Estimated Total Annual Burden Hours: 2,014.

Authority: 42 U.S.C. 1310.

Mary C. Jones,

ACF/OPRE Certifying Officer.

[FR Doc. 2024–18065 Filed 8–13–24; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2024–N–3677]

International Drug Scheduling; Single Convention on Narcotic Drugs; Convention on Psychotropic Substances; Hexahydrocannabinol; N-Pyrrolidino Protonitazene (Protonitazepyne); N-Pyrrolidino Metonitazene (Metonitazepyne); N-Piperidinyl Etonitazene (Etonitazepipne); N-Desethyl-isotonitazene; 3-Hydroxy-phencyclidine; N-Ethylheptedrone; Carisoprodol; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; request for comments.

SUMMARY: The Food and Drug Administration (FDA or Agency) is inviting interested persons to submit comments concerning abuse potential, actual abuse, medical usefulness, trafficking, and impact of scheduling changes on availability for medical use of eight drug substances. These comments will be considered in preparing a response from the United States to the World Health Organization (WHO) regarding the abuse liability and diversion of these drugs. WHO will use this information to consider whether to recommend that certain international restrictions be placed on these drug substances. This notice requesting comments is required by the Controlled Substances Act (CSA).

DATES: Either electronic or written comments must be submitted by August 23, 2024.

ADDRESSES: You may submit comments as follows. Please note that late, untimely filed comments will not be considered. The *https://www.regulations.gov* electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of August 21, 2024. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are received 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–2024–N–3677 for ''International Drug Scheduling; Single Convention on Narcotic Drugs; Convention on Psychotropic Substances; Hexahydrocannabinol (HHC); *N*-Pyrrolidino Protonitazene (Protonitazepyne); *N*-Pyrrolidino Metonitazene (Metonitazepyne); *N*-Piperidinyl Etonitazene (Etonitazepipne); *N*-Desethyl-isotonitazene; 3-Hydroxy-phencyclidine (3–OH–PCP); *N*-Ethylheptedrone; Carisoprodol; 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, 240–402–7500.

- 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, 240–402–7500.

FOR FURTHER INFORMATION CONTACT: Edward (Greg) Hawkins, Center for Drug Evaluation and Research, Controlled Substance Staff, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 5110, Silver Spring, MD 20993–0002, 301–796–0727, *edward.hawkins@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION:

I. Background

The United States is a party to the 1971 Convention on Psychotropic Substances (Psychotropic Convention). Article 2 of the Psychotropic Convention provides that if a party to the convention or WHO has information about a substance, which in its opinion

may require international control or change in such control, it shall so notify the Secretary-General of the United Nations (U.N. Secretary-General) and provide the U.N. Secretary-General with information in support of its opinion.

Paragraph (d)(2)(A) of the CSA (21 U.S.C. 811(d)(2)(A)) (Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970) provides that when WHO notifies the United States under Article 2 of the Psychotropic Convention that it has information that may justify adding a drug or other substances to one of the schedules of the Psychotropic Convention, transferring a drug or substance from one schedule to another, or deleting it from the schedules, the Secretary of State must transmit the notice to the Secretary of Health and Human Services (Secretary of HHS). The Secretary of HHS must then publish the notice in the **Federal Register** and provide opportunity for interested persons to submit comments that will be considered by HHS in its preparation of the scientific and medical evaluations of the drug or substance.

II. WHO Notification

The Secretary of HHS received the following notice from WHO (nonrelevant text removed):

Ref.: C.L.29.2024

The World Health Organization (WHO) presents its compliments to Member States and Associate Members and would like to inform that all recommendations made by the 46th WHO Expert Committee on Drug Dependence (ECDD), held in October 2023, were accepted by the 67th UN Commission on Narcotic Drugs.

WHO further has the pleasure of announcing that the 47th Expert Committee on Drug Dependence (ECDD) will meet from 14 to 18 October 2024 in Geneva, Switzerland. Given that WHO Expert Committee meetings are of a closed nature, this circular letter serves to notify Member States of the agenda of the 47th ECDD, which are in the Annex I file, attached for reference.

WHO is mandated by the 1961 and 1971 International Drug Control Conventions to make recommendations to the UN Secretary-General on the need for and level of international control of psychoactive substances. To fulfil this mandate, WHO convenes the ECDD to advise on appropriate international drug control measures in view of a substance's ability to lead to public health harms as a result of their psychoactive properties, as well as its therapeutic applications.

Although the meetings are of a closed nature, Member States, Associate Members, individuals, and representatives of public and private institutions and civil society who wish to present information to the Expert Committee on issues related to the meeting agenda are invited to attend a virtual information meeting (public consultation) on 14 October 2024. The purpose of the information meeting is to afford the Expert Committee the opportunity to receive presentations and to question representatives of interested parties concerning data that have been provided about substances on the ECDD agenda. Registration information will be made available on the ECDD website in due course: Forty-seventh Expert Committee on Drug Dependence (who.int).

As in the past and in line with the publication ''Guidance on the WHO review of psychoactive substances for international control'' (EB126/2010/REC1, Annex 6), Member States and Associate Members can also contribute to the ECDD review process by providing up to date and accurate information concerning the substances under review in advance of the meeting. For this purpose, and as per previous practice, a questionnaire will be sent to Member States and Associate Members to gather country information on the legitimate use, harmful use, status of national control and potential impact of international control for each substance under evaluation.

The World Health Organization takes this opportunity to renew to Member States and Associate Members the assurance of its highest consideration.

GENEVA, 3 July 2024

Annex I

47th Expert Committee on Drug Dependence (ECDD) Substances for Review 14–18 October 2024

Critical reviews: The substances listed below have been proposed by WHO for critical review and are not currently under international control. Information was brought to WHO's attention that these substances are clandestinely manufactured, of especially serious risk to public health and society, and of no recognized therapeutic use by any Party. The Expert Committee will consider whether information presented during a critical review may justify the scheduling or a change in the scheduling of the substance in the 1961 or 1971 Conventions.

Synthetic Cannabinoids

1. Hexahydrocannabinol (HHC)

Novel Synthetic Opioids

1. *N*-Pyrrolidino protonitazene (protonitazepyne)
2. *N*-Pyrrolidino metonitazene (metonitazepyne)
3. *N*-Piperidinyl etonitazene (etonitazepipne)
4. *N*-Desethyl-isotonitazene

Dissociative-Type Substances

1. 3-Hydroxy-phencyclidine (3–OH–PCP)

Cathinone/Stimulant

1. *N*-Ethylheptedrone

Medicine

1. Carisoprodol

FDA has verified the website addresses contained in the WHO notice as of the date this document publishes in the **Federal Register**; however, websites are subject to change over time. Access to view the WHO questionnaire can be found at *https://www.who.int/groups/ecdd/forty-seventh-ecdd-documents.*

III. Substances Under WHO Review

Hexahydrocannabinol (HHC) is a semi-synthetic cannabinoid. Several synthetic mechanisms for HHC have been published, which involve hydrogenating tetrahydrocannabinol (THC). In vitro receptor binding and activity studies indicate that HHC has higher affinity and agonist activity at the cannabinoid type 1 (CB1) receptor compared to that of the CB2 receptor. These data suggest that HHC produces effects similar to CB1 agonists, such as sedation, analgesia, mood changes, altered memory, psychosis, and panic. According to the National Forensic Laboratory Information System (NFLIS) database, HHC was first detected in the United States in 2022 with a total of 54 law enforcement seizures. There are no commercial uses or approved medical uses for HHC in the United States, and it is not controlled under the CSA.

N-Pyrrolidino protonitazene (protonitazepyne) is a synthetic opioid of the nitazene family that is similar in structure to protonitazene. In vitro binding and activity data indicate that protonitazepyne is approximately 25-fold more potent at the mu opioid receptor than fentanyl. Common adverse events of opioid agonists include nausea, vomiting, constipation, pruritus, dizziness, sedation, and respiratory depression, which can lead to death. Protonitazepyne has been detected in 20 forensic toxicology cases in the United States and the United Kingdom. However, other new psychoactive substances (NPS) or other drugs of abuse were detected in all of these individuals and could have been a contributing factor to the fatality. According to the NFLIS database, protonitazepyne was first detected in 2023 and has been confirmed in 16 law enforcement seizures to date. There are no commercial uses or approved medical uses for protonitazepyne in the United States, and it is not controlled under the CSA.

N-Pyrrolidino metonitazene (metonitazepyne) is a synthetic opioid of the nitazene family that is similar in structure to metonitazene. In vitro binding and activity data indicate that protonitazepyne is approximately 2-fold more potent at the mu opioid receptor than fentanyl. In animal behavior studies it produced subjective effects that were indistinguishable from morphine. As a result, it is assumed that metonitazepyne will have an abuse potential similar to that of other opioid agonists and produce adverse events that include nausea, vomiting,

constipation, pruritus, dizziness, sedation, and respiratory depression, which can lead to death. In the United States, metonitazepyne was detected in six toxicology cases; however, other NPS or other drugs of abuse were detected in all of these individuals and could have been a contributing factor to the fatality. According to the NFLIS database, metonitazepyne was first detected in 2023 and there have been seven confirmed law enforcement seizures to date. There are no commercial uses or approved medical uses for metonitazepyne in the United States, and it is not controlled under the CSA.

N-Piperidynyl etonitazene (etonitazepipne) is a synthetic opioid of the nitazene family and is similar in structure to etonitazene. In vitro binding and activity data indicate that protonitazepyne is approximately 100-fold more potent at the mu opioid receptor than morphine. In animal behavior studies it produced subjective effects that were indistinguishable from morphine. As a result, it is assumed that etonitazepipne will have an abuse potential similar to that of other opioid agonists and produce adverse events that include nausea, vomiting, constipation, pruritus, dizziness, sedation, and respiratory depression, which can lead to death. According to the NFLIS database, etonitazepipne was first detected in 2022 and there have been 10 confirmed law enforcement seizures to date. There are no commercial uses or approved medical uses for etonitazepipne in the United States. As of July 29, 2024, etonitazepipne is temporarily controlled in schedule I under the CSA.

N-Desethyl-isotonitazene is a synthetic opioid of the nitazene family and is similar in structure to isotonitazene and is a known active metabolite of isotonitazene. In vitro binding and activity data indicate that *N*-desethyl-isotonitazene is approximately 20-fold more potent at the mu opioid receptor than fentanyl. In animal behavior studies it produced subjective effects that were indistinguishable from morphine. As a result, it is assumed that *N*-desethyl-isotonitazene will have an abuse potential similar to that of other opioid agonists and produce adverse events that include nausea, vomiting, constipation, pruritus, dizziness, sedation, and respiratory depression, which can lead to death. According to the NFLIS database, *N*-desethyl-isotonitazene was first detected in 2022 and there have been 10 confirmed law enforcement seizures to date. There are no commercial uses or approved medical uses for *N*-desethyl-isotonitazene in the United States. As of July 29, 2024, *N*-desethyl-isotonitazene is temporarily controlled in schedule I under the CSA.

3-Hydroxy-phencyclidine (3–OH–PCP) is a dissociative hallucinogen of the arylcyclohexylamine class that has a structure similar to that of phencyclidine (PCP). In vitro binding and activity data indicate that 3–OH–PCP functions as a high affinity antagonist of the *N*-methyl-*D*-aspartate receptor. Unlike PCP, 3–OH–PCP was also found to have high agonist activity at opioid receptors. In animal behavior studies it produced subjective effects that were indistinguishable from PCP. As a result, it is assumed that it will have a potential of abuse similar to that of PCP and produce effects such as hallucinations, audio and visual distortions, analgesia, and convulsions at high doses. According to the NFLIS database, 3–OH–PCP was first detected in the United States in 2020 with 45 law enforcement seizures. The following years saw a dramatic increase in law enforcement detections with 598 in 2021, 335 in 2022, and 42 in 2023.[1] Since 2020 there have been 34 fatalities in which 3–OH–PCP was determined to be a contributing factor by the medical examiner. There are no commercial uses or approved medical uses for 3–OH–PCP in the United States, and it is not controlled under the CSA.

N-Ethylheptedrone is a stimulant from the substituted cathinone class of drugs that has been used for recreational use. As a stimulant, *N*-ethylheptedrone, would be expected to produce adverse effects consistent with other stimulants such as decreased appetite, anxiety, headaches, weight loss, insomnia, and psychosis. It was first detected in 2019 in Hungry and has since been detected in New Zealand. There are no commercial uses or approved medical uses for *N*-ethylheptedrone in the United States, and it is not controlled under the CSA.

Carisoprodol is a sedative-hypnotic that is used as a centrally acting muscle relaxant and hypnotic. Carisoprodol is a prodrug that is metabolized in the liver to form meprobamate, which functions similarly to benzodiazepines and barbiturates. It was approved for medical use in the United States in 1959 as a muscle relaxant and is typically prescribed in combination with analgesics to treat muscle pain. FDA's Adverse Event Reporting System reported a total of 6,426 adverse events involving carisoprodol since 1969, and 18 of those being reported as drug abuse (data retrieved July 2024). Only 5 of the 18 were reported as abuse of carisoprodol alone. According to the NFLIS database, there were 405 law enforcement seizures of carisoprodol in 2022 alone. Scientific studies indicated that carisoprodol demonstrated abuse potential similar to that of benzodiazepines, resulting in it being controlled in schedule IV under the CSA on January 11, 2012 (76 FR 77330).

[1] The data from 2023 are still being accumulated as of the time of these data were collected (May 2024). As a result, the 2023 data will likely increase.

IV. Opportunity To Submit Domestic Information

As required by paragraph (d)(2)(A) of the CSA, FDA, on behalf of HHS, invites interested persons to submit comments regarding the eight drug substances identified in this document. Any comments received by the deadline will be considered by HHS when it prepares a scientific and medical evaluation for drug substances that is responsive to the WHO Questionnaire for these drug substances. HHS will forward such evaluation of these drug substances to WHO, for WHO's consideration in deciding whether to recommend international control/decontrol of any of these drug substances. Such control could limit, among other things, the manufacture and distribution (import/export) of these drug substances and could impose certain recordkeeping requirements on them.

Although FDA is, through this notice, requesting comments from interested persons, which will be considered by HHS when it prepares an evaluation of these drug substances, HHS will not now make any recommendations to WHO regarding whether any of these drugs should be subjected to international controls. Instead, HHS will defer such consideration until WHO has made official recommendations to the Commission on Narcotic Drugs, which are expected to be made in late 2024. Any HHS position regarding international control of these drug substances will be preceded by another **Federal Register** notice soliciting public comments, as required by paragraph (d)(2)(B) of the CSA (21 U.S.C. 811).

Dated: August 8, 2024.

Lauren K. Roth,

Associate Commissioner for Policy.

[FR Doc. 2024–18045 Filed 8–13–24; 8:45 am]

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