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WHO Expert Committee on Drug Dependence

Twenty-fourth Report

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WHO EXPERT COMMITTEE ON DRUG DEPENDENCE

Geneva, 9-16 April 1987

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WHO EXPERT COMMITTEE ON DRUG DEPENDENCE

Twenty-fourth Report

INTRODUCTION

The WHO Expert Committee on Drug Dependence met in Geneva from 9 to 16 April 1987. The meeting was opened on behalf of the Director-General by Dr Lu Rushan, Assistant Director-General, who drew attention to the important work of the Expert Committee in making recommendations for the international control of narcotic drugs and psychotropic substances. Under the terms of the Single Convention on Narcotic Drugs adopted in 1961 and the Convention on Psychotropic Substances adopted in 1971, WHO must make recommendations to the Secretary-General of the United Nations. This Expert Committee was convened, to assist the Director-General of WHO in accordance with the *Guidelines for the WHO Review of Dependence-producing Psychoactive Substances for International Control*.¹ The request for the review of 6 non-barbiturate sedative hypnotics by the Expert Committee resulted from the meeting of the fourth Programme Planning Working Group (PPWG), based on the original request from the United Nations Commission on Narcotic Drugs. In addition, a notification concerning the rescheduling of secobarbital from the Government of the United States of America was forwarded by the Secretary-General of the United Nations.

Dr Lu Rushan outlined the tasks of the Expert Committee as follows:

(a) To make recommendations regarding the need for, and level of control of, the seven substances under review, i.e., acecarbromal, carbromal, clomethiazole, chloralodol, methylpentynol, triclofos, and secobarbital.

¹ *Executive Board, seventy-seventh session, Geneva, 8-17 January 1986: resolutions and decisions; annexes*. Geneva, 1986 (Annex 9) (unpublished WHO document EB77/1986/REC/1).

(b) To make recommendations on:

1. The rescheduling of methaqualone.
2. The possible scheduling of analogues of various controlled substances.
3. The status of the racemate of metamfetamine under the Convention on Psychotropic Drugs, 1971.
4. Action on the Finnish notification on exempted preparations.
5. The future role of WHO in the handling of exempted preparations.

(c) To advise WHO on how it could best fulfil its obligations under the international drug control treaties.

The Committee was also briefly informed about general WHO activities related to drug use and abuse, as outlined below.

In an effort to promote the rational use of dependence-producing psychoactive substances, both within and outside the practice of psychiatry, WHO recognizes the importance of continuing education for medical professionals. Research will be promoted to establish the most effective educational strategies in rational prescribing of these drugs for use with health care providers. The extent of use of psychoactive substances in the treatment of somatic illness is not fully known, and the Expert Committee advised WHO to examine the use of these drugs in a variety of medical specialities and to develop guidelines for their rational prescription.

Other WHO projects being developed cover the management of pain, and the clinical evaluation of the likelihood of abuse of psychoactive substances. The Expert Committee was also informed that a recent decision had brought together WHO's activities on alcohol and drug abuse into one programme.

1. THE FORMAT OF THIS REPORT

In response to suggestions from the United Nations Commission on Narcotic Drugs and the WHO Executive Board, the PPWG at its third meeting proposed a format for the Expert Committee on Drug Dependence to use in reporting its review of each substance. The Expert Committee used this format in its twenty-third report where it was recommended that '*Similarity to already scheduled compounds*' and '*Effects on the central nervous system and mental functions*' be combined. This recommendation was discussed and approved at the

fourth meeting of the PPWG¹ and the new format has been used in this report.

The WHO procedures for review of dependence-producing psychoactive substances were followed in preparation for this Expert Committee.²

2. ASSESSMENT OF SUBSTANCES

2.1 Acecarbromal

2.1.1 *Substance identification*

Acecarbromal (INN, CAS 77-66-7) chemically, *N*-[(acetylamino) carbonyl]-2-bromo-2-ethylbutanamide, is also known as acetcarbromalum (NFN), acetylcarbromal and sedacetyl. No isomeric forms are possible.

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

Acecarbromal has been classified as a non-barbiturate sedative-hypnotic with a profile similar to that of glutethimide. In single doses the substance produces barbiturate-like sedative-hypnotic effects. Dose-related drowsiness, vertigo, confusion, and motor incoordination can occur. After prolonged use, the pharmacological profile becomes more like that of bromide ion. Chronic bromism leads to signs and symptoms such as loss of memory, confusion, inability to concentrate, hallucinations (both transitory and prolonged), delusions, and delirium, which often occur in other severe psychiatric disturbances. Indeed, until bromism was recognized as a toxicological syndrome, it accounted for a large number of admissions to psychiatric hospitals. Acecarbromal, like the barbiturates, is metabolized by hepatic microsomal enzymes and probably stimulates the production of these enzymes. It should be pointed out that this may increase the range of toxicological effects, owing to the production of increasing amounts of bromide ion.

¹ *Report of the 4th meeting of the Programme Planning Working Group, 2-7 March 1987, Geneva* (unpublished WHO document MNH/PAD/87.2).

² *Critical review of information on six uncontrolled non-barbiturate sedative hypnotic drugs, secobarbital and controlled substance analogues for the 24th Expert Committee on drug dependence, Geneva, 9-16 April 1987* (unpublished WHO document MNH/PAD/86.11. Rev. 1).

2.1.3 *Dependence potential*

There is no information on the ability of acecarbromal to produce physical or psychic dependence in either animals or human subjects in controlled laboratory studies. In recent animal studies carbromal (see Section 2.2.3), a similar substance, produced little barbiturate-like physical dependence at doses limited by solubility. Self-administration was marginal.

2.1.4 *Actual abuse and/or abuse liability (likelihood of abuse)*

Significant abuse of the bromocarbamides was reported in the Federal Republic of Germany in the 1970s. Acecarbromal represented only a small portion of this abuse and at present poses no serious problem to public health and social welfare. Fifty-eight countries submitted reports on acecarbromal, but no others reported a problem with the drug. The drug is subject to national control in three countries. No cases of illicit manufacture or traffic were reported.

2.1.5 *Therapeutic usefulness*

Acecarbromal has been used as a sedative and a hypnotic, and in a variety of combination preparations. It appears to be marketed only in the Federal Republic of Germany. The therapeutic use of this substance has been largely replaced by other more effective drugs. The Committee rated the therapeutic usefulness of acecarbromal as low.

2.1.6 *Recommendation*

On the basis of the available data concerning its pharmacological profile, dependence potential, and actual abuse, the Committee rated the likelihood of abuse of acecarbromal as moderate. The degree of seriousness of the public health and social problems associated with the substance was found to be low, as was its therapeutic usefulness.

The Committee found that there was insufficient evidence that acecarbromal is being, or is likely to be, abused so as to constitute a public health and social problem warranting the placing of the substance under international control.

In the light of this assessment, the Committee did not recommend scheduling of the substance.

2.2 Carbromal

2.2.1 *Substance identification*

Carbromal (INN, CAS 77-65-6), chemically, *N*-(aminocarbonyl)-2-bromo-2-ethylbutanamide, is also known as bromadalum (*Ph. Helv. V.*), bromdiaethylacetylcarbamidum (*OeAB IX*), bromodiethylacetylurea (*Ph. Jap. 1961*), carbromalum (*Ph. Helv. VI*). No isomeric forms are possible.

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

Accecarbromal has been classified as a non-barbiturate sedative-hypnotic with a profile similar to that of glutethimide. In single doses the substance produces barbiturate-like sedative-hypnotic effects. Dose-related drowsiness, vertigo, confusion, and motor incoordination can occur. After prolonged use, the pharmacological profile becomes more like that of bromide ion. Chronic bromism leads to signs and symptoms such as loss of memory, confusion, inability to concentrate, hallucinations (both transitory and prolonged), delusions, and delirium, which are often presented as other severe psychiatric disturbances. Indeed, until bromism was recognized as a toxicological syndrome, it accounted for a large number of admissions to psychiatric hospitals. Carbromal, like the barbiturates, is metabolized by hepatic microsomal enzymes and probably stimulates the production of these enzymes. It should be pointed out that this may increase the range of toxicological effects, owing to the production of increasing amounts of bromide ion.

2.2.3 *Dependence potential*

In drug discrimination studies carbromal was identified as pentobarbital-like by the pigeon, but only partially by the rhesus monkey. The substance showed little evidence of barbiturate-like physical dependence in the rat intraperitoneal infusion model. It should be noted, however, that doses were low relative to pharmacodynamic doses because of difficulties in dissolving the substance. In self-administration studies in the pentobarbital-trained rhesus monkey, carbromal was marginal in two animals and positive in one at only one dose level. It was self-administered in only one of

three monkeys when substituted for cocaine. The results indicate that carbromal is only marginally self-administered. There are no reported controlled human dependence studies.

2.2.4 Actual abuse and/or abuse liability (likelihood of abuse)

There was a significant level of abuse of carbromal in the Federal Republic of Germany in the mid-1970s. Since 1978, abuse has been seen only sporadically and at a rather low level. Belgium reported some abuse of carbromal in 1981 and seven cases were reported in Finland from 1983 to 1985. Data on national control was available for 59 countries. The drug is under national control, at least at the prescription level, in seven countries. A small number of seizures or diversions were reported by Finland, USA and the Federal Republic of Germany. No illicit manufacture or traffic was reported.

2.2.5 Therapeutic usefulness

Carbromal has been used as a sedative-hypnotic alone and in a variety of combination products. Carbromal is known to be marketed in Finland, France, the Federal Republic of Germany, and Switzerland. The drug appears in several pharmacopoeias and may be widely used in generic drugs. The therapeutic use of this substance has been largely replaced by other more effective drugs. The Committee rated the therapeutic usefulness of carbromal as low.

2.2.6 Recommendation

On the basis of the available data concerning its pharmacological profile, dependence potential and actual abuse, the Committee rated the likelihood of abuse of carbromal as moderate. The degree of seriousness of the public health and social problems associated with the substance was found to be low, as was its therapeutic usefulness.

The Committee found that there was insufficient evidence that carbromal is currently being, or is likely to be, abused so as to constitute a public health and social problem warranting the placing of the substance under international control.

In light of this assessment, the Committee did not recommend scheduling of carbromal.

2.3 Clomethiazole

2.3.1 *Substance identification*

Clomethiazole (INN, CAS 533-45-9 for the base; CAS 1867-58-9 for the edisylate), chemically, the base is 5-(2-chloroethyl)-4-methylthiazole and the edisylate is the 1,2-ethanedisulfonate (2:1). Other names include chlormethiazole (BAN), chlormethiazole edisylate (*BP 1980*) and clomethiazolum (NFN). No isomeric forms are possible.

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

Clomethiazole has been classified as an anticonvulsant, sedative and hypnotic, with some anti-anxiety effects. It is viewed as an effective agent in the treatment of alcoholic delirium tremens. It possesses minor pharmacological cross-tolerance to alcohol in animals. Its mode of action differs from both benzodiazepines and barbiturates. Its anticonvulsant activity is apparently mediated through chloride ion channels coupled to GABA-receptors and glycine-receptors. It is extensively metabolized and does not seem to induce as much liver microsomal enzyme production as do barbiturates, which may account for the less marked development of tolerance to it.

Clomethiazole produces a dose-related protection from convulsions induced by a wide range of chemicals, in particular isoniazid. The anticonvulsant dose is much lower than sedative-hypnotic doses. Clomethiazole appears to activate beta rhythms, preferentially in subcortical regions and in the reticular formation.

2.3.3 *Dependence potential*

Controlled studies have shown that clomethiazole does not support barbiturate dependence or produce primary physical dependence in animals. In drug discrimination studies, clomethiazole was recognized as pentobarbital-like by the pigeon but not by the rhesus monkey. Rats and baboons did not discriminate clomethiazole as a benzodiazepine. Intravenous self-administration studies in the codeine-trained rhesus monkey were negative but the substance was self-administered in pentobarbital-

maintained animals. When given by the intracerebroventricular route in the rat it was not self-administered. In this model the standards, diazepam and amobarbital, were self-administered. There are no controlled human studies on the dependence potential of clomethiazole. There are, however, a number of case reports of tolerance and withdrawal signs following clomethiazole abuse.

2.3.4 *Actual abuse and/or abuse liability (likelihood of abuse)*

A significant level of abuse has been reported in the Federal Republic of Germany. In addition, there have been cases reported from Finland, Poland, Sweden, and the United Kingdom. Most cases of abuse reported have been in patients known to be dependent on alcohol or other substances. Abuse of the drug by the intravenous route has been reported from the Federal Republic of Germany. Of 80 countries reporting on the national control status of clomethiazole, 48 reported that it was registered and/or available on the market. The drug is available only on prescription in all countries where it is approved for marketing, purchased on government tenders, or available on an individual patient basis. Forty-eight countries reported no abuse, seizure, or clandestine laboratories. Four countries reported seizures of small amounts of the drug from 1983 to 1985. No diversions were reported.

2.3.5 *Therapeutic usefulness*

Clomethiazole has two major therapeutic indications: (a) treatment of delirium tremens after alcohol withdrawal as well as after the withdrawal of certain other drugs, and (b) treatment of certain convulsive disorders such as eclampsia convulsions, status epilepticus, and myoclonic seizures. It is also indicated in gerontopsychiatric states of insomnia and restlessness, and in anaesthesia (as a hypnotic in patients who require regional anaesthesia). It is an effective drug for inpatient treatment of delirium tremens. However, outpatient treatment of alcoholic cases with clomethiazole may lead to abuse. The Committee rated the therapeutic usefulness of clomethiazole in the treatment of delirium tremens associated with alcohol withdrawal and selective convulsive states as significant, while usefulness for other indications was rated as moderate.

2.3.6 Recommendation

On the basis of available data concerning its pharmacological profile, dependence potential, and actual abuse, the Committee rated the likelihood of abuse of clomethiazole as moderate. The Committee noted that any drug that is used extensively in the treatment of chemical dependency or its consequences is likely to be abused to a certain degree by patients. The degree of seriousness of the public health and social problems associated with the substance was found to be moderate and its therapeutic usefulness moderate to high.

The Committee found that there was insufficient evidence that clomethiazole is currently being, or is likely to be, abused so as to constitute a public health and social problem warranting the placing of the substance under international control.

In light of this assessment, the Committee did not recommend the scheduling of clomethiazole. However, the Committee recognized that this substance may present future problems and recommended that it be monitored closely.

2.4 Chloralodol

2.4.1 Substance identification

Chloralodol (INN, CAS 3563-58-4), chemically 2-methyl-4-(2,2,2-trichloro-1-hydroxyethoxy)-2-pentanol, is also known as chlorhexadol (BAN) and chloralodolum (NFN). There are two chiral carbon atoms in the structure. Thus there are two diastereomeric substances each of which consists of two enantiomers.

2.4.2 Similarity to already known compounds and effects on the central nervous system

Chloralodol is a pro-drug of chloral hydrate and like chloral hydrate it is a hypnotic agent. The slow hydrolysis of the drug reduces the local irritation on the mucous membrane and therefore makes it better tolerated than chloral hydrate.

The total spectrum of adverse reactions and toxic signs due to chloral hydrate are also found with chloralodol, such as dose-related ataxia and confusion. There is no information in the literature on adverse effects, intoxication, and poisoning directly related to

chloralodol. The drug is metabolized to 2,2,2-trichloroethanol which is responsible for its hypnotic effects.

2.4.3 *Dependence potential*

Controlled dependence studies in animals have not been carried out, but cases of moderate psychic and physical dependence on chloral hydrate have been documented with the full clinical picture of 'chloralism'. No specific information is available on the dependence potential of chloralodol.

2.4.4 *Actual abuse and/or abuse liability (likelihood of abuse)*

Few cases of abuse have been reported. From all the information gathered, abuse of chloralodol does not occur at present in any country. The substance is under national control in three of 59 reporting countries, and requires prescription in ten of these countries. No case of illicit manufacture or traffic has been reported.

2.4.5 *Therapeutic usefulness*

The substance is available in very few countries. It has the same therapeutic uses as chloral hydrate and is of very little use at present. The Committee rated the therapeutic usefulness of chloralodol as low.

2.4.6 *Recommendation*

On the basis of the available data concerning its pharmacological profile, dependence potential and actual abuse, the Committee rated the likelihood of abuse of chloralodol as moderate. The degree of seriousness of the public health and social problems associated with the drug was found to be low, as was its therapeutic usefulness.

The Committee found that there was insufficient evidence that chloralodol is being, or is likely to be, abused so as to constitute a public health or social problem warranting the placing of the substance under international control.

In the light of this assessment, the Committee did not recommend scheduling of the drug.

2.5 Methylpentynol

2.5.1 *Substance identification*

Methylpentynol (INN, CAS 77-75-8); chemical name: 3-methyl-1-pentyn-3-ol, is also known as meparfynol and oblivon.

Methylpentynol has a carbamate (1-ethyl-1-methyl-2 propynyl carbamate CAS 302-66-9) and a phthalate derivative (CAS 131-67-9). Methylpentynol has one asymmetric centre and exists as a racemate with two stereoisomers.

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

As a mild sedative and hypnotic, methylpentynol is similar in activity to ethchlorvynol. In higher doses the effects resemble those of acute alcohol intoxication. Methylpentynol possesses no antispasmodic or analgesic activity. Large doses are reported to have no significant depressant effects upon respiration. Only a small percentage of the substance is eliminated unchanged in the urine.

At low doses methylpentynol has a mild sedative activity and at higher doses a mild hypnotic one. Chronic intoxication may induce a decrease in vitality, slurred speech, giddiness, and stupor. Fatigue, insomnia, and psychotic symptoms have been reported with methylpentynol.

Little information specific to the carbamate derivative is available but the pharmacology and toxicology of this derivative appear similar to methylpentynol.

No information specific to the phthalate derivative is available. This compound is only known for its anthelmintic activity.

2.5.3 *Dependence potential*

Controlled animal studies with methylpentynol show that it partially supports pentobarbital dependence and produces physical dependence. In drug discrimination studies, pigeons and rhesus monkeys did not discriminate methylpentynol as pentobarbital. The substance was self-administered by rhesus monkeys. The carbamate showed a similar profile. No controlled human dependence studies have been reported.

2.5.4 *Actual abuse/or abuse liability (likelihood of abuse)*

Chronic abuse has been reported to produce symptoms of intoxication and lead to dependence formation with a withdrawal syndrome. Available information reveals few demonstrable public health or social problems associated with methylpentynol or its carbamate derivative. Only a few cases of abuse have been reported in recent years. The substance or its carbamate derivative is under national control in two countries and requires prescription in 10 of the 60 reporting countries. No case of illicit manufacture or illicit traffic has been reported.

No information is available for the methylpentynol phthalate derivative.

2.5.5 *Therapeutic usefulness*

Methylpentynol has been used as a sedative-hypnotic and in a variety of combination products. It is available on the market in ten of the 60 countries reporting. The therapeutic use of this drug has been largely replaced by more effective drugs. The Committee rated the therapeutic usefulness of methylpentynol as low.

2.5.6 *Recommendation*

On the basis of the available data concerning its pharmacological profile, dependence potential and actual abuse, the Committee rated the likelihood of abuse of methylpentynol and its derivatives as moderate. The degree of seriousness of the public health and social problems associated with the drug and its derivatives was found to be low as was its therapeutic usefulness.

Despite its close relationship to ethchlorvynol, the Committee found that there was insufficient evidence that methylpentynol and its derivatives are being, or are likely to be, abused so as to constitute a public health and social problem warranting the placing of the substance and its derivatives under international control.

In the light of this assessment, the Committee did not recommend scheduling of the drug.

2.6 Triclofos

2.6.1 *Substance identification*

Triclofos (INN, CAS 306-52-5, CAS 7246-20-0 for the sodium salt); chemical name: 2,2,2-trichloroethanol dihydrogen phosphate. No isomeric forms are possible.

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

Triclofos sodium has been classified pharmacologically as a sedative-hypnotic with a profile similar to that of chloral hydrate, a substance to which it is chemically related. Triclofos is rapidly biotransformed to trichloroethanol, a pharmacologically active metabolite of chloral hydrate. Triclofos is more palatable and believed to produce less gastric irritation than chloral hydrate.

Triclofos sodium has mostly hypnotic but also sedative actions similar to those of chloral hydrate. The principal effects are sedation at low doses and sleep induction at higher ones. Overdose may cause loss of reflex, respiratory depression, and, occasionally, death.

2.6.3 *Dependence potential*

In drug discrimination studies triclofos was identified as a benzodiazepine by the rat but not by the baboon. Pigeons, rhesus monkeys, and baboons did not discriminate triclofos as pentobarbital. The substance did substitute for pentobarbital in the dependent rat but itself produced only mild withdrawal symptoms. Self-administration studies have not been reported. Controlled human dependence studies have not been carried out.

2.6.4 *Actual abuse and/or abuse liability (likelihood of abuse)*

There were two abuse cases reported in Finland between 1983 and 1985. In the Drug Abuse Warning Network (DAWN) reports from the USA there were twelve mentions of triclofos from emergency rooms and two from medical examiners from 1979 to 1985. Concerning illicit manufacturing and illicit traffic of the substance, no seizures or clandestine laboratories were reported from 53 countries. Triclofos is available on prescription in eight, and under national control in three out of 57 reporting countries. The foregoing

evidence as well as the low predicted dependence potential of the substance may indicate a low abuse liability.

2.6.5 Therapeutic usefulness

Triclofos is a hypnotic that is reported to be effective in the treatment of insomnia, and can also be employed as a mild sedative and to premedicate children before surgery. The therapeutic use of this substance has been largely replaced by other more effective drugs. The Committee rated the therapeutic usefulness of triclofos as low.

2.6.6 Recommendation

On the basis of the available data concerning its pharmacological profile, dependence potential, and actual abuse, the Committee rated the likelihood of abuse of triclofos as low. The degree of seriousness of the public health and social problems associated with the substance were also estimated to be low as was its therapeutic usefulness.

The Committee found that there was insufficient evidence that triclofos is being, or is likely to be, abused so as to constitute a public health and social problem warranting the placing of the substance under international control.

In the light of this assessment, the Committee did not recommend scheduling of the drug.

2.7 Secobarbital

A notification (NAR/CL.9/1986, DND 411/1(2))¹ from the Government of the United States of America concerning the rescheduling of secobarbital has been transmitted to the Director-General of the World Health Organization pursuant to Article 2, Paragraph 2 of the Convention on Psychotropic Substances, 1971.

Secobarbital is an intermediate-acting sedative-hypnotic barbiturate with a high potential for abuse and a high level of actual abuse with demonstrated adverse effects on public health and social well-being. The substance is currently controlled under the

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

Convention on Psychotropic Substances, 1971, in Schedule III along with cyclobarbital, pentobarbital and amobarbital, three other intermediate-acting sedative-hypnotic barbiturates. Since the original scheduling, the therapeutic usefulness of these drugs has declined remarkably and they have been replaced by more effective drugs. The Committee regards the current therapeutic usefulness of these drugs as low. Recent information from the Secretary-General of the United Nations and INTERPOL on the international illicit traffic of secobarbital indicates that there has been an increasing problem in several countries with the substance as compared to the other controlled barbiturates. For instance, INTERPOL reports the following seizure patterns:

	Dosage units		
	Secobarbital	Pentobarbital	Amobarbital
1983	1 136 647	60	169
1984	1 718 565	66	20
1985	4 360 304	70	3 630 019 ¹
1986 ²	1 197 133	118 707	0

¹This represents seizures of Binocetol and Noctadiol which are preparations that contain both secobarbital and amobarbital. These figures are also contained in those listed under secobarbital.

²Preliminary statistics from 36 reporting members.

The problem is particularly acute in Africa and the eastern Mediterranean and south-east Asia. Also the United States of America reports a large illicit traffic in secobarbital being sold as methaqualone.

2.7.1 Recommendation

There is good evidence from controlled studies in animals and human subjects that secobarbital produces both physical and psychological dependence of a severe nature. There is evidence for a high incidence of actual abuse with attendant public health and social problems. The therapeutic usefulness of the drug is low.

There is evidence of a high and increasing illicit traffic with secobarbital as compared with other barbiturates already controlled in Schedule III of the Convention on Psychotropic Substances, 1971. Thus, the Committee recommends that secobarbital be moved from Schedule III to Schedule II of the Convention. The additional control measures associated with this change should permit a more effective control of the illicit traffic in secobarbital.

2.8 Methaqualone

The fourth PPWG¹ suggested that the Expert Committee should consider the need to recommend the rescheduling of methaqualone from Schedule II to Schedule I of the Convention on Psychotropic Substances, 1971. The Expert Committee noted the continuing widespread abuse of methaqualone, the existing large stocks of the drug and its low therapeutic usefulness. It was felt, however, that the data available were not complete or sufficiently up-to-date for consideration at the present meeting. In addition, the Committee was of the opinion that a decision of this magnitude required that the established WHO procedures for review of psychoactive substances be followed. In particular, the Committee believed it was especially important in this case for the Secretary-General of the United Nations to notify the governments of Member Countries that the drug was being considered for rescheduling to Schedule I in order to facilitate the gathering of data. Therefore, it recommended that a critical review be prepared for methaqualone for consideration at the 25th meeting of the Expert Committee.

2.9 Analogues of controlled substances

In recent years, a new drug abuse problem of considerable magnitude has arisen. This involves the synthesis of analogues of substances already controlled under national or international laws. These so-called 'designer drugs' are often highly potent substances which, when introduced on to the illicit market, have caused severe public health and social problems. The PPWG, at its fourth meeting, requested the Expert Committee on Drug Dependence to consider the need to recommend the control of analogues of fentanyl or pethidine which have produced abuse problems in the USA. The Committee has examined these substances and, having noted the absence of any known therapeutic use as well as the urgency for scheduling, recommends the early control of five of them. Detailed reports on the individual analogues are presented below.

2.9.1 *Alpha-methylfentanyl*

2.9.1.1 *Substance identification.* Alpha-methylfentanyl (CAS 79704-88-4); chemical name: (1) CAS: N-[1-(1-methyl-2-

¹ Report of the 4th meeting of the Programme Planning Working Group, 2-7 March 1987, Geneva (unpublished WHO document MNH/PAD/87.2).

phenylethyl)-4-piperidinyl]-*N*-phenylpropanamide; (2) IUFA: *N*-(1-(α -methyl- β -phenyl)-ethyl-4-piperidyl-propionanilide; is also known as 'China white' or 'synthetic heroin'.

2.9.1.2 *Similarity to already scheduled substances and effects on the central nervous system.* Alpha-methylfentanyl has been classified pharmacologically as an agonist of mu-type opioid receptors with a profile similar to that of fentanyl. As a mu-type opioid agonist it possesses analgesic activity and produces morphine-like euphoric effects. Its analgesic potency is three times that of fentanyl and 900 times that of morphine. Its analgesic effect has a rapid onset and a short duration, but its respiratory depressant effect may last longer. The effects of alpha-methylfentanyl on the central nervous system can be reversed by narcotic antagonists such as naloxone.

2.9.1.3 *Dependence potential.* Alpha-methylfentanyl substitutes for morphine in the morphine-dependent monkey and produces primary physical dependence of the opiate type. The substance is self-administered by rhesus monkeys. The substance is recognized as an opiate by heroin abusers and may produce physical dependence in human subjects.

2.9.1.4 *Actual abuse and/or abuse liability (likelihood of abuse).* Street abuse of alpha-methylfentanyl has been reported in the United States of America. At least 16 overdose deaths have been associated with the drug. It has appeared frequently in illicit traffic and is clandestinely manufactured.

2.9.1.5 *Therapeutic usefulness.* At present alpha-methylfentanyl has no known therapeutic use.

2.9.1.6 *Recommendation.* The Committee found that there was sufficient evidence to indicate that alpha-methylfentanyl is liable to similar abuse as, and produces ill-effects similar to those seen with, drugs in Schedule I of the Single Convention on Narcotic Drugs, 1961 and that Convention as amended by the 1972 Protocol. The Committee rated the abuse liability of the substance as high. The degree of seriousness of the public health and social problems associated with the substance was found to be high and there is no known therapeutic usefulness.

Therefore, the Committee recommended that alpha-methylfentanyl be controlled in Schedules I and IV of the Single

Convention on Narcotic Drugs, 1961 and that Convention as amended by the 1972 Protocol.

2.9.2 3-Methylfentanyl

2.9.2.1 *Substance identification.* 3-Methylfentanyl (CAS 42045-86-3); chemical name: (1) CAS: *N*-[3-methyl-1-(2-phenylethyl)-4-piperidinyl]-*N*-phenylpropanamide; (2) IUFA: *N*-(3-Methyl-1-(2-phenylethyl)-4-piperidyl)propionanilide. The drug is also known as F7209. Two racemates and four stereoisomers are possible for 3-methylfentanyl.

2.9.2.2 *Similarity to already scheduled substances and effects on the central nervous system.* 3-Methylfentanyl has been classified pharmacologically as an agonist of mu-type opioid receptors with a profile similar to that of fentanyl. It possesses analgesic activity and produces morphine-like euphoric effects. Its analgesic potency is about four times that of fentanyl and 1100 times that of morphine. Like other mu-type opioids, 3-methylfentanyl depresses respiration, and its effects on the central nervous system can be reversed by narcotic antagonists such as naloxone.

Cis-3-methylfentanyl has a rapid onset of activity and duration of activity of at least 2½ hours. Its potency is estimated to be 1000 times that of morphine. *Trans*-3-methylfentanyl also has a rapid onset of activity but a shorter duration of action than the *cis*-isomer. Its potency is about 600 times that of morphine. The analgesic activity was greatest for the (+) *cis*-isomer ($ED_{50} = 0.00058$ mg/kg of body weight in mice).

2.9.2.3 *Dependence potential.* 3-Methylfentanyl (both *cis*- and *trans*-isomers) substitutes for morphine in the morphine-dependent monkey and produces physical dependence of the morphine type. The substance is self-administered by rhesus monkeys. The substance is recognized as an opiate by heroin abusers and may produce physical dependence in subjects.

2.9.2.4 *Actual abuse and/or abuse liability (likelihood of abuse).* Street abuse of 3-methylfentanyl has been reported in the United States of America. Over 60 cases of death due to an overdose have been reported to be associated with the substance. It has appeared frequently in illicit traffic and is clandestinely manufactured. On the

basis of urine analysis, it was suspected that the substance was being abused by approximately 10% of 500 individuals enrolled in drug treatment programmes in California, USA.

2.9.2.5 *Therapeutic usefulness.* At present, 3-methylfentanyl has no known therapeutic use.

2.9.2.6 *Recommendation.* The Committee found that there was sufficient evidence to indicate that 3-methylfentanyl is liable to similar abuse as, and produces ill-effects similar to those seen with, drugs in Schedule I of the Single Convention on Narcotic Drugs, 1961 and that Convention as amended by the 1972 Protocol. The Committee rated the abuse liability of the drug as high. The degree of seriousness of the public health and social problems associated with the drug was also found to be high, and there is no known therapeutic use.

Therefore, the Committee recommended that 3-methylfentanyl be controlled in Schedules I and IV of the Single Convention on Narcotic Drugs, 1961 and that Convention as amended by the 1972 Protocol.

2.9.3 *Acetyl-alpha-methylfentanyl*

2.9.3.1 *Substance identification.* Acetyl-alpha-methylfentanyl (CAS 101860-00-8); chemical name: (1) CAS: *N*-[1-(1-methyl-2-phenylethyl)-4-piperidinyl]-*N*-phenylacetamide; (2) IUPAC: *N*-[1-(α -methyl-1-phenylethyl)-4-piperidinyl]acetamide. There is one asymmetric centre and the compound can exist as a racemate or two stereoisomers.

2.9.3.2 *Similarity to already scheduled substances and effects on the central nervous system.* Acetyl-alpha-methylfentanyl has been classified pharmacologically as a mu-type opioid receptor agonist with a profile similar to that of fentanyl. As a mu-type opioid agonist it possesses analgesic activity and produces morphine-like euphoric effects. Its analgesic potency is ten times that of morphine. Like other mu-opioids, acetyl-alpha-methylfentanyl can depress respiration, and its effects on the central nervous system can be reversed by narcotic antagonists such as naloxone.

2.9.3.3 *Dependence potential.* Acetyl-alpha-methylfentanyl substitutes completely for morphine in the morphine-dependent monkey.

2.9.3.4 *Actual abuse and/or abuse liability (likelihood of abuse).* Street abuse of acetyl-alpha-methylfentanyl has been reported in the United States of America. It has appeared in the illicit traffic and is clandestinely produced.

2.9.3.5 *Therapeutic usefulness.* At present, acetyl-alpha-methylfentanyl has no known therapeutic use.

2.9.3.6 *Recommendation.* The Committee found that there was sufficient evidence to indicate that acetyl-alpha-methylfentanyl is liable to similar abuse as, and produces ill-effects similar to those seen with, drugs in Schedule I of the Single Convention on Narcotic Drugs, 1961 and that Convention as amended by the 1972 Protocol. The Committee rated the abuse liability of the drug as high. The degree of seriousness of the public health and social problems associated with the drug was also found to be high and there is no known therapeutic usefulness.

Therefore, the Committee recommended that acetyl-alpha-methylfentanyl be controlled in Schedules I and IV of the Single Convention on Narcotic Drugs, 1961 and that Convention as amended by the 1972 Protocol.

2.9.4 MPPP

2.9.4.1 *Substance identification.* MPPP (CAS 13147-09-06); chemical name: (1) CAS: 1-methyl-4-phenyl-4-piperidinol propanoate (ester); (2) IUPAC: 1-methyl-4-phenyl-4-propionoxypiperidine. The drug is also known as 3-demethylprodine or desmethylprodine. No isomers are possible.

2.9.4.2 *Similarity to already scheduled substances and effects on the central nervous system.* MPPP has been classified pharmacologically as an agonist of mu-type opioid receptors with a profile similar to that of pethidine. It possesses an analgesic activity and produces morphine-like euphoric effects. Its analgesic potency is 1½ times that of morphine. Like other mu-opioids, MPPP depresses respiration and its effects on the central nervous system can be reversed by narcotic antagonists such as naloxone. One of the impurities in the synthesis of MPPP is MPTP (1-methyl-4-phenyl-tetrahydropyridine), a neurotoxin that destroys the dopaminergic neurones in the substantia nigra of the brain and leads to a

permanent Parkinsonian syndrome. A large number of individuals abusing MPPP have developed Parkinsonian symptoms. This represents a severe public health problem.

2.9.4.3 *Dependence potential.* MPPP substitutes for morphine in the morphine-dependent monkey. The substance is recognized as an opiate in heroin abusers and may produce physical dependence in man.

2.9.4.4 *Actual abuse and/or abuse liability (likelihood of abuse).* More than 100 cases of actual abuse of MPPP by the heroin-abusing population have been reported from the USA. Many deaths have been associated with the substance. Several outbreaks of MPTP-induced Parkinsonism have been related to MPPP abuse. Canada and France have also reported cases of MPPP abuse.

MPPP is controlled as a narcotic substance in France and the USA.

2.9.4.5 *Therapeutic usefulness.* At present, MPPP has no known therapeutic use.

2.9.4.6 *Recommendation.* The Committee found that there was sufficient evidence to indicate that MPPP is liable to similar abuse as, and produces ill-effects similar to those seen with, drugs in Schedule I of the Single Convention on Narcotic Drugs, 1961 and that Convention as amended by the 1972 Protocol. The Committee rated the abuse liability of the substance as high. The degree of seriousness of the public health and social problems associated with the substance was also found to be high and there is no known therapeutic use.

Therefore, the Committee recommended that MPPP be controlled in Schedules I and IV of the Single Convention on Narcotic Drugs, 1961 and that Convention as amended by the 1972 Protocol.

2.9.5 PEPAP

2.9.5.1 *Substance identification.* PEPAP (CAS 64-52-8); chemical name: (1) CAS: 4-phenyl-1-(2-phenylethyl)-4-piperidinol acetate (ester); (2) IUFA: 1-phenylethyl-4-phenyl-4-acetoxy-piperidine. No isomers are possible.

2.9.5.2 *Similarity to already scheduled substances and effects on the central nervous system.* PEPAP has been classified pharmacologically as an agonist of mu-type opioid receptors with a profile similar to that of pethidine. It possesses analgesic activity and produces morphine-like euphoric effects. Its analgesic potency is about twice that of morphine. Like other mu-type opioids, PEPAP depresses respiration and its effects on the central nervous system can be reversed by narcotic antagonists such as naloxone.

2.9.5.3 *Dependence potential.* PEPAP substitutes completely for morphine in morphine-dependent monkeys.

2.9.5.4 *Actual abuse and/or abuse liability (likelihood of abuse).* Seizure of a clandestine laboratory and confiscation of numerous street samples containing PEPAP have been reported by the USA. PEPAP is controlled as a narcotic substance in France and the USA.

2.9.5.5 *Therapeutic usefulness.* At present, PEPAP has no known therapeutic use.

2.9.5.6 *Recommendation.* The Committee found that there was sufficient evidence to indicate that PEPAP is liable to similar abuse as, and produces ill-effects similar to those seen with, drugs in Schedule I of the Single Convention on Narcotic Drugs, 1961 and that Convention as amended by the 1972 Protocol. The Committee rated the abuse liability of the drug as high. The degree of seriousness of the public health and social problems associated with the drug was found to be high, and there is no known therapeutic use.

Therefore, the Committee recommended that PEPAP be controlled in Schedules I and IV of the Single Convention on Narcotic Drugs, 1961 and that Convention as amended by the 1972 Protocol.

2.10 Metamfetamine racemate

The PPWG¹, at its fourth meeting, requested the advice of the Expert Committee on Drug Dependence on the status of the racemate of metamfetamine (chemical name: (±)-N,α-dimethylbenzeneethanamine; (1) CAS: (±)-N,α-dimethylphen-

¹ Report of the 4th meeting of the Programme Planning Working Group, 2-7 March, 1987, Geneva (unpublished WHO document MNH/PAD/87.2).

ethylamine) under the Convention on Psychotropic Substances, 1971. The drafters of the Convention placed amphetamine (the racemate) and dextroamphetamine (the (+)-isomer) in Schedule II of the 1971 Convention. Subsequently the (–)-isomer was also placed under control. It should be noted that the earlier INN methamphetamine refers to the (+)-isomer and the racemate was not specifically named in the schedules. This left the control status of the racemate open to possible misinterpretation.

2.10.1 *Recommendation*

On the basis of the foregoing discussions, the Committee recommends that metamfetamine racemate be specifically controlled under Schedule II of the Convention on Psychotropic Substances, 1971.

The Committee noted that WHO had convened a group of experts to discuss chemical and pharmacological specifications of substances for control under the International Conventions. Their report clearly delineated procedures for the future handling of isomers.¹ The Expert Committee recommended that these procedures be initiated in all future reviews of substances being considered for control under the International Conventions.

3. RECOMMENDATIONS FOR EXEMPT PREPARATIONS

3.1 Notification by the Finnish Government concerning exempt preparations – DND 421/12(1) Finl. DND 411/1(2)²

On 2 May 1985, the Finnish Government sent a notification to the Secretary-General of the United Nations with the information that the Government, pursuant to Article 3, Paragraph 3, of the Convention on Psychotropic Substances, 1971, had exempted 14 preparations containing psychotropic substances, as provided for by that Convention. The preparations were exempted from all measures of control except for the mandatory measures required by

¹ *Report of the meeting on chemical and pharmacological specifications of substances for control* (unpublished WHO document MNH/PAD/86.13).

² A copy of this notification can be obtained by writing to: United Nations Division of Narcotic Drugs, Vienna International Centre, P.O. Box 500, A-1400 Vienna, Austria.

Article 3, Paragraphs 3(a) to (7), and the requirements of Article 9, Paragraph 1.

On 7 August 1985 the Secretary-General of the United Nations informed WHO of the Finnish notification. The United Nations Division of Narcotic Drugs, in a letter dated 15 October 1985, supplied WHO with further details about domestic use and/or possible exportation.

A WHO Consultative Group reviewed the Finnish exemptions in 1985 and noted that this group of exempt preparations was unique since it represented the first group containing benzodiazepines. The Consultative Group was of the opinion that the exemption of the preparations listed below need not be terminated except for the mandatory provision of Article 3, Paragraph 3, Subparagraphs (a) to (f). It noted that the Government of Finland had indicated that these preparations are for domestic use only and will remain under prescription control:

Klorriptyl
Klorriptyl
Librax
Limbitrol
Aminopam¹
Aspam
Diapantin
Dolapam
Relapam
Nitrapamil
Vertipam
Spasmo-Oxepam

The Consultative Group came to the conclusion that the exemption of the following preparations by the Government of Finland should be terminated in part, and accordingly recommended that the requirements of Article 8, Paragraph 1, and of Article 11, Paragraph 5 apply to such preparations to the extent that the provisions relate to importers and exporters:

Gastrodyn comp.
Trimigrin.

¹ This preparation is no longer available on the market in Finland.

The PPWG examined the recommendations of the WHO Consultative Group at its third meeting and expressed its full agreement. In the light of the United Nations Commission on Narcotic Drugs Resolution 3(S-IX) of February 1986, the PPWG recommended that the findings of the Consultative Group need not yet be brought to the attention of the Expert Committee but might remain in the WHO files.

The United Nations Commission on Narcotic Drugs, at its thirty-second session in February 1987, however, decided that WHO should resume the review of the pending notification of the Government of Finland. Thus, the PPWG took up the matter at its fourth meeting and had before it additional information from the Finnish Government. In agreement with the recommendations of the 1985 Consultative Group, the PPWG proposed that the Expert Committee should review the notification at its twenty-fourth meeting.

3.1.1 *Recommendation*

The Expert Committee agreed with the recommendation of the PPWG that 12 of the 14 exemptions should be accepted and that the exemptions concerning Gastrodyn comp. (diazepam 2 mg per tablet, glycopyrronium bromide 1 mg per tablet), and Trimigrin (diazepam, 2 mg per tablet, ergotamine tartrate 1 mg per tablet, prochlorperazine 8 mg per tablet) should be terminated in part, so that the requirements of Article 8, Paragraph 1, and Article 11, Paragraph 5, should apply to the extent that the provisions relate to importers and exporters.

3.2 **Procedural recommendations concerning exempt preparations**

The PPWG, at its fourth meeting, suggested that the Expert Committee should examine in detail the WHO activities relating to the exemption of preparations under the Convention on Psychotropic Substances, 1971.

The Committee considered two informal reports by Professor B. Rexed: "Development of a WHO procedure for review of exempted preparations under the Convention on Psychotropic Substances, 1971," and "Rev. 1: WHO review of exempted preparations under the Convention on Psychotropic Substances, 1971", including some alterations of the proposed WHO review

procedure taking into account the discussion at the fourth meeting of the PPWG. The PPWG had, in a general way, endorsed the proposals contained in the reports referred to above.

The Expert Committee supported the procedure for a WHO review of exempted preparations as outlined below.

I. The exempting party

1. A Party, exempting a preparation from measures of control provided under the Convention on Psychotropic Substances, 1971, for any of its constituent psychotropic substances, must follow the special provisions regarding the control of preparations of Article 3, Paragraphs 2 and 3, of that Convention.

2. The Party, in compounding and controlling the preparation, should follow the recommendations of the United Nations Commission on Narcotic Drugs as contained in Resolutions 1(S-VIII) and 3(S-IX).

3. The Party must, as provided by Article 3, Paragraph 3, notify the Secretary-General of any new exemption as well as any change, or the termination, of any exemption.

II. The World Health Organization

1. The responsibility of WHO:

(a) When notified of an exempted preparation, WHO has the obligation, as provided by Article 3, Paragraph 4, of the Convention, to make an assessment and, as appropriate, to make a recommendation to the United Nations Commission on Narcotic Drugs of the control measures, if any, from which the preparation should cease to be exempted.

(b) In its assessment upon notification of an exempted preparation, WHO should take into account the guidelines of United Nations Commission on Narcotic Drugs, as put forth in Resolutions 2(S-VI), 1(S-VIII) and 3(S-IX).

2. The WHO review procedure:

(a) Non-exported preparations.

(i) The exemption is for domestic use only, and the exempting Party gives assurance in its notification that, to the best of its knowledge, there is no significant abuse.

This exemption does not require an immediate WHO evaluation. It is, without further action by the WHO Secretariat, referred to storage for later study.

- (ii) The exemption is for domestic use only, and information has been received by WHO, that there is evidence of national abuse.

This exemption is evaluated by WHO, and any resulting recommendation(s) as to change or termination of the exemption is brought to the attention of the Party.

- (iii) The exemption is for domestic use only, and information has been received by WHO, that it may constitute a public health and social problem to another Party (for example, as a result of illicit trade and/or abuse):

This exemption is evaluated by WHO, and any resulting recommendation(s) as to change or termination of the exemption are communicated by the Director-General of WHO to the country of origin of the preparation, or if the abuse problems are widespread, to the Secretary-General of the United Nations.

(b) Exported preparations.

All such exemptions are evaluated by WHO, and recommendations are formulated according to the following considerations:

- (i) the degree of conformity with the requirements of Article 3, Paragraph 2, of the Convention (that is, degree of abuse liability and recoverability of the psychotropic substance(s)) as well as with the United Nations Commission on Narcotic Drugs Resolution 1(S-VIII).
- (ii) information that the preparation constitutes a public health and social problem to an importing country or to a country where it is illicitly traded.

If under (i) and (ii) above there are no negative findings, then no further action is required by WHO. If, however, under either (i) or (ii) or both, there are negative findings, any resulting recommendation(s) are communicated to the Secretary-General of the United Nations.

The Expert Committee considered this procedure to correspond with the relevant work plan of the WHO Secretariat and accepted,

in a general way, the considerations underlying this procedure made in the two reports by Professor B. Rexed. The Expert Committee proposed that the outline of the procedure be communicated together with a short summary of the underlying considerations to the United Nations Commission on Narcotic Drugs for comments and for any further suggestions as to WHO activities concerning exempted preparations.

4. RECOMMENDATIONS AND CONCLUSIONS

1. At the request of the World Health Organization, information on specific psychoactive substances is collected by the Secretary-General of the United Nations and INTERPOL to help the Expert Committee on Drug Dependence in its evaluation. The Expert Committee recommended that, in addition, the Director-General of WHO should collect information officially through a circular letter addressed to the ministries of health in order to bring out additional information from health care institutions.

2. The Expert Committee considered that drug registration authorities at the national level have an important role to play in promoting the rational use of psychoactive drugs. When a drug is registered, made available on the market, or re-registered, it is essential to obtain data on the dependence potential of the drug, the likely public health and social problems, and the identified need of the society for the drug. Data are needed on dependence potential both in experimental animals and in human subjects as well as on the merit of the drug for therapeutic use. WHO should encourage, together with national health authorities, the development of laboratories and clinical services that can provide data on dependence potential and actual abuse.

3. The Expert Committee noted that many psychoactive substances with dependence potential are being replaced by safer drugs. The use and production of such substances has ceased in many countries. Since some of these substances may not be scheduled under any of the Conventions the possibility of their being still made available in developing countries remains. The drug control administrations in the Member States may need assistance to check the national availability of these drugs.

The Expert Committee, therefore, recommended that WHO, in cooperation with the United Nations Division of Narcotic Drugs,

should develop suitable mechanisms to make information available to the national drug control administrations of developed and developing countries, on substances whose therapeutic usefulness has diminished, that are not being widely produced and that fall within the scope of the Conventions.

4. The Expert Committee recommended that parties to the Convention on Psychotropic Substances, 1971, take full advantage of Article 13, which allows parties to prohibit the importation of controlled substances into their country. The use of Article 13 to prohibit the importation of methaqualone was felt to be a good example of how this mechanism can help solve a serious drug abuse problem.

5. The Expert Committee noted that epidemiological data concerning the public health consequences of drug abuse were very inadequate. It recommended that governments should collect, on a regular basis, data on substances covered by the Conventions that are involved in drug overdose or suicide attempts from the casualty emergency services of general hospitals, and other services.

6. Following successful working group meetings on the rational use of psychoactive drugs and the use of psychotropic substances outside psychiatry, the Expert Committee recommended that WHO, in collaboration with governments, should (a) encourage, initiate and organize regional and national training courses/seminars on psychotropic substances for all health personnel, especially general practitioners, pharmacists, physicians and psychiatrists to improve their knowledge of these drugs, and (b) liaise with health care training schools and encourage them to include or expand the training curricula and syllabi with respect to psychotropic substances.

7. The Expert Committee has considered in detail the sections of the Critical Review (MNH/PAD/86.11.Rev.1) concerning analogues of controlled substances (the so-called "designer drugs"), as well as additional information on the relevant experience in the USA, including a list of 13 substances recently nationally controlled there, and additional information from France. As indicated in Section 2.9 of this report, the Committee decided to recommend inclusion of five of these substances under the Single Convention on Narcotic Drugs, 1961 and that Convention as amended by the 1972 Protocol. The Committee further recommended that the WHO Secretariat should continue to collect information, with the help of concerned countries, on the remaining substances on the list of 13,

and on other analogues of controlled substances that may be trafficked illicitly and abused.

Additionally, the Expert Committee drew attention to the possibility of instituting relevant and special legal controls as regards the illicit analogues of controlled substances. The Committee contended that there is a need to be able to control such analogues more rapidly at the national level than is possible under the international treaties. One country has already developed such legislation. The Expert Committee proposed that WHO should develop guidelines for the preparation of such legislation for national use. A meeting between health and law enforcement authorities, to be held in Morocco, has already been organized by WHO and the US Drug Enforcement Administration.

8. The Expert Committee recommended further review of methaqualone, amphetamine and metamfetamine for possible rescheduling to Schedule I of the 1971 Convention.

9. The Expert Committee noted, with satisfaction, that WHO and the pharmaceutical industry have discussed the possibility of collaboration on reducing the problems associated with the abuse of psychoactive substances. The Expert Committee strongly encouraged WHO to continue the dialogue with the industry and to explore activities for implementing the proposals contained in the report,¹ in particular for helping in the future work of the Expert Committee.

5. ACKNOWLEDGEMENTS

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¹ *Collaboration between the pharmaceutical industry and international agencies in reducing drug abuse* (unpublished WHO document MNH/PAD/87.1).

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