



DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-495]

Schedules of Controlled Substances: Placement of *N*-Ethylhexedrone, *alpha*-Pyrrolidinohexanophenone, 4-Methyl-*alpha*-ethylaminopentiophenone, 4'-Methyl-*alpha*-pyrrolidinohexiophenone, *alpha*-Pyrrolidinoheptaphenone, and 4'-Chloro-*alpha*-pyrrolidinovalerophenone in Schedule I

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Drug Enforcement Administration proposes placing six synthetic cathinones, as identified in this proposed rule, in schedule I of the Controlled Substances Act. If finalized, this action would make permanent the existing regulatory controls and administrative, civil, and criminal sanctions applicable to schedule I controlled substances on persons who handle (manufacture, distribute, reverse distribute, import, export, engage in research, conduct instructional activities or chemical analysis, or possess), or propose to handle these six specified controlled substances.

DATES: Comments must be submitted electronically or postmarked on or before [INSERT DATE 30 DAYS AFTER PUBLICATION IN THE FEDERAL REGISTER].

Requests for hearing and waivers of an opportunity for a hearing or to participate in a hearing must be received on or before [INSERT DATE 30 DAYS AFTER PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: To ensure proper handling of comments, please reference “Docket No. DEA-495” on all electronic and written correspondence, including any attachments.

- *Electronic comments:* The Drug Enforcement Administration (DEA) encourages that all comments be submitted electronically through the Federal eRulemaking Portal which provides the ability to type short comments directly into the comment field on the Web page or attach a file for lengthier comments. Please go to <http://www.regulations.gov> and follow the online instructions at that site for submitting comments. Upon completion of your submission you will receive a Comment Tracking Number for your comment. Please be aware that submitted comments are not instantaneously available for public view on Regulations.gov. If you have received a Comment Tracking Number, your comment has been successfully submitted and there is no need to resubmit the same comment.

- *Paper comments:* Paper comments that duplicate the electronic submission are not necessary. Should you wish to mail a paper comment, *in lieu of* an electronic comment, it should be sent via regular or express mail to: Drug Enforcement Administration, Attn: DEA Federal Register Representative/DPW, 8701 Morrisette Drive, Springfield, Virginia 22152.

- *Hearing requests:* All requests for a hearing and waivers of participation, together with a written statement of position on the matters of fact and law asserted in the hearing, must be sent to: Drug Enforcement Administration, Attn: Administrator, 8701 Morrisette Drive, Springfield, Virginia 22152. All requests for hearing and waivers of participation should also be sent to: (1) Drug Enforcement Administration, Attn: Hearing Clerk/OALJ, 8701 Morrisette Drive, Springfield, Virginia 22152; and (2) Drug Enforcement Administration, Attn: DEA Federal Register Representative/DPW, 8701 Morrisette Drive, Springfield, Virginia 22152.

FOR FURTHER INFORMATION CONTACT: Terrence L. Boos, Ph.D., Drug and Chemical Evaluation Section, Drug Enforcement Administration; Telephone: (571) 362-3249.

SUPPLEMENTARY INFORMATION:

In this proposed rule, the Drug Enforcement Administration (DEA) proposes to permanently schedule the following six controlled substances in schedule I of the Controlled Substances Act (CSA), including their salts, isomers, and salts of isomers whenever the existence of such salts, isomers, and salts of isomers is possible within the specific chemical designation:

- *N*-ethylhexedrone (other names: α -ethylaminohexanophenone, ethyl hexedrone, HEXEN, 2-(ethylamino)-1-phenylhexan-1-one),
- *alpha*-pyrrolidinohexanophenone (other names: α -pyrrolidino-hexanophenone, *alpha*-PHP, α -PHP, PV7, 1-phenyl-2-(pyrrolidin-1-yl)hexan-1-one),
- 4-methyl-*alpha*-ethylaminopentiophenone (other names: *N*-ethyl-4-methylnorpentedrone, 4-methyl- α -ethylaminopentiophenone, 4-MEAP, 2-(ethylamino)-1-(4-methylphenyl)pentan-1-one),
- 4'-methyl-*alpha*-pyrrolidinohexiophenone (other names: 4'-methyl- α -PHP, 4'-methyl PHP, PV4, 4-MPHP, MPHP, 4-methyl-*alpha*-pyrrolidino hexanophenone, , 1-(4-methylphenyl)-2-(pyrrolidin-1-yl)hexan-1-one),
- *alpha*-pyrrolidinoheptaphenone (other names: *alpha*-pyrrolidinoheptiophenone, *alpha*-PHpP, PV8, 1-phenyl-2-(pyrrolidin-1-yl)heptan-1-one),
and
- 4'-chloro-*alpha*-pyrrolidinovalerophenone (other names: 4-chloro- α -pyrrolidinopentiophenone, 4-chloro- α -PVP, 4-Cl- α -PVP, 4-chloro-2-(1-pyrrolidinyl)-valerophenone, 1-(4-chlorophenyl)-2-(pyrrolidin-1-yl)pentan-1-one).

Posting of Public Comments

Please note that all comments received in response to this docket are considered part of the public record. They will, unless reasonable cause is given, be made available

by DEA for public inspection online at <http://www.regulations.gov>. Such information includes personal identifying information (such as your name, address, etc.) voluntarily submitted by the commenter. The Freedom of Information Act applies to all comments received. If you want to submit personal identifying information (such as your name, address, etc.) as part of your comment, but do not want it to be made publicly available, you must include the phrase “PERSONAL IDENTIFYING INFORMATION” in the first paragraph of your comment. You must also place all of the personal identifying information you do not want made publicly available in the first paragraph of your comment and identify what information you want redacted.

If you want to submit confidential business information as part of your comment, but do not want it to be made publicly available, you must include the phrase “CONFIDENTIAL BUSINESS INFORMATION” in the first paragraph of your comment. You must also prominently identify the confidential business information to be redacted within the comment.

Comments containing personal identifying information or confidential business information identified as directed above will be made publicly available in redacted form. If a comment has so much confidential business information that it cannot be effectively redacted, all or part of that comment may not be made publicly available. Comments posted to <http://www.regulations.gov> may include any personal identifying information (such as name, address, and phone number) included in the text of your electronic submission that is not identified as directed above as confidential.

An electronic copy of this document and supplemental information to this proposed rule are available at <http://www.regulations.gov> for easy reference.

Request for Hearing or Waiver of Participation in Hearing

Pursuant to 21 U.S.C. 811(a), this action is a formal rulemaking “on the record after opportunity for a hearing.” Such proceedings are conducted pursuant to the

provisions of the Administrative Procedure Act, 5 U.S.C. 551–559. 21 CFR 1308.41–1308.45; 21 CFR part 1316, subpart D. Interested persons may file requests for hearing or notices of intent to participate in a hearing in conformity with the requirements of 21 CFR 1308.44(a) or (b), and include a statement of interest in the proceeding and the objections or issues, if any, concerning which the person desires to be heard. Any interested person may file a waiver of an opportunity for a hearing or to participate in a hearing together with a written statement regarding the interested person’s position on the matters of fact and law involved in any hearing as set forth in 21 CFR 1308.44(c).

All requests for a hearing and waivers of participation, together with a written statement of position on the matters of fact and law involved in such hearing, must be sent to DEA using the address information provided above.

Legal Authority

The CSA provides that proceedings for the issuance, amendment, or repeal of the scheduling of any drug or other substance may be initiated by the Attorney General on his own motion. 21 U.S.C. 811(a). This proposed action is supported by a recommendation from the Assistant Secretary for Health of the Department of Health and Human Services (HHS) and an evaluation of all other relevant data by DEA. If finalized, this action would make permanent the existing temporary regulatory controls and administrative, civil, and criminal sanctions for schedule I controlled substances on any person who handles (manufactures, distributes, imports, exports, engages in research, conducts instructional activities or chemical analysis, or possesses) or proposes to handle *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, or 4-chloro- α -PVP.

Background

On July 18, 2019, pursuant to 21 U.S.C. 811(h)(1), DEA published an order in the *Federal Register* (84 FR 34291) temporarily placing *N*-ethylhexedrone, *alpha*-pyrrolidinohexanophenone (α -PHP), 4-methyl-*alpha*-ethylaminopentiophenone (4-

MEAP), 4'-methyl-*alpha*-pyrrolidinohexiophenone (MPHP), *alpha*-pyrrolidinoheptaphenone (PV8), and 4'-chloro-*alpha*-pyrrolidinovalerophenone (4-chloro- α -PVP) in schedule I of the CSA upon finding that these synthetic cathinones pose an imminent hazard to the public safety. That temporary order was effective on the date of publication. Pursuant to 21 U.S.C. 811(h)(2), the temporary control of these substances is set to expire on July 18, 2021. However, this same subsection also provides that, during the pendency of proceedings under 21 U.S.C. 811(a)(1) with respect to a substance, the temporary scheduling of that substance may be extended for up to one year. Proceedings for the scheduling of a substance under 21 U.S.C. 811(a) may be initiated by the Attorney General (delegated to the Administrator of DEA (Administrator) pursuant to 28 CFR 0.100) on his own motion, at the request of the Secretary of HHS,¹ or on the petition of any interested party. An extension of the existing temporary order is being ordered by the Administrator in a separate action, and is being simultaneously published elsewhere in this issue of the *Federal Register*.

The Administrator, on her own motion, is initiating proceedings under 21 U.S.C. 811(a)(1) to permanently schedule *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP. DEA has gathered and reviewed the available information regarding the pharmacology, chemistry, trafficking, actual abuse, pattern of abuse, and the relative potential for abuse for these synthetic cathinones. On October 22, 2020, the Acting Administrator of DEA submitted a request to the Assistant Secretary for Health of HHS (Assistant Secretary) to provide DEA with a scientific and medical evaluation of available information and a scheduling recommendation for *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP, in accordance with 21 U.S.C. 811(b) and (c).

¹ Because the Secretary of HHS has delegated to the Assistant Secretary for Health (Assistant Secretary) the authority to make domestic drug scheduling recommendations, for purposes of this proposed rulemaking, all subsequent references to “Secretary” have been replaced with “Assistant Secretary.”

Upon evaluating the scientific and medical evidence, on July 8, 2021, the Assistant Secretary submitted to the Acting Administrator HHS's scientific and medical evaluation and scheduling recommendation for these substances. Upon receipt of the scientific and medical evaluation and scheduling recommendation from HHS, DEA reviewed the document and all other relevant data, and conducted its own eight-factor analysis of the abuse potential of *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP in accordance with 21 U.S.C. 811(c).

Proposed Determination of Schedule *N*-Ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-Chloro- α -PVP

As discussed in the background section, the Administrator is initiating proceedings, pursuant to 21 U.S.C. 811(a)(1), to add *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP permanently to schedule I. DEA has reviewed the scientific and medical evaluation and scheduling recommendation, received from HHS, and all other relevant data and conducted its own eight-factor analysis of the abuse potential of *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP pursuant to 21 U.S.C. 811(c). Included below is a brief summary of each factor as analyzed by HHS and DEA, and as considered by DEA in its proposed scheduling action. Please note that both the DEA and the HHS 8-Factor analyses and the Assistant Secretary's July 8, 2021 letter are available in their entirety under the tab "Supporting Documents" of the public docket of this rulemaking action at <http://www.regulations.gov>, under Docket Number "DEA-495."

1. *The Drug's Actual or Relative Potential for Abuse:* Both the DEA and the HHS 8-factor analyses found that *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP have abuse potential associated with its abilities to produce psychoactive effects that are similar to those produced by schedule I synthetic cathinones such as methcathinone, mephedrone, methylone, pentylone, and 3,4-methylenedioxypropylone

(MDPV) and schedule II stimulants such as methamphetamine and cocaine that have a high potential for abuse. In particular, the responses in humans to *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP are stimulant-like and include paranoia, agitation, palpitations, tachycardia, hypertension, and hyperthermia.

N-Ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP have no approved medical uses in the United States but there have been reports of individuals experiencing adverse outcomes after taking these substances. Because these substances are not approved drug products, a practitioner may not legally prescribe them, and they cannot be dispensed to an individual. The use of these substances without medical advice leads to the conclusion that these synthetic cathinones are being abused for their psychoactive properties.

Reports from public health and law enforcement state that these substances are being abused and taken in amounts sufficient to create a hazard to an individual's health. This hazard is evidenced by emergency department admissions or deaths, representing a significant safety issue for those in the community. Further, from January 2012 through December 2020 (query date: May 3, 2021), the National Forensic Laboratory Information System (NFLIS) databases registered a total of 2,289 reports by participating DEA, State, local, and other forensic laboratories, as applicable, pertaining to *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP.² NFLIS registered these reports identifying these substances in drug-related exhibits from more than 40 States. MPHP was first identified in June 2012 in seized drug evidence (although MPHP was identified in blood samples from a 27-year-old decedent in 2011), followed by 4-MEAP and PV8 (August and December 2013, respectively), alpha-PHP (May 2014), 4-chloro- α -PVP

² NFLIS is a national drug forensic laboratory reporting system that systematically collects results from drug chemistry analyses conducted by state and local forensic laboratories across the country. The NFLIS participation rate, defined as the percentage of the national drug caseload represented by laboratories that have joined NFLIS, is over 97 percent. NFLIS includes drug chemistry results from completed analyses only.

(December 2015) and most recently *N*-ethylhexedrone (August 2016). Consequently, the data indicate that *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP are being abused, and they present safety hazards to the health of individuals who consume them due to their stimulant properties.

2. *Scientific Evidence of the Drug's Pharmacological Effects, if Known:* As described by HHS, studies show that *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP produce pharmacological effects that are similar to those produced by schedule I and II substances such as methamphetamine (II), cocaine (II), mephedrone (I), MDPV (I), and methylone (I). Similar to these schedule I and II substances, *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP bind to monoamine transporters for dopamine and norepinephrine, and block the uptake of these neurotransmitters at their transporters. *N*-Ethylhexedrone, α -PHP, and MPHP (4-MEAP, PV8, and 4-chloro- α -PVP were not tested in this assay) do not promote the release of these monoamines. Additionally, behavioral studies in animals demonstrate that *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP produce locomotor behavior and discriminative stimulus effects that are similar to those of methamphetamine and cocaine. Overall, these data indicate that *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP produce pharmacological effects and stimulant-like behaviors that are similar to those of other schedule I synthetic cathinones such as methcathinone, mephedrone, MDPV, and methylone, as well as schedule II stimulants methamphetamine and cocaine.

3. *The State of Current Scientific Knowledge Regarding the Drug or Other Substance:* *N*-Ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP are designer drugs of the phenethylamine class and they are structurally similar to permanently controlled schedule I synthetic cathinones and schedule II stimulants like methamphetamine.

Pharmacokinetic studies show that humans, in general, metabolize synthetic cathinones to their corresponding amphetamines followed by reduction of the beta-keto group to the corresponding alcohol which can involve hydrogenation, deethylation, demethylation, or hydroxylation. Given that *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP are synthetic cathinones, it is likely that these six synthetic cathinones are also metabolized to their corresponding amphetamines and alcohols.

Neither DEA nor HHS is aware of any currently accepted medical use for *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP. According to HHS's 2021 scientific and medical evaluation and scheduling recommendation, the Food and Drug Administration (FDA) has not approved marketing applications for drug products containing *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP for any therapeutic indication, nor is HHS aware of any reports of clinical studies or claims of accepted medical use for *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP in the United States.

A drug has a "currently accepted medical use" if DEA concludes that it satisfies a five-part test. Specifically, with respect to a drug that has not been approved by FDA, all of the following must be demonstrated: the drug's chemistry is known and reproducible; there are adequate safety studies; there are adequate and well-controlled studies proving efficacy; the drug is accepted by qualified experts; and the scientific evidence is widely available.³ Based on this analysis, *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP have no currently accepted medical use in the United States.

Furthermore, DEA has not found any references regarding clinical testing of these substances in the scientific and medical literature. Although the chemistry of synthetic

³ 57 FR 10499 (1992), *pet. for rev. denied*, *Alliance for Cannabis Therapeutics v. DEA*, 15 F.3d 1131, 1135 (D.C. Cir. 1994).

cathinones, in general, is known and has been reproduced, as mentioned above there are no clinical studies involving *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP. Taken together with HHS's conclusion, DEA finds that there is no legitimate medical use for *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP in the United States.

4. *History and Current Pattern of Abuse:* Available evidence suggests that the history and pattern of abuse of *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP parallel that of permanently controlled schedule I cathinone stimulants. *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP are synthetic cathinones of the phenethylamine class and they are structurally and pharmacologically similar to schedule I and II substances such as methcathinone (I) and methamphetamine (II). Like these schedule I and II substances, *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP are most likely ingested by swallowing capsules or tablets or snorted by nasal insufflation of the powder tablets. As reported by DEA and HHS, products containing *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, or 4-chloro- α -PVP, similar to schedule I synthetic cathinones, are likely to be falsely marketed as "research chemicals," "jewelry cleaner," "stain remover," "plant food or fertilizer," "insect repellants," or "bath salts;" sold at smoke shops, head shops, convenience stores, adult book stores, or gas stations; and purchased on the Internet. Like those seen with commercial products that contain synthetic cathinones, the packages of products that contain *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, or 4-chloro- α -PVP also probably contain the warning "not for human consumption," most likely in an effort to circumvent statutory restrictions for these substances. Law enforcement data indicate that *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP are available for illicit use and are being abused. Demographic data collected from published reports and mortality records suggest that the main users of *N*-ethylhexedrone, α -PHP, 4-MEAP,

MPHP, PV8, and 4-chloro- α -PVP, similar to other schedule I synthetic cathinones permanently placed in schedule I, are young adults. Toxicology reports also revealed that *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP are being ingested with other substances including other synthetic cathinones, common cutting agents, or other recreational substances. Consequently, products containing synthetic cathinones, including *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, or 4-chloro- α -PVP, are distributed to users, often with unpredictable outcomes. Thus, the recreational abuse of *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP is a significant concern. These data indicate that *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP have a history and current pattern of abuse.

5. *Scope, Duration and Significance of Abuse:* *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP are recreational drugs that emerged on the United States' illicit drug market after the scheduling of other synthetic cathinones (*e.g.*, *N*-ethylpentylone, ethylone, mephedrone, methylone, pentylone, and MDPV) (*see* DEA's Eight Factor Analysis for a full discussion). Forensic laboratories have confirmed the presence of *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP in drug exhibits received from Federal, State, and local law enforcement agencies. MPHP was first identified in June 2012 in seized drug evidence (although MPHP was identified in blood samples from a 27-year-old decedent in 2011 - *see* Factor 6 for details), followed by 4-MEAP and PV8 (August and December 2013, respectively), alpha-PHP (May 2014), 4-chloro- α -PVP (December 2015) and most recently *N*-ethylhexedrone (August 2016). From January 2012 through December 2020 (query date: May 3, 2021), NFLIS database registered a total of 2,289 reports from forensic laboratories pertaining to the 6 synthetic cathinones (*N*-ethylhexedrone, 613 reports; α -PHP – 984 reports; 4-MEAP – 131 reports; MPHP – 92 reports; PV8 – 174 reports; and 4-chloro- α -PVP – 295 reports). HHS reported that there were 13,238 calls to United States poison control centers

(PCCs)⁴ involving synthetic cathinones from 2010 to 2019 and 39 mentions of cathinones of which 23 were for α -PHP on the Dashboard⁵ from July 2018 to July 2020.

Accordingly, concerns over the continuing abuse of synthetic cathinones have led to the control of many synthetic cathinones. A full presentation of the NFLIS reports by substance and year, PCC, and Dashboard data are available in both DEA's and HHS's eight-factor analyses within the Supporting Documents section of the public docket available at <http://www.regulations.gov>.

6. *What, if Any, Risk There Is to the Public Health:* HHS reported that the public health risks of *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP result from their ability to induce stimulant-like responses, which may lead to impaired judgement and dangerous behavior. Adverse health effects associated with the abuse of *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP include a number of stimulant-like adverse health effects such as diaphoresis, insomnia, mydriasis, hyperthermia, vomiting, agitation, disorientation, paranoia, and abdominal pain. Serious adverse events such as acute kidney failure, cardiac arrest, rhabdomyolysis, and coma have been associated with the use of *N*-ethylhexedrone, α -PHP, 4-MEAP, and PV8. In addition, *N*-ethylhexedrone, α -PHP, MPHP, and PV8 have been involved in the deaths of individuals. The identification of *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, or 4-chloro- α -PVP in toxicological samples associated with fatal and non-fatal overdoses as reported in the medical and scientific literature, forensic laboratory reports, and public health documents confirms these adverse effects of *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, or 4-chloro- α -PVP. Like schedule I synthetic cathinones, *N*-

⁴ PCC data are derived from the National Poison Data System, a database managed by the American Association of Poison Control Centers (AAPCC). AAPCC is a nationwide network of PCCs that receive calls from individuals, healthcare professionals, and other interested persons in the general U.S. population regarding exposures to prescription drugs and other substances.

⁵ The Dashboard is an online, interactive tool that reports on the identification of certain novel psychoactive substances in de-identified sample extracts from forensic investigations, including medicolegal death investigations and toxicology testing. The Dashboard was accessed on February 26, 2021.

ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP have caused acute health problems leading to emergency department (ED) admissions, violent behaviors causing harm to self or others, and/or death. Specifically, evidence demonstrate that all six synthetic cathinones have resulted in ED visits that required medical attention, but only *N*-ethylhexedrone, α -PHP, MPHP, and PV8 abuse have been associated with the deaths of individuals. It remains highly likely that additional cases of adverse health effects involving *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP in the United States have occurred and will continue to be under-reported as these substances are not part of standard panels for toxicological analyses of biological specimens. Thus, the abuse of *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP, like that of the abuse of schedule I synthetic cathinones and stimulant drugs, poses significant adverse health risks including death.

Furthermore, because abusers of synthetic cathinones obtain these substances through unregulated sources, the identity, purity, and quantity are uncertain and inconsistent. These unknown factors pose an additional risk for significant adverse health effects to the end user.

Based on information received by DEA, the abuse of *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP has led to, at least, the same qualitative public health risks as other schedule I synthetic cathinones and the schedule II stimulant methamphetamine. The public health risks attendant to the abuse of synthetic cathinones, including *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, or 4-chloro- α -PVP, are well established and have resulted in large numbers of ED visits and fatal overdoses.

7. Its Psychic or Physiological Dependence Liability: According to HHS, the psychic or physiological dependence liability of *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP is demonstrated by their positive abuse-related studies in animals and reported stimulant effects in humans. The results from two behavioral

studies (drug discrimination and locomotor studies) demonstrate that *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, or 4-chloro- α -PVP produced behavioral effects that are similar to those of substances with stimulant effects such as the schedule II stimulants cocaine and methamphetamine. Thus, based on the structural and pharmacological similarities of *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP to schedule II stimulant substances that have demonstrated psychic or physiological dependence liability, it is anticipated that the stimulant properties of *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP produce psychic dependence liability.

8. *Whether the Substance is an Immediate Precursor of a Substance Already Controlled Under the CSA:* *N*-Ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP are not immediate precursors of any controlled substance under the CSA as defined by 21 U.S.C 802(23).

Conclusion: After considering the scientific and medical evaluation conducted by HHS, HHS's scheduling recommendation, and DEA's own eight-factor analysis, DEA finds that the facts and all relevant data constitute substantial evidence of the potential for abuse of *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP. As such, DEA hereby proposes to permanently schedule *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP as controlled substances under the CSA.

Proposed Determination of Appropriate Schedule

The CSA establishes five schedules of controlled substances known as schedules I, II, III, IV, and V. The CSA also outlines the findings required to place a drug or other substance in any particular schedule. 21 U.S.C. 812(b). After consideration of the analysis and recommendation of the Assistant Secretary for Health of HHS and review of all other available data, the Administrator of DEA, pursuant to 21 U.S.C. 811(a) and 812(b)(1), finds that:

1. *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP have a high potential for abuse;
2. *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP have no currently accepted medical use in treatment in the United States; and
3. There is a lack of accepted safety for use of *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP under medical supervision.

Based on these findings, the Administrator concludes that *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP, including their salts, isomers, and salts of isomers, whenever the existence of such salts, isomers, and salts of isomers is possible within the specific chemical designation, warrant control in schedule I of the CSA. 21 U.S.C. 812(b)(1).

Requirements for Handling *N*-Ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-Chloro- α -PVP

If this rule is finalized as proposed, *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, or 4-chloro- α -PVP would continue⁶ to be subject to the CSA's schedule I regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, reverse distribution, importation, exportation, research, and conduct of instructional activities involving the handling of schedule I controlled substances including the following:

1. *Registration.* Any person who handles (manufactures, distributes, reverse distributes, imports, exports, engages in research, or conducts instructional activities or

⁶ *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP are currently subject to schedule I controls on a temporary basis, pursuant to 21 U.S.C. 811(h). 84 FR 34291, July 18, 2019. An order extending the temporary scheduling of *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP for one year is published elsewhere in this issue of the Federal Register, on the same day as this notice of proposed rulemaking.

chemical analysis with, or possesses) or who desires to handle *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, or 4-chloro- α -PVP is required to be registered with DEA to conduct such activities pursuant to 21 U.S.C. 822, 823, 957, and 958, and in accordance with 21 CFR parts 1301 and 1312.

2. *Security.* *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP are subject to schedule I security requirements and must be handled and stored pursuant to 21 U.S.C. 823 and in accordance with 21 CFR 1301.71–1301.76. Non-practitioners handling *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, or 4-chloro- α -PVP must also comply with the employee screening requirements of 21 CFR 1301.90–1301.93.

3. *Labeling and Packaging.* All labels, labeling, and packaging for commercial containers of *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP must be in compliance with 21 U.S.C. 825, and be in accordance with 21 CFR part 1302.

4. *Quota.* Only registered manufacturers are permitted to manufacture *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, or 4-chloro- α -PVP in accordance with a quota assigned pursuant to 21 U.S.C. 826 and in accordance with 21 CFR part 1303.

5. *Inventory.* Any person registered with DEA to handle *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, or 4-chloro- α -PVP must have an initial inventory of all stocks of controlled substances (including *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP) on hand on the date the registrant first engages in the handling of controlled substances pursuant to 21 U.S.C. 827 and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11.

After the initial inventory, every DEA registrant must take an inventory of all controlled substances (including *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP) on hand every two years, pursuant to 21 U.S.C. 827 and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11.

6. *Records and Reports.* Every DEA registrant is required to maintain records and submit reports with respect to *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, or 4-chloro- α -PVP pursuant to 21 U.S.C. 827, and in accordance with 21 CFR 1301.74(b) and (c) and parts 1304, 1312, and 1317. Manufacturers and distributors must submit reports regarding these substances to the Automation of Reports and Consolidated Order System pursuant to 21 U.S.C. 827 and in accordance with 21 CFR parts 1304 and 1312.

7. *Order Forms.* Every DEA registrant who distributes *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, or 4-chloro- α -PVP is required to comply with the order form requirements, pursuant to 21 U.S.C. 828 and 21 CFR part 1305.

8. *Importation and Exportation.* All importation and exportation of *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, or 4-chloro- α -PVP must be in compliance with 21 U.S.C. 952, 953, 957, and 958, and in accordance with 21 CFR part 1312.

9. *Liability.* Any activity involving *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, or 4-chloro- α -PVP not authorized by, or in violation of the CSA or its implementing regulations, is unlawful, and could subject the person to administrative, civil, and/or criminal sanctions.

Regulatory Analyses

Executive Orders 12866 (Regulatory Planning and Review) and 13563 (Improving Regulation and Regulatory Review)

In accordance with 21 U.S.C. 811(a), this proposed scheduling action is subject to formal rulemaking procedures performed “on the record after opportunity for a hearing,” which are conducted pursuant to the provisions of 5 U.S.C. 556 and 557. The CSA sets forth the criteria for scheduling a drug or other substance. Such actions are exempt from review by the Office of Management and Budget (OMB) pursuant to section 3(d)(1) of Executive Order (E.O.) 12866 and the principles reaffirmed in E.O. 13563.

Executive Order 12988, Civil Justice Reform

This proposed regulation meets the applicable standards set forth in sections 3(a) and 3(b)(2) of E.O. 12988 to eliminate drafting errors and ambiguity, minimize litigation, provide a clear legal standard for affected conduct, and promote simplification and burden reduction.

Executive Order 13132, Federalism

This proposed rulemaking does not have federalism implications warranting the application of E.O. 13132. The proposed rule does not have substantial direct effects on the States, on the relationship between the national government and the States, or the distribution of power and responsibilities among the various levels of government.

Executive Order 13175, Consultation and Coordination with Indian Tribal Governments

This proposed rule does not have tribal implications warranting the application of E.O. 13175. It does not have substantial direct effects on one or more Indian tribes, on the relationship between the Federal government and Indian tribes, or on the distribution of power and responsibilities between the Federal government and Indian tribes.

Regulatory Flexibility Act

The Administrator, in accordance with the Regulatory Flexibility Act, 5 U.S.C. 601–612, has reviewed this proposed rule and by approving it certifies that it will not have a significant economic impact on a substantial number of small entities. On July 18, 2019, DEA published an order to temporarily place *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP in schedule I of the CSA pursuant to the temporary scheduling provisions of 21 U.S.C. 811(h). DEA estimates that all entities handling or planning to handle these substances have already established and implemented the systems and processes required to handle *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, or 4-chloro- α -PVP. There are currently 34 unique registrations authorized to handle *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, or 4-chloro- α -PVP specifically,

as well as a number of registered analytical labs that are authorized to handle schedule I controlled substances generally. From review of entity names, DEA estimates these 34 registrations represent 29 entities. Some of these entities are likely to be large entities. However, since DEA does not have information of registrant size and the majority of DEA registrants are small entities or are employed by small entities, DEA estimates a maximum of 29 entities are small entities. Therefore, DEA conservatively estimates as many as 29 small entities are affected by this proposed rule.

A review of the 34 registrations indicates that all entities that currently handle *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, or 4-chloro- α -PVP also handle other schedule I controlled substances, and thus they have established and implemented (or maintain) the systems and processes required to handle *N*-ethylhexedrone, α -PHP, 4-MEAP, MPHP, PV8, and 4-chloro- α -PVP as a schedule I substance. Therefore, DEA anticipates that this proposed rule will impose minimal or no economic impact on any affected entities, and, thus, will not have a significant economic impact on any of the 29 affected small entities. Therefore, DEA has concluded that this proposed rule will not have a significant economic impact on a substantial number of small entities.

Unfunded Mandates Reform Act of 1995

In accordance with the Unfunded Mandates Reform Act (UMRA) of 1995, 2 U.S.C. 1501 *et seq.*, DEA has determined and certifies that this proposed action would not result in any Federal mandate that may result “in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100,000,000 or more (adjusted annually for inflation) in any 1 year * * * .” Therefore, neither a Small Government Agency Plan nor any other action is required under UMRA of 1995.

Paperwork Reduction Act of 1995

This proposed action does not impose a new collection of information under the Paperwork Reduction Act of 1995. 44 U.S.C. 3501–3521. This proposed action would

not impose recordkeeping or reporting requirements on State or local governments, individuals, businesses, or organizations. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, DEA proposes to amend 21 CFR part 1308 as follows:

PART 1308 – SCHEDULES OF CONTROLLED SUBSTANCES

1. The authority citation for part 1308 continues to read as follows:

Authority: 21 U.S.C. 811, 812, 871(b), 956(b), unless otherwise noted.

2. Amend § 1308.11 by:

a. Adding paragraphs (d)(94) through (99); and

b. Removing and reserving paragraphs (h)(42) through (h)(47).

The additions to read as follows:

§ 1308.11 Schedule I.

* * * * *

(d) * * *

(94) *N*-Ethylhexedrone (Other name: α -ethylaminohexanophenone).....7246

(95) *alpha*-Pyrrolidinohexanophenone (Other names: α -PHP, α -pyrrolidino-hexanophenone, 1-phenyl-2-(pyrrolidin-1-yl)hexan-1-one).....7544

(96) 4-Methyl-*alpha*-ethylaminopentiophenone (Other names: 4-MEAP, 2-(ethylamino)-1-(4-methylphenyl)pentan-1-one).....7245

(97) 4'-Methyl-*alpha*-pyrrolidinohexiophenone (Other names: MPHP, 4'-methyl-*alpha*-pyrrolidino hexanophenone; 1-(4-methylphenyl)-2-(pyrrolidin-1-yl)hexan-1-one).....7446

(98) *alpha*-Pyrrolidinoheptaphenone (Other names: PV8, 1-phenyl-2-(pyrrolidin-1-yl)heptan-1-one).....7548

(99) 4'-Chloro-*alpha*-pyrrolidinovalerophenone (Other names: 4-chloro- α -PVP, 4-chloro- α -pyrrolidinopentiophenone, 1-(4-chlorophenyl)-2-(pyrrolidin-1-yl)pentan-1-one).....7443

* * * * *

Anne Milgram,
Administrator.

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