

part 601 have been approved under OMB control number 0910-0338; and the collections of information in 21 CFR parts 801 and 809 have been approved under OMB control number 0910-0485.

Dated: January 21, 2016.

Leslie Kux,

Associate Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2016-N-0117]

International Drug Scheduling; Convention on Psychotropic Substances; Single Convention on Narcotic Drugs; World Health Organization; Scheduling Recommendations; Acetylfentanyl; MT-45; para-Methoxymethylamphetamine (PMMA); α -Pyrrolidinovalerophenone (α -PVP); para-Methyl-4-methylaminorex (4,4'-DMAR); Methoxetamine (MXE); Phenazepam; 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 2016. This notice is issued under the Controlled Substances Act (the CSA).

DATES: Submit either electronic or written comments by February 25, 2016. Submit requests for a public meeting on or before February 5, 2016. 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: <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-2015-N-0117 for "International Drug Scheduling; Convention on Psychotropic Substances; Single Convention on Narcotic Drugs; World Health Organization; Scheduling Recommendations; Acetylfentanyl; MT-45; para-Methoxymethylamphetamine (PMMA); α -Pyrrolidinovalerophenone (α -PVP); para-Methyl-4-methylaminorex (4,4'-DMAR); Methoxetamine (MXE); Phenazepam; Request for Comments." 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 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 <http://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 5 substances to be considered for control under the Psychotropic Convention. This notification reflects the recommendation from the 36th WHO Expert Committee for Drug Dependence (ECDD), which met in June 2014. In the **Federal Register** of December 30, 2013 (78 FR 79465), 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 2 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:

Reference:

NAR/CL.5/2015

WHO/ECDD37; 1961C-Art.3; 1971C-

Art.2

CU 2014/288/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:

Acetylfentanyl be placed in Schedule I and in Schedule IV of the 1961 Convention

and

MT-45 be placed in Schedule I of the 1961 Convention

and

para-Methoxymethylamphetamine (PMMA) be placed in Schedule I of the 1971 Convention

and

α -Pyrrolidinovalerophenone (α -PVP); para-Methyl-4-methylaminorex (4,4'-DMAR) and methoxetamine (MXE) be placed in Schedule II of the 1971 Convention

and

Phenazepam be placed in Schedule IV of the 1971 Convention.

In the letter from the Director-General of the World Health Organization to the Secretary-General reference is also made to Commission on Narcotic Drugs decision 58/2 of 13 March 2015, by which the Commission decided to postpone the consideration of the proposal concerning the recommendation to place ketamine in Schedule IV of the Convention on Psychotropic Substances of 1971 and to request additional information from the World Health Organization and other relevant sources.

His Excellency

Mr. John Kerry

Secretary of State of the United States of America

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 fifty-ninth session of the Commission on Narcotic Drugs, 14–22 March 2016.

In connection with the notification, WHO has also submitted the relevant extract from the report of the thirty-seventh session 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 under the 1961 Convention and the 1971 Convention, at the latest by 1 February 2016 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.

30 December 2015

NAR/CL.5/2015

Annex I

Annex I

Letter addressed to the Secretary-General of the United Nations from the Director-General of the World Health Organization

“The Thirty-seventh meeting of the WHO Expert Committee on Drug Dependence was convened from 16 to 20 November 2015, at WHO headquarters in Geneva.

With reference to Article 2, paragraphs 1, 4 and 6 of the Convention on Psychotropic Substances (1971) and Article 3, paragraphs 1, 3 and 5 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:

—Acetylfentanyl be placed in Schedule I and in Schedule IV of the Single Convention on Narcotic Drugs (1961), and that:

—MT-45 be placed in Schedule I of the Single Convention on Narcotic Drugs (1961), and that:

- para-Methoxymethylamphetamine (PMMA) be placed in Schedule I of the Convention on Psychotropic Substances (1971), and that:
- α -Pyrrolidinovalerophenone (α -PVP); para-Methyl-4-methylaminorex (4,4'-DMAR) and methoxetamine (MXE) be placed in Schedule II of the Convention on Psychotropic Substances (1971), and that:
- Phenazepam be placed in Schedule IV of the Convention on Psychotropic Substances (1971).

The recommendations and the assessments and findings on which they are based are set out in detail in the Report of the 37th 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.

In decision 58/2 of 13 March 2015, the Commission on Narcotic Drugs decided to postpone the consideration of the proposal concerning the recommendation to place ketamine in Schedule IV of the Convention on Psychotropic Substances of 1971 and to request additional information from the World Health Organization and other relevant sources. Consequentially, an update review paper on ketamine was commissioned and provided to the Expert Committee. Following its deliberations the Committee unanimously agreed that it found nothing in the updates, nor in what was disclosed during its deliberations, that would give it reason to recommend a new pre-review or critical review of ketamine with a view to potentially change its standing recommendation of 2014 that ketamine should not be placed under international control. The current standing recommendation is consistent with the earlier recommendation made in 2012.

I am very pleased with the ongoing collaboration between UNODC, INCB and WHO, in particular, the support to the work of the WHO Expert Committee on Drug Dependence and preparations for the Special Session of the United Nations General Assembly on the World Drug Problem in 2016."

NAR/CL.5/2015

Annex II

Annex II

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

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

Acetylfentanyl

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

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

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

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

MT-45

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

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

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

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

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

para-Methoxymethylamphetamine (PMMA)

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

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

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

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

α -Pyrrolidinovalerophenone (α -PVP)

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

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

The Committee considered that the degree of risk to public health and

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

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

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

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

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

Methoxetamine (MXE)

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

During its 36th meeting, the WHO Expert Committee on Drug Dependence discussed the critical review report on methoxetamine and concluded that

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

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

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

Phenazepam

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

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

Substance recommended for critical review:

Etizolam (INN)

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

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

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

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

Substance recommended for surveillance:

4-Fluoroamphetamine (4-FA)

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

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

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

Update on cannabis:

The Commission on Narcotic Drugs, in Resolution 52/5, expressed that it "... looks forward to an updated

report on cannabis by the Expert Committee, subject to the availability of extra budgetary resources”, and the Report of the International Narcotics Control Board for 2014 reiterated, “. . . its invitation to WHO to evaluate the potential medical utility of cannabis and the extent to which cannabis poses a risk to human health.” WHO therefore commissioned an update report paper on cannabis and cannabis resin.

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

Update on ketamine:

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

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

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.

Acetylfentanyl (N-(1-phenethylpiperidin-4-yl)-N-phenylacetamide) is a potent opioid analgesic in the phenylpiperidine class of synthetic opioids. On July 17, 2015, acetylfentanyl 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 U.S. Attorney General (the Attorney General), though, may extend this temporary scheduling for up to 1 year. The WHO ECDD met in November 2015 and recommended that acetylfentanyl be placed in Schedule I and in Schedule IV of the 1961 Single Convention. On July 17, 2015, acetylfentanyl was temporarily placed in Schedule I of the CSA under the temporary scheduling provision of section 201(h) of the CSA. These provisions provide the Attorney General with the authority to temporarily place a substance into Schedule I of the CSA for 2 years, without regard to the requirements of 21 U.S.C. 811(b), if he finds that such action is necessary to avoid an imminent hazard to the public safety. In addition, if proceedings to control a substance are initiated under 21 U.S.C. 811(a)(1), the Attorney General may extend the temporary scheduling for up to 1 year (21 U.S.C. 811(h)(2)). Therefore, considering the previously mentioned time limitations of temporary scheduling under section 201(h) of the CSA, it will be necessary to adopt non-temporary controls to fulfill U.S. obligations if acetylfentanyl is controlled under Schedule I and Schedule IV of the 1961 Single Convention.

1-cyclohexyl-4-(1,2-diphenylethyl)-piperazine (MT-45) is a synthetic opioid with potent analgesic activity comparable to morphine despite being structurally unrelated to most other opioids. MT-45 use has been associated with deaths in the United States and in other countries. The WHO ECDD met in November 2015 and recommended that MT-45 be placed in Schedule I of the 1961 Single Convention. MT-45 is not currently controlled in the United States under the CSA. As such, additional controls will be necessary to fulfill U.S. obligations if MT-45 is controlled under Schedule I of the 1961 Single Convention.

Phenazepam belongs 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. The WHO ECDD at its 37th meeting recommended that Phenazepam be placed in Schedule IV of the Psychotropic Convention. While Phenazepam is currently prescribed in some countries, it is not approved for medical use or controlled in the United States under the CSA. Additional controls will be necessary to fulfill U.S. obligations if Phenazepam is controlled under Schedule IV of the Psychotropic Convention.

Para-Methoxymethylamphetamine (PMMA) is a substituted amphetamine of the phenethylamine class, as well as a structural analog of paramethoxyamphetamine (PMA) which produces effects similar but not identical to that of MDMA. The WHO ECDD at its 37th meeting recommended PMMA be placed in Schedule I of the Psychotropic Convention. PMMA is not currently controlled in the United States under the CSA. Additional controls will be necessary if PMMA is placed in Schedule I of the Psychotropic Convention.

Para-Methyl-4-methylaminorex (4,4'-DMAR) is a derivative of the stimulant drug 4-methylaminorex and has been involved in several deaths in the United States. The WHO ECDD at its 37th meeting recommended 4,4'-DMAR be placed in Schedule II of the Psychotropic Convention. 4,4'-DMAR is not currently controlled in the United States under the CSA. Additional controls will be necessary to fulfill U.S. obligations if 4,4'-DMAR is controlled under Schedule II of the Psychotropic Convention.

α -Pyrrolidinovalerophenone (α -PVP or alpha-PVP) is a synthetic cathinone structurally and pharmacologically similar to amphetamine; 3,4-methylenedioxymethamphetamine (MDMA); cathinone; and other related substances. On March 7, 2014, α -PVP 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. The WHO ECDD at its 37th meeting recommended that α -PVP be placed in Schedule II of the Psychotropic Convention. Therefore, considering the previously mentioned time limitations of temporary scheduling under section 201(h) of the CSA, additional controls will be necessary to fulfill U.S. obligations if α -PVP is controlled under Schedule II of the Psychotropic Convention.

Methoxetamine (MXE) is a synthetic drug substance and belongs in the arylcyclohexamine class. The WHO

ECDD at its 37th meeting recommended that MXE be placed in Schedule II of the Psychotropic Convention. MXE is not currently controlled under the CSA in the United States. Additional controls will be necessary to fulfill U.S. obligations if MXE is controlled under Schedule II of the Psychotropic 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 Psychotropic Convention at the CND meeting in March 2015.

Comments regarding the WHO recommendations for control of acetylfentanyl and MT-45 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 February 5, 2016.

Dated: January 20, 2016.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2016-01474 Filed 1-25-16; 8:45 am]

BILLING CODE 4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2015-P-3053]

Determination That IZBA (Travoprost Ophthalmic Solution), 0.003 Percent, Was Not Withdrawn From Sale for Reasons of Safety or Effectiveness

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) has determined that IZBA (travoprost ophthalmic solution), 0.003 percent, was not withdrawn from sale for reasons of safety or effectiveness. This determination will allow FDA to approve abbreviated new drug applications (ANDAs) for travoprost ophthalmic solution/drops, 0.003 percent, if all other legal and regulatory requirements are met.

FOR FURTHER INFORMATION CONTACT: Kate Greenwood, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6286, Silver Spring, MD 20993-0002, 240-402-1748.

SUPPLEMENTARY INFORMATION: In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act of 1984 (Pub. L. 98-417) (the 1984 amendments), which authorized the approval of duplicate versions of drug products under an ANDA procedure. ANDA applicants must, with certain exceptions, show that the drug for which they are seeking approval contains the same active ingredient in the same strength and dosage form as the “listed drug,” which is a version of the drug that was previously approved. ANDA applicants do not have to repeat the clinical testing otherwise necessary to gain approval of a new drug application (NDA).

The 1984 amendments include what is now section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)), which requires FDA to publish a list of all approved drugs. FDA publishes this list as part of the “Approved Drug Products With Therapeutic Equivalence Evaluations,” which is known generally as the “Orange Book.” Under FDA regulations, drugs are removed from the list if the Agency withdraws or suspends approval of the drug’s NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (21 CFR 314.162).

A person may petition the Agency to determine, or the Agency may determine on its own initiative, whether a listed drug was withdrawn from sale for reasons of safety or effectiveness. This determination may be made at any time after the drug has been withdrawn from sale, but must be made prior to approving an ANDA that refers to the listed drug (§ 314.161 (21 CFR 314.161)). FDA may not approve an ANDA that does not refer to a listed drug.

IZBA (travoprost ophthalmic solution), 0.003 percent, is the subject of

NDA 204822, held by Alcon Laboratories, Inc., and initially approved on May 15, 2014. IZBA is indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

In a letter dated September 4, 2015, Alcon Laboratories, Inc. notified FDA that IZBA (travoprost ophthalmic solution), 0.003 percent, was discontinued. IZBA (travoprost ophthalmic solution), 0.003 percent, is currently listed in the “Discontinued Drug Product List” section of the Orange Book.

Jonathan Goodman of Florek & Endres PLLC submitted a citizen petition dated August 20, 2015 (Docket No. FDA-2015-P-3053), under 21 CFR 10.30, requesting that the Agency determine whether IZBA (travoprost ophthalmic solution), 0.003 percent, was withdrawn from sale for reasons of safety or effectiveness.

After considering the citizen petition and reviewing Agency records and based on the information we have at this time, FDA has determined under § 314.161 that IZBA (travoprost ophthalmic solution), 0.003 percent, was not withdrawn for reasons of safety or effectiveness. The petitioner has identified no data or other information suggesting that IZBA (travoprost ophthalmic solution), 0.003 percent, was withdrawn for reasons of safety or effectiveness. We have carefully reviewed our files for records concerning the withdrawal of IZBA (travoprost ophthalmic solution), 0.003 percent, from sale. We have also independently evaluated relevant literature and data for possible postmarketing adverse events. We have found no information that would indicate that this product was withdrawn from sale for reasons of safety or effectiveness.

Accordingly, the Agency will continue to list IZBA (travoprost ophthalmic solution), 0.003 percent, in the “Discontinued Drug Product List” section of the Orange Book. The “Discontinued Drug Product List” delineates, among other items, drug products that have been discontinued from marketing for reasons other than safety or effectiveness. ANDAs that refer to IZBA (travoprost ophthalmic solution), 0.003 percent, may be approved by the Agency as long as they meet all other legal and regulatory requirements for the approval of ANDAs. If FDA determines that labeling for this drug product should be revised to meet current standards, the Agency will advise ANDA applicants to submit such labeling.