DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary

Office of the Assistant Secretary for Health
Washington, D.C. 20201

DEC - 4 2013

Mr. Thomas M. Harrigan
Deputy Administrator
Drug Enforcement Administration
U. S. Department of Justice
8701 Morrissette Drive
Springfield, VA 22152

Dear Mr. Harrigan:

Thank you for your recent letter notifying me of your intention to temporarily place 4-methyl-*N*-ethylcathinone (4-MEC), 4-methyl-α-pyrrolidinopropiophenone (4-MePPP), alpha-pyrrolidinopentiophenone (α-PVP), 1-(1,3-benzodioxol-5-yl)-2-(methylamino)butan-1-one (butylone), 2-(methylamino)-1-phenylpentan-1-one (pentedrone), 1-(1,3-benzodioxol-5-yl)-2-(methylamino)pentan-1-one (pentylone), 4-fluoro-*N*-methylcathinone (4-FMC), 3-fluoro-*N*-methylcathinone (3-FMC), naphthylpyrovalerone (naphyrone), and alpha-pyrrolidinobutiophenone (α-PBP) into Schedule I of the Controlled Substances Act (CSA).

I asked the Food and Drug Administration to review its files and the agency has advised me that there are currently no approved new drug applications or investigational new drug applications for any of these substances. Therefore, the Department of Health and Human Services has no objection regarding your plans to temporarily place 4-MEC, 4-MePPP, a-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and a-PBP into Schedule I of the CSA.

Sincerely yours,

Howard K. Koh

Howard K. Koh, M.D., M.P.H.
Assistant Secretary for Health

4-Methyl-*N*-ethylcathinone (4-MEC), 4-Methyl-*alpha*-pyrrolidinopropiophenone (4-MePPP), Alpha-pyrrolidinopentiophenone (α-PVP), 1-(1,3-Benzodioxol-5-yl)-2-(methylamino)butan-1-one (Butylone), 2-(Methylamino)-1-phenylpentan-1-one (Pentedrone), 1-(1,3-Benzodioxol-5-yl)-2-(methylamino)pentan-1-one (Pentylone), 4-Fluoro-*N*-methylcathinone (4-FMC), 3-Fluoro-*N*-methylcathinone (3-FMC), 1-(Naphthalen-2-yl)-2-(pyrrolidin-1-yl)pentan-1-one (Naphyrone), and Alpha-pyrrolidinobutiophenone (α-PBP)

Background Information and Evaluation of 'Three Factor Analysis' (Factors 4, 5 and 6) for Temporary Scheduling

Drug and Chemical Evaluation Section, Office of Diversion Control, Drug Enforcement Administration, Washington, DC 20537

January 2014

I. Introduction

Synthetic cathinones (also commonly referred to as substituted cathinones or cathinone derivatives) are β-keto-phenethylamine derivatives. A number of synthetic cathinones produce pharmacological effects that are substantially similar to those of the Schedule I substances cathinone, methcathinone, and 3,4-methylenedioxymethamphetamine (MDMA) and Schedule II stimulants amphetamine, methamphetamine, and cocaine. Products that contain synthetic cathinones have been falsely marketed as "research chemicals," "jewelry cleaner," "stain remover," "plant food or fertilizer," "insect repellants" or "bath salts." These products are sold at smoke shops, head shops, convenience stores, adult book stores, and gas stations and can also be purchased on the Internet. The packages of these commercial products usually contain the warning "not for human consumption" most likely in an effort to circumvent statutory restrictions for these substances.

The Drug Enforcement Administration (DEA) temporarily placed three synthetic cathinones, namely, 4-methyl-*N*-methylcathinone (mephedrone), 3,4-methylenedioxy-*N*-methylcathinone (methylone), and 3,4-methylenedioxypyrovalerone (MDPV), in Schedule I of

the Controlled Substances Act (CSA) on October 21, 2011. 76 FR 65371. On July 9, 2012, President Obama signed the Food and Drug Administration Safety and Innovation Act (FDASIA), which made the manufacturing, distribution, dispensing, and possession of mephedrone and MDPV illegal[1]. On October 18, 2012, a final order was issued by DEA placing methylone in Schedule I of the CSA. 77 FR 64032.

Around the time that these three synthetic cathinones were scheduled, other synthetic cathinone substances, as evidenced by law enforcement encounters, emerged in the U.S. illicit drug market. These synthetic cathinone substances contain slight alterations of the chemical structure of known Schedule I or II psychoactive substances (phenethylamines and β-keto-phenethylamines). The other synthetic cathinone substances are (1) 4-methyl-*N*-ethylcathinone ("4-MEC"); (2) 4-methyl-*alpha*-pyrrolidinopropiophenone ("4-MePPP"); (3) alpha-pyrrolidinopentiophenone ("α-PVP"); (4) 1-(1,3-benzodioxol-5-yl)-2-(methylamino)butan-1-one ("butylone"); (5) 2-(methylamino)-1-phenylpentan-1-one ("pentedrone"); (6) 1-(1,3-benzodioxol-5-yl)-2-(methylamino)pentan-1-one ("pentylone"); (7) 4-fluoro-*N*-methylcathinone ("4-FMC"); (8) 3-fluoro-*N*-methylcathinone ("3-FMC"); (9) 1-(naphthalen-2-yl)-2-(pyrrolidin-1-yl)pentan-1-one ("naphyrone"); and (10) alpha-pyrrolidinobutiophenone ("α-PBP").

Evidence indicates that 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP, like the Schedule I cathinones mephedrone, methylone, and MDPV, are being abused for their psychoactive properties. Many of these synthetic cathinone substances share many substantial similarities with Schedule I and Schedule II substances including reported desired and adverse effects. In general, desired effects reported by abusers of synthetic cathinone substances include euphoria, sense of well-being, increased sociability, energy, empathy, increased alertness, and improved concentration and focus. Abusers also report experiencing unwanted effects such as tremor, vomiting, agitation, sweating, fever, chest pain. Other adverse or toxic effects that have been reported with the abuse of synthetic cathinones include tachycardia, hypertension, hyperthermia, mydriasis,

[1] Subtitle D of the FDASIA titled the "Synthetic Drug Abuse Prevention Act of 2012," (SDAPA) amended Schedule I of section 202 of the CSA.

rhabdomyolysis, hyponatremia, seizures, altered mental status (paranoia, hallucinations, delusions), and even death. These 10 synthetic cathinone substances have no known medical use in the United States but evidence demonstrates that these substances are being used by individuals. There have been documented reports of emergency room admissions and deaths associated with the abuse of synthetic cathinone substances. Thus, the abuse of synthetic cathinone substances including these 10 synthetic cathinone substances continues to be a serious public health threat.

Evidence from poison centers, emergency departments (EDs), and law enforcement indicates that synthetic cathinone substances continue to be abused in the United States. According to a press release from the American Association of Poison Control Centers (AAPCC),[2] there were 306 exposure calls related to synthetic cathinones in 2010, 6,137 calls in 2011, and 2,691 calls in 2012 (AAPCC, 2013). As of October 31, 2013, poison centers received 833 calls relating to human exposures to bath salts. In addition, according to the Drug Abuse Warning Network (DAWN) report released by the Substance Abuse and Mental Health Services Administration (SAMHSA)[3], in 2011, "bath salts" were involved in 22,904 ED visits.

Both the National Forensic Laboratory Information System (NFLIS), a DEA sponsored program that systematically collects drug identification results and associated information from drug cases analyzed by Federal, State, and local forensic laboratories, and the System To Retrieve Information from Drug Evidence (STRIDE), a federal database for the drug samples analyzed by DEA forensic laboratories, registered encounters of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP (Table 1, Factor 5, and the Appendix). In 2009, NFLIS registered no reports in state and local law enforcement laboratories regarding these synthetic cathinone substances. However, in 2010, there were 13 reports from 5 states related to these substances registered in NFLIS, in 2011 there were 800 reports from 32 states, in 2012 there were 5,485 reports from 41 states, and from January to

[2] AAPCC is a non-profit, national organization that represents the poison control centers of the United States.
[3] DAWN is a public health surveillance system that monitors drug-related ED visits in the United States.

November 2013 there were 2,509 reports from 41 states.[4] From January 2010 to November 2013, 1,732 drug exhibits pertaining to the trafficking, distribution and abuse of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP were recorded in the STRIDE database (which reports data from DEA laboratories).[5] Law enforcement have encountered these synthetic cathinones substances mainly in powder, crystal, resin, tablet, and capsule forms.

With no legitimate medical use and limited pharmacological information, these substances (4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP) have emerged on the designer drug market and are being abused for their psychoactive properties. To protect the public health and safety, DEA intends to temporarily place 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP in Schedule I of the CSA. With respect to finding an imminent hazard to the public safety, DEA has considered the factors required under the CSA for the temporary scheduling of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP. 21 U.S.C. 811(h)(3) and 811(c)(4)-(6).

Synthetic Cathinones

4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP are synthetic cathinones (β-keto-phenethylamines) of the larger phenethylamine structural class (amphetamines, cathinones, 2C compounds, aminoindanes, etc.). They are designer drugs of the phenethylamine class which are structurally and pharmacologically similar to amphetamine, MDMA, cathinone and other related substances. Synthetic cathinones share a core phenethylamine structure with substitutions at the β-position, α-position, phenyl ring, or nitrogen atom (Figure 1). The addition of a beta-keto (β-keto) substituent [i.e., carbonyl (C=O)] to the phenethylamine core structure along with substitutions on the alpha (α) carbon (C) atom

[4] NFLIS analyzed on 12/20/ 2013 for state and local forensic drug reports.
[5] STRIDE data was queried on 12/20/2013 by date submitted to Federal forensic laboratories.

or the nitrogen (N) atom produce a variety of substances called cathinones or synthetic cathinones.

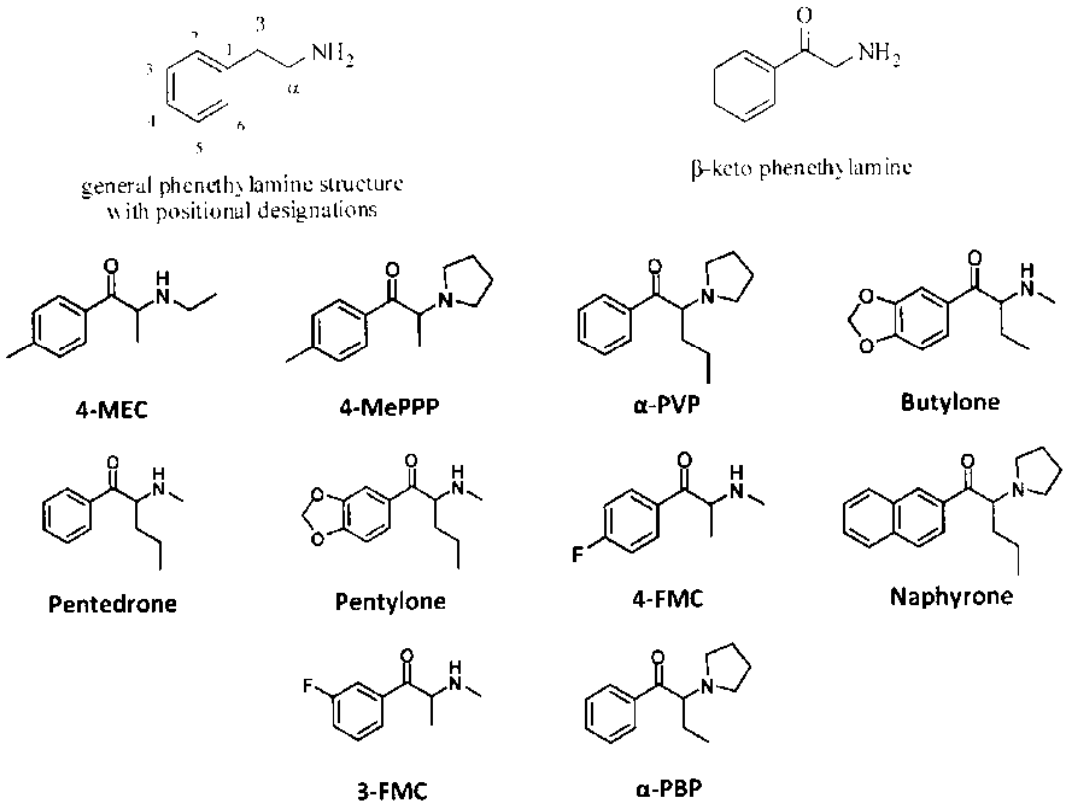

Figure 1: Chemical Structures

Although the abuse potential of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP has not been systematically studied in humans, the available data indicate that the pharmacological actions of these substances are substantially similar to those of stimulants and hallucinogens such as mephedrone, MDPV, cathinone methcathinone, and MDMA which are Schedule I substances with high potential for abuse. Scientific studies, which include those done by contract researchers for the National Institute on Drug Abuse (NIDA), evaluating the pharmacological activity of these synthetic cathinone substances demonstrate that these substances have pharmacological effects on the central nervous system that are substantially similar to those of the Schedule I and II substances, MDPV, methylone, mephedrone, methamphetamine, MDMA, methcathinone, and

cocaine. Like these Schedule I and II substances, 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP bind to monoamine transporters for dopamine, serotonin, or norepinephrine and promote the release of these monoamines or block their uptake (Han and Gu, 2006; Howell and Kimmel, 2008). Actions at these transporters, especially actions that alter dopaminergic neurotransmission, are believed to be involved in the production of the stimulant effects of the phenethylamine class of drugs (Rothman et al., 2001; Mori et al., 2012). Data also demonstrate that these synthetic cathinone substances are locomotor stimulants and produce discriminative stimulus effects (as determined in drug discrimination studies) that are substantially similar to those of the Schedule I and II substances, methamphetamine and cocaine. In the drug discrimination paradigm, if a new drug or substance has discriminative stimulus effects in animals similar to a known drug of abuse, it is highly likely that this new drug will produce pharmacological effects (including subjective effects) in humans similar to the known drug of abuse and would be similarly abused by humans (Balster and Bigelow, 2003).

4-Methyl-N-ethylcathinone (4-MEC)

4-MEC, in addition to the β-keto substituent [a carbonyl (C=O) group which is common amongst synthetic cathinones], has a ring substitution of a methyl ($-CH_3$) group on the phenethylamine core structure and the nitrogen atom is substituted with an ethyl group ($-CH_2CH_3$) (Figure 1). Scientific studies evaluating the pharmacological activity of 4-MEC demonstrate that 4-MEC has pharmacological effects that are substantially similar to those of mephedrone, MDPV, cathinone, methcathinone, and other related substances, which are Schedule I substances with high potential for abuse. In laboratory studies investigating the effects of drugs on monoaminergic systems, 4-MEC, like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone) and methamphetamine, inhibits the uptake of the monoamine neurotransmitter dopamine in transfected cells (Cozzi et al., 1999; Eshleman et al., 2013; NIDA, 2013; Simmler et al., 2013). In locomotor activity assays, 4-MEC, like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone) and methamphetamine, is a locomotor stimulant in rodents (Glennon et al., 1995; Baumann et

al., 2012; NIDA, 2012; Gatch et al., 2013). In drug discrimination studies, 4-MEC (ED_{50}[6] = 18.6 and 11.4 mg/kg), like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone), fully substitutes for the discriminative stimulus effects produced by 1 mg/kg methamphetamine and 10 mg/kg cocaine, respectively, indicating that it is highly likely that this new drug will produce pharmacological effects (including subjective effects) in humans similar to the known drugs of abuse (i.e. methamphetamine or cocaine) and, thus, would be similarly abused by humans (Balster and Bigelow, 2003; NIDA, 2012, 2013; Gatch et al., 2013).

4-Methyl-α-pyrrolidinopropiophenone (4-MePPP)

4-MePPP, in addition to the β-keto substituent, has a ring substitution of a methyl (-CH_3) group on the phenethylamine core structure and is substituted on the nitrogen atom to form a pyrrolidine ring (Figure 1). Scientific studies evaluating the pharmacological activity of 4-MePPP demonstrate that 4-MePPP has pharmacological effects that are substantially similar to those of mephedrone, MDPV, cathinone and methcathinone, which are Schedule I substances with high potential for abuse. In laboratory studies investigating the effects of drugs on monoaminergic systems 4-MePPP, like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone) and methamphetamine, inhibits the uptake of the monoamine neurotransmitter dopamine in transfected cells (Eshleman et al., 2013; NIDA, 2013; Simmler et al., 2013). In locomotor activity assays, 4-MePPP, like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone) and methamphetamine, increases locomotor activity in rodents (Glennon et al., 1995; NIDA, 2012; Baumann et al., 2013; Gatch et al., 2013). In drug discrimination studies, 4-MePPP (ED_{50} = 13.35 and 8.91 mg/kg), like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone), fully substitutes for the discriminative stimulus effects produced by 1 mg/kg methamphetamine and 10 mg/kg cocaine, respectively (NIDA, 2012; Gatch et al., 2013).

[6] ED_{50} for drug discrimination studies is the dose at which the subjects would be expected to make 50% of their responses on the drug-appropriate lever

Alpha-pyrrolidinopentiophenone (α-PVP)

In addition to the β-keto substituent, α-PVP has a substitution on the nitrogen atom of the phenethylamine core structure to form a pyrrolidine ring and a chain of three carbon atoms attached to the α-carbon position (Figure 1). α-PVP has pharmacological effects on the central nervous system that are substantially similar to those of mephedrone, MDPV, cathinone and methcathinone, which are Schedule I substances with high potential for abuse. In laboratory studies investigating the effects of drugs on monoaminergic systems, α-PVP, like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone) and methamphetamine, inhibits the uptake of the monoamine neurotransmitter dopamine in rat brain synaptosomes or in cells that have been transfected with the corresponding transporter (Cozzi et al., 1999; Meltzer, 2006; Baumann et al., 2013; Eshleman et al, 2013; NIDA, 2013; Simmler et al., 2013). In locomotor activity assays, α-PVP, like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone) and methamphetamine, increases locomotor activity in rodents (Glennon et al., 1995; Baumann et al., 2013; Gatch et al., 2013; NIDA, 2013). In drug discrimination studies, α-PVP (ED_{50} = 0.46 and 2.77 mg/kg), like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone), fully substitutes for the discriminative stimulus effects produced by 1 mg/kg methamphetamine and 10 mg/kg cocaine, respectively (NIDA, 2012, 2013; Gatch et al., 2013).

1-(1,3-Benzodioxol-5-yl)-2-(methylamino)butan-1-one (butylone)

Butylone, in addition to the β-keto substituent, has an ethyl group ($-CH_2CH_3$) at the α-position, a methylenedioxy ring attached to the phenyl ring, and a methyl group ($-CH_3$) attached to the nitrogen atom (Figure 1). The pharmacological effects of butylone on the central nervous system are substantially similar to those of mephedrone, MDPV, cathinone and methcathinone, which are Schedule I substances with high potential for abuse. In laboratory studies investigating the effects of drugs on monoaminergic systems, butylone, like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone) and methamphetamine, inhibits the uptake of the monoamine neurotransmitter dopamine in transfected cells (Cozzi et al., 1999; Eshleman et al., 2013; Simmler et al., 2013). In locomotor activity assays, butylone, like several other synthetic cathinones (methcathinone, methylone,

MDPV, and mephedrone) and methamphetamine, has been shown to stimulate locomotor activity in mice (Glennon et al., 1995; NIDA, 2012; Gatch et al., 2013). In drug discrimination studies, butylone (ED_{50} = 2.52 and 4.78 mg/kg), like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone), fully substitutes for the discriminative stimulus effects produced by 1 mg/kg methamphetamine and 10 mg/kg cocaine, respectively (NIDA, 2012; Gatch et al., 2013).

2-(Methylamino)-1-phenylpentan-1-one (pentedrone)

Pentedrone, in addition to the β-keto substituent, has a chain of three carbon atoms, a propyl group ($-CH_2CH_2CH_3$) attached to the α-carbon position, and a methyl group ($-CH_3$) attached to the nitrogen atom (Figure 1). Pentedrone has pharmacological effects that are substantially similar to those of mephedrone, MDPV, cathinone and methcathinone, which are Schedule I substances with high potential for abuse. In laboratory studies investigating the effects of drugs on monoaminergic systems, pentedrone, like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone) and methamphetamine, inhibits the uptake of the monoamine neurotransmitter dopamine in transfected cells (Cozzi et al., 1999; Eshlemen et al., 2013; NIDA, 2013; Simmler et al., 2013). In locomotor activity assays, pentedrone, like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone) and methamphetamine, increases locomotor activity in rodents (Glennon et al., 1995; Baumann et al., 2012; NIDA, 2012). In drug discrimination studies, pentedrone (ED_{50}= 2.67 and 2.58 mg/kg) like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone), fully substitutes for the discriminative stimulus effects produced by 1 mg/kg methamphetamine and 10 mg/kg cocaine, respectively (NIDA, 2012, 2013; Gatch et al., 2013).

1-(1,3-Benzodioxol-5-yl)-2-(methylamino)pentan-1-one (pentylone)

In addition to the β-keto substituent, the α-position alkyl group for pentylone is a propyl ($-CH_2CH_2CH_3$) group, the nitrogen atom substitution is a methyl ($-CH_3$) group, and the phenyl ring substitution is a methylenedioxy group (Figure 1). Pentylone as pharmacological effects that are substantially similar to those of mephedrone, MDPV, cathinone and methcathinone,

which are Schedule I substances with high potential for abuse. In laboratory studies investigating the effects of drugs on monoaminergic systems, pentylone, like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone) and methamphetamine, inhibits the uptake of the monoamine neurotransmitter dopamine in transfected cells (Cozzi et al., 1999; Eshlemen et al., 2013; NIDA, 2013). In locomotor activity assays, pentylone, like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone) and methamphetamine, is a locomotor stimulant (Glennon et al., 1995; Baumann et al., 2012; Gatch et al., 2013; NIDA, 2012). In drug discrimination studies, pentylone (ED_{50} = 3.86 and 2.33 mg/kg), like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone), fully substitutes for the discriminative stimulus effects produced by 1 mg/kg methamphetamine and 10 mg/kg cocaine, respectively (NIDA, 2012; Gatch et al., 2013).

4-Fluoro-N-methylcathinone (4-FMC)

4-FMC (also known as flephedrone), in addition to the β-keto substituent, incorporates a methyl (-CH_3) group at the α-carbon and a phenyl ring substitution of a fluorine (F) atom (Figure 1). Additionally, the nitrogen atom is substituted with a methyl group. 4-FMC has pharmacological effects that are substantially similar to those of mephedrone, MDPV, cathinone and methcathinone, which are Schedule I substances with high potential for abuse. In laboratory studies investigating the effects of drugs on monoaminergic systems, 4-FMC, like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone) and methamphetamine, inhibits the uptake of the monoamine neurotransmitter dopamine in transfected cells (Cozzi et al., 1999; Eshleman et al., 2013; Simmler et al., 2013). In locomotor activity assays, 4-FMC, like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone) and methamphetamine, increases locomotor activity in rodents (Glennon et al., 1995; Baumann et al., 2012; Marusich et al., 2012; Gatch et al., 2013). In drug discrimination studies, 4-FMC (ED_{50} = 2.69 and 3.24 mg/kg), like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone), fully substitutes for the discriminative stimulus effects produced by 1 mg/kg methamphetamine and 10 mg/kg cocaine, respectively (NIDA, 2012; Gatch et al., 2013).

3-Fluoro-N-methylcathinone (3-FMC)

3-FMC, in addition to the β-keto substituent, incorporates a methyl (-CH_3) group at the α-carbon and a phenyl ring substitution of a fluorine (F) atom (Figure 1). Additionally, the nitrogen atom is substituted with a methyl group. 3-FMC has pharmacological effects that are substantially similar to those of mephedrone, MDPV, cathinone and methcathinone, which are Schedule I substances with high potential for abuse. In laboratory studies investigating the effects of drugs on monoaminergic systems, 3-FMC, like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone) and methamphetamine, inhibits the uptake of the monoamine neurotransmitter dopamine in transfected cells (Cozzi et al., 1999; Eshlemen et al., 2013; NIDA, 2013). In locomotor activity assays, 3-FMC, like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone) and methamphetamine, increases locomotor activity in rodents (Glennon et al., 1995; NIDA, 2012; Baumann et al., 2012; Marusich et al., 2012; Gatch et al., 2013). In drug discrimination studies, 3-FMC (ED_{50}=0.84 and 0.82 mg/kg), like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone), fully substitutes for the discriminative stimulus effects produced by 1 mg/kg methamphetamine and 10 mg/kg cocaine, respectively (Gatch et al., 2013; NIDA, 2013).

Napthylpyrovalerone (naphyrone)

Naphyrone, in addition to the β-keto substituent, has a propyl group (-$CH_2CH_2CH_3$) at the α-position and the nitrogen atom is incorporated into a five membered ring known as a pyrrolidine ring (Figure 1). The phenyl ring of naphyrone is in the formation of bicyclic ring systems. Naphyrone has pharmacological effects that are substantially similar to those of mephedrone, MDPV, cathinone and methcathinone, which are Schedule I substances with high potential for abuse. In laboratory studies investigating the effects of drugs on monoaminergic systems, naphyrone, like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone) and methamphetamine, inhibits the uptake of the monoamine neurotransmitter dopamine in rat brain synaptosomes or cells that have been transfected with the corresponding transporter (Gygi et al., 1997; Meltzer et al., 2006; Kehr et al., 2011; Hadlock et al., 2011; Martinez-Clemente et al., 2011; Bauman et al., 2012; NIDA, 2012; Simmler et al.,

2013; Eshleman et al., 2013; Iversen et al., 2013). In locomotor activity assays, naphyrone, like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone) and methamphetamine, increases locomotor activity in mice. In drug discrimination studies, naphyrone (ED_{50} = 2.96 and 3.20 mg/kg), like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone), fully substitutes for the discriminative stimulus effects produced by 1 mg/kg methamphetamine and 10 mg/kg cocaine, respectively (NIDA, 2011; NIDA, 2012).

Alpha-pyrrolidinobutiophenone (α-PBP)

α-PBP, in addition to the β-keto substituent, has a chain of two carbon atoms attached to the α-carbon position and the nitrogen atom is incorporated into a pyrrolidine ring (Figure 1). α-PBP has pharmacological effects that are substantially similar to those of mephedrone, MDPV, cathinone and methcathinone, which are Schedule I substances with high potential for abuse. In laboratory studies investigating the effects of drugs on monoaminergic systems, α-PBP, like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone) and methamphetamine, inhibits the uptake of the monoamine neurotransmitter dopamine in cells that have been transfected with the corresponding transporter (Cozzi et al., 1999; Eshleman et al., 2013; NIDA, 2013). In locomotor activity assays, α-PBP, like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone) and methamphetamine, increases locomotor activity in rodents (Baumann et al., 2013; Gatch et al., 2013; NIDA, 2013). In drug discrimination studies, α-PBP (ED_{50} = 2.68 and 3.70 mg/kg), like several other synthetic cathinones (methcathinone, methylone, MDPV, and mephedrone), fully substitutes for the discriminative stimulus effects produced by 1 mg/kg methamphetamine and 10 mg/kg cocaine, respectively (Gatch et al., 2013; NIDA, 2013).

Factor 4: Its History and Current Pattern of Abuse

The synthetic cathinones 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP have emerged on the United States' illicit drug market and are being perceived as being 'legal' alternatives to mephedrone, methylone, MDPV, cocaine, methamphetamine, and MDMA. Products containing these substances are falsely marketed as "research chemicals," "jewelry cleaner," "stain remover," "plant food or fertilizer," "insect repellants" or "bath salts." They are sold at smoke shops, head shops, convenience stores, adult book stores, and gas stations and can also be purchased on the Internet. These substances are commonly encountered in the form of powders, crystals, resins, tablets, and capsules. The packages of these commercial products usually contain the warning "not for human consumption," most likely in an effort to circumvent statutory restrictions for these substances. Some products found to contain 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP include, but are not limited to: "Doves," "White Ice," "Oceanic Deeper," "Enchanted," "Platinum," and others.

4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP are likely to be abused in the same manner as other synthetic cathinones such as mephedrone, methylone, and MDPV. Information from published scientific studies indicate that the most common routes of administration for synthetic cathinones like mephedrone, methylone, and MDPV are nasal insufflation by snorting the powder and ingestion by swallowing capsules or tablets (Psychonaut, 2010a; EMCDDA, 2011; Kelly, 2011; Prosser and Nelson, 2012; Vardakou et al., 2011; Forrester, 2012, 2013; Warrick et al., 2013; Zawilska and Wojcieszak, 2013). The powder can also be injected or swallowed (EMCDDA et al., 2011; Zawilska and Wojcieszak, 2013). Other methods of intake include rectal administration, ingestion by "bombing" (wrapping a dose of powder in a paper wrap and swallowing) and intramuscular injection (ACMD, 2010; Psychonaut, 2010a, c; Miotto et al., 2013; Zawilska and Wojcieszak, 2013).

As demonstrated with the Schedule I synthetic cathinones (i.e., MDPV, mephedrone, and methylone), the main users of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone,

4-FMC, 3-FMC, naphyrone, and α-PBP are likely to be youths and young adults (EMCDDA, 2011; Coppola and Mondola, 2012; Forrester, 2012, 2013; Warrick et al., 2013; Stogner and Miller, 2013; Zawilska and Wojcieszak, 2013). Synthetic cathinone exposures reported to the Texas Poison Center Network during 2010 and 2011 involved mostly adolescents (12 to 19-years-old) and young adults (mean age was 30-years-old) with the majority of patients being males (Forrester, 2012, 2013). Stogner and Miller (2013) reported that the lifetime use (used at least once) of synthetic cathinones among college students (at a large Southeastern U.S. university) in the United States is 25 out of 2,349 students surveyed. A survey of college students in 2012 by the Monitoring the Future (MTF)[7] showed that 0.2% of full-time college students used synthetic cathinone substances (Johnston et al., 2013). The use of synthetic cathinone substances among 8th, 10th, and 12th grade students and young adults (non-college peers aged 19 to 28-years-old) was 0.8%, 0.6%, 1.3%, and 0.8%, respectively.

4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP are likely to have duration of effects like those of Schedule I synthetic cathinones because of their structural and pharmacological similarities. Users report (AAPCC, drug surveys, medical literature) that the effects of synthetic cathinones occur a few minutes to 15 minutes after administration, depending on the synthetic cathinone and the route of administration (oral, insufflation, intravenous, etc.), and the effects can last up to three hours (Karila et al., 2010; Psychonaut, 2010b; EMCDDA, 2011; German et al., 2013).

As found with the Schedule I synthetic cathinones (mephedrone, methylone, and MDPV) and sympathomimetic agents (e.g., cocaine, methamphetamine, amphetamine), 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP are likely to cause stimulant related psychological and somatic effects. Desired effects reported by abusers of synthetic cathinone substances include euphoria, sense of well-being, increased sociability, energy, empathy, increased alertness, and improved concentration and focus. Schedule I synthetic cathinones have also been reported to cause stimulant related

[7] MTF is a research program conducted at the University of Michigan's Institute for Social Research under grants from NIDA. MTF tracks drug use trends among American adolescents in the 8th, 10th, and 12th grades and high school graduates into adulthood by conducting national surveys.

psychological and somatic adverse effects such as headache, nausea, palpitations, seizures, increased sex drive, paranoia, agitation, tachycardia, hypertension, hyperthermia, mydriasis, rhabdomyolysis, hyponatremia, and excessive sweating (ACMD, 2010; Frohlich et al., 2011; Karila et al., 2011; Kelly, 2011; Jerry et al., 2012; Prosser and Nelson, 2012; Rojek et al., 2012; German et al., 2013; Zawilska and Wojcieszak, 2013). Other adverse effects reported by synthetic cathinone users include bruxism (teeth grinding), tremor, chest pain, sore nasal passages, hot flashes, fever, sore mouth/throat, nose bleed, suppressed appetite, blurred vision, insomnia, hallucinations, addiction/dependence, nausea/vomiting, and nasal burns (EMCDDA, 2011; Prosser and Nelson, 2012; Derung et al., 2011).

There is evidence that 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP are ingested with other substances. This is likely to either heighten the effects or ameliorate the come-down effects of the synthetic cathinones (EMCDDA, 2011; Vardakou et al., 2011; Zawilska and Wojcieszak, 2013). Co-ingestions can be from the ingestion of multiple products separately or a single product that is composed of multiple substances (e.g., one tablet containing both 4-MEC and MDPV). Substances found in combination with 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, or naphyrone are: other synthetic cathinones (e.g., methylone and MDPV), common cutting agents (e.g., lidocaine, caffeine, lignocaine, ephedrine etc.), or other recreational substances (e.g., 4-fluoroamphetamine, cocaine, methamphetamine, amphetamine) (EMCDDA, 2011; Vardakou et al., 2011; Coppola and Mondola, 2012; Zuba and Byrska, 2013; Caudevilla-Gálligo et al., 2013). Multiple drug use and co-ingestions are confirmed by forensic analysis of seized and purchased synthetic cathinone products. Forensic analysis data also showed that some products contained multiple substances.

Summary

4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP are synthetic cathinones that emerged on the United States' illicit drug market around the time of the scheduling of mephedrone, methylone, and MDPV. These synthetic cathinones substances, like the Schedule I synthetic cathinones (mephedrone, methylone, and

MDPV), are promoted as being a 'legal' alternative to cocaine, methamphetamine, and MDMA. Products that contain 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP are falsely marketed as "research chemicals," "jewelry cleaner," "stain remover," plant food or fertilizer," "insect repellants" or "bath salts" and are 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 (e.g., "White Dove", "Explosion", "Tranquility"). They are commonly encountered in the form of powders, crystals, resins, tablets, and capsules. The packages of these commercial products usually contain the warning "not for human consumption." Information from published scientific studies indicate that the most common routes of administration for synthetic cathinone substances is ingestion by swallowing capsules or tablets or nasal insufflation by snorting the powder tablets (Psychonaut, 2010a; EMCDDA, 2011; Kelly, 2011; Prosser and Nelson, 2012; Vardakou et al., 2011; Forrester, 2012, 2013; Warrick et al., 2013; Zawilska and Wojcieszak, 2013). Evidence from poison centers and published reports suggest that the main users of methylone are young adults (EMCDDA, 2011; Coppola and Mondola, 2012; Forrester, 2012, 2013; Warrick et al., 2013; Stogner and Miller, 2013; Zawilska and Wojcieszak, 2013). There is evidence that these synthetic cathinone substances are ingested with other substances including other synthetic cathinones, common cutting agents, or other recreational substances.

Factor 5: The Scope, Duration, and Significance of Abuse

Around the time that the legislation made the manufacturing, distribution, dispensing, and possession of mephedrone, MDPV, and methylone illegal[8], other synthetic cathinone substances, as evidenced by law enforcement encounters, emerged in the U.S. illicit drug market. These substances include but are not limited to 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP.

[8] Subtitle D of the FDASIA titled the "Synthetic Drug Abuse Prevention Act of 2012," (SDAPA) amended Schedule I of section 202 of the CSA to include MDPV and mephedrone. Methylone was permanently controlled via the administrative process. 77 FR 64032.

The popularity of synthetic cathinones, including these 10 synthetic cathinone substances, as recreational drugs increased since they first appeared on the U. S. illicit drug market in 2009. 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP are prevalent and they are abused throughout the United States as evidenced by law enforcement seizures. These substances are readily available from the Internet, retail suppliers (e.g., head shops, tobacco shops, convenience stores, adult book stores, and gas stations) or street dealers. Data, including law enforcement data, indicate that products that contain synthetic cathinone substances are generally sold in 50 to 500 milligram packets with prices ranging from $25-$70 per 50 mg packet and $60-$70 per gram (Fass et al., 2012; Miotto et al., 2013). These substances can also be bought in bulk quantities (e.g., 100 g to over 5 kg). Companies located overseas are primarily responsible for the trafficking of these substances.

Studies suggest that synthetic cathinones may be used as an alternative to illicit substances like MDMA and cocaine (ACMD, 2010; EMCDDA, 2011; Ojanperä et al., 2011; Coppola and Mondola, 2012). ACMD reported that "Toot" (most commonly identified as a mixture of butylone and methylone) and mephedrone were popular among users of heroin (ACMD, 2010).

Information from poison centers and emergency departments indicates that synthetic cathinones continue to be abused by individuals (see Factor 5). AAPCC reported in a press release that there were 306 exposure calls related to synthetic cathinones in 2010, 6,137 calls in 2011, and 2,691 calls in 2012 (AAPCC, 2013). As of October 31, 2013, poison centers received 833 calls relating to human exposures to bath salts. According to the Drug Abuse Warning Network (DAWN) report released by SAMHSA, 22,904 ED visits involved "bath salts" in 2011.

There are convictions of drug traffickers and indictments against alleged drug traffickers in the United States involving most of these substances indicating that these substances are being distributed throughout the United States (see Appendix for a list of some of these cases). For example, two individuals were convicted of conspiracy to distribute, or to possess with intent to distribute a controlled substance analogue (one of the substances was 4-MEC) in

violation of 21 USC 846 and conspiracy to import a controlled substance analogue in violation of 21 USC 963 and other violations after a jury trial in the United States District Court Northern District of New York. In another case, the jury returned a guilty verdict in the United States District Court for the Western District of Virginia against an individual for the conspiracy to distribute, or to possess with intent to distribute a controlled substance analogue (one of the substances was 4-MEC) in violation of 21 USC 846. Several individuals were indicted and subsequently convicted in the United States District Court for the District of Arizona for violations of the analogue drug provision (substances included α-PVP, α-PBP, 4-MePPP, pentedrone, pentylone, butylone, and MDPV).

Table 1: Synthetic Cathinones - Number of Reports (State and Local)

Synthetic Cathinone	NFLIS (2010)	NFLIS (2011)	NFLIS (2012)	NFLIS (2013*)
4-MEC	5	175	1,052	644
4-MePPP	0	91	181	16
α-PVP	0	17	2,730	1,583
Butylone	3	173	258	52
Pentedrone	0	122	913	125
Pentylone	0	34	169	32
FMC**	4	168	106	13
Naphyrone	1	20	19	3
α-PBP	0	0	57	41

NFLIS database was queried for drug reports on 12/20/2013 by date submitted to state and local forensic laboratories.
*2013 Data are January – November (data are still being reported for November)
**FMC consists of isomers of FMC including 3-FMC and 4-FMC

Evidence from law enforcement indicates that 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP are being abused in the United States (see Table 1 and Appendix). In 2010, NFLIS, a DEA sponsored forensic database, registered 13 reports from 5 states regarding many of these synthetic cathinone substances that were analyzed by state and local forensic laboratories.[9] In 2011, there were 800 reports from 33 states related to these substances registered in NFLIS, and in 2012, there were 5,485 reports from 41 states, and from January to November 2013 there were 2,509 reports from 41 states. From January 2010 to November 2013, 1,732 drug exhibits pertaining to the trafficking,

[9] NFLIS state and local forensic drug reports queried on December 20, 2013.

distribution and abuse of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP were recorded in the STRIDE database, a federal database for drug items analyzed by DEA forensic laboratories.[10] Among the synthetic cathinone substances, 4-MEC, butylone, FMC and pentedrone were the most prevalent substances encountered by law enforcement as reported in NFLIS in 2011. However, in 2012 and 2013, α-PVP is the most prevalent substances encountered.

Table 2: Encounters of Synthetic Cathinone Substances by CBP (518 Total Shipments)

	Synthetic Cathinone	2010	2011	2012	2013	2010 - 2013	
1	4-MEC	2	29	28	19	78	42 kg, 4000 packets
2	4-MePPP		3	4	1	8	3.6 kg
3	α-PVP		1	18	21	40	70 kg
4	Butylone	2	12	5	2	21	8.4 kg
5	Pentedrone		8	9	1	18	43 kg
6	Pentylone		6	4		10	21.7 kg, 2000 packets
7, 8	FMC*	3	7		3	13	5.4 kg
9	Naphyrone		3			3	4 kg
10	α-PBP		2	8	1	11	7 kg

Data analyzed on December 18, 2013

*FMC consists of isomers of FMC including 3-FMC and 4-FMC

At selected United States ports of entry, the U.S. Customs and Border Protection (CBP) has encountered several shipments of products from April 2010 to November 2013 containing these 10 synthetic cathinone substances (see Table 2). These encounters of 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP indicate that these substances are popular drugs of abuse. Most of the shipments of these synthetic cathinones originated overseas and were destined for delivery throughout the United States to places like Arizona, Arkansas, California, Colorado, Florida, Hawaii, Idaho, Illinois, Michigan, Missouri, Nebraska, Nevada, New Jersey, New Mexico, Oklahoma, Oregon, Texas, Virginia, Washington, and Wyoming.

Concerns over the abuse of synthetic cathinones have prompted many states to control these substances. Some states have enacted legislation to capture a broad range of synthetic cathinones by utilizing a broad definition to define synthetic cathinones. For example, some

[10] STRIDE data was queried on 12/20/2013 by date submitted to Federal forensic laboratories.

states like Arkansas, Idaho, Mississippi, and North Carolina define controlled synthetic cathinones as substances that have certain substitutions (e.g., by substitution in the ring system to any extent with alkyl, alkylenedioxy, etc; by substitution at the 2-amino nitrogen atom with alkyl, dialkyl, benzyl, etc.) on a defined structure (i.e., 2-aminopropan-1-one, 2-amino-1-phenyl-1-propanone). In contrast, other states, like Arizona, Delaware, Massachusetts, Tennessee, and Washington specifically control one or more of the synthetic cathinones by name. As of June 24, 2013, more than half of the states in the United States have emergency scheduled or enacted legislation placing regulatory controls on some or many of the synthetic cathinones that are listed in this document. In addition, the U.S. Armed Forces prohibited the use of synthetic cathinones for intoxication purposes due to its use by service members of the U.S. armed forces (Berry-Caban et al., 2012; Loeffler et al., 2012). Internationally, several member countries of the European Union have enacted laws placing controls on the possession and/or sale of one or more of these substances (Winstock et al., 2010; EMCDDA, 2011; Morris, 2010).

Summary

4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP, like mephedrone, methylone, and MDPV, are popular recreational drugs. Evidence that these synthetic cathinone substances are being abused is confirmed by law enforcement encounters of these substances. Forensic laboratories have analyzed drug exhibits received from state, local, or federal law enforcement agencies that were found to contain 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP. NFLIS registered over 8,000 reports from state and local forensic laboratories identifying these substances in drug-related exhibits for a period from January 2010 to December 2013 from 42 states. STRIDE registered over 1,700 reports from DEA forensic laboratories from January 2010 to November 2013. Additionally, large seizures of these substances have occurred by the U.S. Customs and Border Protection (CBP). Concerns over the abuse of these synthetic cathinone substances have prompted many states to regulate them.

Factor 6: What, If Any, Risk There is to the Public Health

Synthetic cathinones, in general, have been reported to cause a number of stimulant-like adverse effects (ACMD, 2010; Karila et al., 2010; Psychonaut, 2010a, c; EMCDDA, 2011; Prosser and Nelson, 2012; Capriola, 2013). Stimulant-like adverse effects include tachycardia, hypertension, hyperthermia, palpitations, hyponatremia, tremor, seizures, vomiting, sweating, headache, rhabdomyolysis, etc. (Frohlich et al., 2011; Spiller et al., 2011; Vardakou et al., 2011; Derung et al., 2012; Rojek et al., 2012; Warrick et al., 2012; Zawilska and Wojcieszak, 2013). Hyperthermia can be a serious adverse effect and can lead to metabolic acidosis, rhabdomyolysis, renal failure, disseminated intravascular coagulation, coma, and death. The clinical presentation of intoxication from synthetic cathinones shares some features seen with MDMA and stimulants like cocaine. Clinical case reports indicate that synthetic cathinones also produce other adverse effects such as hallucinations, psychosis, paranoia, delusions, etc. (Frohlich et al., 2011; Spiller et al., 2011; Vardakou et al., 2011; Derung et al., 2011; Thorton et al., 2012).

Law enforcement, forensic laboratories, case reports, and public health officials have reported toxic exposure to some of the synthetic cathinone substances that demonstrate the public health risks associated with these substances. Substances that have been specifically identified include 4-MEC, butylone, 4-FMC, α-PVP, pentylone and naphyrone. According to the DAWN report that was released by SAMHSA, 22,904 visits to the emergency department in 2011 involved "bath salts." As described below, many individuals have presented at emergency departments following exposure to these synthetic cathinone substances or products containing these substances.

Serious adverse effects including hyperthermia have resulted in documented hospital emergency department (ED) admissions from the ingestion of butylone, 4-FMC, or naphyrone.

Frohlich et al. (2011) described a case of acute liver failure after the ingestion of synthetic cathinones which included butylone. A 28-year-old male suffering from bipolar affective disorder (but otherwise healthy) ingested 12 stimulant tablets. Following ingestion he suffered a seizure. He was transported to the emergency department. He also had

tachycardia, hypertension, hyperpyrexia, and profuse sweating. Rhabdomyolysis, a syndrome caused by injury to skeletal muscle, developed two days after ingestion and likely caused renal failure. The liver failure eventually resolved following treatment and the patient was discharged into psychiatric care. The pills that the patient had ingested were analyzed and found to contain MDPV and butylone.

Derungs et al. (2012) described the case of a 31-year-old male who suffered sympathomimetic toxicity after ingesting naphyrone. The patient purchased the powder over the internet. He believed that he was purchasing MDMA but instead received naphyrone. The patient had no knowledge about naphyrone but chose to ingest the amount that he would have ingested if the substance had been MDMA, so he ingested 100 mg of the powder with fruit juice. After administration, he developed blurred visions, increasing restlessness, and could not concentrate. He also experienced insomnia for two nights, hallucinations, paranoia and felt nervous. The patient had a history of heroin use and was on substitution therapy with buprenorphine. He presented to the emergency room exhibiting psychotic symptoms. Upon examination he had mydriasis and elevated blood pressure indicating that he was suffering from acute sympatomimetic toxidrome. Later in the same day of admission, the patient discharged himself. A toxicological screen of specimens from the patient identified naphyrone. A urine drug screen was positive for benzodiazepines but did not detect other cathinones, cocaine, or amphetamine derivatives.

Thorton et al. (2012) described the case of a 23-year-old male who insufflated 4-FMC. After snorting a white powder the patient was agitated, suicidal, and complained of hallucinations. He was taken to the hospital via ambulance. Emergency personnel reported that the patient was hyperthermic, diaphoretic, and tachycardic with mydriasis. The patient was chemically and physically restrained because he was agitated. Symptoms eventually resolved and the patient was discharged. The patient was diagnosed to suffer from schizoaffective disorder, bipolar disorder, or psychosis secondary to bath salt (4-FMC) ingestion. Testing of the bath salt product revealed MDPV and 4-FMC. A toxicological screen of specimens from the patient identified MDPV and 4-FMC. A higher concentration of 4-FMC (346

and 257 ng/mL in serum and urine, respectively) compared to MDPV (186 and 136 ng/mL in serum and urine, respectively) was detected.

Some individuals under the influence of these synthetic substances have acted violently and unpredictably causing harm, or even death, to themselves or others.

Gil et al. (2013) described the case of a 30-year-old male who died in a road traffic accident after an alleged ingestion of 4-MEC. 4-MEC was identified in a zipper bag found on the decedent. 4-MEC at a concentration of 152 ng/ml (blood) and 122 ng/ml (urine) was also detected in biological specimens from the decedent. Ethanol (0.12 g/dL in blood and 0.19 g/dL in urine) was also present in these specimens.

Another case reported by Gil et al. (2013) described the case of a 27-year-old male who was arrested by the police on suspicion of possession of narcotics (white powder) (Gil et al., 2013). 4-MEC was identified in the white powder seized from the subject. A toxicological screen identified 4-MEC in blood samples from this subject.

Butylone has been directly implicated in two fatalities reported in the medical literature.

Warrick et al. (2012) described the death of a 24-year-old female who ingested two capsules of what was thought to be "Ecstasy" at a concert. After being found unconscious by emergency personnel, the decedent was taken to the emergency department. The comatose patient suffered from hyperthermia, tachycardia, mydriasis, tachypnea and some tremors. Despite efforts to save her life the decedent died. Toxicology tests identified methylone and butylone in specimens from this individual. Laboratory analysis also identified methylone and butylone in the powder obtained from a capsule that was found on the decedent. The cause of death determined by the medical examiner was serotonin syndrome secondary to methylone and butylone ingestion.

Rojek et al. (2012) described the death of a 21-year-old male who ingested butylone for suicidal intentions. The decedent was admitted to the hospital after ingesting 10 tablets of a substance called "Amph-i-bia." The decedent purchased the substances at a retail shop. On admission, the patient suffered tachycardia, hypertension, mydriasis and was disoriented. He

subsequently developed seizures and suffered a cardiac and respiratory arrest. Despite efforts to save his life he died. A toxicological screen of specimens from this patient identified butylone. The cause of death was reported as multi-organ failure resulting from malignant serotonin syndrome.

Other synthetic cathinones, like α-PVP and pentylone, have also been implicated in the deaths of individuals.

Marinetti and Antonides (2013) described several postmortem cases in which synthetic cathinones such as MPDV, α-PVP, pentylone, methylone and methedrone were detected in biological, postmortem specimens. A 44-year-old female with a history of bipolar disorder and previous suicide and drug abuse died from multiple drug intoxication. She tested positive for pentylone, α-PVP, hydrocodone, promethazine, and other pharmaceutical drugs. A 35-year-old female with a history of drug abuse including intravenous drug abuse was found unresponsive in bed. A toxicological screen detected morphine, codeine, citalopram, α-PVP, and 6-MAM (6-monoacetylmorphine; an active metabolite of heroin) in biological specimen from this individual. A 50-year-old female with a history of heroin abuse was found unresponsive on a sofa at her home. A toxicological screen detected α-PVP, morphine, codeine, 6-MAM, and pharmaceutical drugs in biological specimen from this individual. A 51-year-old male was fatally shot by police officers after a chase. A toxicological screen detected α-PVP in biological specimen from this individual. A 34-year-old male was found dead in his basement from hanging. A toxicological screen detected α-PVP and pentylone in biological specimen from this individual. A 32-year-old female who was morbidly obese was found unresponsive on the floor in her home. A toxicological screen detected MDPV, α-PVP, morphine, methedrone, 6-MAM, and pharmaceutical drugs in biological specimen from this individual.

The products containing synthetic cathinone substances often do not bear labeling information regarding its ingredients or the health risks and potential hazards associated with these products. In addition, products may not contain the expected active ingredients (Davies et al., 2010; Spiller et al., 2011; Ayres and Bond, 2012; Zuba and Byrska, 2013). Thus, individuals who purchase these products likely have insufficient knowledge of the exact product

contents. This lack of information poses significant risk to users who may not know what they are purchasing or the risk associated with the abuse of those products. In a study that analyzed products offered for sale over a 6 month period, there was significant variation in the active substance (i.e., the products did not contain the active ingredients listed or products marketed to contain a specific legal substance contained a different substance) in one quarter (5 of 20) of the products that were purchased (the same named products such as Head rush, Pure bliss, or Xtacy were purchased repeatedly during a 6 month period) and tested (Davies et al., 2010). In a separate study, the analysis of a specific brand name synthetic cathinone product (e.g., white lightening), that appeared identical in packaging but obtained at different locations, revealed different synthetic cathinones as the primary ingredient (Spiller et al., 2011). Accordingly, 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP have been identified in varying combinations in packages that have been seized by law enforcement. A study by Brandt et al. (2010) showed that 70% of the products analyzed contained an illicit substance. Another study showed that there was poor quality of product information (Schmidt et al., 2010). Of 1,308 products evaluated, 40% (524) did not list ingredients, 92% (1,202) failed to list any side effects, and 86% (1,129) failed to list any warnings about potential interactions with other substances or medications. Since abusers obtain these drugs through unknown sources, the purity of these drugs is uncertain presenting another level of risk to users (EMCDDA, 2011). Thus, the limited knowledge about product content and its purity and lack of information about its effects pose significant risks to the users.

Summary

In summary, available evidence on the overall public health risks associated with the use of synthetic cathinones indicates that 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP can cause acute health problems leading to ED admissions, violent behaviors causing harm to self or others, or death. In addition, products containing these synthetic cathinone substances 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. Acute effects of

these substance are those typical of a sympathomimetic agents (e.g., cocaine, methamphetamine, amphetamine) and include among other effects tachycardia, headache, palpitations, agitation, anxiety, mydriasis, tremor, fever or sweating, and hypertension (ACMD, 2010; Karila and Reynaud, 2010; EMCDDA, 2011; Prosser and Nelson, 2012; Derung et al., 2011; Rojek et al., 2012; Thorton et al., 2012; Capriola, 2013). Other effects, with possible public health risk implications, that have been reported from the use of synthetic cathinone substances include psychological effects such as psychosis, paranoia, hallucinations, and agitation (Derung et al., 2011; Rojek et al., 2012; Thorton et al., 2012). Finally, the possibility of death for individuals abusing 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP also indicates that these substances are a serious public health threat.

Conclusion of 3-Factor Analysis

After a careful review of the scientific literature, Factors 4, 5, and 6, NFLIS, STRIDE, and other law enforcement data and other data and information, it is evident that 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP are trafficked and abused and pose a significant public health risk. These drugs have become popular among drug abusers due to their stimulant-like effects and pharmacological similarity to mephedrone, MDPV, methylone, cocaine, and methamphetamine.

DEA has considered the three criteria for placing a substance into Schedule I of the CSA (21 U.S.C. 812). The data available and reviewed for 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, and α-PBP indicated that these substances, including their salts, isomers, and salts of isomers, pose an imminent hazard to public safety and health, have no currently accepted medical use in treatment in the United States, and lack accepted safety for use under medical supervision.

References

AAPCC. American Association of Poison Control Centers. 2013. Bath Salts Data. Updated October 31, 2013.

ACMD. Advisory Council on the Misuse of Drugs (ACMD). 2010. Consideration of the cathinones. (Iversen). London.

Ayres TC, Bond TW. 2012. A chemical analysis examining the pharmacology of novel psychoactive substances freely available over the internet and their impact on public (ill) health. Legal highs or illegal highs? BMJ Open, 2: doi:pii e000977. 10.11/bmjopen-2012-000977.

Balster RL, Bigelow GE. 2003. Guidelines and methodological reviews concerning drug abuse liability assessment. Drug and Alcohol Dependence, 70: S13-40.

Baumann MH, Ayestas MA, Partilla JS, Sink JR, Shulgin AT, Daley PF, Brandt SD, Rothman RB, Ruoho AE, Cozzi NV. 2012. The designer methcathinone analogs, mephedrone and methylone, are substrates for monoamine transporters in brain tissue. Neuropsychopharmacology. 37: 1192-1203.

Baumann MH, Partilla JS, Lehner KR, Thorndike EB, Hoffman AF, Holy M, Rothman RB, Goldberg SR, Lupica CR, Sitte HH, Brandt SD, Tella SR, Cozzi NV, Schindler CW. 2013. Powerful cocaine-like actions of 3,4-methylenedioxypyrovalerone (MDPV), a principal constituent of psychoactive 'bath salts' products. Neuropsychopharmacology, 38: 552-562.

Berry-Caban CS, Kleinschmidt PE, Rao DS, Jenkins J. 2012. Synthetic cannabinoid and cathinone use among US soldiers. The United States Army Medical Department Journal, October – December: 19-24.

Brandt SD, Sumnal HR, Measham F, Cole J. 2010. Analysis of second-generation 'legal highs' in the UK: Initial findings. Drug Testing and Analysis, 2: 377-382.

Caudevilla-Gálligo F, Ventura M, Ruiz BII, Fornís I. 2013. Presence and composition of cathinone derivative in drug samples taken from a drug test service in Spain. Human Psychopharmacology, 28: 341-344.

Capriola M. 2013. Synthetic cathinone abuse. Clinical Pharmacology: Advance and Applications, 5: 109-115.

Coppola M, Mondola R. 2012. Synthetic cathinones: chemistry, pharmacology and toxicology of a new class of designer drugs of abuse marketed as "bath salts" or "plant food." Toxicology Letters, 211: 144-149.

Cozzi NV, Sievert MK, Shulgin AT, Jacob III P, Ruoho AE. 1999. Inhibition of plasma membrane monoamine transporters by β-ketoamphetamines. European Journal of Pharmacology, 381: 63-69.

Davies S, Wood DM, Smith G, Button J, Ramsy J, Archer R, Holt DW, Dargan PI. 2010. Purchasing 'legal highs' on the Internet-is there consistency in what you get? QJM: An International Journal of Medicine, 103: 489–493.

Derung A, Schietzel S, Meyer MM, Maurer HH, Krahenbuhl S, Liechti ME. 2011. Sympathomimetic toxicity in a case of analytically confirmed recreational use of naphyrone (naphthylpyrovalerone). Clinical Toxicology, 49: 691-693.

Eshleman AJ, Wolfrum KM, Hatfield MG, Johnson RA, Murphy KV, Janowsky A. 2013. Substituted methcathinones differ in transporter and receptor interactions. Biochemical Pharmacology, 85: 1803-1815.

EMCDDA. European Monitoring Centre for Drugs and Drug Addiction. 2011. Report of the risk assessment of mephedrone in the framework of the Council Decision on new psychoactive substances. Luxembourg: Publications Office of the European Union, doi: 10.2810/40800.

Fass JA, Fass AD, Garcia AS. 2012. Synthetic cathinones (bath salts): legal status and patterns of abuse. The Annals of Pharmacotherapy, 46: 436-41.

Forrester M. 2012. Synthetic cathinone exposures reported to Texas poison centers. The American Journal of Drug and Alcohol Abuse, 38: 609-615.

Forrester M. 2013. Adolescent synthetic cathinone exposure reported to Texas poison centers. Pediatric Emergency Care, 29: 151-155.

Frohlich S, Lambe E, O'Dea J. 2011. Acute liver failure following recreational use of psychotropic "head shop" compounds. Irish Journal of Medical Science, 180: 263-264.

Gatch MB, Taylor C, Forster MJ. 2013. Locomotor stimulant and discriminative stimulus effects of "bat salt" cathinones. Behavioral Pharmacology, 24: 437-447.

German CL, Fleckenstein AE, Hanson GR. 2013. Bath salts and synthetic cathinones: An emerging designer drug phenomenon. Life Sciences, http://dx/dpo/prg/10.1016/j.lfs.2013.07.023.

Gil D, Adamowicz P, Skulska A, Tokarczyk B, Stanaszed R. 2013. Analysis of 4-MEC in biological and non-biological material – Three case reports. Forensic Science International, 228: e11-e15.

Glennon RA, Young R, Martin BR, Dal Cason TA. 1995. Methcathinone ("Cat"): An enantiomeric potency comparison. Pharmacology Biochemistry and Behavior, 50: 601-606.

Gygi M, Fleckenstein, Gibb J, Hanson G. 1997. Role of endogenous dopamine in the neurochemical deficits induced by methcathinone. The Journal of Pharmacology and Experimental Therapeutics, 283: 1350-1355.

Hadlock GC, Webb KM, McFadden LM, Chu PW, Ellis JD, Allen SC, Andrenyak DM, Vieira-Brock PL, German CL, Conrad KM, Hoonakker AJ, Gibb JW, Wilkins DG. 2011. 4-Methymethcathinone

(mephedrone): neuropharmacological effects of a designer stimulant of abuse. Journal of Pharmacology and Experimental Therapeutics, 339: 530-536.

Han D, Gu H. 2006. Comparison of the monoamine transporters from human and mouse in their sensitivities to psychostimulant drugs. BMC Pharmacology, 6: 6.

Howell, LL, Kimmel, HL. 2008. Monoamine transporters and psychostimulant addiction. Biochemical Pharmacology, 75: 196-217.

Iversen L, Gibbons S, Treble R, Setola V, Huang XP, Roth BL. 2013. Neurochemical profiles of some novel psychoactive substances. European Journal of Pharmacology, 700: 147-151.

Jerry J, Collins G, Streem D. 2012. Synthetic legal intoxicating drugs: The emerging 'incense' and 'bath salt' phenomenon. Cleveland Clinic Journal of Medicine, 79: 258-264.

Johnston LD, O'Malley PM, Bachman JG, Schulenberg JE. 2013. Monitoring the Future national survey results on drug use, 1975-2012: Volume 2, College students and adults ages 19-50. Ann Arbor: Institute for Social Research, The University of Michigan.

Karila L, Reynaud M. 2010. GHB and synthetic cathinones: clinical effects and potential consequences. Drug Testing and Analysis, 3: 552-559.

Kehr J, Ichinose F, Yoshitake S, Goiny M, Sievertsson T, Nyberg F, Yoshitake T. 2011. Mephedrone, compared to MDMA (ecstasy) and amphetamine, rapidly increases both dopamine and serotonin levels in nucleus accumbens of awake rats. British Journal of Pharmacology, 164: 1949-1958.

Kelly J. 2011. Cathinone derivatives: A review of their chemistry, pharmacology and toxicology. Drug Testing and Analysis, 3: 439-453.

Loeffler G, Hurst D, Penn A, Yung K. 2012. Spice, bath salts, and the U.S. military: the emergence of synthetic cannabinoid receptor agonists and cathinones in the U.S. Armed Forces. Military Medicine, 177: 1041-1048.

Marinetti LJ, Antonides HM. 2013. Analysis of synthetic cathinones commonly found in bath salts in human performance and postmortem toxicology: method development, drug distribution and interpretation of results. Journal of Analytical Toxicology, doe:10.1093/jat/bks136

Martinez-Clemente J, Escubedo E, Pubill D, Camarasa J. 2011. Interaction of mephedrone with dopamine and serotonine targets in rats. European Neuropsyopharmacology, 22: 231-236.

Marusich JA, Grant KR, Blough BE, Wiley JL. 2012. Effects of synthetic cathinones contained in "bath salts" on motor behavior and a functional observational battery in mice. NeuroToxicology, 33: 1305-1313.

Meltzer PC, Butler D, Deschanps JR, Madras BK. 2006. 1-(4-Methylphenyl)-2-pyrrolidin-1-yl-pentan-1-one (pyrovalerone) analogues. A promising class of monoamine uptake inhibitors. Journal of Medicinal Chemistry, 49: 1420-1432.

Miotto K, Striebel J, Cho AK, Wang C., 2013. Clinical and pharmacological aspects of bath salt use: A review of the literature and case reports. Drug and alcohol Dependence, 132: 1-12.

Mori T, Yoshizawa K, Shibasaki M, Suzuki T. 2012. Discriminative stimulus effects of hallucinogenic drugs: a possible relation to reinforcing and aversive effects. Journal of Pharmacological Sciences, 120: 70-76.

Morris K. 2010. UK places generic ban on mephedrone drug family. Lancet, 375: 1333-1334.

NIDA. National Institute on Drug Abuse (NIDA). 2011 - 2013. Reports. Contract: N01DA-7-8872, N01DA-13-8908, or ADA12013. Unpublished data.

Ojanpera IK, Heikman PK, Rasanen IJ. 2011. Urine analysis of 3,4-methylenedioxypyrovalerone in opioid-dependent patients by gas-chromatography-mass spectrometry. Therapeutic Drug Monitoring, 33: 257-263.

Prosser JM, Nelson LS. 2012. The toxicology of bath salts: a review of synthetic cathinones. Journal of Medical Toxicology, 8: 33-42.

Psychonaut WebMapping Research Group. 2010a. Mephedrone report, Institute of Psychiatry, King's College London: London, UK. [Paolo Deluca et al.]

Psychonaut WebMapping Research Group. 2010b. Ivory Wave report, Institute of Psychiatry, King's College London: London, UK. [Paolo Deluca et al.]

Psychonaut WebMapping Research Group. 2010c. MDPV report, Institute of Psychiatry, King's College London: London, UK. [Paolo Deluca et al.]

Rothman R, Baumann M, Dersch C, Romero D, Rice K, Carroll F, Partilla J. 2001. Amphetamine-type central nervous system stimulants release norepinephrine more potently than they release dopamine and serotonin. Synapse, 39: 32-41.

Rojek S, Klys M, Strona M, Maciow M, Kula K. 2012. "Legal highs"-Toxicity in the clinical and medico-legal aspect as exemplified by suicide with bk-MBDB administration. Forensic Science International, 222: e1-e6.

Schmidt MM, Sharm A, Schifano F, Feinmann C. 2010. "Legal highs" on the net-Evaluation of UK-based Websites, products and product information. Forensic Science International, 206: 92-97.

Simmler LD, Buser TA, Donzelli M, Schramm Y, Dieu L-H, Huwyler J, Chaboz S, Hoener MC, Liechti ME. 2013. Pharmacological characterization of designer cathinones in vitro. British Journal of Pharmacology, 168: 458-470.

Spiller HA, Ryan ML, Weston RG, Jansen J. 2011. Clinical experience with and analytical confirmation of "bath salts" and "legal highs" (synthetic cathinones) in the United States. Clinical Toxicology, 49: 499-505.

Stogner JM, Miller BL. 2013 Investigating the 'bath salt' panic: The rarity of synthetic cathinone use among students in the United States. Drug and Alcohol Review, 32: 545-549.

Thorton SL, Gerona RR, Tomaszewski CA. 2012. Psychosis from a bath salt product containing flephedrone and MDPV with serum, urine, and product quantification. Journal of Medical Toxicology, 8: 310-313.

Vardakou I, Pistos C, Spiliopolou. 2011. Drugs for youth via Internet and the example of mephedrone. Toxicology Letters, 201: 191-195.

Warrick BJ, Wilson J, Hedge M, Freeman S, Leonard K, Aaron C. 2012. Lethal serotonin syndrome after methylone and butylone ingestion. Journal of Medical Toxicology, 8: 65-68.

Warrick BJ, Hill M, Kekman K, Christensen R, Goetz R, Casavant MJ, Wahl M, Mowry JB, Spiller H, Anderson D, Aleguas A, Gummin D, Thomas R, Nezlek C, Smolinske S. 2013. A 9-state analysis of designer stimulant, "bath salt," hospital visits reported to poison control centers. Annals of Emergency Medicine, 62: 244-251.

Winstock A, Mitcheson L, Marsden. 2010. Mephedrone: still available and twice the price. The Lancet, 376: 1537.

Zawilska JB, Wojcieszak. 2013. Designer cathinones – An emerging class of novel recreational drugs. Forensic Science International, 231: 42-53.

Zuba D, Byrska B. 2013. Prevalence and co-existence of active components of 'legal high.' Drug Testing and Analysis, 5: 420-429.

II. APPENDIX

STRIDE, NFLIS, and Examples of Enforcement Activities

System To Retrieve Information from Drug Evidence (STRIDE) Reports

Data from the forensic laboratory database STRIDE, a federal database for the drug samples analyzed by DEA forensic laboratories, indicate illicit activity involving 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, 4-FMC, 3-FMC, naphyrone, or α-PBP. From January 2010 to November 2013, Federal law enforcement authorities encountered 1,732 drug exhibits pertaining to the trafficking, distribution and abuse of these synthetic cathinone substances (Table II.1).

Table II.1: Synthetic Cathinones Reports (Federal)

Synthetic Cathinone	STRIDE (2010)	STRIDE (2011)	STRIDE (2012)	STRIDE (2013*)	STRIDE (2010-2013*)
4-MEC	4	142	162	66	374
4-MePPP	0	10	101	11	122
α-PVP	0	7	544	108	659
Butylone	0	14	56	4	74
Pentedrone	0	11	262	15	288
Pentylone	0	5	107	7	119
FMC**	0	10	21	6	37
Naphyrone	0	5	17	0	22
α-PBP	0	1	32	4	37
TOTAL	4	205	1,302	221	1,732

STRIDE database was queried on 12/20/2013 by date submitted to federal forensic laboratories.
*2013 Data are January – November (data are still being reported for November).
**FMC consists of isomers of FMC including 3-FMC and 4-FMC

National Forensic Laboratory Information System (NFLIS) Reports

In 2010, the NFLIS registered 13 reports from 5 states containing 4-MEC, butylone, FMC, and naphyrone (Table II.2, II.4, and II.5) analyzed by state and local forensic laboratories. However, in 2011, there were 800 reports from 32 states related to these substances (exclude α-PBP) registered in NFLIS, in 2012 there were 5,485 reports from 41 states, and in the first eleven months of 2013, there were 2,509 reports from 41 states. These substances

represented approximately 29% (8,807/30,448) of all the reports to NFLIS involving synthetic cathinones from January 2010 to November 2013 (Table II.3).

Table II.2: Synthetic Cathinones - Number of Reports (State and Local)

Synthetic Cathinone	NFLIS (2010)	NFLIS (2011)	NFLIS (2012)	NFLIS (2013*)	NFLIS (2010-2013*)
4-MEC	5	175	1,052	644	1,876
4-MePPP	0	91	181	16	288
α-PVP	0	17	2,730	1,583	4,330
Butylone	3	173	258	52	486
Pentedrone	0	122	913	125	1,160
Pentylone	0	34	169	32	235
FMC**	4	168	106	13	291
Naphyrone	1	20	19	3	43
α-PBP	0	0	57	41	98
TOTAL	**13**	**800**	**5,485**	**2,509**	**8,807**

NFLIS database was queried for drug reports on 12/20/2013 by date submitted to state and local forensic laboratories

*2013 Data are January – November (data are still being reported for November)

**FMC consists of isomers of FMC including 3-FMC and 4-FMC

Table II.3: Number of Reports (State and Local) of All Synthetic Cathinones

Substance Category	2010	2011	2012	2013*	2010-2013*
Ten Synthetic Cathinones[‡]	13	800	5,485	2,509	8,807
All Synthetic Cathinones	636	6,345	12,959	10,508	30,448
% Ten Synthetic Cathinones[‡]	2%	13%	42%	24%	29%

NFLIS database was queried for drug reports on 12/20/2013 by date submitted to state and local forensic Laboratories.

*2013 Data are January – November (data are still being reported for November)

[‡]Ten Synthetic Cathinones include 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, FMC, naphyrone, and α-PBP

Table II.4: Number of States where Synthetic Cathinones[‡] was Identified (State and Local)

Synthetic Cathinone	2010	2011	2012	2013	2010-2013*
4-MEC	3	24	37	35	**38**
4-MePPP	0	13	21	12	**26**
α-PVP	0	6	38	33	**40**
Butylone	1	22	28	16	**34**
Pentedrone	0	17	28	17	**33**
Pentylone	0	8	23	16	**29**
FMC**	2	22	26	6	**29**
Naphyrone	1	9	10	2	**16**
α-PBP	0	0	16	9	**19**
TOTAL STATES	**5**	**32**	**41**	**41**	**42**

NFLIS database was queried on 12/20/2013 by date submitted to state and local forensic laboratories.

*2013 Data are January – November (data are still being reported for November)

**FMC consists of isomers of FMC including 3 FMC and 4-FMC

[‡]Synthetic Cathinones are 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, FMC, naphyrone, and α-PBP

Table II.5: States where Synthetic Cathinones[‡] were Identified

	States with Exhibits from 2010-2013*				
Synthetic Cathinones	Arizona	Arkansas	California	Colorado	Connecticut
	Florida	Georgia	Illinois	Indiana	Iowa
	Kansas	Kentucky	Louisiana	Maine	Maryland
	Massachusetts	Michigan	Minnesota	Mississippi	Missouri
	Nebraska	Nevada	New Hampshire	New Jersey	New Mexico
	New York	North Carolina	North Dakota	Ohio	Oklahoma
	Oregon	Pennsylvania	South Carolina	South Dakota	Tennessee
	Texas	Utah	Virginia	Washington	West Virginia
	Wisconsin	Wyoming			

NFLIS database was queried on 12/20/2013 by date submitted to state and local forensic laboratories.
*2013 Data are January – November (data are still being reported for November)
[‡]Synthetic Cathinones are 4-MEC, 4-MePPP, α-PVP, butylone, pentedrone, pentylone, FMC, naphyrone, and α-PBP

Examples of Enforcement Activities

1. On May 14, 2013, two individuals were convicted after a jury trial in the United States District Court Northern District of New York. The individuals were convicted of conspiracy to distribute, or to possess with intent to distribute controlled substance analogues (4-MEC and mephedrone) in violation of 21 USC 846 and conspiracy to import a controlled substance analogue in violation of 21 USC 963 and/or 19 counts of money laundering in violation of 18 USC 1956. A third individual who was arrested in this investigation failed to show for trial and is currently a fugitive. Also indicted in this investigation was a foreign individual who allegedly shipped the substances to the convicted individuals. Eighteen other defendants pled guilty to conspiracy to distribute, or to possess with intent to distribute a controlled substance analogue in violation of 21 USC 846.

2. The jury in the United States District Court for the Western District of Virginia returned a guilty verdict (May 2013) on nine counts against an individual for the conspiracy to distribute, or to possess with intent to distribute a controlled substance analogue (4-MEC, methylone, and MDPV) in violation of 21 USC 846.

3. Several individuals were indicted (July 2012) in the United States District Court for the District of Arizona for the alleged violation of the analogue drug provision (substances

included α-PVP, α-PBP, 4-MePPP, pentedrone, pentylone, butylone, and MDPV). Many of the indicted pled guilty and one individual was found guilty in a jury trial in July 2013.

4. An individual was indicted (October 2012) in the United States District Court for the Western District of Virginia for the alleged violation of the analogue drug provision (substance is α-PVP). Two other individuals were also indicted in this case. One individual pled guilty and one individual was found guilty in a jury trial in July 2013.

5. Individuals were indicted (July 2012) in the United States District Court for the Southern District of New York for conspiring to distribute and possess with intent to distribute a controlled substance analogue (the synthetic designer drugs was α-PVP) in violation of 21 USC 846. The defendants plead guilty (April 2013).

6. Four individuals were indicted (April 2012) in the United States District Court for the Northern District of West Virginia for the conspiracy to distribute controlled substance analogues (α-PVP was one of the substances) and other related charges in violation of 21 USC 846. Three of the individuals pled guilty to some of the charges.