regulated drug products on a variety of topics related to consumer, patient, or healthcare professional perceptions and use of drug products and related materials. These materials may include, but are not limited to direct-to-consumer prescription drug promotion, physician labeling of prescription drugs, medication guides, over-the-counter drug labeling, emerging risk communications, patient labeling, online sales of medical products, and consumer and professional education.

In the **Federal Register** of July 17, 2019 (84 FR 34186), FDA published a 60-day notice requesting public comment on the proposed collection of information. No comments were received.

Annually, we project that 20 studies will be initiated using 160 focus groups with an average of 9 persons per group. We assume each focus group will last an average of 1.75 hours.

We estimate the burden for the information collection as follows:

TABLE 1—ESTIMATED ANNUAL REPORTING BURDEN [1]

Activity	Number of respondents	Number of responses per respondent	Total annual responses	Average burden per response	Total hours
Focus Group Study	1,440	1	1,440	1.75	2,520

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.

Based on a review of the information collection since our last request for OMB approval, we have made no adjustments to our burden estimate.

Dated: December 18, 2019.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

[FR Doc. 2019–28247 Filed 12–30–19; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2019–N–5955]

International Drug Scheduling; Convention on Psychotropic Substances; Single Convention on Narcotic Drugs; World Health Organization; Scheduling Recommendations; AB-FUBINACA; 5F-AMB-PINACA; 5F-MDMB-PICA; 4-F-MDMB-BINACA; 4-CMC; N-ethylhexedrone; alpha-PHP; DOC; Crotonyl Fentanyl; Valeryl Fentanyl; Flualprazolam and Etizolam; 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 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 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 2020. This notice is issued under the Controlled Substances Act (CSA).

DATES: Submit either electronic or written comments by January 30, 2020. The short time period for the submission of comments is needed to ensure that Health and Human Services (HHS) may, in a timely fashion, carry out the required action and be responsive to the United Nations.

ADDRESSES: You may submit comments as follows. Please note that late, untimely filed comments will not be considered. Electronic comments must be submitted on or before January 30, 2020. The *https://www.regulations.gov* electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of January 30, 2020. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

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):* Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, 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-2019-N-5955 for ''International Drug Scheduling; Convention on Psychotropic Substances; Single Convention on Narcotic Drugs; World Health Organization; Scheduling Recommendations; AB-FUBINACA; 5F-AMB-PINACA; 5F-MDMB-PICA; 4-F-MDMB-BINACA; 4-CMC; N-ethylhexedrone; alpha-PHP; DOC; Crotonyl Fentanyl; Valeryl Fentanyl; Flualprazolam and Etizolam; Request for Comments.'' Received comments, those filed in a timely manner (see **ADDRESSES**), will be placed in the docket and, except for those submitted as ''Confidential Submissions,'' publicly viewable at *https://www.regulations.gov* or at the Dockets Management Staff 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 Dockets Management Staff. 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: *https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf.*

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 Dockets Management Staff, 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 (1971 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 1971 Convention that the CND proposes to decide whether to add a drug or other substance to one of the schedules of the 1971 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 ten substances to be considered for control under the 1971 Convention. This notification reflects the recommendation from the 42nd WHO Expert Committee for Drug Dependence (ECDD), which met in October 2019. In the **Federal Register** of September 10, 2019 (84 FR 47521), 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. 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 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, to provide interested and affected persons an opportunity to submit comments regarding the WHO recommendations for drugs under the 1961 Convention, 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 Convention.

II. United Nations Notification

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

Reference: NAR/CL.10/2019 WHO/ECDD42; 1961C-Art.3, 1971C-Art.2 CU 2019/462/DTA/SGB (A)

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 in a letter dated 15 November 2019 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 added to Schedule I of the 1961 Convention:

Crotonyl fentanyl
chemical name: (2E)-N-phenyl-N-[1-(2-phenylethyl)piperidin-4-yl]but-2-enamide

Valeryl fentanyl
chemical name: N-phenyl-N-[1-(2-phenylethyl)piperidin-4-yl]pentanamide

Substance recommended to be added to Schedule I of the 1971 Convention:

DOC
chemical name: 1-(4-chloro-2,5-dimethoxyphenyl)propan-2-amine

Substances recommended to be added to Schedule II of the 1971 Convention:

AB-FUBINACA
chemical name: N-[1-amino-3-methyl-1-oxobutan-2-yl]-1-[(4-fluorophenyl)methyl]-1H-indazole-3-carboxamide

5F-AMB-PINACA (5F-AMB, 5F-MMB-PINACA)
chemical name: methyl 2-{[1-(5-fluoropentyl)-1H-indazole-3-carbonyl]amino}-3-methylbutanoate

5F-MDMB-PICA (5F-MDMB-2201)
chemical name: methyl 2-{[1-(5-fluoropentyl)-1H-indole-3-carbonyl]amino}-3,3-dimethylbutanoate

4F-MDMB-BINACA
chemical name: methyl 2-{[1-(4-fluorobutyl)-1H-indazole-3-carbonyl]amino}-3,3-dimethylbutanoate

4-CMC (4-chloromethcathinone; clephedrone)
chemical name: 1-(4-chlorophenyl)-2-(methylamino)propan-1-one

N-Ethylhexedrone
chemical name: 2-(ethylamino)-1-phenylhexan-1-one
Alpha-PHP
chemical name: 1-phenyl-2-(pyrrolidine-1-yl)hexan-1-one

Substances recommended to be added to Schedule IV of the 1971 Convention:

Flualprazolam
chemical name: 8-chloro-6-(2-fluorophenyl)-1-methyl-4*H*-benzo[*f*][1,2,4]triazolo[4,3-*a*][1,4]diazepine
Etizolam
chemical name: 4-(2-chlorophenyl)-2-ethyl-9-methyl-6H-thieno[3,2f][1,2,4]triazolo[4,3 a][1,4]diazepine

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 connection with the notification, WHO also submitted a summary of the rationale of the recommendations which is hereby transmitted as annex II. For time reasons, this notification and its annexes I and II are transmitted in English only. The notification and its annexes will be transmitted in French and Spanish as soon as available.

Also in accordance with the same provisions, the notification from WHO will be brought to the attention of the 63rd session of the Commission on Narcotic Drugs (2–6 March 2020) in a pre-session document that will be made available in the six official languages of the United Nations on the website of the 63rd session of the CND: *https://www.unodc.org/unodc/en/commissions/CND/session/63_Session_2020/session-63-of-the-commission-on-narcotic-drugs.html.*

In order to assist the Commission in reaching a decision, it would be appreciated if the Government could communicate any comments it considers relevant to the possible scheduling of substances recommended by WHO to be placed under international control under the 1961 Convention, namely: Crotonyl fentanyl, Valeryl fentanyl, as well as any economic, social, legal, administrative or other factors that it considers relevant to the possible scheduling of substances recommended by WHO to be placed under international control under the 1971 Convention, namely: DOC, AB-FUBINACA, 5F-AMB-PINACA (5F-AMB, 5F-MMB-PINACA), 5F-MDMB-PICA (5F-MDMB-2201), 4F-MDMB-BINACA, 4-CMC (4-chloromethcathinone; clephedrone), N-Ethylhexedrone, Alpha-PHP, Flualprazolam, Etizolam.

Communications should be sent 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, email: *unodc-sgb@un.org* (fax: +43–1–26060–5885), no later than by 31 January 2020.

2 December 2019

His Excellency,
Mr. Rex Tillerson,
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 Forty-second meeting of the WHO Expert Committee on Drug Dependence was convened from 21 to 25 October 2019 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 WHO should recommend these substances to be placed under international control or if their level of control should be changed.

The Forty-second Meeting reviewed thirteen psychoactive substances, five of which are synthetic cannabinoids, four synthetic stimulants, two fentanyl analogues, and two benzodiazepines. In addition, the Meeting carried out a pre-review of preparations of acetyldihydrocodeine, codeine, dihydrocodeine, ethylmorphine, nicocodine, nicodicodine, norcodeine and pholcodine that are listed in Schedule III of the 1961 Convention on Narcotic Drugs.

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

To be added to Schedule I of the Single Convention on Narcotic Drugs (1961):

Crotonyl fentanyl
chemical name: (2E)-N-phenyl-N-[1-(2-phenylethyl)piperidin-4-yl]but-2-enamide
Valeryl fentanyl
chemical name: N-phenyl-N-[1-(2-phenylethyl)piperidin-4-yl]pentanamide

To be added to Schedule I of the Convention on Psychotropic Substances (1971):

DOC
chemical name: 1-(4-chloro-2,5-dimethoxyphenyl)propan-2-amine

To be added to Schedule II of the Convention on Psychotropic Substances (1971):

AB-FUBINACA
chemical name: N-[1-amino-3-methyl-1-oxobutan-2-yl]-1-[(4-fluorophenyl)methyl]-1H-indazole-3-carboxamide
5F-AMB-PINACA (5F-AMB, 5F-MMB-PINACA)
chemical name: methyl 2-{[1-(5-fluoropentyl)-1H-indazole-3-carbonyl]amino}-3-methylbutanoate
5F-MDMB-PICA (5F-MDMB-2201)
chemical name: methyl 2-{[1-(5-fluoropentyl)-1H-indole-3-carbonyl]amino}-3,3-dimethylbutanoate
4-F-MDMB-BINACA
chemical name: methyl 2-{[1-(4-fluorobutyl)-1H-indazole-3-carbonyl]amino}-3,3-dimethylbutanoate
4-CMC (4-chloromethcathinone; clephedrone)
chemical name: 1-(4-chlorophenyl)-2-(methylamino)propan-1-one
N-ethylhexedrone
chemical name: 2-(ethylamino)-1-phenylhexan-1-one
Alpha-PHP
chemical name: 1-phenyl-2-(pyrrolidine-1-yl)hexan-1-one

To be added to Schedule IV of the Convention on Psychotropic Substances (1971):

Flualprazolam
chemical name: 8-chloro-6-(2-fluorophenyl)-1-methyl-4*H*-benzo[*f*][1,2,4]triazolo[4,3-*a*][1,4]diazepine
Etizolam
chemical name: 4-(2-chlorophenyl)-2-ethyl-9-methyl-6H-thieno[3,2f][1,2,4]triazolo [4,3-a][1,4]diazepine

To be kept under surveillance:

APINACA (AKB-48)
chemical name: N-(adamantan-1-yl)-1-pentyl-1H-indazole-3-carboxamide

To proceed to critical review:

—Preparations of acetyldihydrocodeine, codeine, dihydrocodeine, ethylmorphine, nicocodine, nicodicodine, norcodeine and pholcodine listed in Schedule III of the 1961 Single Convention on Narcotic Drugs

The assessments and findings on which these recommendations are based are set out in detail in the report of the Forty-second Meeting of the WHO Expert Committee on Drug Dependence.

A summary of the rationale of these recommendations is attached in Annex 1 of this letter.

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

Annex II

Summary of the Rationale for the Recommendations of the 42nd Expert Committee on Drug Dependence

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

Crotonyl fentanyl

The chemical name for crotonyl fentanyl is (2E)-N-phenyl-N-[1-(2-phenylethyl)piperidin-4-yl]but-2-enamide.

Crotonyl fentanyl binds to mu opioid receptors and acts as an opioid agonist. In animal models, crotonyl fentanyl produces antinociception, actions predictive of oxycodone-like subjective effects and both central nervous system stimulation and depression. The opioid antagonist naltrexone blocks the effects of crotonyl fentanyl. This pharmacological profile indicates that crotonyl fentanyl is an opioid and comparative studies suggest that it has a potency intermediate between oxycodone and fentanyl.

Consistent with the results from animal studies, the effects of crotonyl fentanyl were reversed by an opioid antagonist in a clinical admission due to overdose. Due to its opioid mechanism of action, crotonyl fentanyl has the potential to be associated with substantial harm.

Crotonyl fentanyl has been found in seized material from countries across several regions. It has no veterinary or medical use.

Based on its opioid mechanism of action and similarity to drugs such as oxycodone and fentanyl that are controlled under Schedule I of the Single Convention on Narcotic Drugs, it is recommended that crotonyl fentanyl also be controlled under Schedule I of the Single Convention on Narcotic Drugs (1961).

Valeryl fentanyl

The chemical name for valeryl fentanyl is N-phenyl-N-[1-(2-phenylethyl)piperidin-4-yl]pentanamide.

Valeryl fentanyl binds to mu opioid receptors and acts as an opioid agonist. In animal models, valeryl fentanyl suppresses opioid withdrawal symptoms, produces antinociception and has actions predictive of oxycodone-like subjective effects. The opioid antagonist naltrexone blocks the effects of valeryl fentanyl. This pharmacological profile indicates that valeryl fentanyl is an opioid and comparative studies suggest that it has a potency less than that of fentanyl.

Valeryl fentanyl has been detected in biological samples from a small number of deaths and cases of driving under the influence of drugs.

Valeryl fentanyl has been detected in seizures from countries across several regions. It has no veterinary or medical use.

Based on the evidence of its opioid mechanism of action and similarity to drugs such as fentanyl that are controlled under Schedule I of the Single Convention on Narcotic Drugs, it is recommended that valeryl fentanyl also be controlled under Schedule I of the Single Convention on Narcotic Drugs (1961).

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

DOC

DOC is also known as 4-chloro-2,5-DMA or 2,5-dimethoxy-4-chloroamphetamine. Its chemical name is 1-(4-chloro-2,5-dimethoxyphenyl)propan-2-amine.

DOC is an agonist at the serotonergic 5–HT2A receptor, a mechanism it shares with hallucinogens such as LSD.

In animal models, DOC has actions predictive of hallucinogenic subjective effects (similar to LSD and DOM) and shows evidence of rewarding effects. It can produce both central nervous system stimulation and depression.

Based on clinical admissions due to overdose, the adverse effects associated with use of DOC include agitation, aggression, hallucinations, tachycardia, hyperthermia and seizures.

DOC has been detected in 40 countries. It has no veterinary or medical use.

Based on its similarity in mechanism of action and effects to currently scheduled hallucinogens such as LSD and DOM, and the evidence that it is abused so as to constitute a public health and social problem, it is recommended that DOC be controlled under the 1971 Convention on Psychotropic Substances. As it has no medical use and its use constitutes a serious risk to public health, it is recommended that it be controlled under Schedule I of 1971 Convention on Psychotropic Substances.

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

AB-FUBINACA

The chemical name for AB-FUBINACA is N-[1-amino-3-methyl-1-oxobutan-2-yl]-1-[(4-fluorophenyl)methyl]-1H-indazole-3-carboxamide.

In common with other synthetic cannabinoids, AB-FUBINACA is a full agonist at the cannabinoid CB1 receptor that mediates the psychoactive effects of cannabinoids. In animal studies, it produced central nervous system depression and other typical cannabinoid behavioural effects and had actions predictive of cannabinoid subjective effects.

AB-FUBINACA produces neurological signs in animals that are indicative of toxicity, including seizures, hyperreflexia and aggression. Based on its mechanism of action, it would be expected to produce a range of adverse effects in human users that include tachycardia, nausea, vomiting, confusion and hallucinations. There are a large number of cases of intoxication resulting from AB-FUBINACA, often in combination with other drugs, and at least one death has been reported that is attributable to the effects of AB-FUBINACA.

AB-FUBINACA use has been reported in over 30 countries across different regions. It has no veterinary or medical use.

Based on its capacity to produce a state of dependence, its ability to produce central nervous system depression and the evidence that it is abused so as to constitute a public health and social problem, it is recommended that AB-FUBINACA be controlled under the 1971 Convention on Psychotropic Substances. As it has no medical use and its use constitutes a substantial risk to public health, it is recommended that it be controlled under Schedule II of 1971 Convention on Psychotropic Substances.

5F-AMB-PINACA

5F-AMB-PINACA is also known as 5F-AMB and 5F-MMB-PINACA. Its chemical name is methyl 2-{[1-(5-fluoropentyl)-1H-indazole-3-carbonyl]amino}-3-methylbutanoate.

In common with other synthetic cannabinoids, 5F-AMB-PINACA is a full agonist at the cannabinoid CB1 receptor that mediates the psychoactive effects of cannabinoids. In animal studies it

produced central nervous system depression and had actions predictive of cannabinoid-like subjective effects. 5F-AMB-PINACA produces impairment of memory and seizures in animals.

5F-AMB-PINACA use has been associated with a number of cases of fatal and non-fatal intoxication often in combination with other drugs. In a case of non-fatal intoxication due to 5F-AMB-PINACA alone, the effects included cognitive impairment, slowed movement, slurred speech and poor coordination. Based on its mechanism of action, it would also be expected to produce a range of other effects in human users that include tachycardia, nausea, vomiting, confusion and hallucinations. 5F-AMB-PINACA has been identified as a causal factor in motor vehicle accidents, some of which were fatal.

5F-AMB-PINACA use has been reported in over 30 countries across different regions. It has no veterinary or medical use.

Based on its capacity to produce a state of dependence, its ability to produce central nervous system depression and the evidence that it is abused so as to constitute a public health and social problem, it is recommended that 5F-AMB-PINACA be controlled under the 1971 Convention on Psychotropic Substances. As it has no medical use and its use constitutes a substantial risk to public health, it is recommended that it be controlled under Schedule II of the 1971 Convention on Psychotropic Substances.

5F-MDMB-PICA

5F-MDMB-PICA is also known as 5F-MDMB-2201. Its chemical name is methyl 2-{[1-(5-fluoropentyl)-1H-indole-3-carbonyl]amino}-3,3-dimethylbutanoate.

In common with other synthetic cannabinoids, 5F-MDMB-PICA is a full agonist at the cannabinoid CB1 receptor that mediates the psychoactive effects of cannabinoids.

Its use has been associated with a number of fatal and non-fatal intoxications that have been characterised by effects such as decreased mental status, agitated delirium and seizures. While 5F-MDMB-PICA has been present in biological samples mostly in combination with other drugs, in at least some of these cases 5F-MDMB-PICA has been assessed as having a high contribution to the effects produced. It has been used by victims of three apparent mass overdose events, but at least one other synthetic cannabinoid was also detected in biological fluids from the victims.

5F-MDMB-PICA has been detected in 20 countries. It has no veterinary or medical use.

Based on its mechanism of action, 5F-MDMB-PICA has the ability to produce a state of dependence and central nervous system depression. There is evidence that it is abused so as to constitute a public health and social problem. It is therefore recommended that 5F-MDMB-PICA be controlled under the 1971 Convention on Psychotropic Substances. As it has no medical use and its use constitutes a substantial risk to public health, it is recommended that it be controlled under Schedule II of the 1971 Convention on Psychotropic Substances.

4F-MDMB-BINACA

4F-MDMB-BINACA is also known as 4F-MDMB-BUTINACA. Its chemical name is methyl 2-{[1-(4-fluorobutyl)-1H-indazole-3-carbonyl]amino}-3,3-dimethylbutanoate.

In common with other synthetic cannabinoids, 4F-MDMB-BINACA is a full agonist at the CB1 receptor that mediates the psychoactive effects of cannabinoids.

Self-reported effects provided by individuals who had used cannabinoid products that included 4F-MDMB-BINACA as the major constituent, included auditory and visual hallucinations, vomiting, paranoia, euphoria, relaxation, irregular heartbeat, agitation, confusion, insomnia, and chest pain. These effects are consistent with the cannabinoid full agonist mechanism of action of 4F-MDMB-BINACA. Its use has been associated with a number of fatal and non-fatal intoxications and of cases of driving under the influence of drugs. However, other synthetic cannabinoids have been detected in most of these cases.

4F-MDMB-BINACA has been detected in a small number of countries to date, but its use may be increasing. It has no veterinary or medical use.

Based on its mechanism of action, 4F-MDMB-BINACA has the ability to produce a state of dependence and central nervous system depression. There is evidence that it is abused so as to constitute a public health and social problem. It is therefore recommended that 4F-MDMB-BINACA be controlled under the 1971 Convention on Psychotropic Substances. As it has no medical use and its use constitutes a substantial risk to public health, it is recommended that it be controlled under Schedule II of the 1971 Convention on Psychotropic Substances.

4-CMC

4-CMC is also known as 4-chloromethcathinone and clephedrone. Its chemical name is 1-(4-chlorophenyl)-2-(methylamino)propan-1-one.

In common with other stimulants used non-medically, 4-CMC increases neuronal concentrations of the neurotransmitter dopamine. It also has effects on serotonin and, to a lesser extent, noradrenaline.

In animal models, 4-CMC has effects predictive of abuse potential, including actions predictive of MDMA-like subjective effects and stimulation of brain reward centres. It also produces central nervous system stimulation. Users of the drug report effects similar to other stimulants, particularly MDMA-like effects, including increased energy, mood elevation and increased sociability.

4-CMC use has been associated with adverse effects typical of stimulant drugs, including tachycardia, agitation and impaired movement. Based on these effects and its mechanism of action, major risks associated with use of this drug will include cardiac failure and psychosis. In association with other drugs, 4-CMC has been involved in fatalities due to overdose, suicide and traffic accidents. It has been detected in used syringes, indicating the potential for injection related health problems in association with its use.

4-CMC has been detected in many countries across different regions. It has no veterinary or medical use.

Based on its mechanism of action and effects, 4-CMC has the ability to produce a state of dependence and central nervous system stimulation. There is evidence that it is abused so as to constitute a public health and social problem. It is therefore recommended that 4-CMC be controlled under the 1971 Convention on Psychotropic Substances. As it has no medical use and its use constitutes a substantial risk to public health, it is recommended that it be controlled under Schedule II of the 1971 Convention on Psychotropic Substances.

N-Ethylhexedrone

The chemical name for N-ethylhexedrone is 2-(ethylamino)-1-phenylhexan-1-one.

In common with other stimulants used non-medically, N-ethylhexedrone increases neuronal concentrations of the neurotransmitter dopamine. It also has effects on noradrenaline.

In preclinical models, N-ethylhexedrone has actions predictive of methamphetamine-like subjective effects and produces central nervous system stimulation. Users of the drug

report effects similar to other stimulants, including increased energy, mood elevation, perceptual changes and increased sociability.

Information on the adverse effects is limited, but the effects reported are consistent with the effects of stimulant drugs and include tachycardia, tremor, seizures and hyperthermia. N-ethylhexedrone has been implicated as the cause of at least one fatality and of cases of impaired driving. It has been detected in used syringes, indicating the potential for injection related health problems in association with its use.

N-ethylhexedrone has been detected in 30 countries across different regions. It has no veterinary or medical use.

Based on its mechanism of action and effects, N-ethylhexedrone has the ability to produce a state of dependence and central nervous system stimulation. There is evidence that it is abused so as to constitute a public health and social problem. It is therefore recommended that N-ethylhexedrone be controlled under the 1971 Convention on Psychotropic Substances. As it has no medical use and its use constitutes a substantial risk to public health, it is recommended that it be controlled under Schedule II of the 1971 Convention on Psychotropic Substances.

Alpha-PHP

Alpha-PHP is also known as alpha-pyrrolidinohexanophenone. Its chemical name is 1-phenyl-2-(pyrrolidine-1-yl)hexan-1-one.

In common with other stimulants used non-medically, alpha-PHP increases neuronal concentrations of the neurotransmitter dopamine. It also has effects on noradrenaline.

In animal models, alpha-PHP has effects predictive of abuse and dependence potential, including actions predictive of methamphetamine-like subjective effects and reinforcing properties. It produces central nervous system stimulation in animals. Users of the drug report effects similar to other stimulants, including increased energy, mood elevation, perceptual changes and appetite suppression.

The adverse effects of the drug include tachycardia, paranoia and hallucinations. It has been identified as the cause of multiple deaths and clinical admissions.

Alpha-PHP has been detected in over 20 countries across different regions. It has no veterinary or medical use.

Based on its mechanism of action and effects, alpha-PHP has the ability to produce a state of dependence and central nervous system stimulation. There is evidence that it is abused so as to constitute a public health and social problem. It is therefore recommended that alpha-PHP be controlled under the 1971 Convention on Psychotropic Substances. As it has no medical use and its use constitutes a substantial risk to public health, it is recommended that it be controlled under Schedule II of the 1971 Convention on Psychotropic Substances.

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

Flualprazolam

The chemical name for flualprazolam is 8-chloro-6-(2-fluorophenyl)-1-methyl-4*H*-benzo[*f*][1,2,4]triazolo[4,3-*a*][1,4] diazepine.

Flualprazolam is chemically similar to the benzodiazepines alprazolam and triazolam and in animal models it produces the typical benzodiazepine effects of sedation, muscle relaxation and anticonvulsant actions. Users have reported effects such as sedation, disinhibition and memory impairment that are common with benzodiazepines and have described it as similar to alprazolam and clonazepam.

In toxicology reports, flualprazolam has been documented as contributing to forensic and clinical events, including fatal and non-fatal intoxications and cases of driving under the influence. It has no medical use.

There is limited information on the extent of global use of flualprazolam with most reported identifications coming from two countries. There are numerous reports of its use on internet forums.

Based on its capacity to produce a state of dependence and central nervous system depression similar to the controlled benzodiazepine alprazolam, which is controlled under Schedule IV of the1971 Convention on Psychotropic Substances, as well as evidence that it is likely to be abused so as to constitute a public health and social problem, it is recommended that flualprazolam be controlled under Schedule IV of the 1971 Convention on Psychotropic Substances.

Etizolam

The chemical name for etizolam is 4-(2-chlorophenyl)-2-ethyl-9-methyl-6H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepine. It has been previously reviewed by the ECDD, most recently at its 39th meeting in 2017.

Etizolam is an agonist at the benzodiazepine site on the GABAA receptor, inducing central nervous system depression. It has typical benzodiazepine effects that include sedation and muscle relaxation as well as anxiolytic and anticonvulsant actions. Adverse effects include drowsiness, ataxia, slurred speech, cognitive impairment and loss of consciousness.

Etizolam use has been associated with a large number of deaths, generally along with another drug or drugs. Benzodiazepines such as etizolam pose a significant risk when combined with opioids as they can potentiate the respiratory depressant effects of opioids.

Etizolam has been used in a number of countries and in some of these countries has been associated with reports of fatal and no-fatal intoxication as well as cases of driving under the influence. It has marketing authorization for medical use in three countries.

Based on its capacity to produce a state of dependence and central nervous system depression similar to other controlled benzodiazepines, as well as evidence that it is abused so as to constitute a public health and social problem, it is recommended that etizolam be controlled under Schedule IV of the 1971 Convention on Psychotropic Substances.

Substance recommended for surveillance:

APINACA

The chemical name for APINACA (also known as AKB-48) is N-(adamantan-1-yl)-1-pentyl-1H-indazole-3-carboxamide. It was previously reviewed at the 36th meeting of the WHO Expert Committee on Drug Dependence in 2014 but was not recommended for control at that time.

In common with other synthetic cannabinoids, APINACA is an agonist at the CB1 receptor that mediates the psychoactive effects of cannabinoids. In animal studies it produced central nervous system depression and had actions predictive of cannabinoid-like subjective effects.

APINACA produces neurological signs in animals that include seizures, hyperreflexia and aggression. However, there are no studies of the adverse effects of APINACA in human users of the drug and no available information regarding fatal or non-fatal intoxications.

APINACA use has been reported in a number of countries but its use has been declining since 2015 and it is now detected very infrequently if at all.

Owing to the lack of significantly more information since the review conducted by the 36th ECDD in 2014, and considering the current insufficiency of data regarding dependence, abuse and risks to public health (including risks to the

individual), the Committee recommended that APINACA be kept under surveillance.

Preparations recommended for critical review:

—Preparations of acetyldihydrocodeine, codeine, dihydrocodeine, ethylmorphine, nicocodine, nicodicodine, norcodeine and pholcodine listed in Schedule III of the 1961 Single Convention on Narcotic Drugs

The Committee considered a pre-review of the following preparations listed in Schedule III of the 1961 Single Convention on Narcotic Drugs: acetyldihydrocodeine, codeine, dihydrocodeine, ethylmorphine, nicocodine, nicodicodine, norcodeine and pholcodine, when compounded with one or more other ingredients and containing not more than 100 milligrams of the drug per dosage unit and with a concentration of not more than 2.5 per cent in undivided preparations.

These preparations have not been previously reviewed. The ECDD Secretariat commissioned a pre-review of these preparations, on the basis of concerns regarding abuse and harm of preparations of codeine that were conveyed to the Secretariat. As many of the substances listed in the first entry of Schedule III of the 1961 Single Convention are chemically and pharmacologically similar to codeine, the eight preparations were considered together.

These preparations have been marketed and used as antitussive medicines and analgesics for mild to moderate pain. In many countries these preparations are available without medical prescription. The active substances in the preparations are opioids and all substances themselves are controlled under Schedule II of the 1961 Single Convention on Narcotic Drugs. Misuse of and dependence on preparations of codeine and dihydrocodeine have been well described. The pre-review suggested that there may be less evidence regarding the other preparations. The Committee also noted evidence of separation of the opioid drug such as codeine from the other ingredients in these preparations by people misusing these preparations.

Based on the evidence available regarding dependence, abuse and risks to public health, the Committee recommended a critical review of the following preparations included in Schedule III of the 1961 Convention at a future meeting: acetyldihydrocodeine, codeine, dihydrocodeine, ethylmorphine, nicocodine, nicodicodine, norcodeine, and pholcodine when compounded with one or more other ingredients and containing not more than 100 milligrams of the drug per dosage unit and with a concentration of not more than 2.5 per cent in undivided preparations.

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 1971 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.

Crotonyl fentanyl (chemical name: *N*-(1-phenethylpiperidin-4-yl)-*N*-phenylbut-2-enamide) and valeryl fentanyl (chemical name: *N*-(1-phenethylpiperidin-4-yl)-*N*-phenylpentanamide) are synthetic opioids that have a pharmacological profile similar to other Schedule I and II opioid substances controlled under the CSA such as cyclopropyl fentanyl, fentanyl, and other related mu-opioid receptor agonist substances. They are clandestinely produced and associated with adverse events typically associated with opioid use such as respiratory depression, anxiety, constipation, tiredness, hallucinations, and withdrawal. Crotonyl fentanyl and valeryl fentanyl have been encountered by law enforcement and/or reported in the scientific literature by public health officials as being illicitly distributed and abused. Crotonyl fentanyl and valeryl fentanyl have no commercial or currently accepted medical uses in the United States. On February 1, 2018, valeryl fentanyl was temporarily placed into Schedule I of the CSA. The chemical structure of crotonyl fentanyl defines it as a fentanyl-related substance, as defined in 21 CFR 1308.11(h)(30); therefore, crotonyl fentanyl was temporarily controlled as a Schedule I controlled substance under the CSA as of February 6, 2018. As such, additional controls will be necessary to fulfill United States obligations if crotonyl fentanyl and valeryl fentanyl are placed in Schedules I of the Single Convention on Narcotic Drugs (1961).

DOC (chemical names: 2,5-Dimethoxy-4-chloroamfetamine; 2,5-dimethoxy-4-chloroamphetamine; 1-(4-chloro-2,5-dimethoxyphenyl)propan-2-amine) is a hallucinogenic substance with psychedelic effects. Law enforcement has encountered DOC in tablet, capsule, powder, liquid, and blotter paper forms. Its use has been associated with at least one death. DOC has no currently accepted medical use in treatment in the United States. DOC is not controlled under the CSA but is a Schedule I controlled substance in the state of Florida. As such, additional permanent controls will be necessary to fulfill United States obligations if DOC is controlled under Schedule I of the 1971 Convention.

AB-FUBINACA (chemical name: *N*-(1-amino-3-methyl-1-oxobutan-2-yl)-1-(4-fluorobenzyl)-1*H*-indazole-3-carboxamide) is a synthetic cannabinoid that is a potent full agonist at CB1 receptors. This substance functionally (biologically) mimics the effects of structurally unrelated THC, a Schedule I substance under the CSA, and the main psychoactive chemical constituent in cannabis. Synthetic cannabinoids have been marketed under the guise of ''herbal incense,'' and promoted by drug traffickers as legal alternatives to cannabis. AB-FUBINACA use has been associated with serious adverse events including death in the United States. There are no commercial or approved medical uses for AB-FUBINACA. On September 6, 2016, AB-FUBINACA was permanently placed as a Schedule I controlled substance under the CSA. As such, additional permanent controls will not be necessary to fulfill United States obligations if AB-FUBINACA is controlled under Schedule II of the 1971 Convention.

5F-AMB (5F-AMB-PINACA, 5F-MMB-PINACA) (chemical name: methyl 2-(1-(5-fluoropentyl)-1*H*-indazole-3-carboxamido)-3-methylbutanoate) is a synthetic cannabinoid that is a potent full agonist at CB1 receptors. This substance functionally (biologically) mimics the effects of THC, a Schedule I substance under the CSA, and the main psychoactive chemical constituent in cannabis. Synthetic cannabinoids have been marketed under the guise of ''herbal incense,'' and promoted by drug traffickers as legal alternatives to cannabis. The use of synthetic cannabinoids, including, 5F–AMB has been associated with nausea and vomiting, shortness of breath or depressed breathing, hypertension, tachycardia, chest pain, muscle twitching, acute renal failure, anxiety, agitation, psychosis, suicidal ideation, and/or cognitive impairment. There are no commercial or approved medical uses for 5F–AMB. On April 8, 2019, a Drug Enforcement Administration Notice of Proposed Rulemaking proposed permanently placing 5F–AMB

into Schedule I of the CSA. As such, additional permanent controls will not be necessary to fulfill United States obligations if 5F–AMB is controlled under Schedule II of the 1971 Convention.

5F-MDMB-PICA (5F-MDMB-2201) (chemical name: methyl 2-(1-(5-fluoropentyl)-1*H*-indazole-3-carboxamido)-3,3-dimethylbutanoate) is a synthetic cannabinoid that has been sold online and used to mimic the biological effects of THC, the main psychoactive chemical constituent in cannabis. Research and clinical reports have demonstrated that synthetic cannabinoids are applied onto plant material so that the material may be smoked as users attempt to obtain a euphoric and psychoactive ''high.'' Synthetic cannabinoids have been marketed under the guise of ''herbal incense,'' and promoted by drug traffickers as legal alternatives to cannabis. 5F-MDMB-PICA has been associated with law enforcement seizures and overdoses requiring emergency medical intervention. On April 16, 2019, 5F-MDMB-PICA was temporarily controlled as a Schedule I substance under the CSA. As such, additional permanent controls will be necessary to fulfill United States obligations if 5F-MDMB-PICA is controlled under Schedule II of the 1971 Convention.

4F-MDMB-BINACA (4F-ADB) (chemical name: methyl 2-(1-(4-fluorobutyl)-1*H*-indazole-3-carboxamido)-3,3-dimethylbutanoate) is a synthetic cannabinoid that is a potent full agonist at CB1 receptors. This substance functionally (biologically) mimics the effects of THC, a Schedule I substance, and the main psychoactive constituent in cannabis. 4F-MDMB-BINACA has been encountered in numerous synthetic cannabinoid products that are smoked for their psychoactive effects. Multiple law enforcement encounters of 4F-MDMB-BINACA have been reported involving overdose deaths, illicit use, and seizures of drug evidence between December 2018 and February 2019. There are no commercial or approved medical uses for 4F-MDMB-BINACA. 4F-MDMB-BINACA is a positional isomer of 5F-AMB (chemical name: methyl 2-(1-(5-fluoropentyl)-1H-indazole-3-carboxamido)-3-methylbutanoate), as defined by 21 CFR 1300.01, and has been a Schedule I controlled substance under the CSA since April 10, 2017. As such, additional permanent controls will not be necessary to fulfill United States obligations if 4F-MDMB-BINACA is controlled under Schedule II of the 1971 Convention.

4-CMC (4-chloromethcathinone; clefedrone, clephedrone) (chemical name: 1-(4-chlorophenyl)-2-(methylamino)propan-1-one) is a synthetic cathinone. 4-CMC produces central nervous system stimulant effects and is abused for its psychoactive properties. 4-CMC abuse has been associated with adverse health effects. 4-CMC has no currently accepted medical use in treatment in the United States. 4-CMC is not controlled under the CSA, but it is considered a Schedule I controlled substance by a number of states in the United States. As such, additional permanent controls will be necessary to fulfill United States obligations if 4-CMC is controlled under Schedule II of the 1971 Convention.

N-Ethylhexedrone (chemical name: 2-(ethylamino)-1-phenylhexan-1-one; NEH, hexen, Ethyl-Hex) and *alpha*-PHP (chemical name: 1-phenyl-2-(pyrrolidin-1-yl)hexan-1-one; PV-7, α-pyrrolidinohexanophenone) are synthetic cathinones. *N*-Ethylhexedrone and *alpha*-PHP produce central nervous system stimulant effects and are abused for their psychoactive properties. *N*-Ethylhexedrone and *alpha*-PHP have been associated with adverse health effects leading to emergency department admissions, and deaths. *N*-Ethylhexedrone and *alpha*-PHP have no currently accepted medical use in treatment in the United States. On July 18, 2019, *N*-Ethylhexedrone and *alpha*-PHP were temporarily controlled as a Schedule I substance under the CSA. As such, additional permanent controls will be necessary to fulfill United States obligations if *N*-Ethylhexedrone and *alpha*-PHP are controlled under Schedule II of the 1971 Convention.

Flualprazolam and etizolam belong to a class of substances known as benzodiazepines. Benzodiazepines produce central nervous system depression and are commonly used to treat insomnia, anxiety, and seizure disorders. Etizolam is currently prescribed in some countries; however, neither drug substance is approved for medical use in the United States. Currently, flualprazolam and etizolam are not controlled under the CSA, but are controlled in a number of states in the United States. As such, additional permanent controls will be necessary to fulfill United States obligations if flualprazolam and etizolam are controlled under Schedule IV of the 1971 Convention.

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 1971 Convention at the CND meeting in March 2020.

Comments regarding the WHO recommendations for control of crotonyl fentanyl and valeryl fentanyl; under the 1961 Single Convention will also be forwarded to the relevant Agencies for consideration in developing the United States position regarding narcotic substances at the CND meeting.

Dated: December 23, 2019.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Advisory Council on Alzheimer's Research, Care, and Services; Meeting

AGENCY: Assistant Secretary for Planning and Evaluation, HHS.

ACTION: Notice of meeting.

SUMMARY: This notice announces the public meeting of the Advisory Council on Alzheimer's Research, Care, and Services (Advisory Council). The Advisory Council provides advice on how to prevent or reduce the burden of Alzheimer's disease and related dementias on people with the disease and their caregivers. During the January 27, 2020 meeting, an invited panel will present lessons from epidemiology on understanding current rates of dementia, future trends, and potential preventive strategies. The Advisory Council will hear about the Department of Defense's Peer Reviewed Alzheimer's Research Program as well as an update on the recommendations from the Alzheimer's Disease-Related Dementias Research Summit. Federal workgroups will also provide updates on work completed in the last quarter.

DATES: The meeting will be held on January 27, 2020 from 9:30 a.m. to 4:15 p.m. EST.

ADDRESSES: The meeting will be held in Room 800 in the Hubert H. Humphrey Building, 200 Independence Avenue SW, Washington, DC 20201.

Comments: Time is allocated on the agenda to hear public comments. The time for oral comments will be limited