

is responsible for oversight and implementation of the MSP provisions as part of its overall authority for the Medicare program. The CMS accomplishes this through a combination of direct CMS action and work by CMS' contractors. The CMS efforts include policy and operational guidelines, including regulations (as necessary), as well as oversight over contractor MSP responsibilities. As a result of litigation in the mid-1990's, certain GHP insurers were mandated to report coverage information for a number of years. Subsequent to this litigation related mandatory reporting, CMS instituted a Voluntary Data Sharing Agreement (VDSA) effort which expanded the scope of the GHP participants and added some NGHP participants. This VDSA process complemented the IRS/SSA/CMS Data Match reporting by employers, but clearly did not include the universe of primary payers and had few NGHP participants. Both GHP and NGHP entities have had and continue to have the responsibility for determining when they are primary to Medicare and to pay appropriately, even without the mandatory Section 111 process. In order to make this determination, they should already and always be collecting most of the information CMS will require in connection with Section 111 of the MMSEA. Section 111 establishes separate mandatory reporting requirements for GHP arrangements as well as for liability insurance (including self-insurance), no-fault insurance, and workers' compensation, these may collectively be referred to as "Non-GHP or NGHP." *Form Number:* CMS-10265 (OMB control number: 0938-1074); *Frequency:* Yearly, Quarterly; *Affected Public:* Private Sector (Business or other for-profits); *Number of Respondents:* 19,248; *Total Annual Responses:* 5,019,248; *Total Annual Hours:* 557,826. (For policy questions regarding this collection contact John Albert at 410-786-7457.)

Dated: January 5, 2017.

William N. Parham, III,

Director, Paperwork Reduction Staff, Office of Strategic Operations and Regulatory Affairs.

[FR Doc. 2017-00298 Filed 1-10-17; 8:45 am]

BILLING CODE 4120-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2016-N-4619]

International Drug Scheduling; Convention on Psychotropic Substances; Single Convention on Narcotic Drugs; World Health Organization; Scheduling Recommendations; 4-Methylethcathinone and Nine Other Substances; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is providing interested persons with the opportunity to submit written comments, and to request an informal public meeting concerning recommendations by the World Health Organization (WHO) to impose international manufacturing and distributing restrictions, under international treaties, on certain drug substances. The comments received in response to this notice and/or public meeting will be considered in preparing the United States' position on these proposals for a meeting of the United Nations Commission on Narcotic Drugs (CND) in Vienna, Austria, in March 2017. This notice is issued under the Controlled Substances Act (CSA).

DATES: Submit either electronic or written comments by February 10, 2017. Submit requests for a public meeting on or before January 23, 2017. The short time period for the submission of comments and requests for a public meeting is needed to ensure that HHS may, in a timely fashion, carry out the required action and be responsive to the United Nations. For additional information, see section IV of this document.

ADDRESSES: You may submit comments as follows:

Electronic Submissions

Submit electronic comments in the following way:

- **Federal eRulemaking Portal:** <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted,

such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.

- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- **Mail/Hand delivery/Courier (for written/paper submissions):** Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

- For written/paper comments submitted to the Division of Dockets Management, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2016-N-4619 for "International Drug Scheduling; Convention on Psychotropic Substances; Single Convention on Narcotic Drugs; World Health Organization; Scheduling Recommendations; 4-Methylethcathinone and Nine Other Substances; Request for Comments." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at <https://www.regulations.gov> or at the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

- **Confidential Submissions—**To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on

<https://www.regulations.gov>. Submit both copies to the Division of Dockets Management. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <http://www.fda.gov/regulatoryinformation/dockets/default.htm>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: James R. Hunter, Center for Drug Evaluation and Research, Controlled Substance Staff, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 5150, Silver Spring, MD 20993-0002, 301-796-3156, james.hunter@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

The United States is a party to the 1971 Convention on Psychotropic Substances (Psychotropic Convention). Section 201(d)(2)(B) of the CSA (21 U.S.C. 811(d)(2)(B)) provides that when the United States is notified under Article 2 of the Psychotropic Convention that the CND proposes to decide whether to add a drug or other substance to one of the schedules of the Psychotropic Convention, transfer a drug or substance from one schedule to another, or delete it from the schedules, the Secretary of State must transmit notice of such information to the Secretary of Health and Human Services (Secretary of HHS). The Secretary of HHS must then publish a summary of such information in the **Federal Register** and provide opportunity for interested persons to submit comments. The Secretary of HHS must then evaluate the proposal and furnish a recommendation to the Secretary of State that shall be binding on the representative of the United States in

discussions and negotiations relating to the proposal.

As detailed in the following paragraphs, the Secretary of State has received notification from the Secretary-General of the United Nations (the Secretary-General) regarding eight substances to be considered for control under the Psychotropic Convention. This notification reflects the recommendation from the 38th WHO Expert Committee for Drug Dependence (ECDD), which met in November 2016. In the **Federal Register** of September 19, 2016 (81 FR 64162), FDA announced the WHO ECDD review and invited interested persons to submit information for WHO's consideration.

The full text of the notification from the Secretary-General is provided in section II of this document. Section 201(d)(2)(B) of the CSA requires the Secretary of HHS, after receiving a notification proposing scheduling, to publish a notice in the **Federal Register** to provide the opportunity for interested persons to submit information and comments on the proposed scheduling action.

The United States is also a party to the 1961 Single Convention on Narcotic Drugs (1961 Single Convention). The Secretary of State has received a notification from the Secretary-General regarding two substances to be considered for control under this convention. The CSA does not require HHS to publish a summary of such information in the **Federal Register**. Nevertheless, in an effort to provide interested and affected persons an opportunity to submit comments regarding the WHO recommendations for narcotic drugs, the notification regarding these substances is also included in this **Federal Register** notice. The comments will be shared with other relevant Agencies to assist the Secretary of State in formulating the position of the United States on the control of these substances. The HHS recommendations are not binding on the representative of the United States in discussions and negotiations relating to the proposal regarding control of substances under the 1961 Single Convention.

II. United Nations Notification

The formal notification from the United Nations that identifies the drug substances and explains the basis for the recommendations is reproduced as follows (non-relevant text removed):

Reference:
NAR/CL.8/2016
WHO/ECDD38; 1961C-Art.3; 1971C-Art.2
CU 2016/495/DTA/SGB

The Secretary-General of the United Nations presents his compliments to the

Secretary of State of the United States of America and has the honour to inform the Government that the Director-General of the World Health Organization (WHO), pursuant to article 3, paragraphs 1 and 3 of the Single Convention on Narcotic Drugs of 1961 as amended by the 1972 Protocol (1961 Convention) and article 2, paragraphs 1 and 4 of the Convention on Psychotropic Substances of 1971 (1971 Convention) notified the Secretary-General of the following recommendations:

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

- U-4770
chemical name: 3,4-dichloro-N-(2-dimethylamino-cyclohexyl)-N-methylbenzamide
- butorfentanyl
chemical name: N-phenyl-N-[1-(2-phenylethyl)-4-piperidinyl]butanamide
- Substances recommended to be placed in Schedule II of the 1971 Convention:
- 4-MEC (4-methylethcathinone)
chemical name: 2-(ethylamino)-1-(4-methylphenyl)propan-1-one
- ethylone
chemical name: 1-(2H-1,3-benzodioxol-5-yl)-2-(ethylamino)propan-1-one
- pentedrone
chemical name: 2-(methylamino)-1-phenylpentan-1-one
- ethylphenidate
chemical name: ethyl phenyl(piperidin-2-yl)acetate
- MPA (methiopropamine)
chemical name: N-methyl-1-(thiophen-2-yl)propan-2-amine
- MDMB-CHMICA
chemical name: methyl N-([1-(cyclohexylmethyl)-1H-indol-3-yl]carbonyl)-3-methyl-L-valinate
- 5F-APINACA (5F-AKB-48)
chemical name: N-(adamantan-1-yl)-1-(5-fluoropentyl)-1H-indazole-3-carboxamide
- XLR-11
chemical name: [1-(5-fluoropentyl)-1H-indol-3-yl](2,2,3,3-tetramethylcyclopropyl)methanone

In addition, in the letter from the Director-General of the World Health Organization to the Secretary-General, reference is also made to the recommendations by the thirty-eighth meeting of the WHO Expert Committee on Drug Dependence (ECDD) for carrying out a critical review of one substance at a subsequent Expert Committee meeting, as well as for one substance to continue to be kept under surveillance. Furthermore, the letter also makes reference to the recommendation by the Expert Committee with regard to cannabis and its component substances.

In accordance with the provisions of article 3, paragraph 2 of the 1961 Convention and article 2, paragraph 2 of the 1971 Convention, the Secretary-General hereby transmits the notification as annex I to the present note. In accordance with the provisions of article 3, paragraph 2 of the 1961 Convention and article 2, paragraph 2 of the 1971 Convention, the notification from WHO will be brought to

the attention of the sixtieth session of the Commission on Narcotic Drugs (13–17 March 2017).

In connection with the notification, WHO has also submitted the relevant extract from the report of the thirty-eighth meeting of the WHO Expert Committee on Drug Dependence which is hereby transmitted as annex II.

In order to assist the Commission in reaching a decision, it would be appreciated if the Government could communicate any economic, social, legal, administrative or other factors that it considers relevant to the possible scheduling of the afore-mentioned substances that are recommended by WHO to be placed under international control under the 1961 Convention (namely: U-4770 and butyrfentanyl) and the 1971 Convention (namely: 4-MEC, ethylone, pentadone, ethylphenidate, MPA, MDMB-CHMICA, 5F-APINACA, and XLR-11).

Communications are to be sent at the latest by 20 January 2017 to the Executive Director of the United Nations Office on Drugs and Crime, c/o Secretary, Commission on Narcotic Drugs, P.O. Box 500, 1400 Vienna, Austria, fax: +43-1-26060-5885, email: sgb@unodc.org.

21 December 2016

His Excellency
Mr. John Kerry
Secretary of State of the United States of America

Annex I

Letter Addressed to the Secretary-General of the United Nations From the Director-General of the World Health Organization

“The Thirty-eighth meeting of the WHO Expert Committee on Drug Dependence convened from 14 to 18 November 2016, at WHO headquarters in Geneva. The objective of this meeting was to carry out an in-depth evaluation of psychoactive substances in order to determine whether or not WHO should recommend these substances to be placed under international control.

With reference to Article 2, paragraphs 1 and 4 of the Convention on Psychotropic Substances (1971) and Article 3, paragraphs 1 and 3 of the Single Convention on Narcotic Drugs (1961), as amended by the 1972 Protocol, I am pleased to submit recommendations of the World Health Organization as follows:

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

—U-47700

chemical name: 3,4-dichloro-N-(2-dimethylamino-cyclohexyl)-N-methylbenzamide

—butyrfentanyl

chemical name: N-phenyl-N-[1-(2-phenylethyl)-4-piperidinyl]butanamide to be placed in Schedule II of the Convention on Psychotropic Substances (1971):

—4-MEC (4-methylethcathinone)

chemical name: 2-(ethylamino)-1-(4-methylphenyl)propan-1-one

—ethylone

chemical name: 1-(2H-1,3-benzodioxol-5-yl)-2-(ethylamino)propan-1-one

—pentadone

chemical name: 2-(methylamino)-1-phenylpentan-1-one

—ethylphenidate

chemical name: ethyl phenyl(piperidin-2-yl)acetate

—MPA (methiopropamine)

chemical name: N-methyl-1-(thiophen-2-yl)propan-2-amine

—MDMB-CHMICA

chemical name: methyl N-[(1-(cyclohexylmethyl)-1H-indol-3-yl)carbonyl]-3-methyl-L-valinate

—5F-APINACA (5F-AKB-48)

chemical name: N-(adamantan-1-yl)-1-(5-fluoropentyl)-1H-indazole-3-carboxamide

—XLR-11

chemical name: [1-(5-fluoropentyl)-1H-indol-3-yl](2,2,3,3-tetramethylcyclopropyl)methanone.

In addition, the Expert Committee recommended to carry out a critical review at a subsequent Expert Committee meeting for:

—3-MMC (3-Methylmethcathinone)

chemical name: 2-(methylamino)-1-(3-methylphenyl)propan-1-one

It also recommended to continue to keep the following substance under surveillance:

—JWH-073

chemical name: (1-butyl-1H-indol-3-yl)(1-naphthyl)methanone

The Committee recommended that a specific ECDD meeting dedicated to cannabis and its component substances should be held within the next eighteen months from the 38th meeting, and will carry out 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 recommendations and the assessments and findings on which they are based are set out in detail in the Report of the 38th Expert Committee on Drug Dependence, which is the Committee that advises me on these issues. An extract of the Committee's Report is attached in Annex 1 to this letter.

I am very pleased with the ongoing collaboration among the United Nations Office on Drugs and Crime (UNODC), International Narcotics Control Board (INCB) and WHO, in particular, how this collaboration has supported the work of the WHO Expert Committee on Drug Dependence, and more generally, the implementation of operational recommendations from the United Nations General Assembly Special Session (UNGASS) 2016.”

NAR/CL.8/2016

Annex II

Extract From the Report of the 38th Expert Committee on Drug Dependence

Substances recommended to be scheduled in Schedule I and Schedule IV 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-methylbenzamide. U47700 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-methylbenzamide) 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-piperidinyl]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 UN 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 UN 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 UN 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 UN 1971 Convention on Psychotropic Substances.

Pentedrone (α -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 UN 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 UN 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 UN 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 UN 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 UN 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 UN 1971 Convention on Psychotropic Substances.

MDMB-CHMICA

Chemically, MDMB-CHMICA is methyl N-{{[1-(cyclohexylmethyl)-1H-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)-1H-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 UN 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 UN 1971 Convention on Psychotropic Substances.

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

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

5F-APINACA has not been previously pre-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 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)-1H-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 UN 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 UN 1971 Convention on Psychotropic Substances.

XLR-11

Chemically, XLR-11 is [1-(5-fluoropentyl)-1H-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)-1H-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 UN 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 UN 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-1H-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-1H-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 UN 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.

III. Discussion

Although WHO has made specific scheduling recommendations for each of the drug substances, the CND is not obliged to follow the WHO recommendations. Options available to the CND for substances considered for control under the Psychotropic Convention include the following: (1) Accept the WHO recommendations; (2) accept the recommendations to control, but control the drug substance in a schedule other than that recommended; or (3) reject the recommendations entirely.

U-47700 is a synthetic opioid drug developed in the 1970s. U-47700 is structurally related to the opioid AH-7921. U-47700 is selective for the μ -opioid receptor. U-47700 has never been studied on humans, but would be expected to produce effects similar to those of other potent opioid agonists, including strong analgesia, sedation, euphoria, constipation, itching, and respiratory depression which could be harmful or fatal. Overdoses and

overdose fatalities have been directly attributed to U-47700 misuse. There have been reports of U-47700 being encountered in counterfeit pills. On November 14, 2016, the U.S. Drug Enforcement Administration (DEA) temporarily scheduled U-47700 into schedule I pursuant to the temporary scheduling provisions of the Controlled Substances Act. As such, additional permanent controls will be necessary to fulfill U.S. obligations if U-47700 is controlled under Schedule I of the 1961 Single Convention.

Butyrylfentanyl (butyrylfentanyl) is a synthetic opioid and analog of fentanyl. Fentanyl is controlled in Schedule II of the CSA, and an active ingredient in drug products approved for medical use and marketed in the United States. Butyrylfentanyl has a pharmacological profile similar to that of fentanyl and other μ -opioid receptor agonists. Risks associated with abuse of butyrylfentanyl include development of substance use disorder, overdose, and death similar to that of other μ -opioid agonists. The DEA is aware of at least 40 confirmed fatalities associated with butyrylfentanyl. It has no approved medical use in the United States. On May 12, 2016, butyrylfentanyl was temporarily placed into Schedule I of the CSA for 2 years upon finding that it posed an imminent hazard to the public safety. The Attorney General, though, may extend this temporary scheduling for up to 1 year. As such, additional permanent controls will be necessary to fulfill U.S. obligations if butyrylfentanyl is controlled under Schedule I of the 1961 Single Convention.

4-Methylethcathinone (4-MEC), 3-Methylmethcathinone (3-methyl-N-methylcathinone; 3-MMC): 3-methylmethcathinone (3-MMC), pentadrone, and ethylone (3,4-methylenedioxy-N-ethylcathinone; bk-MDEA; MDEC) are synthetic cathinones that are structurally and pharmacologically similar to amphetamine, 3-4-methylenedioxymethamphetamine (MDMA), cathinone, and other related substances. These substances are central nervous system stimulants with psychoactive properties similar to Schedule I and II amphetamine type substances. Public health risks associated with the use of synthetic cathinones suggest that these substances are associated with cardiac, psychiatric, and neurological symptoms that may lead to emergency department admissions, violent behaviors causing harm to self or others, or death. 4-MEC and pentadrone have no known medical use in the United States. On March 7, 2014, the DEA published a final order

in the **Federal Register** amending 21 CFR 1308.11(h) to temporarily place 4-MEC and pentadrone into Schedule I of the CSA pursuant to the temporary scheduling provisions of 21 U.S.C. 811(h). On March 4, 2016, the temporary Schedule I status of 4-MEC and pentadrone was extended for 1 year, or until permanent scheduling is completed. Permanent scheduling for 4-MEC and pentadrone was initiated on March 4, 2016, upon publication of the notice of proposed rulemaking. As such, additional permanent controls will be necessary to fulfill U.S. obligations if 4-MEC and pentadrone is controlled under Schedule II of the 1971 Convention on Psychotropic Substances.

In the United States, ethylone has been sold as the street drug “Molly” and encountered as a replacement for methylone. Ethylone has no known medical use in the United States. As a positional isomer of the controlled drug butylone, ethylone is considered a Schedule I controlled substance under the CSA. As such, no additional controls will be necessary to fulfill U.S. obligations if ethylone is controlled under Schedule II of the 1971 Convention on Psychotropic Substances.

Ethylphenidate is structurally related to methylphenidate. Methylphenidate is controlled in Schedule IV of the CSA, and an active ingredient in drug products approved for medical use and marketed in the United States. Ethylphenidate is not approved for medical use in the United States. Ethylphenidate is structurally related to methylphenidate are being marketed as novel psychoactive substances with psychoactive effects similar to methylphenidate, therefore posing similar health risks to the users. Ethylphenidate is a controlled substance in several European countries, and is not a controlled substance in the United States under the CSA. As such, additional permanent controls will be necessary to fulfill U.S. obligations if ethylphenidate is controlled under Schedule II of the 1971 Convention on Psychotropic Substances.

Methiopropamine (MPA) is a structural analogue of the Schedule II controlled substance methamphetamine. Pharmacologically, it functions as a norepinephrine-dopamine reuptake inhibitor and, secondarily, as a serotonin reuptake inhibitor. MPA is a thiophene based analog of methamphetamine. It has stimulant properties as an inhibitor of dopamine, norepinephrine transporters in the central nervous system. MPA is not approved for medical use or controlled

in the United States under the CSA. As such, additional permanent controls will be necessary to fulfill U.S. obligations if MPA is controlled under Schedule II of the 1971 Convention on Psychotropic Substances.

MDMB-CHMICA is an indole-based synthetic cannabinoid that is a potent full agonist at cannabinoid type 1 (CB1) receptors and mimics functionally (biologically) the effects of the structurally unrelated delta-9-tetrahydrocannabinol, a Schedule I substance, and the main active ingredient of marijuana. Synthetic cannabinoids are marketed under the guise of “herbal incense,” and promoted by drug traffickers as legal alternatives to marijuana. MDMB-CHMICA use is associated with serious adverse events including death in several European countries. There are no commercial or approved medical uses for MDMB-CHMICA. MDMB-CHMICA is not controlled under the CSA, but may be treated as a “controlled substance analogue” under the CSA pursuant to 21 U.S.C. 802(32)(A) and 813, and is a controlled substance in the State of Louisiana. As such, additional permanent controls will be necessary to fulfill U.S. obligations if MDMB-CHMICA is controlled under Schedule II of the 1971 Convention on Psychotropic Substances.

5F-APINACA (5F-AKB48) is a synthetic cannabinoid belonging to a chemical structural class with an indazole core. In vitro studies show that it binds to the CB1 receptors and displays agonist properties in functional assays, suggesting that it would share in vivo effects with delta-9-THC and various synthetic cannabinoids. There are no commercial or medical uses for 5F-APINACA. Synthetic cannabinoids are marketed under the guise of “herbal incense,” and promoted by drug traffickers as legal alternatives to marijuana. SF-APINACA is not a controlled substance under the CSA, but may be treated as a “controlled substance analogue” under the CSA pursuant to 21 U.S.C. 802(32)(A) and 813. As such, additional permanent controls will be necessary to fulfill U.S. obligations if SF-APINACA is controlled under Schedule II of the 1971 Convention on Psychotropic Substances.

XLR-11 (5-Fluoro-UR-144, 5F-UR-144) is an indole-based synthetic cannabinoid and acts as an agonist at CB1 receptors. Animal studies indicate that it mimics functionally (biologically) the effects of the structurally unrelated delta-9-THC, a Schedule I substance, and the main active ingredient of marijuana and numerous other

Schedule I synthetic cannabinoids. Synthetic cannabinoids are marketed under the guise of “herbal incense,” and promoted by drug traffickers as legal alternatives to marijuana. On May 11, 2016, XLR11 was permanently controlled as a Schedule I substance under the CSA. As such, additional permanent controls will not be necessary to fulfill U.S. obligations if XLR-11 is controlled under Schedule II of the 1971 Convention on Psychotropic Substances.

FDA, on behalf of the Secretary of HHS, invites interested persons to submit comments on the notifications from the United Nations concerning these drug substances. FDA, in cooperation with the National Institute on Drug Abuse, will consider the comments on behalf of HHS in evaluating the WHO scheduling recommendations. Then, under section 201(d)(2)(B) of the CSA, HHS will recommend to the Secretary of State what position the United States should take when voting on the recommendations for control of substances under the Psychotropic Convention at the CND meeting in March 2017.

Comments regarding the WHO recommendations for control of U-47700 and Butyrylfentanyl under the 1961 Single Convention will also be forwarded to the relevant Agencies for consideration in developing the U.S. position regarding narcotic substances at the CND meeting.

IV. Opportunity for Public Meeting

FDA does not presently plan to hold a public meeting. If any person believes that, in addition to written comments, a public meeting would contribute to the development of the U.S. position on the substances to be considered for control under the Psychotropic Convention, a request for a public meeting and the reasons for such a request should be sent to James R. Hunter (see **FOR FURTHER INFORMATION CONTACT**) on or before January 23, 2017.

Dated: January 5, 2017.

Leslie Kux,

Associate Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2014-D-1862]

Recommended Warning for Over-the-Counter Acetaminophen-Containing Drug Products and Labeling Statements Regarding Serious Skin Reactions; Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a guidance for industry entitled “Recommended Warning for Over-the-Counter Acetaminophen-Containing Drug Products and Labeling Statements Regarding Serious Skin Reactions.” This guidance is intended to inform manufacturers, members of the medical and scientific community, and other interested persons that at this time FDA does not intend to take action against the marketing of single- and combination-ingredient, acetaminophen-containing, nonprescription (commonly referred to as over-the-counter (OTC)) drug products bearing a warning as described in the guidance alerting consumers that the use of acetaminophen may cause severe skin reactions.

DATES: Submit either electronic or written comments on Agency guidances at any time.

ADDRESSES: You may submit comments as follows:

Electronic Submissions

Submit electronic comments in the following way:

- **Federal eRulemaking Portal:** <http://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <http://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <http://www.regulations.gov>.

- If you want to submit a comment with confidential information that you do not wish to be made available to the public submit the comment as a written/paper submission and in the manner detailed (see “Written/Paper Submissions” and “Instructions”).

Written/Paper Submissions

Submit written/paper submissions as follows:

- **Mail/Hand delivery/Courier (for written/paper submissions):** Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

- For written/paper comments submitted to the Division of Dockets Management, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in “Instructions.”

Instructions: All submissions received must include the Docket No. FDA-2014-D-1862 for “Recommended Warning for Over-the-Counter Acetaminophen-Containing Drug Products and Labeling Statements Regarding Serious Skin Reactions; Guidance for Industry.” Received comments will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at <http://www.regulations.gov> or at the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

- **Confidential Submissions—**To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <http://www.regulations.gov>. Submit both copies to the Division of Dockets Management. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other