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**Commission on Narcotic Drugs**

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Agenda item 6 (b)

**Implementation of the international drug control**

**treaties: changes in the scope of control of substances**

**Extract from the Report of the 38th Expert Committee on  
Drug Dependence, convened from 14 to 18 November 2016, at  
WHO headquarters in Geneva\***

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## Annex 1

### Extract from the Report of the 38th Expert Committee on Drug Dependence

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

##### U-47700

Chemically, U-47700 is 3,4-dichloro-*N*-(2-dimethylamino-cyclohexyl)-*N*-methyl-benzamide. U-47700 has two chiral centres resulting in four isomers; cis and trans conformations each have two enantiomers [cis: are (1R,2R), and (1S,2S); trans are (1R,2S) and (1S,2R)].

U-47700 was not previously pre-reviewed or critically reviewed by the Committee. A direct critical review is proposed based on information brought to the attention of the WHO that U-47700 is clandestinely manufactured, poses risk to public health and society, and has no recognized therapeutic use by any Party.

U-47700 (3,4-dichloro-*N*-(2-dimethylamino-cyclohexyl)-*N*-methyl-benzamide) is a compound liable to similar abuse and with similar ill-effects to controlled opioids such as morphine and AH-7921 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. There is sufficient evidence that it 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. Thus, because it meets the required condition of similarity, it is recommended that U-47700 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.

##### Butyrfentanyl

Chemically, butyrfentanyl is *N*-phenyl-*N*-[1-(2-phenylethyl)-4-iperidinyl]butanamide.

Butyrfentanyl has not been previously pre-reviewed or critically reviewed by the Committee. A direct critical review is proposed based on information brought to the attention of the WHO that butyrfentanyl is clandestinely manufactured, poses risk to public health and society, and has no recognized therapeutic use by any Party.

Butyrfentanyl (*N*-phenyl-*N*-[1-(2-phenylethyl)-4-piperidinyl]butanamide) is a compound liable to similar abuse and with similar ill-effects to controlled opioids such as morphine and fentanyl that are included in Schedule I of the 1961 Single Convention on Narcotic Drugs. It can be converted into fentanyl as well. It has no recorded therapeutic use and its use has resulted in fatalities. There is sufficient evidence that it 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. Thus, because it meets either of the required conditions of similarity or convertibility, it is recommended that butyrfentanyl 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.

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

### **4-MEC (4-Methylethcathinone)**

Chemically, 4-methylethcathinone (4-MEC) is 2-(ethylamino)-1-(4-methylphenyl)propan-1-one. 4-MEC has a chiral centre giving rise to an enantiomeric pair of (S)-4-MEC and (R)-4-MEC isomers.

A critical review report on 4-MEC was discussed in June 2014 at the 36th meeting of the WHO Expert Committee on Drug Dependence. The Committee recommended that 4-MEC not be placed under international control at that time due to insufficiency of data regarding dependence, abuse and risks to public health, but be kept under surveillance. 4-MEC continues to appear as a psychostimulant with monoamine transporter activity with indications of abuse liability. New data have emerged from *in vitro* and *in vivo* studies since the 36th ECCD meeting that has prompted the current critical review.

The Committee considered that the degree of risk to public health and society associated with the abuse of 4-MEC (2-(ethylamino)-1-(4-methylphenyl)propan-1-one) is substantial. Therapeutic usefulness has not been recorded. It recognized that it has similar abuse and similar ill-effects as substances in Schedule II of the United Nations 1971 Convention on Psychotropic Substances. The Committee considered that there is sufficient evidence that 4-MEC 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. 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 4-MEC be placed in Schedule II under the United Nations 1971 Convention on Psychotropic Substances.

### **Ethylone**

Chemically, ethylone is 1-(2H-1,3-benzodioxol-5-yl)-2-(ethylamino)propan-1-one. It is a chiral compound with isomers, and its hydrochloride salt can exist in two conformations (polymorphs) at the C-C bond linking the side chain to the aromatic ring.

Ethylone was not previously pre-reviewed or critically reviewed. A direct critical review is proposed based on information brought to the attention of the WHO that ethylone is clandestinely manufactured, poses serious 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 ethylone (1-(2H-1,3-benzodioxol-5-yl)-2-(ethylamino)propan-1-one) is substantial. Therapeutic usefulness has not been recorded. It recognized that it has similar abuse and similar ill-effects as substances in Schedule II of the United Nations 1971 Convention on Psychotropic Substances. The Committee considered that there is sufficient evidence that ethylone 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. 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 ethylone be placed in Schedule II under the United Nations 1971 Convention on Psychotropic Substances.

**Pentedrone ( $\alpha$ -Methylaminovalerophenone)**

Chemically, pentedrone is 2-(methylamino)-1-phenylpentan-1-one. It has a chiral centre giving rise to two stereoisomers, (*S*)- and (*R*)- pentedrone.

Pentedrone has not been previously reviewed or critically reviewed by the Expert Committee on Drug Dependence of the WHO. A direct critical review is proposed based on information brought to WHO's attention that pentedrone is clandestinely manufactured, poses serious 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 pentedrone (2-(methylamino)-1-phenylpentan-1-one) is substantial. Therapeutic usefulness has not been recorded. It recognized that it has similar abuse and similar ill-effects as substances in Schedule II of the United Nations 1971 Convention on Psychotropic Substances. The Committee considered that there is sufficient evidence that pentedrone 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. 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 pentedrone be placed in Schedule II under the United Nations 1971 Convention on Psychotropic Substances.

**Ethylphenidate (EPH)**

Chemically, ethylphenidate is ethyl phenyl(piperidin-2-yl)acetate.

Ethylphenidate was not previously pre-reviewed or critically reviewed. A direct critical review is proposed based on information brought to the attention of the WHO that ethylphenidate is clandestinely manufactured, poses serious 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 ethylphenidate (ethyl phenyl(piperidin-2-yl)acetate) is substantial. Therapeutic usefulness has not been recorded. It recognized that it has similar abuse and similar ill-effects as substances in Schedule II of the United Nations 1971 Convention on Psychotropic Substances. The Committee considered that there is sufficient evidence that ethylphenidate 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. 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 ethylphenidate be placed in Schedule II under the United Nations 1971 Convention on Psychotropic Substances.

**MPA (Methiopropamine)**

Chemically, methiopropamine is *N*-methyl-1-(thiophen-2-yl)propan-2-amine. It has a chiral centre with two enantiomers.

Methiopropamine was previously critically reviewed by the Committee at its 36th meeting. Owing to the insufficiency of data regarding dependence, abuse and risks to public health, the Committee recommended that methiopropamine not be placed under international control but be kept under surveillance. Subsequent data collected from the literature and from different countries indicated that this substance may cause substantial harm and that it has no medical use warranting an updated critical review.

The Committee considered that the degree of risk to public health and society associated with the abuse of methiopropamine (*N*-methyl-1-(thiophen-2-yl)propan-2-amine) is substantial. Therapeutic usefulness has not been recorded. It recognized that it has similar abuse and similar ill-effects as substances in Schedule II of the United Nations 1971 Convention on Psychotropic Substances. The Committee considered that there is sufficient evidence that methiopropamine 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. 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 methiopropamine be placed in Schedule II under the United Nations 1971 Convention on Psychotropic Substances.

#### **MDMB-CHMICA**

Chemically, MDMB-CHMICA is methyl *N*-{[1-(cyclohexylmethyl)-1*H*-indol-3-yl]carbonyl}-3-methyl-L-valinate. MDMB-CHMICA has a chiral carbon in the butanoic chain. Therefore, two stereoisomers exist: (*S*)-MDMB-CHMICA and (*R*)-MDMB-CHMICA.

MDMB-CHMICA has not been previously pre-reviewed or critically reviewed. A direct critical review is proposed based on information brought to the attention of the WHO that MDMB-CHMICA is clandestinely manufactured, poses serious 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 MDMB-CHMICA (methyl *N*-{[1-(cyclohexylmethyl)-1*H*-indol-3-yl]carbonyl}-3-methyl-L-valinate) is substantial. Therapeutic usefulness has not been recorded. It recognized that it has similar abuse and similar ill-effects as substances in Schedule II of the United Nations 1971 Convention on Psychotropic Substances. The Committee considered that there is sufficient evidence that MDMB-CHMICA 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. 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 MDMB-CHMICA be placed in Schedule II under the United Nations 1971 Convention on Psychotropic Substances.

#### **5F-APINACA (5F-AKB-48)**

Chemically, 5F-APINACA is *N*-(adamantan-1-yl)-1-(5-fluoropentyl)-1*H*-indazole-3-carboxamide.

5F-APINACA has not been previously pre-reviewed or critically reviewed by the Expert Committee on Drug Dependence of WHO. A direct critical review is proposed based on information brought to the attention of the WHO that 5F-APINACA is clandestinely manufactured, poses serious 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 5F-APINACA (*N*-(adamantan-1-yl)-1-(5-fluoropentyl)-1*H*-indazole-3-carboxamide) is substantial. Therapeutic usefulness has not been recorded. It recognized that it has similar abuse and similar ill-effects as substances in Schedule II of the United Nations 1971 Convention on Psychotropic Substances. The Committee considered that there is sufficient evidence that 5F-APINACA 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. 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 5F-APINACA be placed in Schedule II under the United Nations 1971 Convention on Psychotropic Substances.

#### **XLR-11**

Chemically, XLR-11 is [1-(5-fluoropentyl)-1*H*-indol-3-yl](2,2,3,3-tetramethylcyclopropyl)methanone.

XLR-11 has not been previously pre-reviewed or critically reviewed. A direct critical review is proposed based on information brought to WHO's attention that XLR-11 is clandestinely manufactured, poses serious 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 XLR-11 ([1-(5-fluoropentyl)-1*H*-indol-3-yl](2,2,3,3-tetramethylcyclopropyl)methanone) is substantial. Therapeutic usefulness has not been recorded. It recognized that it has similar abuse and similar ill-effects as substances in Schedule II of the United Nations 1971 Convention on Psychotropic Substances such as JWH-018 and AM-2201. The Committee considered that there is sufficient evidence that XLR-11 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. 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 XLR-11 be placed in Schedule II under the United Nations 1971 Convention on Psychotropic Substances.

#### **Substance recommended for critical review:**

##### **3-Methylmethcathinone (3-methyl-N-methylcathinone; 3-MMC)**

Chemically, 3-MMC is 2-(methylamino)-1-(3-methylphenyl)propan-1-one. 3-MMC contains a chiral centre at the C-2 carbon of the propane sidechain, so two enantiomers exist: (*R*)-3-MMC and (*S*)-3-MMC.

3-MMC was not previously pre-reviewed or critically reviewed. A direct critical review is proposed based on information brought to the attention of the WHO that 3-MMC is clandestinely manufactured, poses serious risk to public health and society, and has no recognized therapeutic use by any Party.

The Committee deliberated at length regarding the information available pertinent to the degree of risk to public health and society associated with the abuse of 3-MMC (2-(methylamino)-1-(3-methylphenyl)propan-1-one). The Committee decided that the information as currently provided, and the ensuing discussions that had occurred, were inadequate to form a consensus and confident recommendation regarding the scheduling of 3-MMC. As per paragraph 59 of the *Guidance on the WHO review of psychoactive substances for international control*, and as supported by its procedural reference to the *Thirty-fourth report of the WHO Expert Committee on Drug Dependence*, "... in cases where additional information concerning the substance under review is required, the Committee may decide that it will reach a final opinion at a subsequent meeting." "... then it should request another critical review in order to refer the matter to a subsequent Expert Committee." As directed by these guidelines, the Committee requested that the Secretariat arrange another critical review of 3-MMC at a subsequent Expert Committee.

## Substance recommended for surveillance:

### JWH-073

Chemically, JWH-073 is (1-butyl-1*H*-indol-3-yl)(1-naphthyl)methanone.

During its 36th meeting, the WHO Expert Committee on Drug Dependence discussed the critical review report on JWH-073 and concluded that owing to the current insufficiency of data regarding dependence, abuse and risks to public health, JWH-073 should not be placed under international control at that time but be kept under surveillance. New information on its pharmacology and abuse potential warranted an update of the critical review report for discussion at the 38th ECDD.

The available pharmacodynamic data related to JWH-073 (1-butyl-1*H*-indol-3-yl)(1-naphthyl)methanone) demonstrates that this substance has the capacity to produce some effects similar to its homologue, JWH-018, that is included in Schedule II of the United Nations 1971 Convention on Psychotropic Substances. However, the data currently available does not make it possible to establish a direct link between JWH-073 abuse and appearance of public health and social problems that would be a requirement for placing this substance under international control. It is therefore recommended not to place JWH-073 under international control but to continue to keep it under surveillance.

## Update on cannabis and cannabis resin:

At the 37th ECDD meeting the Committee requested that Secretariat begin collecting data towards a pre-review of cannabis, cannabis resin, extracts and tinctures of cannabis at a future meeting. Consistent with this request, two updates on the scientific literature on cannabis were prepared and subsequently presented to the Expert Committee. Following its deliberations the Committee noted that the current Schedule I of the 1961 Convention groups together cannabis and cannabis resin, extracts and tinctures of cannabis. Cannabis plant and cannabis resin are also in Schedule IV of the 1961 Convention. The Committee further noted that there are natural and synthetic cannabinoids in Schedule I and Schedule II of the 1971 Convention. The committee recognized:

- An increase in the use of cannabis and its components for medical purposes
- The emergence of new cannabis-related pharmaceutical preparations for therapeutic use
- Cannabis has never been subject to a formal pre-review or critical review by the ECDD.

The Committee requested that the Secretariat prepare relevant documentation in accordance with the *Guidance on the WHO review of psychoactive substances for international control* in order to conduct pre-reviews for the following substances:

- Cannabis plant and cannabis resin
- Extracts and tinctures of cannabis
- Delta-9-tetrahydrocannabinol (THC)
- Cannabidiol (CBD)
- Stereoisomers of THC.

The Committee recommended that these pre-reviews be evaluated at a specific ECDD meeting dedicated to cannabis and its component substances to be held within the next eighteen months from the 38th meeting.

The purpose of the pre-review is to determine whether current information justifies an Expert Committee critical review. The categories of information for evaluating substances in pre-reviews are identical to those used in critical reviews. The pre-review is a preliminary analysis, and findings at this stage should not determine whether the control status of a substance should be changed.

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