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Agenda item 6
Implementation of the international drug control treaties:
Changes in the scope of control of substances

Extract from the Report of the 37th Expert Committee on Drug Dependence, convened from 16 to 20 November 2015, at WHO headquarters in Geneva*

* The present document is reproduced in the form in which it was received.

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Annex 1

Extract from the Report of the 37th Expert Committee on Drug Dependence

Substance recommended to be scheduled in Schedule I and Schedule IV of the Single Convention on Narcotic Drugs (1961), as amended by the 1972 Protocol:

Acetylfentanyl

Chemically, acetylfentanyl is *N*-phenyl-*N*-[1-(2-phenylethyl)-4-piperidinyl]acetamide. It is in the phenylpiperidine class of synthetic opioids that includes fentanyl, a Schedule I drug under the UN 1961 Single Convention on Narcotic Drugs. Acetylfentanyl has also been referred to as "desmethyl fentanyl".

Acetylfentanyl has not been previously reviewed by the Committee. A critical review was proposed based on information brought to WHO's attention that acetylfentanyl is clandestinely manufactured, poses a risk to public health and society, and has no recognized therapeutic use by any Party.

Acetylfentanyl has effects similar to those of morphine and fentanyl that are included in Schedule I of the 1961 Single Convention on Narcotic Drugs. It has no recorded therapeutic use and its use has resulted in fatalities. Thus, because it meets the required condition of similarity, it is recommended that acetylfentanyl be placed in Schedule I of the Single Convention on Narcotic Drugs, 1961, as consistent with Article 3, paragraph 3 (iii) of that Convention in that the substance is liable to similar abuse and productive of similar ill effects as drugs in Schedule I. In addition, in accordance with Article 3, paragraph 5 of that Convention, considering acetylfentanyl is particularly liable to abuse and to produce ill-effects, and its liability is not offset by substantial therapeutic advantages, it is recommended it be included in Schedule IV of the Single Convention on Narcotic Drugs, 1961.

Substance recommended to be scheduled in Schedule I of the Single Convention on Narcotic Drugs (1961), as amended by the 1972 Protocol:

MT-45

Chemically, MT-45 is 1-cyclohexyl-4-(1,2-diphenylethyl)piperazine. MT-45 has two enantiomers and is commonly available as the racemic mixture.

MT-45 has not been previously reviewed by the Committee. A critical review was proposed based on information brought to WHO's attention that MT-45 is clandestinely manufactured, poses a risk to public health and society, and has no recognized therapeutic use by any Party.

MT-45 is a compound with morphine-like effects. The Committee considered that the degree of risk to public health and society associated with the abuse liability and accompanying evidence warranted its placement under international control. Therapeutic use in humans has not been recorded. The Committee recommended

that MT-45 be placed in Schedule I of the 1961 Single Convention, as amended by the 1972 Protocol.

Substance recommended to be scheduled in Schedule I of the Convention on Psychotropic Substances (1971):

para-Methoxymethylamphetamine (PMMA)

Chemically, PMMA (*para*-methoxymethylamphetamine) is 1-(4-methoxyphenyl)-*N*-methylpropan-2-amine. PMMA has two enantiomers and is commonly available as the racemic mixture.

PMMA has not been previously reviewed by the Committee. A critical review was proposed based on information brought to WHO's attention that PMMA is clandestinely manufactured, poses a risk to public health and society, and has no recognized therapeutic use by any Party.

The Committee considered that the effects of PMMA are similar to PMA, a drug listed in Schedule I of the Convention on Psychotropic Substances of 1971, and the degree of risk to public health and society associated with its abuse is especially serious. The Committee also noted it has no recorded therapeutic use. The Committee considered that the evidence of its abuse warranted its placement under international control and recommended that PMMA be placed in Schedule I of the 1971 Convention.

Substances recommended to be scheduled in Schedule II of the Convention on Psychotropic Substances (1971):

α-Pyrrolidinovalerophenone (α-PVP)

Chemically, α-PVP (α-pyrrolidinovalerophenone) is 1-phenyl-2-(pyrrolidin-1-yl)pentan-1-one. This synthetic cathinone is the desmethyl analogue of pyrovalerone that is listed in Schedule IV of the 1971 United Nations Convention on Psychotropic Substances. α-PVP has two enantiomers and is commonly available as the racemic mixture. α-PVP is closely related to 3',4'-methylenedioxypyrovalerone (MDPV) that has recently been placed in Schedule II of the UN Convention on Psychotropic Substances (1971).

α-PVP has not been previously reviewed by the Committee. A direct critical review was proposed based on information brought to WHO's attention that α-PVP is clandestinely manufactured, poses a risk to public health and society, and has no recognized therapeutic use by any Party.

The Committee considered that the degree of risk to public health and society associated with the abuse of α-PVP is substantial. Therapeutic usefulness has not been recorded. Its pharmacological effects are similar to methamphetamine and MDPV, psychostimulants listed in Schedule II of the 1971 Convention. The Committee considered that the evidence of its abuse warranted its placement under international control. As per the *Guidance on the WHO review of psychoactive substances for international control*, higher regard was accorded to the substantial public health risk than to the lack of therapeutic usefulness. The Committee recommended that α-PVP be placed in Schedule II of the 1971 Convention.

para-Methyl-4-methylaminorex (4,4'-DMAR)

Chemically, 4,4'-DMAR (*para*-methyl-4-methylaminorex) is 4-methyl-5-(4-methylphenyl)-4,5-dihydro-1,3-oxazol-2-amine. 4,4'-DMAR has four enantiomers and exists as racemic *cis*- or *trans*- forms. It is a synthetic substituted oxazoline derivative interpretable as an analogue of 4-methylaminorex (4-MAR) and aminorex, which are psychostimulants listed as Schedule I and Schedule IV substances, respectively, under the 1971 United Nations Convention on Psychotropic Substances.

4,4'-DMAR has not been previously reviewed by WHO. A critical review was proposed based on information brought to WHO's attention that 4,4'-DMAR is clandestinely manufactured, poses a risk to public health and society, and has no recognized therapeutic use by any Party.

As per the *Guidance on the WHO review of psychoactive substances for international control*, higher regard was accorded to the substantial public health risk than to the lack of therapeutic usefulness. The Committee considered that the degree of risk to public health and society associated with the abuse of 4,4'-DMAR is substantial. The Committee recommended that 4,4'-DMAR be placed in Schedule II of the 1971 Convention.

Methoxetamine (MXE)

Chemically, methoxetamine (MXE) is 2-(ethylamino)-2-(3-methoxyphenyl)cyclohexanone. It is a synthetic drug and belongs to the arylcyclohexylamine class like phencyclidine. Methoxetamine has two enantiomers and is commonly available as the racemic mixture.

During its 36th meeting, the WHO Expert Committee on Drug Dependence discussed the critical review report on methoxetamine and concluded that owing to the insufficiency of data regarding dependence, abuse and risks to public health, methoxetamine should not be placed under international control at that time, but be kept under surveillance. In 2014 the European Union decided to bring methoxetamine under control after a risk assessment by the EMCDDA. Furthermore new information on its abuse potential and more reports of fatal and non-fatal intoxications warranted a critical review for the 37th ECDD.

Methoxetamine has been shown to have effects similar to phencyclidine, a compound listed in Schedule II of the Convention on Psychotropic Substances of 1971. The Committee considered that the degree of risk to public health and society associated with the abuse liability of methoxetamine is substantial. The Committee also noted it has no recorded therapeutic use. The Committee considered that the evidence of its abuse warranted its placement under international control. The Committee recommended that methoxetamine be placed in Schedule II of the 1971 Convention.

Substance recommended to be scheduled in Schedule IV of the Convention on Psychotropic Substances (1971):

Phenazepam

Chemically, phenazepam is 7-bromo-5-(2-chlorophenyl)-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one.

Phenazepam has not been previously reviewed by the Committee. The Committee undertook a pre-review of the substance and considered that the information provided in the pre-review report was sufficient and indicated that dependence and harm caused by phenazepam was of such magnitude that proceeding directly into critical review within the meeting was warranted. All procedural requirements for a critical review, including two peer reviews, were fulfilled. Phenazepam has been shown to have effects similar to diazepam that is in Schedule IV of the Convention on Psychotropic Substances of 1971. The Committee considered that the degree of risk to public health and society associated with the abuse of phenazepam has a smaller but still significant risk to public health compared to substances in Schedules I-III and has a therapeutic usefulness from little to great. The Committee considered that the evidence of its abuse warranted its placement under international control. The Committee further recommended that phenazepam be placed in Schedule IV of the 1971 Convention.

Substance recommended for critical review:

Etizolam (INN)

Chemically, etizolam is 4-(2-chlorophenyl)-2-ethyl-9-methyl-6*H*-thieno[3,2-*f*][1,2,4]triazolo[4,3-*a*][1,4]diazepine.

The Expert Committee on Drug Dependence (ECDD) reviewed etizolam for the first time at its 26th meeting in 1989. At that time, the Committee rated the abuse liability of etizolam as moderate and the therapeutic usefulness as moderate to high. In view of the lack of clear-cut abuse, and of public health and social problems associated with its use, the Committee was unable to come to a decision concerning the scheduling of etizolam and recommended that a decision be deferred to the 27th meeting of the Committee.

At its 27th meeting in 1990, the Committee again rated the abuse liability of etizolam as low to moderate and the therapeutic usefulness as moderate to high. The Committee noted few public health and social problems associated with its use at that time and considered that the degree of seriousness of these problems was not great enough to warrant international control. Consequently, the Committee did not recommend scheduling of etizolam in 1990.

At the 37 ECDD, on the basis of the evidence available regarding dependence, abuse and risks to public health, the Committee recommended that a critical review of etizolam is warranted for a future meeting.

Substance recommended for surveillance:

4-Fluoroamphetamine (4-FA)

Chemically, 4-FA (4-fluoroamphetamine) is 1-(4-fluorophenyl)propan-2-amine. 4-FA has two enantiomers and is commonly available as the racemic mixture.

4-FA has not been previously reviewed by the Committee. A critical review was proposed based on information brought to WHO's attention that 4-FA is clandestinely manufactured, poses a risk to public health and society, and has no recognized therapeutic use by any Party.

Owing to the current insufficiency of data regarding dependence, abuse and risks to public health (including risks to the individual), the Committee recommended that 4-FA not be placed under international control at this time, but be kept under surveillance.

Update on cannabis:

The Commission on Narcotic Drugs, in Resolution 52/5, expressed that it "... looks forward to an updated report on cannabis by the Expert Committee, subject to the availability of extra budgetary resources", and the Report of the International Narcotics Control Board for 2014 reiterated, "... its invitation to WHO to evaluate the potential medical utility of cannabis and the extent to which cannabis poses a risk to human health." WHO therefore commissioned an update report paper on cannabis and cannabis resin.

An update on the scientific literature of cannabis was presented and reviewed during the session including the pharmacology, toxicology and the claimed therapeutic applications. The Committee then deliberated about the content of the material presented. The Committee requested the Secretariat to begin collecting data towards a pre-review of cannabis, cannabis resin, extracts and tinctures of cannabis at a future meeting. Furthermore it specifically requested the Secretariat to place emphasis on any therapeutic advantages that they may have relative to other existing therapeutics.

Update on ketamine:

Updates on ketamine were presented in which the levels and consequences of its abuse, and new potential medical applications were identified. Levels of ketamine abuse appeared to be declining in many countries world-wide. Potential new therapeutic uses were identified including depression and refractory status epilepticus. Evaluation of ketamine for treating depression is in Phase III studies. Ketamine is widely used as an anaesthetic agent for human and veterinary use globally. Ketamine is the anaesthetic agent of choice in low income countries and emergency situations where there are limitations in trained medical personnel, anesthesia machines, and consistent sources of electricity.

Following its deliberations, the Committee unanimously agreed that it found nothing in the updates, nor that which was disclosed during its deliberations, that would give it reason to recommend a new pre-review or critical review of ketamine with a view to potentially change its standing recommendation of 2014 that ketamine should not be placed under international control.