number and diversity. These difficulties have become increasingly apparent and various attempts have been made to find a term that could be applied to drug abuse generally. The component in common appears to be dependence, whether psychic or physical or both. Hence, use of the term " drug dependence ", with a modifying phrase linking it to a particular drug type in order to differentiate one class of drugs from another, has been given most careful consideration.

" Drug dependence " is defined as a state arising from repeated administration of a drug on a periodic or continuous basis. Its characteristics will vary with the agent involved and this must be made clear by designating the particular type of drug dependence in each specific case—for example, drug dependence of morphine type, of cocaine type, of cannabis type, of barbiturate type, of amphetamine type, etc. (See Annex 1 for descriptions of specific types of drug dependence.)

The Expert Committee recommends substitution of the term " drug dependence " for the terms " drug addiction " and " drug habituation ".

It must be emphasized that drug dependence is a general term selected for its applicability to all types of drug abuse and carries no connotation of the degree of risk to public health or need for a particular type of drug control. The agents controlled internationally continue to be those that are morphine-like, cocaine-like, and cannabis-like, however produced, the use of which results in drug dependence of morphine type, drug dependence

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[1] *Wld Hlth Org. techn. Rep. Ser.*, 1952, **57**, 9 (section 6.1).

[2] *Wld Hlth Org. techn. Rep. Ser.*, 1957, **116**, 9 (section 8).

of cocaine type, and drug dependence of cannabis type. Other types of drug dependence (barbiturate, amphetamine, etc.) continue to present problems, but their description under the general term " drug dependence " does not in any way affect the measures taken to solve them. The general term will help to indicate a relationship by drawing attention to a common feature associated with drug abuse and at the same time permit more exact description and differentiation of specific characteristics according to the nature of the agent involved.

### 5. Considerations Governing the Medical Use of Narcotics

The Committee has on many occasions stressed the medical aspects of the treatment of addicts and the precautionary attitude that should be adopted by physicians in this connexion and in the use of narcotics generally in their practice. Its attention was drawn to a recent report setting forth in considerable detail the whole philosophy of the use of narcotics in medical practice.[1] It was felt that this report constituted a useful guide towards the attainment of the objectives that the Committee has stressed.

### 6. Khat (*Catha edulis*)

The Committee studied a report by the Secretariat on the medical aspects of the habitual chewing of khat leaves. In this report the somatic and psychic symptoms brought about by the chewing of the leaves were reviewed and explained as the effects of the specific active principles contained in the leaves. Besides tannins in appreciable amounts, it has been possible to identify (+)-norpseudoephedrine (cathine) and a chemically and pharmacologically closely related substance, which disappears when the plant is dried and is presumably a step in the biosynthesis of cathine. These two substances are amphetamine-like in respect of structure and pharmacodynamics, but there is evidence that their effects are less powerful than those produced by equivalent amounts of, for example, methamphetamine.

The Committee considered that while khat and pure amphetamine substances produced medical effects that were similar although of different degree, the lower activity of khat was due in the main to differences in dosage, route of administration, and the circumstances in which the one or the other were consumed. In addition, khat produced gastro-intestinal symptoms, due partly to its high content of tannins.

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[1] Council on Mental Health (1963) *Narcotics and medical practice*. *J. Amer. med. Ass.*, **185**, 976.

The Committee realized that the habitual chewing of khat had led, in some areas, to socio-economic phenomena detrimental to the individual and the community, such as loss of man hours and diversion of income, with malnutrition and aggravation of disease as consequences.

The Committee was of the opinion that the problems connected with khat and with the amphetamines [1] should be considered in the same light because of the similarity of their medical effects, even though there are quantitative differences and specific socio-economic features; this is all the more desirable since the problems with respect to khat are confined at present to a few countries in one region.

## 7. Abuse of Hallucinogenic Agents

The Committee took note of the increasingly frequent reports of poorly controlled clinical administration and non-medical use of lysergic acid diethylamide (LSD-25). In spite of warnings, irregular use is reaching alarming proportions. The Committee was particularly disturbed by the publicity given to the uncontrolled use of this drug and the damage that the indiscriminate use of so powerful an agent has already produced. The problem is at present a local one. In the Committee's opinion, immediate measures with respect to distribution and availability are necessary.

Other instances of indiscriminate use of agents with related effects, such as peyotl (mescaline), *Piptadenia peregrina* (bufotenine), and *Rivea corymbosa* were noted. The misuse in these instances appears to be less widespread than in the case of LSD-25, but a watch should be kept and corrective measures taken where necessary.

## 8. Coded Information on Narcotics

As indicated in previous reports,[2-5] the Committee maintains an interest in the availability of a centralized source of information on drug dependence in all its aspects, including the agents involved, with easy means of fast retrieval.

Coded data (about 8000 items) on a large part of the material accumulated, have now been transferred to an IBM card system, and the complete bibliographic material microfilmed. Co-operation with the American

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[1] *Wld Hlth Org. techn. Rep. Ser.*, 1956, **102**, 12 (section 7); 1957, **116**, 9 (section 7).

[2] *Wld Hlth Org. techn. Rep. Ser.*, 1957, **116**, 11 (section 11).

[3] *Wld Hlth Org. techn. Rep. Ser.*, 1958, **142**, 11 (section 9).

[4] *Wld Hlth Org. techn. Rep. Ser.*, 1959, **160**, 10 (section 7), 14 (Annex 2).

[5] *Wld Hlth Org. techn. Rep. Ser.*, 1962, **229**, 12 (section 8).

Social Health Association, the Alcoholism and Drug Addiction Research Foundation, Toronto, and the United Nations Division of Narcotic Drugs, has been worked out. This will greatly expedite further work and increase the completeness of coverage of published material in this field. Sets of IBM cards and the microfilm will shortly be available at cost.

### 9. International Classification of Diseases

The Committee was informed of the preparation of the eighth revision of the classification, and would draw attention to the diversity of the items listed under " 316. Drug Addiction ", not all of which are considered addiction-producing in a legal or pharmacological sense. Referring to the recommendation in the present report that the term " drug dependence " be substituted for " drug addiction ", the Committee would invite attention to the application of this recommendation in the international classification of diseases, thereby bringing into better harmony the list of diverse items referred to above.

## Annex 1

## TYPES OF DRUG DEPENDENCE

**Drug dependence of morphine type** is described as a state arising from repeated administration of morphine, or an agent with morphine-like effects, on a periodic or continuous basis. Its characteristics include :

(1) an overpowering desire or need to continue taking the drug and to obtain it by any means ; the need can be satisfied by the drug taken initially or by another with morphine-like properties ;

(2) a tendency to increase the dose owing to the development of tolerance ;

(3) a psychic dependence on the effects of the drug related to a subjective and individual appreciation of those effects ; and

(4) a physical dependence on the effects of the drug requiring its presence for maintenance of homeostasis and resulting in a definite, characteristic, and self-limited abstinence syndrome when the drug is withdrawn.

The abstinence syndrome is the most characteristic and distinguishing feature of drug dependence of morphine type. It appears within a few hours of the last dose of drug taken, reaches peak intensity in 12 hours or more, and subsides spontaneously, most often within a week, the time course varying with the duration of action of the specific morphine-like agent involved. The abstinence syndrome may also be precipitated in a matter of minutes and made to take a more rapid time course by the administration of a specific antagonist while continuing the administration of the agent responsible for the dependence. The complex of symptoms which constitute the abstinence syndrome includes : yawning, lacrimation, rhinorrhoea, perspiration, mydriasis, tremor, gooseflesh, anorexia, anxiety, restlessness, nausea, emesis, diarrhoea, hot flushes, rise in body temperature, increase in respiratory rate and in systolic blood pressure, abdominal or other muscle cramps, and dehydration and loss of body-weight.

**Drug dependence of barbiturate type** is described as a state arising from repeated administration of a barbiturate, or an agent with barbiturate-like effect, on a continuous basis, generally in amounts exceeding therapeutic dose levels. Its characteristics include :

(1) a strong desire or need to continue taking the drug ; the need can be satisfied by the drug taken initially or by another with barbiturate-like properties ;

(2) a tendency to increase the dose, partly owing to the development of tolerance ;

(3) a psychic dependence on the effects of the drug related to subjective and individual appreciation of those effects ; and

(4) a physical dependence on the effects of the drug requiring its presence for maintenance of homeostasis and resulting in a definite, characteristic, and self-limited abstinence syndrome when the drug is withdrawn.

The abstinence syndrome is the most characteristic and distinguishing feature of drug dependence of barbiturate type. It begins to appear within the first 24 hours of cessation of drug taking, reaches peak intensity in two or three days, and subsides slowly. There is at present no known agent that will precipitate the barbiturate abstinence syndrome during continuation of drug administration. The complex of symptoms which constitute the abstinence syndrome, in approximate order of appearance, are : anxiety, involuntary twitching of muscles, intention tremor of hands and fingers, progressive weakness, dizziness, distortion in visual perception, nausea, vomiting, insomnia, weight loss, and a precipitous drop in blood pressure on standing ; convulsions of a grand mal type and/or a delirium resembling alcoholic delirium tremens may occur.

**Drug dependence of cocaine type** is described as a state arising from repeated administration of cocaine or an agent with cocaine-like properties, on a periodic or continuous basis. Its characteristics include :

(1) an overpowering desire or need to continue taking the drug and to obtain it by any means ;

(2) absence of tolerance to the effects of the drug during continued administration ; in the more frequent episodic use, the drug may be taken at short intervals, resulting in the build-up of an intense toxic reaction ;

(3) a psychic dependence on the effects of the drug related to a subjective and individual appreciation of those effects ; and

(4) absence of a physical dependence and hence absence of an abstinence syndrome on abrupt withdrawal ; withdrawal is attended by a psychic disturbance manifested by craving for the drug.

**Drug dependence of amphetamine type** is a state arising from repeated administration of amphetamine or an agent with amphetamine-like effects on a periodic or continuous basis. Its characteristics include :

(1) a desire or need to continue taking the drug ;

(2) consumption of increasing amounts to obtain greater excitatory and euphoric effects or to combat more effectively depression and fatigue, accompanied in some measure by the development of tolerance ;

(3) a psychic dependence on the effects of the drug related to a subjective and individual appreciation of the drug's effects ; and

(4) general absence of physical dependence so that there is no characteristic abstinence syndrome when the drug is discontinued.

**Drug dependence of cannabis type** is described as a state arising from repeated administration of cannabis or cannabis substances, which in some areas is almost exclusively periodic, in others more continuous. Its characteristics include :

(1) a desire (or need) for repeated administration of the drug on account of its subjective effects, including the feeling of enhanced capabilities ;

(2) little or no tendency to increase the dose, since there is little or no development of tolerance ;

(3) a psychic dependence on the effects of the drug related to subjective and individual appreciation of those effects ;

(4) absence of physical dependence so that there is no definite and characteristic abstinence syndrome when the drug is discontinued.

These are concise descriptions which could be expanded, particularly with reference to differences in degree according to dose and duration of administration and to potency among agents within a particular type. The differences between morphine and codeine are a good example of the latter. Descriptions of drug dependence of other types could be written, e.g., for certain sedatives not chemically classified as barbiturates, or for alcohol, to name only two. The characteristics of dependence of the non-barbiturate sedative type are essentially identical with the characteristics of dependence of the barbiturate type and a separate description seems at present unnecessary. Alcohol is outside the terms of reference of this expert committee, but is nevertheless an agent that can admittedly cause psychic and physical dependence.

All the descriptions of types of drug dependence have been confined to medical aspects only, but socio-economic characteristics and implications should not be overlooked. They vary according to the drug type and there are variations in the individual and social harm that accompany drug dependence of different types :

With morphine, the harm to the individual is in the main indirect, arising from preoccupation with drug taking ; personal neglect, malnutrition and infection are frequent consequences. For society also, the harm may be related to the preoccupation of the individual with drug taking ; disruption of interpersonal relationships, economic loss, and crimes against property are frequent consequences.

With the barbiturates, the detrimental effect on the individual stems in part from his preoccupation with drug taking, but more particularly from

persistent effects of the drug—ataxia, dysarthria, and impairment of mental function, with confusion, loss of emotional control, poor judgment, and occasionally a toxic psychosis. The harm to society is related to both the individual's preoccupation with drug taking and the drug's effect on interpersonal relationships.

With cocaine, the individual detrimental effect may be indirect, resulting from the individual's preoccupation with drug taking, again with malnutrition and infection as frequent consequences, or direct, a severe toxic reaction accompanying rapid and repeated administration in episodic drug use. The harm to society is related to preoccupation with drug taking by the individual, with economic loss and crimes against society as consequences. When drug dependence of cocaine type is brought about through chewing of coca leaves, anorexia, a change in working habits, and loss in weight are additional characteristics.

The amphetamines tend to cause anorexia, persistent and exaggerated psychomotor disturbances, and disruption of mental function, even to the occurrence of a toxic psychosis. For society, the harm is related in part to the drug's psychomotor effects (involvement in accidents, for example).

With cannabis, lasting disturbance of mental function has been alleged but not proven. Distortion of perception, one of the effects of the drug, may lead to disruption of interpersonal relationships, and abuse of the drug to criminal behaviour.

The risk to public health should be and usually is of paramount importance as a criterion for the establishment of control for a dependence-producing drug of any of the types described and in deciding on the degree of control. At the same time, socio-economic factors and social harm associated with drug dependence and drug abuse must be taken into account and may determine the appropriateness of control in a particular case. The socio-economic factors largely determine society's attitude towards the individuals involved in drug abuse, but they are not characteristics that need to be considered in medical and scientific differentiation of the types of drug dependence.

## Annex 2

# LIST OF DRUGS UNDER INTERNATIONAL NARCOTICS CONTROL [1]

| *Common name or INN* * | *Chemical designation* | *Expert Committee on Addiction-Producing Drugs* | | *Control regime* | |
|---|---|---|---|---|---|
| | | *Report number* | *Reference* [2] | *Group* | *Convention* |
| acetyldihydrocodeine | acetyldihydrocodeine | 1 | 1949, **19**, 30 | II | 1931 |
| acetylmethadol * | 3-acetoxy-6-dimethylamino-4,4-diphenylheptane | 1 | 1949, **19**, 31 | I | 1931 |
| allylprodine * | 3-allyl-1-methyl-4-phenyl-4-propionoxypiperidine | 10 | 1960, **188**, 3 | I | 1931 |
| alphacetylmethadol * | α-3-acetoxy-6-dimethylamino-4,4-diphenylheptane | 4 | 1954, **76**, 7 | I | 1931 |
| alphameprodine * | α-3-ethyl-1-methyl-4-phenyl-4-propionoxypiperidine | 7 | 1957, **116**, 8 | I | 1931 |
| alphamethadol * | α-6-dimethylamino-4,4-diphenyl-3-heptanol | 4 | 1954, **76**, 7 | I | 1931 |
| alphaprodine * | α-1,3-dimethyl-4-phenyl-4-propionoxypiperidine | 1 | 1949, **19**, 30 | I | 1931 |
| anileridine * | 1-(*p*-aminophenethyl)-4-phenylpiperidine-4-carboxylic acid ethyl ester | 7 | 1957, **116**, 7 | I | 1931 |
| benzethidine * | 1-(2-benzyloxyethyl)-4-phenylpiperidine-4-carboxylic acid ethyl ester | 10 | 1960, **188**, 4 | I | 1931 |
| benzylmorphine | 3-benzylmorphine | | | I | 1931 |
| betacetylmethadol * | β-3-acetoxy-6-dimethylamino-4,4-diphenylheptane | 4 | 1954, **76**, 7 | I | 1931 |
| betameprodine * | β-3-ethyl-1-methyl-4-phenyl-4-propionoxypiperidine | 3 | 1952, **57**, 7 | I | 1931 |
| betamethadol * | β-6-dimethylamino-4,4-diphenyl-3-heptanol | 5 | 1955, **95**, 8 | I | 1931 |
| betaprodine * | β-1,3-dimethyl-4-phenyl-4-propionoxypiperidine | 1 | 1949, **19**, 30 | I | 1931 |
| cannabis | *Cannabis sativa* L. | | | | 1925 |
| clonitazene * | 2-*p*-chlorbenzyl-1-diethylaminoethyl-5-nitrobenzimidazole | 11 | 1961, **211**, 4 | I | 1931 |
| cocaine | methyl ester of benzoylecgonine | | | I | 1931 |
| coca leaf | | | | | 1925 |
| codeine | 3-methylmorphine | | | II | 1931 |
| codeine-N-oxide | | | | I | 1931 |
| desomorphine * | dihydrodeoxymorphine | | | I | 1931 |
| dextromoramide * | (+)-4-[2-methyl-4-oxo-3,3-diphenyl-4-(1-pyrrolidinyl)butyl]morpholine | 8 | 1958, **142**, 8 | I | 1931 |

* Proposed international non-proprietary name (INN).

[1] For details such as synonyms and the date of coming into force of international control, see *Multilingual list of narcotic drugs under international control* (UN document E/CN 7/341) and *List of drugs under international control* (published annually by the UN, Division of Narcotic Drugs) respectively.

[2] The references given in this column are to *World Health Organization : Technical Report Series*, with the exception of the report published in 1949 which appeared in *Official Records of the World Health Organization*, No. 19.

| *Common name or INN* * | *Chemical designation* | *Expert Committee on Addiction-Producing Drugs* | | *Control regime* | |
|---|---|---|---|---|---|
| | | *Report number* | *Reference* [1] | *Group* | *Convention* |
| diampromide * | *N*-[2-(methylphenethylamino)-propyl]-propionanilide | 11 | 1961, **211**, 5 | I | 1931 |
| diethylthiambutene * | 3-diethylamino-1,1-di-(2′-thienyl)-1-butene | 6 | 1956, **102**, 10 | I | 1931 |
| dihydrocodeine | 7,8-dihydrocodeine | 1 | 1949, **19**, 30 | II | 1931 |
| dihydromorphine | 7,8-dihydromorphine | | | I | 1931 |
| dihydromorphine esters | | | | I | 1931 |
| dimenoxadol * | 2-dimethylaminoethyl 1-ethoxy-1,1-diphenylacetate | 9 | 1959, **160**, 9 | I | 1931 |
| dimepheptanol * | 6-dimethylamino-4,4-diphenyl-3-heptanol | 1 | 1949, **19**, 31 | I | 1931 |
| dimethylthiambutene * | 3-dimethylamino-1,1-di-(2′-thienyl)-1-butene | 4 | 1954, **76**, 9 | I | 1931 |
| dioxaphetyl butyrate * | ethyl 4-morpholino-2,2-diphenylbutyrate | 6 | 1956, **102**, 9 | I | 1931 |
| diphenoxylate * | 1-(3-cyano-3,3-diphenyl-propyl)-4-phenylpiperidine-4-carboxylic acid ethyl ester | 11 | 1961, **211**, 5 | I | 1931 |
| dipipanone * | 4,4-diphenyl-6-piperidino-3-heptanone | 5 | 1955, **95**, 8 | I | 1931 |
| ecgonine | (—)-3-hydroxytropane-2-carboxylate | | | I | 1931 |
| ecgonine esters | | | | I | 1931 |
| ethylmethyl-thiambutene * | 3-ethylmethylamino-1,1-di-(2′-thienyl)-1-butene | 4 | 1954, **76**, 9 | I | 1931 |
| ethylmorphine | 3-ethylmorphine | | | II | 1931 |
| etonitazene * | 1-diethylaminoethyl-2-*p*-ethoxybenzyl-5-nitro-benzimidazole | 11 | 1961, **211**, 7 | I | 1931 |
| etoxeridine * | 1-[2-(2-hydroxyethoxy)ethyl]-4-phenylpiperidine-4-carboxylic acid ethyl ester | 8 | 1958, **142**, 9 | I | 1931 |
| fentanyl * | 1-phenethyl-4-*N*-propionylanilinopiperidine | 13 | 1964, **273**, 4 | I | 1931 |
| furethidine * | 1-(2-tetrahydrofurfuryl-oxyethyl)-4-phenylpiperidine-4-carboxylic acid ethyl ester | 10 | 1960, **188**, 5 | I | 1931 |
| heroin | diacetylmorphine | | | I | 1931 |
| hydrocodone * | dihydrocodeinone | | | I | 1931 |
| hydrocodone esters | | | | I | 1931 |
| hydromorphinol * | 14-hydroxydihydromorphine | 11 | 1961, **211**, 7 | I | 1931 |
| hydromorphone * | dihydromorphinone | | | | 1925 |
| hydromorphone esters | | | | | 1925 |
| hydroxypethidine * | 4-(*m*-hydroxyphenyl)-1-methylpiperidine-4-carboxylic acid ethyl ester | 1 | 1949, **19**, 30 | I | 1931 |
| isomethadone * | 6-dimethylamino-5-methyl-4,4-diphenyl-3-hexanone | 1 | 1949, **19**, 31 | I | 1931 |
| ketobemidone * | 4-(*m*-hydroxyphenyl)-1-methyl-4-propionylpiperidine | 1 | 1949, **19**, 30 | I | 1931 |
| levomethorphan * | (—)-3-methoxy-*N*-methyl-morphinan | 3 | 1952, **57**, 6 | I | 1931 |

[1] The references given in this column are to *World Health Organization : Technical Report Series*, with the exception of the report published in 1949 which appeared in *Official Records of the World Health Organization*, No. 19.

| *Common name or INN* * | *Chemical designation* | *Expert Committee on Addiction-Producing Drugs* | | *Control regime* | |
|---|---|---|---|---|---|
| | | *Report number* | *Reference* [1] | *Group* | *Convention* |
| levomoramide * | (—)-4-[2-methyl-4-oxo-3,3-diphenyl-4-(1-pyrrolidinyl)-butyl]morpholine | 8 | 1958, **142**, 8 | I | 1931 |
| levophenacylmorphan * | (—)-3-hydroxy-*N*-phenacylmorphinan | 10 | 1960, **188**, 5 | I | 1931 |
| levorphanol * | (—)-3-hydroxy-*N*-methylmorphinan | 3 | 1952, **57**, 6 | I | 1931 |
| metazocine * | 2′-hydroxy-2,5,9-trimethyl-6,7-benzomorphan | 10 | 1960, **188**, 6 | I | 1931 |
| methadone * | 6-dimethylamino-4,4-diphenyl-3-heptanone | 1 | 1949, **19**, 30 | I | 1931 |
| methadone-intermediate | 4-cyano-2-dimethylamino-4,4-diphenylbutane | 12 | 1962, **229**, 7 | I<br>I | 1931<br>1931 |
| methyldesorphine * | 6-methyl-$\Delta^6$-deoxymorphine | 4 | 1954, **76**, 6 | I | 1931 |
| methyldihydromorphine * | 6-methyldihydromorphine | 5 | 1955, **95**, 5 | I | 1931 |
| metopon * | 5-methyldihydromorphinone | 1 | 1949, **19**, 30 | I | 1931 |
| moramide-intermediate | 2-methyl-3-morpholino-1,1-diphenylpropane carboxylic acid | 12 | 1962, **229**, 7 | I | 1931 |
| morpheridine * | 1-(2-morpholinoethyl)-4-phenylpiperidine-4-carboxylic acid ethyl ester | 8 | 1958, **142**, 8 | I | 1931 |
| morphine | | | | I | 1931 |
| morphine esters | | | | I | 1931 |
| morphine ethers | | | | I | 1931 |
| morphine-N-oxide | | | | I | 1931 |
| morphine-N-oxide derivatives | | | | I | 1931 |
| morphine pentavalent nitrogen derivatives | | | | I | 1931 |
| myrophine * | myristylbenzylmorphine | 5 | 1955, **95**, 6 | II | 1931 |
| nicocodine * | 6-nicotinylcodeine | 12 | 1962, **229**, 6 | II | 1931 |
| nicomorphine * | 3,6-dinicotinylmorphine | 9 | 1959, **160**, 4 | I | 1931 |
| noracymethadol * | (±)-α-3-acetoxy-6-methylamino-4,4-diphenylheptane | 12 | 1962, **229**, 5 | I | 1931 |
| norcodeine * | *N*-demethylcodeine | 9 | 1959, **160**, 5 | II [2] | 1931 |
| norlevorphanol * | (—)-3-hydroxymorphinan | 10 | 1960, **188**, 6 | I | 1931 |
| normethadone * | 6-dimethylamino-4,4-diphenyl-3-hexanone | 5 | 1955, **95**, 7 | I | 1931 |
| normorphine * | demethylmorphine | 9 | 1959, **160**, 5 | I | 1931 |
| norpipanone * | 4,4-diphenyl-6-piperidino-3-hexanone | 13 | 1964, **273**, 4 | I | 1931 |
| opium | | | | | 1925 |
| oxycodone * | 14-hydroxydihydrocodeinone | | | I | 1931 |
| oxycodone esters | | | | I | 1931 |
| oxymorphone * | 14-hydroxydihydromorphinone | 5 | 1955, **95**, 6 | I | 1931 |
| pethidine * | 1-methyl-4-phenylpiperidine-4-carboxylic acid ethyl ester | 1 | 1949, **19**, 30 | I | 1931 |

[1] The references given in this column are to *World Health Organization : Technical Report Series*, with the exception of the report published in 1949 which appeared in *Official Records of the World Health Organization*, No. 19.

[2] Recommended by WHO for this control regime.

| *Common name or INN* * | *Chemical designation* | *Expert Committee on Addiction-Producing Drugs* | | *Control regime* | |
|---|---|---|---|---|---|
| | | *Report number* | *Reference* [1] | *Group* | *Convention* |
| pethidine-intermediate-A | 4-cyano-1-methyl-4-phenylpiperidine | 12 | 1962, **229**, 7 | I | 1931 |
| pethidine-intermediate-B | 4-phenylpiperidine-4-carboxylic acid ethyl ester | 12 | 1962, **229**, 7 | I | 1931 |
| pethidine-intermediate-C | 1-methyl-4-phenylpiperidine-4-carboxylic acid | | | I | 1931 |
| pethidine-intermediate-C, esters of | | 5 | 1955, **95**, 9 | I | 1931 |
| phenadoxone * | 6-morpholino-4,4-diphenyl-3-heptanone | 1 | 1949, **19**, 31 | I | 1931 |
| phenampromide * | *N*-(1-methyl-2-piperidino-ethyl)propionanilide | 11 | 1961, **211**, 7 | I | 1931 |
| phenazocine * | 2'-hydroxy-5,9-dimethyl-2-phenethyl-6,7-benzomorphan | 10 | 1960, **188**, 6 | I | 1931 |
| phenomorphan * | 3-hydroxy-*N*-phenethylmorphinan | 6 | 1956, **102**, 8 | I | 1931 |
| phenoperidine * | 1-(3-hydroxy-3-phenylpropyl)-4-phenylpiperidine-4-carboxylic acid ethyl ester | 11 | 1961, **211**, 8 | I | 1931 |
| pholcodine * | morpholinylethylmorphine | 3 | 1952, **57**, 5 | II | 1931 |
| piminodine * | 4-phenyl-1-(3-phenylamino-propyl)piperidine-4-carboxylic acid ethyl ester | 10 | 1960, **188**, 7 | I | 1931 |
| proheptazine * | 1,3-dimethyl-4-phenyl-4-propionoxyazacycloheptane | 6 | 1956, **102**, 11 | I | 1931 |
| properidine * | 1-methyl-4-phenylpiperidine-4-carboxylic acid isopropyl ester | 5 | 1955, **95**, 9 | I | 1931 |
| racemethorphan * | (±)-3-methoxy-*N*-methylmorphinan | 3 | 1952, **57**, 7 | I | 1931 |
| racemoramide * | (±)-4-[2-methyl-4-oxo-3,3-diphenyl-4-(1-pyrrolidinyl)-butyl]morpholine | 8 | 1958, **142**, 8 | I | 1931 |
| racemorphan * | (±)-3-hydroxy-*N*-methylmorphinan | 3 | 1952, **57**, 6 | I | 1931 |
| thebacon * | acetyldihydrocodeinone | | | I | 1931 |
| thebaine | 3,6-dimethyl-8-dehydromorphine | | | I | 1931 |
| trimeperidine * | 1,2,5-trimethyl-4-phenyl-4-propionoxypiperidine | 8 | 1958, **142**, 9 | I | 1931 |

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