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## DEPARTMENT OF JUSTICE

### Drug Enforcement Administration

#### 21 CFR Part 1308

[Docket No. DEA-357]

### Schedules of Controlled Substances: Placement of Methylone into Schedule I

**AGENCY:** Drug Enforcement Administration, Department of Justice.

**ACTION:** Final Rule.

**SUMMARY:** With the issuance of this final rule, the Administrator of the Drug Enforcement Administration (DEA) places the substance 3,4-methylenedioxy-N-methylcathinone (methylone) including its salts, isomers, and salts of isomers whenever the existence of such salts, isomers, and salts of isomers is possible, into Schedule I of the Controlled Substances Act (CSA). This action is pursuant to the CSA which requires that such actions be made on the record after opportunity for a hearing through formal rulemaking.

**DATES:** *Effective date:* [INSERT DATE OF PUBLICATION IN THE FEDERAL REGISTER].

**FOR FURTHER INFORMATION CONTACT:** John W. Partridge, Executive Assistant, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrisette Drive, Springfield, Virginia 22152; Telephone: (202) 307-7165.

## **SUPPLEMENTARY INFORMATION:**

### **Legal Authority**

The DEA implements and enforces Titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, often referred to as the Controlled Substances Act and the Controlled Substances Import and Export Act (21 U.S.C. 801-971), as amended (hereinafter, “CSA”). The implementing regulations for these statutes are found in Title 21 of the Code of Federal Regulations (CFR), parts 1300 to 1321. Under the CSA, controlled substances are classified in one of five schedules based upon their potential for abuse, their currently accepted medical use, and the degree of dependence the substance may cause. 21 U.S.C. 812. The initial schedules of controlled substances by statute are found at 21 U.S.C. 812(c) and the current list of scheduled substances are published at 21 CFR Part 1308.

Pursuant to 21 U.S.C. 811(a)(1), the Attorney General may, by rule, “add to such a schedule or transfer between such schedules any drug or other substance if he ... (A) finds that such drug or other substance has a potential for abuse, and (B) makes with respect to such drug or other substance the findings prescribed by subsection (b) of section 812 of this title for the schedule in which such drug is to be placed ...” The findings required for the placement of a controlled substance in Schedule I are: “(A) The drug or other substance has a high potential for abuse. (B) The drug or substance has no currently accepted medical use in treatment in the United States (U.S.) (C) There is a lack of accepted safety for use of the drug or other substance under medical supervision.” 21 U.S.C. 812(b). Pursuant to 28 CFR 0.100(b), the Attorney General has delegated this scheduling authority to the Administrator of DEA.

The CSA provides that scheduling of any drug or other substance may be initiated by the Attorney General (1) on his own motion; (2) at the request of the Secretary for Health of the

Department of Health and Human Services (HHS), or (3) on the petition of any interested party. 21 U.S.C. 811(a). This action is based on a recommendation from the Assistant Secretary for Health (Assistant Secretary)<sup>1</sup> of HHS and on an evaluation of all other relevant data by DEA. In light of methylone's current status as a temporarily scheduled, Schedule I controlled substance (see Section titled "Background," below), this action permanently imposes the regulatory controls and criminal sanctions of Schedule I on the manufacture, distribution, dispensing, importation, and exportation of methylone and products containing methylone.

Pursuant to 21 CFR 1308.44(e), the Administrator of DEA may issue her final order "[I]f all interested persons waive or are deemed to waive their opportunity for the hearing or to participate in the hearing." As no requests for a hearing were filed on this proposed scheduling action, all interested persons are deemed to have waived their opportunity for a hearing pursuant to 21 CFR 1308.44(d), and the Administrator may issue her final order without a hearing.

## **Background**

On September 8, 2011, DEA published a Notice of Intent to temporarily place 3,4-methylenedioxy-N-methylcathinone (methylone) along with two other synthetic cathinones (4-methyl-N-methylcathinone (mephedrone) and 3,4-methylenedioxypropylone (MDPV)) into Schedule I pursuant to the temporary scheduling provisions of the CSA. 76 FR 55616.

Following this, on October 21, 2011, DEA published a Final Order in the Federal Register amending 21 CFR 1308.11(g) to temporarily place these three synthetic cathinones into Schedule I of the CSA pursuant to the temporary scheduling provisions of 21 U.S.C. 811(h). 76 FR

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<sup>1</sup> As set forth in a memorandum of understanding entered into by HHS, the Food and Drug Administration (FDA), and the National Institute on Drug Abuse (NIDA), FDA acts as the lead agency within HHS in carrying out the Secretary's scheduling responsibilities under the CSA, with the concurrence of NIDA. 50 FR 9518. In addition, because the Secretary of the Department of Health and Human Services has delegated to the Assistant Secretary for Health of the Department of Health and Human Services the authority to make domestic drug scheduling recommendations, for purposes of this document, all subsequent references to "Secretary" have been replaced with "Assistant Secretary."

65371. This Final Order, which became effective on the date of publication, was based on findings by the DEA Administrator that the temporary scheduling of these three synthetic cathinones was necessary to avoid an imminent hazard to the public safety pursuant to 21 U.S.C. 811(h)(1). At the time the Final Order took effect, the CSA (21 U.S.C. 811(h)(2) (2011)) required that the temporary scheduling of a substance expire at the end of one year from the date of issuance of the scheduling order, and it also provided that, during the pendency of proceedings under 21 U.S.C. 811(a)(1) with respect to the substance, the temporary scheduling of that substance could be extended for up to six months.<sup>2</sup> Under this provision, the temporary scheduling of methylone expired on October 20, 2012. Pursuant to 21 U.S.C. 811(h)(2), an extension until April 20, 2013, was ordered by the DEA Administrator. 77 FR 64032. In addition, on October 17, 2012, DEA published a Notice of Proposed Rulemaking (NPRM) which proposed the permanent placement of methylone in Schedule I of the CSA. 77 FR 63766. This action finalizes the scheduling action proposed in the October 17, 2012, NPRM.

As described in the October 21, 2011, Final Order, methylone is a designer drug of the phenethylamine class and is structurally and pharmacologically similar to amphetamine, 3,4-methylenedioxymethamphetamine (MDMA), cathinone and other related substances. The addition of a beta-keto ( $\beta$ -ketone) substituent to the phenethylamine core structure produces a group of substances that have  $\beta$ -keto-phenethylamine as the core structure. Methylone has a  $\beta$ -keto-phenethylamine core structure. Methylone has been used lawfully as a research chemical, but based on the review of the scientific literature, there are no known medical uses for methylone. Furthermore, the Assistant Secretary has advised that there are no exemptions or

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<sup>2</sup> On July 9, 2012, President Obama signed the Food and Drug Administration Safety and Innovation Act (Pub. L. 112-144) (FDASIA), which amended several provisions of the CSA. Subtitle D of FDASIA is titled the “Synthetic Drug Abuse Prevention Act of 2012.” In particular, FDASIA amended Schedule I of section 202(c) of the CSA to include mephedrone and MDPV but not methylone, and amended section 201(h)(2) to increase the maximum timeframes for temporary scheduling. Pub. L. 112-144, Sections 1152(b) and 1153.

approvals in effect for methylone under section 505 (21 U.S.C. 355) of the Federal Food, Drug, and Cosmetic Act.

### **Determination to Schedule Methylone**

Pursuant to 21 U.S.C. 811 (a), proceedings to add a drug or substance to those controlled under the CSA may be initiated by the Attorney General on his own motion. On March 30, 2012, DEA requested a scientific and medical evaluation and scheduling recommendation from the Assistant Secretary for methylone, mephedrone and MDPV pursuant to 21 U.S.C. 811(b). On August 14, 2012, the Assistant Secretary provided DEA with a scientific and medical evaluation and scheduling recommendation document prepared by the Food and Drug Administration (FDA) titled “Basis for the Recommendation to Place 3,4-Methylenedioxymethcathinone (Methylone) and its Salts in Schedule I of the Controlled Substances Act (CSA).” Pursuant to 21 U.S.C. 811(b), this document contained an eight-factor analysis of the abuse potential of methylone, along with HHS’ recommendation to control methylone under Schedule I of the CSA. Upon receipt and evaluation of the scientific and medical evaluation and scheduling recommendation from the Assistant Secretary,<sup>3</sup> and after conducting an eight-factor analysis of methylone’s abuse potential pursuant to 21 U.S.C. 811(c), DEA published the NPRM titled “Schedules of Controlled Substances: Placement of Methylone into Schedule I” on October 17, 2012. 77 FR 63766. This NPRM proposed placement of methylone into Schedule I of the CSA, and provided an opportunity for all interested persons to request a hearing on or before November 16, 2012, or to submit comments on or before December 17, 2012.

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<sup>3</sup> HHS did not provide a scientific and medical evaluation and scheduling recommendation regarding mephedrone and MDPV. However, mephedrone and MDPV were listed as Schedule I substances under the FDASIA (see Footnote 2, above).

Included below is a brief summary of each factor as analyzed by HHS and DEA, and as considered by DEA in the scheduling decision. Please note that both the DEA and HHS analyses are available under “Supporting and Related Material” of the public docket for this rule at [www.regulations.gov](http://www.regulations.gov) under docket number DEA-357.

1. The Drug’s Actual or Relative Potential for Abuse: The abuse potential of methylone is associated with its ability to evoke pharmacological effects similar to those evoked by the Schedule I and II substances such as cathinone (Schedule I), methcathinone (Schedule I), MDMA (Schedule I), amphetamine (Schedule II), methamphetamine (Schedule II), and cocaine (Schedule II). These Schedule I and II substances have a high potential for abuse.

The legislative history of the CSA suggests the following four prongs to consider in determining whether a particular drug or substance has potential for abuse:<sup>4</sup>

- i. There is evidence that individuals are taking the drug or other substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community; or
- ii. There is significant diversion of the drug or substance from legitimate drug channels; or
- iii. Individuals are taking the substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such drugs; or
- iv. The drug is a new drug so related in its action to a drug or other substance already listed as having a potential for abuse to make it likely that the drug or other substance will have the same potential for abuse as such drugs, thus

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<sup>4</sup> Comprehensive Drug Abuse Prevention and Control Act of 1970, H.R. Rep. No. 91-1444, 91st Cong., Sess. 1 (1970); 1970 U.S.C.A.N. 4566, 4601.

making it reasonable to assume that there may be significant diversion from legitimate channels, significant use contrary to or without medical advice, or that it has a substantial capability of creating hazards to the health of the user or to the safety of the community.

With respect to the first prong, a number of case reports and case series have shown that individuals are taking methylone and products containing methylone in amounts sufficient to induce adverse health effects similar to those induced by amphetamine, methamphetamine, and MDMA, Schedule I and II substances. These effects included elevated body temperature, increases in heart rate and respiratory exchange, changes in blood pressure, seizures, erratic behavior, and coma. Even death has been reported following the abuse of methylone or products containing methylone. Further, law enforcement encounters indicate the occurrence of a fatal automotive accident that was caused by a driver under the influence of a product containing methylone.

In considering evidence of significant diversion of the drug or substance from legitimate drug channels under the second prong, it must be noted that as of October 21, 2011, methylone has been temporarily controlled as a Schedule I substance and thus has not been legally available unless for research purposes. However, the National Forensic Laboratory Information System (NFLIS) details 4,727 reports from state and local forensic laboratories, identifying methylone in drug related exhibits for a period from January 2009 to December 2012 from 42 states.<sup>5</sup> The System to Retrieve Information from Drug Evidence (STRIDE) identified methylone in 404 drug related exhibits from a period from January 2009 to December 2012.<sup>5</sup>

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<sup>5</sup> NFLIS is a program sponsored by DEA's Office of Diversion Control which compiles information on exhibits analyzed in State and local law enforcement laboratories. STRIDE is a DEA database which compiles information on exhibits analyzed in DEA laboratories.

For the third prong, HHS states that there is no currently accepted medical use for methylone and no medical practitioner is currently licensed by law to administer methylone. Indeed, the FDA has not approved a new drug application (NDA) for methylone for any therapeutic indication, and no investigational new drug (IND) application for methylone is currently active. Thus, with no accepted medical use or administering practitioners, individuals currently using products containing methylone are doing so on their own initiative without medical advice from a practitioner licensed to administer methylone.

With regard to the fourth prong, HHS states that methylone produces pharmacological effects similar to those produced by the Schedule I and II central nervous system (CNS) substances such as amphetamine, methamphetamine, cocaine, and MDMA which have a high potential for abuse. Methylone, like these Schedule I and II substances, affects the concentrations of the neurotransmitters dopamine, serotonin and norepinephrine in the CNS. In drug discrimination assays, methylone substitutes for MDMA, amphetamine, methamphetamine, and cocaine, which suggests that methylone will likely produce subjective effects in humans similar to these substances and have a similar pattern of abuse. Methylone, like methamphetamine, amphetamine, and cocaine, is a CNS stimulant and produces locomotor stimulant activity in animals.

Methylone has no known medical use in the U.S. but evidence demonstrates that methylone is being abused by individuals for its psychoactive effects. Methylone has been encountered by law enforcement throughout the U.S. reported in NFLIS and in STRIDE databases suggesting that individuals are abusing methylone. Methylone has also been identified during the toxicological screening of individual human urine samples which also demonstrates that individuals are abusing this substance. In addition, information from poison centers indicates the



abuse of synthetic cathinones which likely includes methylone. The American Association of Poison Control Centers (AAPCC)<sup>6</sup> reported in a press release that poison centers took 304 calls in 2010 regarding synthetic cathinone exposures and 6,136 calls in 2011. As of December 31, 2012, poison centers have received 2,654 calls relating to these products. These calls were received in poison centers representing at least 47 states and the District of Columbia. Although methylone may not be specifically identified during exposure calls or identified by toxicology testing by AAPCC, it is likely that some of these retail products described by the callers contained methylone, based on the identification of methylone in approximately 27% of all synthetic cathinones related exhibits reported to NFLIS from January 2009 to December 2012.

State public health and poison centers have warned of the dangers associated with the use of synthetic cathinones and their associated products that are being found on the designer drug market. In response to the abuse of methylone and other synthetic cathinones, as of March 2013, at least 42 states have emergency scheduled or enacted legislation placing regulatory controls on some or many of the synthetic cathinones including mephedrone, methylone, MDPV or a defined general class of cathinones. Numerous local jurisdictions have also placed controls on methylone and other synthetic cathinones. All five branches of the U.S. military prohibit military personnel from possessing or using synthetic cathinones including methylone.

Methylone has been reported to cause a number of adverse effects that are characteristic of stimulants like methamphetamine, amphetamine, and cocaine. Adverse effects associated with the consumption of methylone include those typical of a sympathomimetic agent such as hyperthermia, seizures, hyponatremia, bruxism, sweating, hypertension, tachycardia, headache, palpitations, thirst, and mydriasis. Other effects that have been reported from the use of methylone include psychological effects such as confusion, psychosis, paranoia, hallucinations,

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<sup>6</sup> AAPCC is a non-profit, national organization that represents the poison centers of the United States.

combativeness, and agitation. Finally, reports of death from individuals abusing methylone indicate that methylone is a serious public health threat.

2. Scientific Evidence of the Drug's Pharmacological Effects, If Known: In the recommendation from HHS for the placement of methylone in Schedule I of the CSA, HHS states that based on the results of preclinical studies and the toxicological profile observed in emergency room cases and medical examiner cases it is highly likely that methylone produces pharmacological effects in humans that are similar to those produced by the Schedule I and II substances amphetamine, methamphetamine, cocaine, and MDMA. These findings are based on published in vitro data such as the release of monoamines, inhibition of reuptake of monoamines, and in vivo studies (microdialysis, locomotor activity, body temperature, drug discrimination) and are also based on data from studies conducted by National Institute on Drug Abuse contract researchers (locomotor, drug discrimination, in vitro receptor binding, and functional assays). The preclinical data show that methylone can substitute for MDMA or amphetamine in rats trained to discriminate amphetamine or MDMA, respectively. Methylone, like methamphetamine, amphetamine, and cocaine, is a CNS stimulant and produces locomotor stimulant effects in animals. Methylone, like methamphetamine, has a rewarding effect as evidenced by conditioned place preference tests. Methylone is an inhibitor of dopamine, serotonin and norepinephrine uptake and also causes the release of these neurotransmitters in the CNS. Furthermore, studies show that methylone, like MDMA, can be cytotoxic to liver cells. HHS further states that the toxicological profile observed in emergency room and medical examiner cases involving methylone demonstrate that the pharmacological profile observed in humans is in accordance with preclinical data.

3. The State of Current Scientific Knowledge Regarding the Drug or Other Substance:

Methylone is a  $\beta$ -ketophenethylamine (i.e., synthetic cathinone) that is structurally and pharmacologically similar to amphetamine, methamphetamine, MDMA, cathinone and other related substances. Methylone can be prepared from its corresponding ketone by a two-step synthesis. Studies indicate that humans metabolize methylone and metabolites of methylone have been found in the urine samples of humans and animals given methylone. Research in anti-depressant and anti-parkinson agents resulted in the synthesis and patenting of methylone. However, according to HHS, methylone has no accepted medical use in the U.S., does not have an approved NDA, and is not currently marketed in the U.S. in an FDA-approved drug product. A drug has a “currently accepted medical use” if all of the following five elements have been satisfied: the drug’s chemistry is known and reproducible; and there are adequate safety studies; and there are adequate and well-controlled studies proving efficacy; and the drug is accepted by qualified experts; and the scientific evidence is widely available. 57 FR 10499. HHS also states that there are no published clinical studies involving methylone. DEA has also not found any references to clinical studies involving methylone’s efficacy and safety in the scientific and medical literature. Although the chemistry of methylone is known and has been reproduced, as mentioned above there are no clinical studies involving methylone. Thus, methylone has no currently accepted medical use in treatment in the U.S. and there is a lack of accepted safety for use of methylone under medical supervision.

4. Its History and Current Pattern of Abuse: Methylone is a synthetic cathinone that emerged on the U.S.’ illicit drug market in 2009 and prior to its temporary control was perceived as being a “legal” alternative to cocaine, methamphetamine, and MDMA. Methylone has been falsely marketed as “research chemicals,” “plant food,” or “bath salts” and has been sold at

smoke shops, head shops, convenience stores, adult book stores, and gas stations and can also be purchased on the Internet under a variety of product names (White Dove, Explosion, Tranquility etc.). It is commonly encountered in the form of powders, capsules, and tablets. The packages of these commercial products usually contain the warning “not for human consumption.” Poison centers reported a large number of toxic exposures to these products as indicated by the number of exposure calls related to synthetic cathinones. A large majority of these exposures were by intentional abuse, misuse, or suspected suicide. Most of these exposures were described as acute. AAPCC data also identified the most common route of administration for the synthetic cathinones as inhalation/nasal. Information from published scientific studies indicate that the most common routes of administration for methylone is ingestion by swallowing capsules or tablets or nasal insufflation by snorting the powder. Evidence from poison centers, published case reports, and law enforcement encounters suggest that the main users of methylone are young adults. These substances are popular among youths and young adults with males appearing to abuse methylone more than females. There is evidence that methylone may be co-ingested with other substances including other synthetic cathinones, pharmaceutical agents, or other recreational substances.

5. The Scope, Duration, and Significance of Abuse: Evidence that methylone is being abused is confirmed by drug courts,<sup>7</sup> calls to poison centers, and encounters by law enforcement. Methylone has been identified in specimens from individuals submitted for testing by drug court participants. Drug courts submitted to DEA 18 reports that detail the analysis of biological specimens that contained synthetic cathinones. Methylone was mentioned in 5 of these reports.

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<sup>7</sup> Drug courts were developed to achieve a reduction in recidivism and substance abuse among nonviolent, substance abusing offenders by increasing their likelihood for successful rehabilitation through early, continuous, and intense judicially supervised treatment, mandatory periodic drug testing, and the use of appropriate sanctions and other rehabilitation services. Drug courts analyze specimens from participants for new and existing drugs of abuse.

Evidence from poison centers also indicates that the abuse of synthetic cathinones like methylone is widespread. The AAPCC reported in a press release that poison centers took 304 calls in 2010 regarding synthetic cathinone exposures and 6,136 calls in 2011. As of December 31, 2012, poison centers have received 2,654 calls relating to these products for calendar year 2012. These calls were received in poison centers representing at least 47 states and the District of Columbia. Methylone may not have been specifically mentioned during the exposure calls but it is likely that some of these retail products described by the callers contained methylone based on the identification of methylone in approximately 27% of all synthetic cathinones related exhibits reported to NFLIS from January 2009 to December 2012. Evidence of the increased abuse of methylone is supported by law enforcement encounters of methylone. Forensic laboratories have analyzed drug exhibits received from state, local, or federal law enforcement agencies that were found to contain methylone.<sup>8</sup> NFLIS details 4,727 reports from state and local forensic laboratories identifying methylone in drug related exhibits for a period from January 2009 to December 2012 from 42 States. NFLIS registered 4 reports identifying methylone from 3 states in 2009. However, there were 71 reports from 18 states related to methylone registered in NFLIS in 2010 and there were 1,712 reports from 41 states in 2011. From January to December 2012 there were 2,940 reports from 40 states. STRIDE also details 404 reports from federal forensic laboratories identifying methylone in drug related exhibits for a period from January 2009 to December 2012. STRIDE (which reports data from 6 DEA laboratories) registered 2 exhibits pertaining to the trafficking, distribution, and abuse of methylone in 2009. There were 13 exhibits pertaining to the trafficking, distribution and abuse of methylone registered in STRIDE in 2010 and 130 drug exhibits in 2011. In 2012, 259 drug

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<sup>8</sup> State and local forensic drug reports from January 2009 to December 2012 analyzed on February 6, 2013 and federal on February 7, 2013. The 2012 drug reports are likely to be incomplete due to laboratory reporting lag time.

exhibits pertaining to the trafficking, distribution and abuse of methylone were recorded in the STRIDE database.

At selected U.S. ports of entry, the U.S. Customs and Border Protection (CBP) has encountered shipments of products containing methylone. The most commonly identified synthetic cathinone was methylone. As of February 2013, methylone was identified in 145 of 352 shipments encountered by CBP from June 2008 to December 2012. These shipments of methylone were in powdered form, ranging from gram to multi-kilogram quantities. Most of the shipments of these synthetic cathinones that contained methylone originated in China and were destined for delivery throughout the U.S. to places like Alaska, Arizona, Arkansas, California, Colorado, Florida, Hawaii, Illinois, Indiana, Kansas, Louisiana, Oklahoma, Oregon, Missouri, Nevada, New Mexico, Tennessee, Texas, Washington, and West Virginia.

Concerns over the abuse of methylone and other synthetic cathinones have prompted many states to control these substances. As of March 2013, at least 42 states have emergency scheduled or enacted legislation placing regulatory controls on some or many of the synthetic cathinones including methylone. In addition, the U.S. Armed Forces prohibited the use of synthetic cathinones including mephedrone, methylone, and MDPV.

6. What, if any, Risk There is to the Public Health: Law enforcement, military, and public health officials have reported exposure incidents that demonstrate the dangers associated with methylone to both the individual abusers and other affected individuals. Numerous individuals have presented at emergency departments following exposure to methylone or products containing methylone. Case reports describe presentations to emergency departments of individuals exposed to methylone with symptoms that include tachycardia, headache, palpitations, agitation, anxiety, mydriasis, tremor, fever, sweating, and hypertension. Some

individuals under the influence of methylone have acted violently and unpredictably causing harm, or even death, to themselves or others. In addition, individuals suspected of driving under the influence of intoxicating substances have been found to have positive test results for methylone and some of these incidents involving methylone intoxications have resulted in the deaths of individuals. There are at least three reported deaths in which methylone was ruled as the cause of death, either by the medical examiner or after an autopsy, and there are many reports in which methylone was implicated (i.e., the primary cause of death is not methylone toxicity) in deaths. Additionally, products containing methylone and other synthetic cathinones often do not bear labeling information regarding their ingredients, and if they do it may not contain the expected active ingredients or identify the health risks and potential hazards associated with these products.

7. Its Psychic or Physiological Dependence Liability: According to HHS, there are no studies or case reports that document the psychic or physiological dependence potential of methylone. However, HHS states that because methylone shares pharmacological properties with those of the Schedule I and II substances amphetamine, methamphetamine, cocaine, and MDMA, it is probable that methylone has a dependence profile similar to that of these substances which are known to cause substance dependence.

8. Whether the Substance is an Immediate Precursor of a Substance Already Controlled Under the CSA: Methylone is not considered an immediate precursor of any controlled substance of the CSA as defined by 21 U.S.C 802(23).

## **Requests for a Hearing and Comments**

DEA received no requests for a hearing on this scheduling action, but did receive 15 comments in response to the October 17, 2012, NPRM to schedule methylone. These comments expressed mixed support for the NPRM.

Comments expressing support for the rule: Five commenters supported the proposal to schedule methylone as a Schedule I substance. One commenter stated that drug forum website accounts regarding methylone indicated elevated heart rates (similar to amphetamines), but that (unlike amphetamines) there was little evidence to suggest any medical benefits from methylone. This commenter concluded that Schedule I placement was appropriate for methylone because of the lack of knowledge regarding the substance and its high potential for harm. Another commenter stated that methylone is a synthetic hallucinogenic amphetamine analogue (similar to MDMA) and that in vitro studies have revealed that methylone is as potent as MDMA in binding to monoamine transporters on the neuronal cell surface, which leads to increased serotonin and dopamine levels in the brain that could enhance the substance's addictive potential. In addition, the commenter stated that subjective comparisons among recreational users regarding methylone's effects suggest subtle differences to those of MDMA. The commenter concluded that due to structural similarities with MDMA, limited safety data, and no identified medical use, classification of methylone as a Schedule I controlled substance was appropriate. Another commenter stated that Schedule I placement for methylone was warranted. The commenter noted that methylone has similar effects to some Schedule I and II controlled substances (such as amphetamine, methamphetamine, cocaine, and MDMA), and that methylone has been used as an alternative to methamphetamine, cocaine, and other illegal drugs. This commenter also stated



that actual abuse data indicates that individuals are abusing methylone and concluded that methylone should be treated like Schedule I drugs.

A social worker emphasized the importance of outreach efforts aimed at educating and informing the public the meaning and consequences of placing methylone in Schedule I of the CSA, the method to identify methylone or substances containing methylone, and the side effects of methylone. The commenter also stated that methylone should be designated as a harmful drug for health care use so that medical costs of treating adverse effects resulting from the use of methylone would be covered by insurance. Finally, the commenter stressed the need for increased law enforcement and drug court funding appropriations in anticipation of the potential increase in drug charges related to methylone.

DEA response: DEA appreciates the support of these commenters for this final rule, but notes that some of the suggestions regarding the consequences of scheduling methylone in Schedule I of the CSA are beyond the scope of the CSA.

Comments expressing opposition to the rule: Nine of the comments were in opposition to the proposed scheduling of methylone in Schedule I of the CSA. Various reasons for the disapproval of the scheduling of methylone were provided. These comments can be grouped in the following general categories: (1) concern over prohibition or restrictions on use in research, (2) concern regarding DEA's findings that methylone has high abuse potential and no currently accepted medical use, (3) concern regarding various procedural aspects of the CSA, and (4) concern about the long-term effects of scheduling methylone.

Concern over prohibition or restriction of use in research: Several commenters claimed that Schedule I placement would put barriers in place for clinicians or researchers who might be interested in investigating the potential benefits of methylone in patients. According to these

commenters, placing methylone in Schedule I would be disastrous for research in the use of serotonin releasing agents to treat anxiety disorders. In addition, the commenters claimed that although recent studies have shown methylone to have tremendous potential and “effectiveness” with regard to post-traumatic stress disorder (PTSD), Schedule I placement “implicitly undermines” and “severely impedes” further research attempts to find medical uses. One of these commenters also claimed that “while, like MDMA, methylone acts to release serotonin, and to a lesser extent dopamine and norepinephrine, it releases these chemicals in different ratios than MDMA.” This commenter reasoned that Schedule I placement would somehow harm efforts to contrast the effects of methylone to MDMA by “essentially silenc[ing]” such research and “hinder[ing] the advancement” of better treatments. Yet another commenter claimed that Schedule I placement would “cripple efforts at learning,” make it “difficult and tedious” to be approved to do research, and “create a stigma” regarding methylone. This commenter reasoned that unknown substances like methylone should be left in a legal status which makes further research into such substances possible.

DEA response: Placement of a substance in Schedule I of the CSA does not preclude scientific research from being conducted using methylone. Any person wishing to conduct research using methylone may do so provided that the person has obtained a Schedule I researcher registration with DEA, has the appropriate research protocols in place with FDA, and meets all other statutory and regulatory requirements. This registration can be obtained by submitting an application for schedule I registration in accordance with 21 CFR 1301.11, 1301.13, 1301.32 and 1301.18.

Concern regarding the pharmacological and abuse potential findings considered by DEA for the purpose of scheduling methylone: Several commenters argued that methylone did not satisfy

the criteria for placement in Schedule I, because it either did not meet the “high potential for abuse” prong or the “no currently accepted medical use in treatment in the U.S.” prong that the CSA requires in order for a substance to be placed in Schedule I. 21 U.S.C. 812(b)(1)(A)-(B).

With regard to methylone’s high potential for abuse, one commenter stated that DEA incorrectly assumed that “methylone” is coextensive with reports of abuse of “synthetic cathinones.” Another commenter stated that scheduling decisions should not be made on the basis of “singular, albeit appalling” “hyperbolic news events.” Yet another commenter stated that the scheduling of methylone was based on “conjecture and one fatality.” Finally, one commenter cited to a published animal study (Baumann et al., 2012, *Neuropsychopharmacology*, 37: 1192-1203) which the commenter claimed “suggests that methylone might have reduced potential for adverse effects and abuse compared to MDMA and methamphetamine.”

With regard to methylone’s currently accepted medical use in treatment in the U.S., one commenter stated that too little is currently known about methylone to conclude that it has no therapeutic value or to justify placement in Schedule I. This commenter claimed that anecdotal reports have shown that methylone has beneficial effects and that it may be of value in treating PTSD or other disorders having an anxiety component. According to the commenter, these facts underscored the need for clinical tests. Another commenter noted that like methylone, Einsteinium, which DEA notes is an element like hydrogen, oxygen, and carbon, lacks a known medical purpose but yet is not a controlled substance.

DEA response: DEA does not agree with these statements. As detailed in the HHS and DEA analyses and the HHS recommendation, studies indicate that the abuse potential and pharmacological effects of methylone are similar to those of Schedule I and II substances. Preclinical studies indicated that methylone, like amphetamine, methamphetamine, cathinone

and methcathinone, has pharmacological effects at monoamine transporters. Furthermore, behavioral effects of methylone in animals and humans were found to be similar to those of Schedule I and II substances which have a high potential for abuse. In humans, methylone is expected to produce subjective responses similar to MDMA, methamphetamine, and cocaine based on drug discriminations studies in rodents. Accordingly, published case reports demonstrate that methylone produces pharmacological effects including adverse effects that are characteristic of substances like MDMA, methamphetamine, amphetamine, and cocaine. In addition, the abuse of methylone presents a safety hazard to the health of individuals. There are reports of emergency room admissions and deaths associated with the abuse of methylone. In addition, there is no currently accepted medical use for methylone (for reasons that have already been provided (see Factor 3, “The State of Current Scientific Knowledge Regarding the Drug or Other Substance,” above)).

Concern regarding various procedural aspects of the CSA: A few commenters raised concerns about the legitimacy of the CSA. One commenter stated that the “CSA should have to prove its effectiveness before expanding its parameters.” Other commenters stated that the CSA is “pointless” and that Schedule I is an unnecessary and harmful classification for any substance.

DEA Response: DEA disagrees with these comments. DEA’s mission is to enforce the controlled substance laws and regulations. Methylone satisfies the CSA’s criteria for placement in Schedule I by virtue of its high potential for abuse, the fact that it has no currently accepted medical use in treatment in the U.S., and its lack of safety for use under medical supervision.

21 U.S.C. 812(b)(1).

Long-term effects: One commenter argued that outlawing methylone would push the market for this dangerous substance further underground and would cause the production of a replacement product.

DEA Response: Persons producing such noncontrolled replacement products may nevertheless subject themselves to criminal prosecution under the Controlled Substances Analogue Enforcement Act of 1986 (Pub. L. 99-570) to the extent such products are intended for human consumption and share sufficient chemical and pharmacological similarities to Schedule I or Schedule II controlled substances. 21 U.S.C. 802(32)(a) and 813.

Allocation of Statutory Responsibilities Between DEA and FDA:

One commenter did not express an opinion either for or against the scheduling of methylone. The commenter stated that FDA should handle pharmacological matters. According to this commenter, DEA is biased which affects its science and taints its decision-making. Thus, FDA's decision would be more objective and science-based. This commenter is concerned that DEA is biased in matters regarding science and this bias taints the DEA's decision making.

DEA Response: Congress has crafted the CSA to ensure a proper balance in scheduling actions by assigning different responsibilities to HHS and to DEA. The CSA requires the Secretary of HHS to consider the scientific evidence of a drug's pharmacological effect (if known) in making its scientific and medical evaluation and scheduling recommendation (21 U.S.C. 811(c)(2)), and provides that "[t]he recommendations of the Secretary to the Attorney General shall be binding on the Attorney General as to such scientific and medical matters ...". 21 U.S.C. 811(b). DEA is directly responsible for review in areas of abuse and diversion.

## **Scheduling Conclusion**

Based on consideration of the scientific and medical evaluation and accompanying recommendation of HHS, and based on DEA's consideration of its own eight-factor analysis, DEA finds that these facts and all relevant data constitute substantial evidence of potential for abuse of methylone. As such, DEA hereby will schedule methylone as a controlled substance under the CSA.

## **Determination of Appropriate Schedule**

The CSA establishes five schedules of controlled substances known as Schedules I, II, III, IV, and V. The statute 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 recommendations of the Assistant Secretary for Health of HHS and review of all available data, the Administrator of DEA, pursuant to 21 U.S.C. 812(b)(1), finds that:

- (1) 3,4-methylenedioxy-N-methylcathinone (methylone) has a high potential for abuse;
- (2) 3,4-methylenedioxy-N-methylcathinone (methylone) has no currently accepted medical use in treatment in the U.S.; and
- (3) there is a lack of accepted safety for use of 3,4-methylenedioxy-N-methylcathinone (methylone) under medical supervision.

Based on these findings, the Administrator of DEA concludes that 3,4-methylenedioxy-N-methylcathinone (methylone) including its salts, isomers and salts of isomers, whenever the existence of such salts, isomers, and salts of isomers is possible, warrants control in Schedule I of the CSA (21 U.S.C. 812(b)(1)).

## **Requirements for Handling Methylone**

Methylone is currently scheduled on a temporary basis in Schedule I and is therefore currently subject to the CSA regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, possession, dispensing, importing, and exporting of a Schedule I controlled substance, including those listed below. These controls on methylone will continue on a permanent basis:

Registration. Any person who manufactures, distributes, dispenses, imports, exports, engages in research or conducts instructional activities with methylone or who desires to manufacture, distribute, dispense, import, export, engage in research or conduct instructional activities with methylone must be registered to conduct such activities pursuant to 21 U.S.C. 822 and 958 and in accordance with 21 CFR Part 1301.

Security. Methylone is subject to Schedule I security requirements and must be manufactured and distributed pursuant to 21 U.S.C. 823 and in accordance with 21 CFR 1301.71, 1301.72(a), (c) and (d), 1301.73, 1301.74, 1301.75(a) and (c), 1301.76.

Labeling and Packaging. All labels and labeling for commercial containers of methylone must be in accordance with 21 CFR 1302.03-1302.07, pursuant to 21 U.S.C. 825.

Quotas. Quotas for methylone have been established based on registrations granted and quota applications received pursuant to part 1303 of Title 21 of the Code of Federal Regulations.

Inventory. Every registrant required to keep records and who possesses any quantity of methylone must keep an inventory of all stocks of methylone on hand pursuant to 21 U.S.C. 827 and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11. Every registrant who desires registration in Schedule I for methylone must conduct an inventory of all stocks of the substance on hand at the time of registration.

Records. All registrants must keep records pursuant to 21 U.S.C. 827 and in accordance with 21 CFR 1304.03, 1304.04, 1304.21, 1304.22, and 1304.23.

Reports. All registrants required to submit reports pursuant to 21 U.S.C. 827 and in accordance with 21 CFR 1304.33 must do so regarding methylene.

Order Forms. All registrants involved in the distribution of methylene must comply with the order form requirements pursuant to 21 U.S.C. 828 and 21 CFR 1305.

Importation and Exportation. All importation and exportation of methylene must be done in accordance with 21 CFR Part 1312, pursuant to 21 U.S.C. 952, 953, 957, and 958.

Criminal Liability. Any activity with methylene not authorized by, or in violation of, the Controlled Substances Act or the Controlled Substances Import and Export Act is unlawful.

## **Regulatory Analyses**

### **Executive Orders 12866 and 13563**

In accordance with 21 U.S.C. 811(a), this scheduling action is subject to formal rulemaking procedures done “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 pursuant to Section 3(d)(1) of Executive Order 12866 and the principles reaffirmed in Executive Order 13563.

### **Executive Order 12988**

This regulation meets the applicable standards set forth in Sections 3(a) and 3(b)(2) of Executive Order 12988 Civil Justice Reform 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**

This rulemaking does not have federalism implications warranting the application of Executive Order 13132. The 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**

This rule does not have tribal implications warranting the application of Executive Order 13175. The rule 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) (RFA), has reviewed this final rule and by approving it certifies that it will not have a significant economic impact on a substantial number of small entities. First, there is no commercial, industrial, or accepted medical use for methylone. At least 42 states have already prohibited the manufacture, distribution, and use of methylone, and all U.S. military service members are prohibited from possessing and using it. There have been 30 entities registered with the DEA to handle methylone since it was temporarily scheduled on October 21, 2011. If the synthetic cannabinoid JWH-018 is used as a reference, as it also has no commercial, industrial, or accepted medical use, there are currently 40 entities registered to handle this substance since it was temporarily scheduled on March 1, 2011, and subsequently placed in Schedule I permanently on July 9, 2012, by the Synthetic Drug Abuse Prevention Act of 2012, Pub. L. 112-144, Title XI, Subtitle D, Sections 1151-1153. Based on this, and because there have been no references to

clinical studies involving methylone in the scientific and medical literature, DEA assumes the number of entities registered to handle methylone will remain relatively small. Secondly, there are approximately 1.4 million controlled substances registrants who represent approximately 381,000 businesses affected by this rule. DEA estimates that 371,000 (97 percent) of the affected businesses are considered “small entities” in accordance with the RFA and Small Business Administration standards. 5 U.S.C. 601(6) and 15 U.S.C. 632. Even if all those registered to handle methylone (30 entities) are considered to be small entities, the number of small entities affected by this rule would not be substantial.

#### **Unfunded Mandates Reform Act of 1995**

This rule does not include a 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 for inflation) in any one year. Therefore, no actions were deemed necessary under provisions of the Unfunded Mandates Reform Act of 1995 (UMRA).

#### **Paperwork Reduction Act of 1995**

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

#### **Congressional Review Act**

This rule is not a major rule as defined by § 804 of the Small Business Regulatory Enforcement Fairness Act of 1996 (Congressional Review Act (CRA)). This rule will not result in: an annual effect on the economy of \$100,000,000 or more; a major increase in costs or prices for consumers, individual industries, Federal, State, or local government agencies, or geographic regions; or significant adverse effects on competition, employment, investment, productivity, innovation, or on the ability of U.S.-based companies to compete with foreign based companies

in domestic and export markets. However, pursuant to the CRA, DEA has submitted a copy of this Final Rule to both Houses of Congress and to the Comptroller General.

**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, 21 CFR Part 1308 is amended to read as follows:

**PART 1308— SCHEDULES OF CONTROLLED SUBSTANCES**

1. The authority citation for 21 CFR Part 1308 continues to read as follows:

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

2. Section 1308.11 is amended by adding a new paragraph (d)(47) to read as follows:

**§ 1308.11 Schedule I.**

\* \* \* \* \*

(d) \* \* \*

(47) 3,4-Methylenedioxy-N-methylcathinone (Methylone) .....(7540)

\* \* \* \* \*

April 5, 2013

Dated:

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Michele M. Leonhart  
Administrator

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