U.S. Department of Justice
Drug Enforcement Administration

Background, Data and Analysis

of Synthetic Cathinones:

Mephedrone (4-MMC), Methylone (MDMC) and 3,4-Methylenedioxypyrovalerone (MDPV)

Prepared by

Office of Diversion Control, Drug and Chemical Evaluation Section
Washington, D.C. 20537
August 2011

Background

The Comprehensive Crime Control Act of 1984 (Pub. L. 98-473), which was signed into law on October 12, 1984, amended section 201 of the Controlled Substances Act (CSA) (21 U.S.C. 811) to give the Attorney General the authority to temporarily place a substance into Schedule I of the CSA for one year without regard to the requirements of 21 U.S.C. 811(b) if he finds that such action is necessary to avoid imminent hazard to the public safety. 21 U.S.C. 811(h); 21 CFR 1308.49. If proceedings to control a substance are initiated under 21 U.S.C. 811(a)(1), the Attorney General may extend the temporary scheduling up to six months. 21 U.S.C. 811(h)(2). Where the necessary findings are made, a substance may be temporarily scheduled if it is not listed in any other schedule under section 202 of the CSA (21 U.S.C. 812) or if there is no exemption or approval in effect under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) for the substance. 21 U.S.C. 811(h)(1). The Attorney General has delegated his authority under 21 U.S.C. 811 to the Administrator of the Drug Enforcement Administration (DEA). 28 CFR 0.100.

Section 201(h)(4) of the CSA (21 U.S.C. 811(h)(4)) requires the Administrator to notify the Secretary of Health and Human Services of her intention to temporarily place a substance into Schedule I of the CSA.[1] The Administrator has transmitted notice of her intent to place 4-methyl-N-methylcathinone (mephedrone), 3,4-methylenedioxy-N-methylcathinone (methylone)

[1] The Secretary 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.

and 3,4-methylenedioxypyrovalerone (MDPV) in Schedule I on a temporary basis to the Assistant Secretary by letter dated June 15, 2011. The Assistant Secretary responded to this notice by letter dated July 25, 2011, and advised that based on review by the Food and Drug Administration (FDA) there are currently no investigational new drug applications (INDs) or approved new drug applications (NDAs) for MDPV, mephedrone, or methylone. The Assistant Secretary also stated that the Department of Health and Human Services has no objection to the temporary placement of MDPV, mephedrone, and methylone into Schedule I of the CSA. DEA has taken into consideration the Assistant Secretary's comments. As MDPV, mephedrone, and methylone are not currently listed in any schedule under the CSA, and as no exemptions or approvals are in effect for MDPV, mephedrone, and methylone under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355), DEA believes that the conditions of 21 U.S.C. 811(h)(1) have been satisfied. Any additional comments submitted by the Assistant Secretary in response to this notice, including whether any exemptions or approvals come into effect for the substances in question under the Federal Food, Drug, and Cosmetic Act, shall also be taken into consideration before a final order is published. 21 U.S.C. 811(h)(4).

To make a finding that placing a substance temporarily into Schedule I of the CSA is necessary to avoid an imminent hazard to the public safety, the Administrator is required to consider three of the eight factors set forth in section 201(c) of the CSA (21 U.S.C. 811(c)). These factors are as follows: the substance's history and current pattern of abuse; the scope, duration and significance of abuse; and what, if any, risk there is to the public health. 21 U.S.C. 811(c)(4)-(6). Consideration of these factors includes actual abuse, diversion from legitimate channels, and clandestine importation, manufacture, or distribution. 21 U.S.C. 811(h)(3).

A substance meeting the statutory requirements for temporary scheduling (21 U.S.C. 811(h)(1)) may only be placed in Schedule I. Substances in Schedule I are those that have a high potential for abuse, no currently accepted medical use in treatment in the United States, and lack accepted safety for use under medical supervision. Available data and information for mephedrone, methylone, and MDPV indicate that these three synthetic cathinones have a high potential for abuse, no currently accepted medical use in treatment in the United States, and lack accepted safety for use under medical supervision.

This review document provides an evaluation of the criteria for this determination for the synthetic cathinones mephedrone, methylone, and MDPV, as of August 2011.

Introduction

Mephedrone, methylone, and MDPV are synthetic cathinones (also commonly referred to as substituted cathinones or cathinone derivatives) that share many similarities with the Schedule I stimulants cathinone and methcathinone. Evidence indicates that these synthetic cathinones are being abused for their psychoactive properties. These substances are falsely marketed as "research chemicals," "plant food," 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. 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. Evidence from law enforcement and poison control centers indicates that the abuse of synthetic

cathinones appears to be widespread and is growing. The American Association of Poison Control Centers (AAPCC)[2] reported that, as of July 31, 2011, poison control centers have received 4,137 calls relating to human exposures to "bath salts" for this year (AAPCC, 2011). These calls were received in poison centers in at least 47 states and the District of Columbia. In 2009, the National Forensic Laboratory Information System (NFLIS) registered 15 reports from 8 states containing these three synthetic cathinones.[3] However, in 2010, there were 560 reports from 29 states related to these substances registered in NFLIS, and from January to March 2011 there were 391 reports. An additional 435 reports to NFLIS were captured from April to June 2011 for a total of 826 reports from January to June 2011.[4]

Mephedrone, methylone, and MDPV have no known medical use in the United States and evidence demonstrates that these substances are being abused by individuals as there have been reports of emergency room admissions and deaths associated with the abuse of these substances. These substances have become a serious drug abuse threat. In light of the above information and to protect the public health and safety, DEA is proposing and intends to temporarily place these synthetic cathinones in Schedule I of the CSA. Under the CSA, before DEA can temporarily schedule a substance, the Administrator must notify the Assistant Secretary for Health, delegate of the Secretary of Health and Human Services (HHS), of her intentions. In accordance with Section 201(h)(4) of the CSA, the Assistant Secretary for Health was notified on June 15, 2011.

To make a finding that placing a substance temporarily into Schedule I of the CSA is necessary to avoid an imminent hazard to the public safety, the Administrator is required to consider three of the eight factors set forth in section 201(c) of the CSA (21 U.S.C. 811(c)). These factors are as follows: the substance's history and current pattern of abuse; the scope, duration and significance of abuse; and what, if any, risk there is to the public health. Pursuant to this action, DEA has reviewed the three factors under the CSA (21 U.S.C. 811(c)(4)-(6)) required for temporary scheduling of mephedrone, methylone, and MDPV.

Synthetic cathinones

Synthetic cathinones are a class of β-ketone amphetamines. Synthetic cathinones include but are not limited to mephedrone, methylone, MDPV, butylone, 4-fluoromethcathinone (4-FMC), 3-fluoromethcathinone (3-FMC), 4-methoxymethcathinone (methedrone), 4-methyl-N-ethylcathinone (4-MEC), ethylone, buphedrone, dimethylcathinone, diethylcathinone, and 3,4-methylenedioxy-α-pyrrolidinopentiophenone (MDPBP). Synthetic cathinones, like cathinone, methcathinone, and amphetamine, are central nervous system stimulants and have been reported to induce subjective effects similar to those induced by Schedule I and II stimulants. Consequently, synthetic cathinones are being abused for their stimulant effects. Synthetic cathinones are also reported to be abused for their hallucinogenic effects. Like Schedule I and II

[2] AAPCC is a non-profit, national organization that represents the poison control centers of the United States.
[3] NFLIS is a DEA sponsored database for seized items analyzed by federal, state, and local forensic laboratories.
[4] Analyzed on August 24, 2011.

stimulants, synthetic cathinones effect monoamine transmission. Synthetic cathinones have been shown to bind to monoamine transporters for dopamine, serotonin, and noradrenaline in the brain and promote release of these monoamines (Cozzi et al., 1998; Cozzi et al., 1999; Fuwa et al., 2007; Nagai et al., 2007; Kehr et al., 2011; Sogawa et al., 2011). Increased monoamine concentration in the central nervous system is thought to be involved in the stimulant and hallucinogenic effects of the phenethylamine class of drugs (Dal Cason et al., 1997).

Mephedrone, methylone, and MDPV are the most commonly encountered synthetic cathinones. These three substances represent more than 98% (1,401 of 1,429) of the synthetic cathinones that have been encountered by law enforcement, as reported to NFLIS. Of all the reports (1,429) of synthetic cathinones recorded by NFLIS from January 2009 to June 2011, 55% (791) were MDPV, 23% (331) were mephedrone, and 20% (279) were methylone.

These three substances have also been identified during screening of individual urine samples. Redwood Toxicology Laboratory screened over 2000 urine samples for the following 14 designer stimulants: amphetamines [3,4-methylenedioxyamphetamine (MDA), MDMA, 3,4-methylenedioxymethamphetamine (MDEA), methylbenzyldioxolylbutanamine (MBDB)], cathinones [(methylone, ethylone, butylone, cathinone, methcathinone, MDPV, mephedrone)] and designer piperazines [N,N-benzylpiperazine (BZP), 1-(3-trifluoromethylphenyl)-piperazine (TFMPP) and 1-(3-chlorophenyl)piperazine (mCPP)] (Rana et al., 2011). Six of these 14 designer stimulants were detected of which MDPV (88% or 1,760) and methylone (21% or 420) were the most common substances detected. The other substances detected were mephedrone, butylone, TFMPP, and BZP. A similar study that screened urine samples (209) from attendees of a Methadone maintenance program in the Republic of Ireland found that 13.9% (29) of samples were positive for mephedrone and 3.3% (7) were positive for methylone (European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), 2011; McNamara et al., 2010).

Drug courts have also detected these three synthetic cathinones during mandatory periodic drug screens. 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. Drug courts submitted to DEA 18 reports from the analysis of biological specimens which contained synthetic cathinones. Mephedrone was mentioned in 10 of these reports, methylone in 5, and MDPV in 7.[5] Other substances detected included butylone, lidocaine, benzocaine, and MDMA. It is possible that drug court participants use synthetic cathinones because they believe that these substances are legal and, thus, they can avoid being charged with violating their parole by using synthetic cathinones.

At a single United States port of entry, the U.S. Customs and Border Protection (CBP) has encountered several shipments of products containing mephedrone, methylone, MDPV, or other synthetic cathinones, thus indicating the popularity of these three substances. Of 96 synthetic cathinone shipments encountered as of July 2011, 14 contained mephedrone, 42

[5] Some specimens contain more than one cathinone.

contained methylone, 17 contained MDPV, and 10 contained 4-MEC. Other synthetic cathinones encountered by CBP were butylone, fluoromethcathinone, and dimethylcathinone. Most of the shipments of these synthetic cathinones originated in China or India and were destined for delivery throughout the United States such as Arizona, Alaska, Hawaii, Kansas, Louisiana, Oklahoma, Oregon, Pennsylvania, Missouri, Virginia, Washington, and West Virginia. These encounters of synthetic cathinones through drug screenings and law enforcement encounters are indications of the popularity of these substances.

Mephedrone

Mephedrone, also known as m-cat, Meow, and mad cow, is a psychoactive chemical that is structurally and pharmacologically similar to the Schedule I and II stimulants cathinone, methcathinone, MDMA, and methamphetamine. There is no evidence that mephedrone has a legitimate non-research use and according to HHS there are no approved drug products or new drug applications that contain mephedrone. Mephedrone is reported to cause both stimulant and hallucinogenic effects. Mephedrone, like Schedule I and II stimulants, increased extracellular serotonin and dopamine in rat brain (Bauman et al., 2011; Kehr et al., 2011). Increased monoamine concentration in the central nervous system is thought to be involved in stimulant and hallucinogenic effects (Dal Cason et al., 1997). Mephedrone, like amphetamine, is a locomotor stimulant (Bauman et al., 2011; Kehr et al., 2011). In rats, mephedrone increased locomotor activity but the effects were weaker and shorter than that induced by amphetamine. Because the effects of mephedrone in rats are like that of Schedule I and II stimulants, it is expected that mephedrone will have pharmacological effects in humans similar to those of Schedule I and II stimulants. Accordingly, the effects of mephedrone have been reported to be similar to that of cocaine and amphetamine.

Methylone

Research in anti-depressant and anti-parkinson agents resulted in the development and patenting of methylone in 1996 (Jacob and Shulgin, 1996). However, there is no evidence that methylone has a legitimate non-research use and according to HHS there are no approved drug products or new drug applications that contain methylone. Methylone has been demonstrated to increase serotonin release and to inhibit serotonin and dopamine reuptake in rat brain synaptosomes and in cells expressing the dopamine transporter (DAT), norepinephrine transporter (NET), and the serotonin transporter (SERT) (Cozzi et al., 1998; Cozzi et al., 1999; Nagai et al., 2007; Sogawa et al., 2011). Like methamphetamine and MDMA, methylone elicited the release of dopamine, norepinephrine and serotonin from cells expressing the DAT, NET, and SERT (Sogawa et al., 2011). Methylone, similar to MDMA, also increased extracellular serotonin and dopamine in rat brain (Bauman et al., 2011). Increased monoamine concentration in the central nervous system is thought to be involved in stimulant and hallucinogenic effects of the phenethylamine class of drugs (Dal Cason et al., 1997). In drug discrimination assays, methylone substituted for MDMA and amphetamine, which suggests that methylone will likely produce subjective effects in humans similar to these substances and have a similar pattern of abuse (Dal Cason et al., 1997; Balster and Bigelow, 2003). Studies also showed methylone to be a weak locomotor stimulant (Bauman et al., 2011).

Little is known about the mechanism of methylone-induced toxicity, but studies show that methylone can be cytotoxic with liver cells as possible targets of the methylone-induced cytotoxicity. Incubation of hepatocytes (liver cells) with methylone or MDMA caused cell death (Nakagawa et al., 2009). In addition, high concentrations of methylone induced the release of lactate dehydrogenase (LDH), an indication of decreased cell viability (Sogawa et al., 2011). Although methylone was not toxic to cells at concentrations that were cytotoxic by methamphetamine, methylone in combination with methamphetamine had a synergistic cytotoxic effect on cells. This is important because users have been reported to use synthetic cathinones in combination with other drugs of abuse. These data suggest that using methylone alone and in combination with other psychoactive substances may cause damage to liver cells. A case of liver toxicity was reported in the scientific literature. Boulanger-Gobeil et al. (2011) described a 22-year-old female who developed rhabdomyolysis (a symptom of liver failure) after ingesting a product called "legal ecstasy" which was analyzed to be a mixture of methylone and ethcathinone.

MDPV

MDPV is closely related in structure to phenethylamines such as the Schedule I and II stimulants methamphetamine, cathinone, and methcathinone. MDPV is also structurally related to pyrovalerone, which is a psychoactive drug that was used to treat chronic lethargy and fatigue. There is no evidence that MDPV has a legitimate non-research use and according to HHS there are no approved drug products or new drug applications that contain MDPV. MDPV and other cathinone derivatives (including those which bear ring-group substituents) have been reported to induce subjective effects similar to those induced by stimulant drugs of abuse such as cocaine, amphetamine, MDMA, and methcathinone. Like other stimulants, MDPV has affinity at the dopamine, noradrenaline, and serotonin transporters (Kelly, 2011). Also like methamphetamine and MDMA, MDPV increased extracellular levels of dopamine in mice brain, although with less potency than these Schedule I and II substances (Fuwa et al., 2007). Increased monoamine concentration in the central nervous system is thought to be involved in stimulant and hallucinogenic effects of the phenethylamine class of drugs (Dal Cason et al., 1997).

FACTOR 4. ITS HISTORY AND CURRENT PATTERN OF ABUSE

The synthetic cathinones mephedrone, methylone, and MDPV have recently emerged on the United States' illicit drug market and are being perceived as being 'legal' alternatives to cocaine, methamphetamine, and MDMA. Although synthetic cathinones are new to the United States' illicit drug market, they have been popular as drugs of abuse in Europe since 2007. These substances are falsely marketed as "research chemicals," "plant food," 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 encountered in the form of capsules, tablets, and powders. 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 of the products found to contain synthetic cathinones include, but are not limited to: Ivory Wave, Vanilla Sky, Energy 1, Explosion, Tranquility, White Rush, Starry Nights, and others.

Drug survey reports suggest that the main users of these and other synthetic cathinones are young male adults (Karila et al., 2010; Winstock et al., 2011b; Vardakou et al., 2011). These substances are popular with youths in urban environments with males appearing to abuse synthetic cathinones more than females. Data also suggest that these substances are used by several population groups, such as young adults, mid-to-late adolescents, and older adults (Newcombe, 2009; EMCDDA, 2011).

The most common routes of administration of mephedrone, methylone, and MDPV are nasal insufflation by snorting the powder and ingestion by swallowing capsules or tablets (Psychonaut, 2010a, c; Winstock et al., 2011a; EMCDDA, 2011; Kelly, 2011; Vardakou et al., 2011). The powder can also be injected or swallowed (Schifano et al., 2011; Wood et al., 2009; Wood et al., 2010a; EMCDDA et al., 2011). Other methods of intake include rectal administration, ingestion by "bombing" (wrapping a dose of powder in a paper wrap and swallowing) and intramuscular injection (Newcombe, 2009; Schifano et al., 2011; Psychonaut, 2010a, c; Wood et al., 2010a). Users have reported switching from snorting to swallowing because of its painful effects on the nasal membranes (Newcombe, 2009; McElrath and O'Neill, 2011). Abusers report that the effects occur a few minutes to 15 minutes after administration, depending on the synthetic cathinones and the route of administration, and the effects can last up to three hours. Following nasal insufflations of MDPV, onset is reported to be within a few minutes with effects lasting for two to three hours (Psychonaut, 2010b; EMCDDA, 2011). Following oral or nasal ingestions of mephedrone, users report that desired effects occur 15 to 45 minutes after administration (Karila et al., 2010; Psychonaut, 2010b; EMCDDA, 2011). Following intravenous injections (typical dose reported to be ½ to ⅓ an oral dose) of MDPV, effects are reported to last 1 to 15 minutes with an overall duration of approximately 30 minutes (EMCDDA, 2011).

Users from drug surveys reported that mephedrone, methylone, MDPV, and other synthetic cathinones have an effect profile similar to known drugs of abuse like cocaine and MDMA. The desired psychoactive effects reported by users include euphoria, general stimulation, empathy, enhanced music appreciation, hallucinations, increased insight, elevated mood, decreased hostility, improved mental function, and mild sexual stimulation (Psychonaut, 2010a, b, c; Winstock, 2011b; Measham, 2010; EMCDDA, 2011). If mephedrone is compared to cocaine, participants in a survey of readers of a popular UK dance music magazine reported that mephedrone gave a better high than cocaine (Winstock, 2011b; EMCDDA, 2011). Another survey that was advertised on websites frequented by drug users found that users considered the effects of mephedrone to be similar to those of MDMA (Carhart-Harris et al., 2011). This is consistent with studies in animals that demonstrated that methylone resembles MDMA in its behavioral profile (Dal Cason et al., 1997; Bossong et al., 2005). In rats trained to discriminate MDMA from saline, methylone substitutes for MDMA.

Like Schedule I stimulants, mephedrone, methylone, and MDPV cause common stimulant-like effects. Stimulant related psychological effects reported by users included headache, nausea, palpitation, increased sex drive, excessive sweating, and cold blue fingers (Dargan et al., 2010; Winstock et al., 2011a, b). Other adverse effects reported by users include bruxism (teeth grinding), paranoia, sore nasal passages, hot flashes, sore mouth/throat, nose bleed, suppressed appetite, blurred vision, insomnia, hallucinations, addiction/dependence, nausea/vomiting, burns, and blue/cold extremities (Newcombe, 2009; Psychonaut, 2010a, b, c; Bajaj et al., 2010; Brunt et al., 2010; Dargan et al., 2010; Wood et al., 2009, 2010a, 2010b, EMCDDA, 2011; Regan et al., 2010; Winstock et al., 2011a).

The reported average amount of use of mephedrone, methylone, or MDPV ranged extensively (from approximately 25 milligrams – 5 grams) depending on the substance, duration of intake, and route of administration. The average amount used for mephedrone ranged from 0.5 to 4 grams depending on the route of administration and the number of doses taken (Newcombe, 2009; James et al., 2010; Schifano et al., 2011; Winstock et al., 2011b). According to self-reported drug users, the amounts for snorting mephedrone ranged from 25 – 75 milligrams whereas for oral administration it ranged from 150 to 250 milligrams (Schifano et al. 2011). The typical oral dose reported for methylone ranged from 100 – 250 mg (Kelly, 2010). The dosage for snorting MDPV ranges from as little as 25 milligrams to as high as 5 grams (ACMD, 2010; Psychonaut, 2010b, c; Durham, 2011).

A number of users of mephedrone, methylone, MDPV, and other synthetic cathinones report using these substances monthly or less often. In a 2009 survey of approximately 947 mephedrone users, the majority (69.7%) of users reported consuming mephedrone monthly or less often (Winstock et al., 2011b). Some users (15.1%) reported weekly or more frequent consumption of mephedrone and 15.2% reported use every two weeks. In another survey, regular users of drugs including mephedrone reported initially using mephedrone occasionally, but the participants in the study reported quickly progressing to weekend use (Newcombe, 2009). There is some evidence of daily use of synthetic cathinones (Dargan et al., 2010; EMCDDA, 2011). In a survey of 1,006 school and college students in Scotland, over 20% (205) reported using mephedrone weekly whereas 4.4% (44) reported using mephedrone on a daily basis (Dargan et al., 2010). Synthetic cathinones have also been reported to be used in binges (Newcombe, 2009; Bajaj et al., 2010; EMCDDA, 2011; Schifano et al., 2011). A young professional male who needed inpatient treatment reported binging twice-weekly on 4 to 5 grams of mephedrone orally (Bajaj et al., 2010). Re-dosing (up to 200 milligrams for MDPV and 4 grams for mephedrone) has been reported by users of MDPV and mephedrone (Psychonaut 2010a; Psychonaut 2010c). Abusers also reported that typical sessions using mephedrone lasted approximately 10.4 hours with some individuals administering several times throughout a session (Winstock et al., 2011b). Because of the short duration of action of synthetic cathinones like mephedrone, one possible reason for binging may be to prolong the duration of effects (ACMD, 2010; Schifano et al., 2011). Accordingly, readers of a popular UK dance music magazine who used drugs including mephedrone reported in a survey that mephedrone had a short duration of action and an urge to use that was similar to that of cocaine (Winstock, 2011b).

Mephedrone, methylone, and MDPV are often co-ingested with other substances (Newcombe, 2009; Debruyne et al., 2010; EMCDDA, 2011; Kriikku et al., 2011; Vardakou et al., 2011). Some co-ingested drugs are used to either heighten the effects or ameliorate the come-down effects of the synthetic cathinones (Newcombe, 2009; Vardakou et al., 2011). 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 MDPV and BZP). Substances reported to have been used in combination with mephedrone, methylone, or MDPV are: other synthetic cathinones (e.g., mephedrone, butylone, fluoromethcathinone, MDPV, etc.), pharmaceutical agents (e.g., lidocaine, caffeine, benzocaine, clonazepam, etc.), or other recreational substances (e.g., amphetamine, MDMA, cocaine, gamma-butyrolactone (GBL), kratom, BZP, and TFMPP) (Newcombe, 2009; EMCDDA, 2011; Vardakou et al., 2011). Multiple drug use is confirmed by 1) investigative toxicology reports of drugs screens of drug users in which more than one substance was detected and 2) seized and purchased synthetic cathinone products in which analyzed data revealed that some products contained multiple substances.

FACTOR 5. THE SCOPE, DURATION, AND SIGNIFICANCE OF ABUSE

The popularity of mephedrone, methylone, MDPV, and other synthetic cathinones as recreational drugs has increased since they first appeared on the United States' illicit drug market. These substances are becoming increasingly prevalent and abused throughout the United States. Consequently, there is increasing evidence of their abuse and availability in the United States. Possible reasons for the increased abuse of mephedrone, methylone, and MDPV and other synthetic cathinones may be attributed to their ease of access, price, and legal status. An additional explanation that has been provided in response to findings in the European designer drug market is that some cathinones are being sold as ecstasy/MDMA (Brunt et al., 2010; EMCDDA, 2011; Griffiths et al., 2010). Griffiths and colleagues (2010) further stated that cathinones are growing in importance as 'legal' alternatives and end-users are seeking out specific substances due to a growing awareness. 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. Law enforcement data indicate that products that contain these substances are generally sold in 50 - 500 milligram packets with prices ranging from $25-$70 per packet and $60-$70 per gram (PACIC, 2011). These substances can also be bought in bulk quantities (e.g., 100 g to over 5 kg). Companies located in China and India are primarily responsible for the export of these substances. The perceived noncontrolled status of these substances may give synthetic cathinones an added appeal (Measham et al., 2010). A web-based survey of individuals who visit drug websites found that mephedrone's popularity was related to its legality (Carhart-Harris et al., 2011).

Surveys suggest a high prevalence of use of mephedrone, methylone, MDPV, and other synthetic cathinones. In a 2009 survey of 2,295 clubbers in the United Kingdom, 41.3% (947) of those surveyed reported ever having used mephedrone, 38.7% (890) reported use of mephedrone within the last year and 33.6% (762) reported within the last month (Winstock, 2011b). This is comparable with other psychoactive substances ever used by these respondents such as amphetamine (51.3% or 1,174) and methamphetamine (5.6% or 129). By comparison, a total of 10.8% (248) and 1.9% (44) reported ever having used methylone and MDPV, respectively. In a 2010 survey of 1,006 school and college students in Scotland, 20.3% (205) of those surveyed had used mephedrone on at least one occasion (Dargan et al., 2010). In specimens collected for drug screens, MDPV and methylone were detected in 88% (1,760) and 21% (420), respectively, of urine samples that were analyzed for designer drugs (Rana et al., 2011).

Evidence of the abuse of mephedrone, methylone, and MDPV is confirmed by drug courts. Drug court reports have identified these and other synthetic cathinones in specimens submitted for testing by drug court participants confirming the use of these substances by supposedly former recovering drug users. Drug court reports have identified mephedrone, methylone, MDPV, and butylone in specimens submitted for testing by drug court participants.

Studies suggest that mephedrone, methylone, MDPV, and other synthetic cathinones may be used as an alternative to illicit substances like MDMA and cocaine (EMCDDA, 2011). A study analyzing the urine of opioid-dependent patients undergoing opioid substitution treatment found nine of thirty-four patients tested positive for MDPV (Ojanperä et al., 2011). In addition, surveys found that participants who reported ever having used cocaine, also used mephedrone (Carhart-Harris et al., 2011; Winstock, 2011a). Debruyne et al. (2010) described two individuals who used mephedrone in place of cocaine. ACMD reported that mephedrone and "Toot" (most commonly identified as a mixture of butylone and methylone) were popular among users of heroin (ACMD, 2010). In fact, 36% of a survey of mephedrone users (United Kingdom magazine readers) reported that they now took less cocaine and 63% reported that they took less ecstasy since they began using mephedrone (EMCDDA, 2011). Moreover, 46% reported they would choose mephedrone over cocaine, and only 26% reported they would take mephedrone over ecstasy.

Evidence from law enforcement and poison control centers indicates that the abuse of mephedrone, methylone, MDPV, and other substances is widespread and growing. In 2009, NFLIS received 15 reports of analyzed seizures from 8 states related to mephedrone, methylone, and MDPV. However, in 2010, there were 560 reports of analyzed seizures from 29 states related to these substances reported to NFLIS and in the first half of 2011 (January to June 2011) there were 826. The Texas Poison Center Network reported an increase in the number of calls regarding mephedrone and MDPV since the beginning of 2010 (Forrester, 2011). In January 2010, there were no calls regarding these substances and only 20 total calls for the entire year of 2010. However, from January to July 2011, they received 237 calls. The callers ranged in age from 15 to 57 and 75.9% (195) of all the callers from January 2010 to April 2011 were male. The New Jersey Division of Consumer Affairs reported an increase in the number of cases involving "bath salts" (New Jersey Poison Information and Education System (NJPIES), 2011). Prior to January 2011, NJPIES received no reports of the use of designer drugs labeled as "bath salts." However, from January 2011 to April 2011, NJPIES received 23 cases of "bath salt" exposures. AAPCC reported that, in 2010, poison control centers took 303 calls about synthetic cathinones (AAPCC, 2011). As of July 31, 2011, poison control centers have received 4,137 calls relating to these products for this year. These calls were received in poison control centers representing at least 47 states and the District of Columbia.

Concerns over the abuse of mephedrone, methylone, MDPV, and other synthetic cathinones have prompted many states to control these substances. As of July 15, 2011, thirty-three states have emergency scheduled or enacted legislation placing regulatory controls on some or many of the synthetic cathinones. These states include Alabama, Arkansas, Florida, Georgia, Hawaii, Idaho, Illinois, Indiana, Kansas, Kentucky, Louisiana, Maine, Michigan, Minnesota, Mississippi, Missouri, New Jersey, New Mexico, New York, North Carolina, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Texas, Tennessee, Utah, Virginia, Washington, West Virginia, Wisconsin and Wyoming. In addition, the use of synthetic cathinones by members of the U.S. Armed Forces is prohibited.

Abuse of these substances is not limited to the United States. 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).

FACTOR 6. WHAT, IF ANY, RISK THERE IS TO THE PUBLIC HEALTH

Law enforcement, forensic laboratories, and public health officials have reported exposure incidents demonstrating the public health risks associated with these synthetic cathinones to both individual abusers and the public.

These synthetic cathinones have been reported to cause a number of stimulant-like adverse effects (ACMD, 2010; Psychonaut, 2010a; Psychonaut, 2010c; EMCDDA, 2011). The clinical presentation of intoxication from synthetic cathinones shares some features seen with MDMA and stimulants like cocaine. Clinical case reports indicate that these synthetic cathinones produce a number of stimulant-like adverse effects such as palpitation, seizure, vomiting, sweating, headache, discoloration of the skin, hypertension, tachycardia and hyper-reflexia (Wood et al., 2009; Durham, 2011; Frohlich et al, 2011; Vardakou et al., 2011). A survey of readers of a popular drug-related magazine on the use, effect profile and abuse liability associated with the use of mephedrone reported that the physical effect profile of mephedrone is very typical of stimulants (EMCDDA, 2011). Adverse effects associated with consumption of these drugs as reported by users include nose-bleeds, bruxism (teeth grinding), paranoia, hot flashes, blurred vision, dry mouth/thirst, fast erratic heart-beats, muscular tension in the jaw and limbs, headache, agitation, anxiety, tremor, fever and sweating (Newcombe, 2009; Dargan et al., 2010; Winstock et al, 2011a, b; EMCDDA, 2011; Vardakou et al., 2011). Hyperthermia, a serious adverse effect, can lead to metabolic acidosis, rhadomyolysis, renal failure, disseminated intravascular coagulation, coma and death. Thus, these serious adverse effects may require visits to the emergency department (ED).

Consequently, numerous individuals have presented at emergency departments in response to exposure incidents. Several cases of acute toxicity have been reported for the ingestion of mephedrone or MDPV. Debruyne et al. (2010) reported seven cases in France that were related to the abuse of mephedrone and were reported to the Center of Evaluation and Information on the Pharmacodependence (Addictovigilance). Wood et al. (2009) reported a case of acute toxicity in the United Kingdom after the abuse of mephedrone. A 22-year-old male presented to the emergency room with sympathomimetic toxicity after ingesting 200 milligrams of mephedrone. He developed palpitation, blurred vision, mydriasis, agitation, tachycardia, and an elevated body temperature. His symptoms resolved after treatment. Mephedrone was the only substance detected in his serum. Nicholson et al. (2010) described the case of a 19-year-old Irish male who presented to the emergency room with central crushing chest pain. Clinical tests showed myocardial inflammation. He admitted to ingesting plant food that contained mephedrone. Toxicology screening of biological samples confirmed the presence of mephedrone and no other neurostimulant drugs. He was successfully treated and discharged to go home five days after his admission. The website for the New Jersey Consumer Affairs, www.njconsumeraffairs.gov (2011), reported several cases of emergency room incidents involving patients who abused “bath salts.” The Michigan Department of Community Health reported 25 cases of severe illness and one fatality caused by drugs marketed as “bath salts” (MMWR, 2011). Frohlich et al. (2011) described a case of acute liver failure after the ingestion of synthetic cathinones. A 28-year-old male suffering from bipolar affective disorder (but otherwise healthy) ingested 12 stimulant tablets. Following ingesting he suffered a seizure. He

was transported to the emergency department suffering tachycardia, hypertension, hyperpyrexia, and profuse sweating. Rhabdomyolysis, a symptom of liver failure, developed two days after ingestion. 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 be MDPV and butylone. In a similar case, a 22-year-old female developed rhabdomyolysis after ingesting "legal ecstasy" which was analyzed to be a mixture of methylone and ethcathinone (Boulanger-Gobeil et al., 2011). She also suffered from recurrent seizures, severe hyponatremia (abnormally high concentration of sodium in the blood), nystagmus (involuntary rapid eye movement), hyperreflexia, and bruxism. All her symptoms resolved after treatment that required hospitalization. Penders and Gestring (2011) reported three cases of paranoid psychotic delirium (presenting as paranoid hallucinatory psychosis) following the alleged abuse of "bath salts" containing MDPV. Interestingly, in these three cases of delirium, some memory loss was reported during the time of abuse of the "bath salts." Cases of acute toxicity were also reported for the ingestion of methylone. Katagi et al. (2010) reported two cases of acute toxicity from the confirmed ingestion of methylone. A 19-year-old male was taken to the emergency department suffering from dementia after ingesting an unknown amount of methylone powder. In the second case, a 29-year-old male was taken to the emergency department suffering from acute toxicity after taking an unknown amount of a mixture of methylone and a hallucinogen.

Abusers suspected of driving under the influence of intoxicating substances have been found to have positive test results for a synthetic cathinone. Kriikku et al. (2011) reported on the prevalence of MDPV use among individuals suspected of driving while under the influence of drugs (DUIDs) in Finland. Blood samples from individuals suspected of DUIDs from August 2009 to August 2010 were screened for the presence of MDPV. Of 3000 samples tested, 259 were found to be positive for MDPV. Although other drugs were detected in some case samples, the authors concluded that MDPV use was a significant problem in DUID cases in Finland. DUIDs have also been reported in Ohio. Urine samples from drivers in Ohio suspected of driving under the influence of drugs have tested positive for MDPV. In one of the DUID cases in Ohio reported to DEA, a 31-year-old female hit three parked cars in different locations and was unaware that she hit anything. MDPV was confirmed in blood specimen from this driver; benzoylecmethylecgonine (a metabolite of cocaine) and fluoxetine were also detected. In another incident, a 37-year-old male died when he collided head on with a passenger van. Samples from the decedent tested positive for tetrahydrocannabinol (THC), MDPV, and methylone. Toxicology screens of drivers suspected of driving under the influence in Maine also identified individuals who tested positive for synthetic cathinones. MDPV was confirmed in samples from some of these drivers. DUID cases have been reported for mephedrone, methylone, and MDPV.

Individuals under the influence of these synthetic cathinones have acted violently and unpredictably causing harm, or even death, to themselves or others, including children. In one incident, a man shot and killed himself and his wife; police had tried to pull him over for speeding but he fled and a police chase ensued. Soon after, the couple's 5-year-old son was discovered dead at home. "Bath salts" packaging was found on the male decedent and at the residence of the decedent. Specimens from the decedents confirmed the presence of MDPV and lidocaine. In another incident, officers responded to a domestic disturbance call at a hotel. At the hotel, a male and his wife appeared to be in a state of paranoia and the male admitted to the

officers that he and his wife had been snorting "bath salts" which was confirmed to be MDPV by laboratory analysis. Officers found several children including a 9-year-old and 3-month-old at the site. One of the children appeared to be under the influence of drugs and was transported to the emergency department. The parents were issued summons including one for child endangering. Rohrig (2011) described the case of a 21-year-old who was struck and killed by a van after he ran into oncoming traffic. A witness reported that the decedent was let out on the side of a local interstate after he acted wildly and belligerently after ingesting "bath salts" and smoking "K2" (a synthetic cannabinoid). MDPV was detected in serum samples from the decedent. In another incident, a 26-year-old male shot and killed a deputy who was responding to a domestic violence call. Toxicological testing confirmed the presence of MDPV and synthetic cannabinoids in specimens from the suspect. Maskell et al. (2011) reported a case of a 17-year-old male who died from injuries sustained in a vehicular collision. While driving on the wrong side of the road, he collided head-on with an oncoming car. Mephedrone was detected in blood samples from this individual and is suspected to have affected the ability of this person to drive. Lusthof et al. (2011) reported a case of extreme agitation and death after the ingestion of mephedrone. A 36-year-old man died from substantial blood loss that may have led to aggravated heart and blood pressure problems after he was arrested by police for extreme agitation. An autopsy revealed high concentrations of mephedrone in the decedent's blood and urine. Other substances including oxazepam, MDMA, and alcohol were also detected but in smaller concentrations. A 21-year-old male committed suicide after snorting "bath salts" marketed under the name "Cloud 9." Family members described the decedent as paranoid before he shot and killed himself. A toxicology laboratory report confirmed the presence of MDPV and citalopram in specimens from the decedent.

There are at least three reported deaths in which mephedrone, methylone, or MDPV was ruled as the cause of death by the medical examiner or after an autopsy. Maskell et al. (2011) described a death in the United Kingdom that was attributable to mephedrone abuse. A 19-year-old male died after taking an unknown amount of mephedrone along with alcohol and MDMA at a party. Others at the party described the 19-year-old as being sweaty and acting strangely. Subsequently he collapsed. Emergency services were called and he was taken to the hospital but efforts to resuscitate him were unsuccessful. Toxicology screens confirmed the presence of mephedrone in urine and blood samples from this individual. Mephedrone was considered to be the principal cause of death. A medical examiner's report described the death of a 23-year-old male from methylone intoxication. The decedent was walking in and out of traffic and acting belligerently. The decedent was detained by law enforcement and transported to the emergency department. The decedent had a high temperature and subsequently went into respiratory failure. After several attempts to stabilize the decedent, he died. The medical examiner listed the cause of death as intoxication by methylone. Wyman et al. (2011) reported the death of a 39-year-old male. Family members indicated that the male, who had a history of schizophrenia, depression, and drug abuse, had been snorting "bath salts." The decedent was found dead in his bed. Empty jars of "bath salts" (TranQuility and Infinity) and synthetic cannabinoids (Demon and Flame) were found in the trash next to the decedent. A toxicological screen detected MDPV distributed among multiple tissues, urine and blood samples from the decedent. Other substances detected were nicotine, cotinine, pseudoephedrine, m-chlorophenylpiperazine and methylone. The cause of death was ruled acute MDPV intoxication.

Mephedrone, methylone, and MDPV have also been implicated in drug induced overdose deaths. Maskell et al. (2011) reported two deaths that were linked to mephedrone. In the first death, a 55-year-old female was found dead in her bed. Multiple drug toxicity (mephedrone and methadone) were considered to be the cause of death, because her death was attributed to the combined effects of mephedrone and methadone. In the second death, a 49-year-old female died after snorting approximately 0.5 grams of mephedrone that she purchased from the Internet. She also consumed alcohol and smoked marijuana. A few hours after consuming mephedrone, she complained of a sore chest, she vomited, and then she collapsed. She was transported to the hospital by emergency services but died despite efforts to resuscitate her. Her death was attributed to the adverse effects of mephedrone. A police report described the death of a 29-year-old female. Emergency personnel responded to a call from the decedent's mother that the subject was experiencing seizures after taking an unknown substance. The decedent complained of hearing things and was acting differently. The decedent was transported to the hospital where she later died. A previously described case of a 39-year-old male with psychiatric complications where the cause of death was ruled acute MDPV intoxication also had in his system methylone, nicotine, cotinine, pseudoephedrine, and m-chlorophenylpiperazine. MDPV and diphenhydramine were detected in blood samples taken from the decedent. In another incident, the death of a 19-year-old was ruled a complication of acute oxymorphone toxicity with alprazolam, ethanol, and mephedrone use as likely contributing factors. The decedent was found dead on the fire escape of an apartment building, partially leaning on and over a railing, along with another individual who was also deceased.

There are reports that synthetic cathinones are highly addictive (Psychonaut, 2010a). Studies show that the abuse of synthetic cathinones can lead to psychological dependence like that reported for other stimulant drugs. For example, a young professional male claimed he could not stop using mephedrone (Bajaj et al., 2010). He presented to the hospital with transient psychosis, hallucination, hypomania and mood disturbances. His symptoms resolved after treatment. Additionally, users report a "craving" for some synthetic cathinones, like MDPV and mephedrone, leading to high/frequent abuse of these substances (Psychonaut, 2010a, b, c; EMCDDA, 2011). A survey of mephedrone users found that for 30% (29 of 100) of users, there was evidence of a strong compulsion to use the drug (Winstock et al., 2011a). These individuals met the Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV dependence criteria. Dargan et al. (2010) also reported that one of six users (17.6%) surveyed (college and university students) reported a strong urge to re-dose.

The manufacturers and retailers who make and sell these products do not fully disclose the product ingredients including the active ingredients or the health risks and potential hazards associated with these products. 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. Thus, individuals who purchase these products likely have insufficient knowledge of the exact product contents. In addition, products may not contain the expected active ingredients. In a study that analyzed products offered for sale, there was significant variation in the content of the cathinones in one quarter (5 of 20) of the products they purchased and tested (Davies et al., 2010). 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. Products marketed to contain a specific legal substance may in fact contain a different substance. A study by Brandt et al. (2010) showed that 70% of the products analyzed contained an illicit substance. Since abusers obtain these drugs through unknown sources, the purity of these drugs is uncertain, thus presenting another level of risk to users (EMCDDA, 2011). Thus, the limited knowledge about product content, purity and lack of information about product effects pose significant risks to the user.

Available evidence on the overall health and social risks of these synthetic cathinones indicates that these substances can cause acute health problems, can potentially lead to dependency, or can cause death. Acute effects include those typical of a sympathomimetic agent including tachycardia, headache, palpitations, agitation, anxiety, mydriasis, tremor, fever or sweating and hypertension (Brunt et al., 2010; Wood et al., 2009; James et al., 2010; Wood et al., 2010b; Wood et al., 2010c; EMCDDA, 2011; Winstock et al., 2011a, b).

Conclusion Regarding 3-Factor Analysis

After a careful review of the scientific literature, Factors 4, 5, and 6, NFLIS, law enforcement data and other sources of information, it is evident that mephedrone, methylone, and MDPV are trafficked and abused and pose a significant public health risk. These drugs have become popular among drug abusers for their stimulant and hallucinogenic effects.

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-methyl-N-methylcathinone (mephedrone), 3,4-methylenedioxy-N-methylcathinone (methylone), and 3,4-methylenedioxypyrovalerone (MDPV) indicate that these substances pose an imminent hazard to public safety and health, have no currently accepted medical use in treatment in the United States, and are not safe for use under medical supervision.

References

ACMD. Advisory Council on the misuse of drugs. 2010. Consideration of the cathinones. (Iversen). London.

AAPCC. American Association of Poison Control Centers. 2011. U.S. Poison Centers Raise Alarm About Toxic Substance Marketed as Bath Salts; States Begin Taking Action. Updated August 2, 2011.

Bajaj N, Mullen D, Wylie S. 2010. Dependence and psychosis with 4-methylmethcathinone (mephedrone) use. British Medical Journal Case Reports, doi: 10.1136/bcr.02.2010.2780.

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

Bauman MH, Ayestas MA, Rothman RB, Cozzi NV. 2011. In vivo neurochemistry of designer methcathinone analogs abused by humans. Abstract in "The College on Problems of Drug Dependence (CPDD) 73rd Annual Meeting". 12.

Boulanger-Gobeil C, St-Onge M, Laliberte M, Auger PL. 2011. Seizures and hyponatremia related to ethcathinone and methylone poisoning. Journal of Medical Toxicology, doi: 10.1007/s13181-011-0159-1.

Bossong MG, Van Dijk JP, Niesink JM. 2005. Methylone and mCPP, two new drugs of abuse: Addiction Biology, 10: 321-323.

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.

Brunt TM, Poortman A, Niesink RJ, van den Brink W. Instability of the ecstasy market and a new kid on the block: mephedrone. Journal of Psychopharmacology, 2010 Sep 8. doi:10.1177/0269881110378370.

Carhart-Harris RL, King LA, Nutt DJ. 2011. A web-based survey on mephedrone. Drug and Alcohol Dependence, doi:10.1016/j.drugalcdep.2011.02.011.

Cozzi N, Sievert M, Shulgin A, Peyton J, Ruopho A. 1998. Methcathinone and 2-methylamino-1-(3,4-methylenedioxyphenyl)propan-1-one selectively inhibit plasma membrane catecholamine reuptake transporters. Society for Neuroscience Abstracts, 24: 381-388.

Cozzi N, Sievert M, Shulgin A, Peyton J, Ruoho A. 1999. Inhibition of plasma membrane monoamine transporters by β-ketoamphetamines. European Journal of Pharmacology, 381: 63-69.

Dal Cason T, Young R, Glennon R. 1997. Cathinone: An investigation of several N-alkyl and methylenedioxy-substituted analogs. Pharmacology Biochemistry and Behavior, 58: 1109-1116.

Dargan PI, Albert A, Wood DM. 2010. Mephedrone use and associated adverse effects in school and college/university students before the UK legislation change. QJM: An International Journal of Medicine, 103: 875-879.

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.

Debruyne D, Courne M, Le Boisselier R, Djezzar S, Gerardin M, Boucher A, Karila L, Coquerel A, Mallaret M. 2010. La mephedrone: une designer drug d'usage recent en France. Therapie, 65: 519-524.

Dickson AJ, Vorce SO, Levine V. Past MR. 2010. Multiple-drug toxicity caused by the coadministration of 4-methymethcathinone (Mephedrone) and Heroin. Journal of Analytical Toxicology, 34: 162–168.

Durham. 2011. Ivory wave: the next mephedrone? Emergency Medicine Journal. doi: 10.1136/emj.2011.112920.

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.

Forrester M, 2011. Mephedrone and methylenedioxypyrovalerone (bath salts) reported to the Texas Poison Center Network Updated: April 25, 2011.

Fuwa T, Fukumori N, Tanaka T, Kubo Y, Ogata A, Uehara S, Honda Y, Kodama T. 2007 Microdialysis study of drug effects on central nervous system - Changes of dopamine levels in mice striatum after oral administration of methylenedioxypyrovalerone. Tokyo-to Kenko Anzen Kenkyu Senta Kenkyu Nenpo, 58: 287-292.

Griffiths P, Lopez D, Sedefov R, Gallegos A, Hughes B, Noor A, Royuela L. 2010. Khat use and monitoring and issues for the future. Journal of Ethnopharmacology, 132: 578-583.

Jacob P III, Shulgin. 1996. Novel N-substituted-2-amino-3',4'-methylene-dioxypropiophenones. Patent Cooperation Treaty (PCT) International Applications, PCT/US06/09603.

James D, Adams, RD, Spears R, Cooper G, Lupton DJ, Thompson JP, Thomas SHL. 2010. Clinical characteristic of mephedrone toxicity reported to the UK National Poisons Information Service. Emerging Medicine Journal, 28: 686-689.

Karila L, Reynaud M. 2010. GHB and synthetic cathinones: clinical effects and potential consequences. Drug Testing and Analysis, doi:10.1002/dta.210.

Katagi, M, Zaitsu K, Shima N, Kamata H, Kamata T, Nakanishi K, Nishioka H, Miki A, Tsuchihashi H. 2010. Metabolism and forensic toxicological analyses of the extensively abused designer drug methylone. TIAFT Bulletin, 40: 30-35.

Kehr J, Ichinose F, Yoshitake S, Goiny M, Sievertsson T, Nyberg F, Yoshitake T. Mephedrone, compared to MDMA (ecstasy) and amphetamine, rapidly increases both dopamine and serotonin levels in nucleus accumbens of awake rats. British Journal of Pharmacology, 2011 May 26. doi: 10.1111/j.1476-5381.2011.01499.x.

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

Kriikku P, Wilhelm L, Schwarz O, Rintatalo J. 2011. New designer drug of abuse: 3,4-Methylenedioxypyrovalerone (MDPV). Findings from apprehended drivers in Finland. Forensic Science International, 210: 195-200.

Lusthof KJ, Oosting R, Maes A, Verschraagen M, Dijkhuizen A, Sprong AG. 2011. Forensic Science International, 206: e93-e95.

Maskell PD, De Paoli G, Seneviratne C, Pounder DJ. 2011. Mephedrone (4-methylmethcathinone)-related deaths. Journal of Analytical Toxicology, 35: 188-191.

McElrath K and O'Neill C. 2011. Experiences with mephedrone pre- and post-legislative controls: Perceptions of safety and sources of supply. International Journal of Drug Policy, 22: 120-127.

McNamara S, Stokes S, Coleman N. 2010. Head shop compound abuse amongst attendees of The Drug Treatment Centre Board. Irish Medical Journal, 103: 134-137.

Measham F, Moore K, Newcombe R, Welch Z. 2010. Tweaking, bombing, dabbing and stockpiling: the emergence of mephedrone and the perversity of prohibition. Drugs and Alcohol Today. 10:14-21.

MMWR. Morbidity and Mortality Weekly Report. 2011. Emergency department visits after use of a drug sold as "bath salts" – Michigan, November 13, 2010-March 31, 2011. 60: 1-4.

Nagai F, Nonaka R, Satoh K, Kamimura H. 2007. The effects of non-medically used psychoactive drugs on monoamine neurotransmission in rat. European Journal of Pharmacology, 559: 132-137.

Nakagawa Y, Suzuki T, Tayama S, Ishii H, Ogata A. 2009. Cytotoxic effects of 3,4-methylenedioxy-N-alkylamphetamines, MDMA and its analogues, on isolated rat hepatocytes. Archives of Toxicology, 83: 69-82.

Newcombe R. 2009. Mephedrone The use of mephedrone (M-CAT, Meow) in Middlesbrough. Lifeline Publications and Research, Manchester.

NJPIES. New Jersey Division of Consumer Affairs. 2011. Designer drugs labeled as "bath salts:" Statistics on abuse in New Jersey. (as of April 20, 2011).

Nicholson PJ, Quinn MJ, Dodd JD. 2010. Headshop heartache: acute mephedrone 'meow' myocardis. Heart, 96: 2051–2052.

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.

Penders TM, Gestring R. 2011. Hallucinatory delirium following use of MDPV: "Bath salts." General Hospital Psychiatry, doi: 10.1016/j.genhosppsych.2011.05.014.

Pennsylvania Criminal Intelligence Center (PACIC). 2009. Information Bulletin, Abuse of Bath Salts. CIKR-03-2011. March 8, 2011.

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.]

Rana S, Uralets V, Ross W. 2011. Society of Forensic Toxicologist (SOFT) & The International Association of Forensic Toxicologist (TIAFT). Routine screening of human urine for 14 new designer stimulants found in "bath salts." In press.

Regan L, Mitchelson M, Macdonald C. 2010. Mephedrone toxicity in a Scottish emergency department. Emerging Medicine Journal, 2010 Dec 23. doi: 10.1136/emj.2010.103093.

Rohrig T. 2011. California Association of Toxicologist (CAT) Proceedings, Designer drugs – The future of drug abuse? Pharmacology of cathinones analogs AKA "Bath salts" May 5-6, 2011. Napa, Ca.

Schifano F, Albanese A, Fergus S, Stair JL, Deluca P, Corazza O, Davey Z, Corkery J, Siemann H, Scherbaum N, Farre' M, Torrens M, Demetrovics Z, Ghodse AH; Psychonaut Web Mapping; ReDNet Research Groups. 2011. Mephedrone (4-methylmethcathinone; 'meow meow'): chemical, pharmacological and clinical issues. Psychopharmacology (Berl), 214: 593-602.

Shimizu E, Watanabe H, Kojima T, Hagiwara H, Fujisake M, Miyatake R, Hashimoto K, Iyo M. 2007. Combined intoxication with methylone and 5-MeO-DIPT. Progress in Neuro-Psychopharmacology & Biological Psychiatry. 31: 571 – 573.

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.

Sogawa C, Sogawa N, Ohyama K, Kikura-Hanajiri R, Goda Y, Sora I, Kitayama. 2011. Methylone and monoamine transporters: Correlation with toxicity. Current Neuropharmacology, 9: 58-62.

Torrance H, Cooper G. 2010. The detection of mephedrone (4-methylmethcathinone) in 4 fatalities in Scotland. Forensic Science International. 202: e62-e63.

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

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

Winstock A, Mitcheson L, Ramsey J, Marsden J. 2011a. Mephedrone: use, subjective effects and health risks. Addiction, doi: 10.1111/j.1360-0443.2011.03502.x.

Winstock AR, Mitcheson LR, Deluca P, Davey Z, Corazza O, Schifano F. 2011b. Mephedrone, new kid for the chop? Addiction, 106: 154-161.

Wood DM, Davies S, Puchnarewicz M, Button J, Archer R, Ramsey J, Lee T, Holt DW, Dargan PL. 2009. Recreational Use of 4-methylmethcathinone (4-MMC) presenting with sympathomimetic toxicity and confirmed by toxicological screening. Clinical Toxicology, 47: 733.

Wood DM, Davies S, Puchnarewicz M, Button J, Archer R, Ovaska H, Ramsey J, Lee T, Holt DW, Dargan PL. 2010a. Recreational use of (4-methylmethcathinone, 4-MMC) with associated sympathomimetic toxicity. Journal of Medical Toxicology, 6: 327–330.

Wood DM, Greene SL, Dargan PI. 2010b. Clinical pattern of toxicity associated with the novel synthetic cathinones mephedrone. Emergency Medicine Journal, 28: 280-282.

Wood DM, Davies S, Greene SL, Button J, Holt DW, Ramsey J, Dargan PI. 2010c. Case series of individuals with analytically confirmed acute mephedrone toxicity. Clinical Toxicology (Phila), 9: 924-927.

Wyman JF, Lavins ES, Sofalvi S, Armstrong EJ, Engelhart DA, Boggs PD, Taylor SM, Naso CK, Stibley JM, Snell KD, Wilkins LD, Gubanich KM, Mazzola CD, Norris RN, Blum LM, Miller FP. 2011. Death by "bath salts": Postmortem tissue distribution of MDPV following lethal Intoxication. Society of Forensic Toxicologist (SOFT) & The International Association of Forensic Toxicologist (TIAFT). In press

Appendix 1

Reports from the Scientific Literature

Case Reports of Fatalities Involving Synthetic Cathinones

1. Torrance and Cooper (2010) reported the death of four Scottish individuals whose blood samples tested positive for mephedrone. These fatalities were not attributed to the sole use of mephedrone but they can be considered to be evidence of the misuse of mephedrone and the subsequent harm they may cause to the user or general public.
2. Maskell et al. (2011) reported four deaths in the United Kingdom related to mephedrone abuse. (1) A 49-year-old female died after snorting approximately 0.5 grams mephedrone that she purchased from the Internet. She also consumed alcohol and smoked marijuana. A few hours after taking mephedrone, she complained of a sore chest, vomited, and then collapsed. She was transported to the hospital by emergency services but died despite efforts to resuscitate her. Her death was attributed to the adverse effects of mephedrone. (2) A 19-year-old male died after taking an unknown amount of mephedrone along with alcohol and MDMA at a party. Others at the party described the 19-year-old as being sweaty and acting strangely, and subsequently he collapsed. Emergency services were called and he was taken to the hospital but efforts to resuscitate him were unsuccessful. Toxicology reports confirmed the presence of mephedrone in urine and blood samples from this individual. Mephedrone toxicity was considered to be the principal cause of death. (3) A 55-year-old female was found dead in bed, her death attributed to the combined effects of mephedrone and methadone. Multiple drug toxicity (mephedrone and methadone) was considered to be the cause of death. (4) A 17-year-old male died from injuries sustained in a vehicular collision. While driving on the wrong side of the road he collided head-on with an oncoming car. Mephedrone was detected in his blood and is suspected to have affected his ability to drive.
3. Dickson et al. (2010) described the case of a 22-year-old male who was found unresponsive at his home in Maryland. He was transported to the hospital where he died, and a subsequent autopsy revealed heroin and high concentrations of mephedrone. The medical examiner reported multiple drug toxicity associated with mephedrone and heroin use as the cause of death.
4. Lusthof et al. (2011) described the death of a 36-year-old man from substantial blood loss that may have led to aggravated heart and blood pressure problems after he was arrested by police for extreme agitation. An autopsy revealed a high concentration of mephedrone in the decedent's blood and urine. Other substances including oxazepam, MDMA, and alcohol were also detected but in smaller concentrations.

Emergency Department Incidents/Visits Involving Synthetic Cathinones

5. Shimizu et al. (2007) reported a case of acute drug intoxication from the ingestion of a mixture of methylone and 5-methoxy-N-methyl-N-isopropyltryptamine (5-MeO-MIPT) powder. A 27-year-old Japanese male presented to the emergency room after taking approximately 200 milligrams of methylone and 5-MeO-MIPT powder by oral ingestion

that he purchased over the Internet. According to the report, the subject was transported to the hospital after reportedly acting strangely. At the hospital, the subject had an elevated heart rate and blood pressure, while exhibiting dilated pupils and sweating. The patient's symptoms resolved after five hours of treatment.

6. Debruyne et al. (2010) reported that seven cases in France related to the use of mephedrone were reported to the Center of Evaluation and Information on Pharmacodependence (Addictovigilance). In one case, a young man was involved in a vehicular accident after snorting mephedrone. His blood tested positive for mephedrone. In another case, an individual used mephedrone in place of cocaine.
7. Wood et al. (2009 and 2010a) described a case of toxicity in the United Kingdom. Mephedrone was reported to produce sympathomimetic effects in a 22-year-old male who used it for recreational purposes.
8. Wood et al. (2010b) described 15 patients who presented to the emergency department in the United Kingdom following self-reported mephedrone use. These patients presented with agitation (53.3%), tachycardia (40%), hypertension (20%) and seizures (20%).
9. Wood et al. (2010c) described reports of acute toxicity associated with seven confirmed cases of mephedrone use. The most common symptoms reported in these patients were agitation, palpitations, and chest pain. All patients had an elevated heart rate (mean rate was 109.1 beats per minute) and blood pressure (mean systolic blood pressure was 153 mmHg). One patient, a 29-year-old male, died. The coroner determined that the cause of death was hypoxic brain injury due to cerebral oedema following ingestion of a psychoactive substance. Although no other drugs were detected in specimens from the patient, the coroner ruled that it was possible that other drugs may have been used which were not detectable at the time the biological specimens were collected.
10. Nicholson et al. (2010) described a case involving a 19-year-old Irish male who presented to the emergency room with central crushing chest pain. Clinical tests showed myocardial inflammation. He admitted to ingesting plant food that contained mephedrone. Toxicology screening of biological samples confirmed the presence of mephedrone and no other neurostimulant drugs. He was successfully treated and discharged home five days after his admission.
11. New Jersey Consumer Affairs, www.njconsumeraffairs.gov (2011), published a report online that described several cases of emergency room incidents involving patients who abused designer drugs. Prior to January 2011, no reports regarding the use of designer drugs had been received by New Jersey Poison Information and Education System. Since January 2011, 23 cases have been reported (NJPIES, 2011).
12. The Centers for Disease Control and Prevention published a report that describes 25 cases in Michigan of severe illness and one fatality caused by drugs marketed as "bath salts" (MMWR, 2011).

Physiological or Psychological Dependence of Synthetic Cathinones

13. Bajaj et al. (2010) reported a case regarding a young man from the United Kingdom who was admitted for treatment after a diagnosis of dependence on stimulants (namely mephedrone) with psychosis. The patient stated that he had used mephedrone recreationally (~4 - 5 grams) by insufflation or rectal administration for over one year.

After a few months, he suffered from difficulty sleeping, poor appetite, weight loss, and auditory and visual hallucinations. He reported that his tolerance to mephedrone increased and he needed more to achieve similar effects. He had tried to stop using mephedrone but could only manage abstinence for a few weeks. He was treated and discharged after four weeks.

Reports Documenting that Individuals are Using Synthetic Cathinones in Environments that Cause Harm to the User or Public

14. Kriikku et al. (2011) described cases involving individuals suspected of DUIDs in Finland. Blood samples from individuals suspected of DUIDs from August 2009 to August 2010 were screened for the presence of MDPV. Of 3000 samples tested, 259 were found to be positive for MDPV. The concentration of MDPV ranged from 0.020 – 8.4 mg/L (limit of detection is 0.003 mg/L). Although other drugs may have been detected, the authors concluded that MDPV is a significant problem in DUID cases in Finland.

Studies on the Use, Effect Profile or Abuse Liability Associated with the Use of Synthetic Cathinones

15. Carhart-Harris et al., 2011. Drug and Alcohol Dependence, doi:10.1016/j.drugalcdep.2011.02.011.
16. Dargan et al., 2010. QJM: An International Journal of Medicine, 103: 875-879.
17. EMCDDA, 2011. Luxembourg: Publications Office of the European Union, doi: 10.2810/40800.
18. James et al., 2010. Emerging Medicine Journal, 28: 686-689.
19. McNamara et al., 2010. Irish Medical Journal, 103: 134-137.
20. Measham et al., 2010. Drugs and Alcohol Today. 10:14-21.
21. Newcombe. 2009. Lifeline Publications and Research, Manchester.
22. Regan et al., 2010. Emerging Medicine Journal, 2010 Dec 23. doi: 10.1136/emj.2010.103093.
23. Vardakou et al., 2011. Toxicology Letters, 201: 191-195.
24. Winstock et al., 2010. Lancet, 376: 1537.
25. Winstock et al., 2011. Addiction, 106: 154-161.

Scientific Literature Detailing Synthetic Cathinone Analyses or Metabolism

26. Jankovics et al., 2011. Forensic Science International, doi: 10.1013/j.forsciint. 2011.03.019.
27. Maheux et al., 2010. Microgram Journal, 7: 42-49.
28. Camilleri et al., 2010. Forensic Science International, 1997: 59-66.
29. Meyer et al., 2010a. TIAFT Bulletin, 40: 36-37.
30. Meyer et al., 2010b. Analytical and Bioanalytical Chemistry, 397: 1225-1233.

31. Awad et al., 2006. Journal of Chromatographic Science, 44: 155-161.
32. Combs, 2010. Journal of the Clandestine Laboratory Investigating Chemists Association, 20: 2-4.
33. Gibbons and Zloh, 2010. Bioorganic & Medicinal Chemistry Letters, 20: 4135-4139.
34. Meyer and Maurer, 2010. Current Drug Metabolism, 11: 468-482.
35. Ojanpera et al., 2011. Therapeutic Drug Monitor, 33: 257-263.
36. Strano-Rossi et al., 2010. Rapid Communication in Mass Spectrometry, 24: 2706-2714.
37. Yohannan and Bozenko, 2010. Microgram Journal, 7: 12-15.
38. Westphal et al., 2009. Forensic Science International, 190: 1-8.
39. Uchiyama et al., 2008. Yakugaka Zasshi, 128: 1499-1505.
40. Brandt et al., 2010. Drug Testing Analysis, doi: 10.1002/dta.155.
41. Meyer et al, 2010c. TIAFT Bulletin, 40: 38-39.
42. Katagi et al., 2010. TIAFT Bulletin, 40: 30-35.
43. Dal Cason, 1997. Forensic Science International, 87: 9-53.
44. Kamata et al., 2006. Xenobiotica, 36: 709-723.
45. Santali et al., 2011. Journal of Pharmaceutical & Biomedical Analysis, 56: 246-255.
46. Maurer, 2010. Therapeutic Drug Monitoring, 32: 544-549.

Reports from Exposure Incidents

Law Enforcement Reports

1. A police report described the death of a 29-year-old female. Emergency personnel responded to a call from the decedent's mother that the subject was experiencing seizures after taking an unknown substance. The decedent complained to the mother of hearing things and was described by the mother as acting different. The decedent was transported to the hospital where she later died. MDPV and diphenhydramine were detected in blood samples taken from the decedent.
2. The U.S. Customs and Border Protection (CBP) encountered shipments of products containing mephedrone, methylone, MDPV, and other synthetic cathinones. Of 96 shipments encountered, 14 were mephedrone, 42 contained methylone, 17 contained MDPV, and 10 contained 4-MEC. Some of the other synthetic cathinones encountered by CBP were butylone, fluoromethcathinone, and dimethylcathinone. Most of these shipments originated in China or India and had destinations throughout the United States such as Arizona, Alaska, Hawaii, Kansas, Louisiana, Oklahoma, Oregon, Pennsylvania, Missouri, Virginia, Washington, and West Virginia. A few shipments were destined for Great Britain, The Netherlands, and Germany.
3. The DEA North Central Laboratory received submissions of tablets (66 blue tablets, 37 purple tablets, and 37 yellow tablets) that were confirmed to contain MDPV and caffeine.

(DEA, 2010, Ecstasy mimic tablets (actually containing 3,4-Methylenedioxypyrovalerone (MDPV) and caffeine). Microgram. 43:124)

4. An Ohio police office has submitted 13 cases since January 2011, some describing child endangerment, where the presence of MDPV was confirmed by laboratory analysis and 13 cases where "bath salts" were suspected.
5. The DEA New York Field Division arrested two individuals who sold 35 kilograms of MDPV to undercover agents.
6. The Harris County Institute of Forensic Sciences Drug Chemistry Section (Texas) received submissions of tablets confirmed to contain MDPV, TFMPP, and caffeine. A syringe containing MDPV, oxymorphone, methylone, and lidocaine was also seized. (DEA, 2011, 3,4-Methylenedioxypyrovalerone (MDPV) tablets seized in Houston, Texas. Microgram. 44:41)
7. A patrol officer from in Wisconsin described a case involving MDPV: a 22-year-old male was arrested for possession of drug paraphernalia and a white powder (suspected to be heroin by the arresting patrol officer) that was located in the suspect's car. The suspect stated that the powder was mephedrone and that he had been "shooting up" mephedrone like heroin. The suspect also stated that he paid $40 for one gram and that he purchased it from a distributer who bought the product online in large quantities from China. Laboratory analysis identified the powder as mephedrone.
8. The DEA South Central Laboratory received a submission of a black zip lock plastic bag containing a teal-colored clumpy powder. The substance was identified to be mephedrone. (DEA, 2011, 4-methylmethcathinone seized in Baton Rouge, Louisiana. Microgram. 44:43)
9. The Oregon State Police Bend Forensic Laboratory received submissions of white powder referred to as "sunshine" by users. The substance was identified to be mephedrone. (DEA, 2009, 4-methylmethcathinone in Oregon. Microgram. 42:62.)
10. The Northeastern Illinois Regional Crime Laboratory received several submissions of white powder. The powder in all the submissions was identified to be mephedrone. (DEA, 2010, 4-methylmethcathinone seized in Mundelein, Illinois. Microgram. 43:31.)
11. The Food and Drug Administration's Forensic Chemistry Center received several submissions of white powder. The powder in all the submissions was identified to be mephedrone. (DEA, 2010, 4-methylmethcathinone (mephedrone) seized in Northumberland County, Virginia. Microgram. 43:51.)
12. The State of Michigan Department of State Police submitted a case report of an individual arrested for possessing mephedrone as identified by laboratory analysis (originally suspected to be amphetamine or MDMA). The individual was arrested at his residence after a search warrant yielded a white powdery substance and drug related paraphernalia.
13. The Las Vegas Metropolitan Police Department received submissions of 44 illicitly manufactured tablets (10 peach and round and imprinted with a trefoil radiation symbol, 34 red and round and imprinted with the Motorola logo). Laboratory analysis of the 10 peach tablets identified methamphetamine, methylone, and caffeine. The red tablets were

identified to be methylone and caffeine. (DEA, 2011, Ecstasy mimic tablets (actually containing methamphetamine, 3,4-methylenedioxypyrovalerone (MDPV) and caffeine seized in Las Vegas, Nevada. Microgram. 44:21)

14. A police report from Minnesota reported two individuals who were arrested for the possession of mephedrone (powder and capsule) and a prescription drug. A complaint from a mother that her son was selling drugs in the garage was received, and upon arriving at the residence officers found two males parked in the driveway of the residence where the complaint had originated. When questioned, the two individuals were evasive in their answers and gave slightly different versions of their reason for their presence at the residence. The individuals were arrested when the officer noticed a small plastic bag with a white powdery substance with a sticker that read "White Gold Plant Food ½ gram" and 22 clear capsule pills. A field kit test of the powder inside the capsule tested positive for the presence of methamphetamine or MDMA. In the course of the arrest, the arresting officer noticed that one of the suspects was acting erratic and unable to sit still. The suspect also complained that his mouth was dry and asked for water. The officer noted that the suspect appeared to be under the influence of a controlled substance.

Product Identification Reports

15. A drug testing laboratory submitted laboratory analysis of the "bath salt" product called "Ivory Wave" that was purchased. The product was mixed with a pre-collected sample of urine to aid in the analysis of product. Laboratory results identified MDPV in the sample.

16. A manufacturing laboratory analyzed the "bath salt" product called "White Rush." Laboratory analysis by GC/MS detected MDPV and inositol in the product.

Poison Control Centers; Press Releases

17. The Texas Poison Center Network reported that no calls were received in January 2010. However, in August 2011, the Texas Poison Center Network received 53 calls. Overall, 257 calls were received from January 2010 to August 2, 2011 (Forrester, 2011).

18. The New Jersey Poison Information and Education System received no reports prior to January 2011. From January 2011 to April 2011, NJPIES received 23 cases of "bath salt" exposures (NJPIES, 2011).

19. The American Association of Poison Control Centers reported that in 2010, poison control centers took 303 calls about synthetic cathinones. As of July 31, 2011, poison control centers have received 4,137 calls relating to these products for this year. These calls were received in poison control centers representing at least 47 states and the District of Columbia (AAPCC, 2011).

Reports from Medical Examiners or Autopsy Reports

20. The death of a 19-year-old was ruled a result of complications of acute oxymorphone toxicity with alprazolam, ethanol, and mephedrone use as likely contributing factors. The decedent was found dead on the fire escape of an apartment building, partially leaning on/over a railing, along with another individual who was also deceased.

21. A death of a 39-year-old male was reported by Wyman et al. (2011). Family members indicated that the male, who had a history of schizophrenia, depression, and drug abuse,

had been snorting "bath salts." The subject was found dead in his bed. Empty jars of "bath salts" (TranQuility and Infinity) and synthetic cannabinoids (Demon and Flame) were found in the trash. A toxicological screen detected MDPV distributed among multiple tissues, urine and blood samples from the decedent. Other substances detected were nicotine, cotinine, pseudoephedrine, m-chlorophenylpiperazine and methylone. The cause of death was ruled acute MDPV intoxication.

22. A 21-year-old male committed suicide after snorting "Cloud 9" bath salts. Family members described the decedent as paranoid before he shot and killed himself. A toxicology laboratory report confirmed the presence of MDPV and citalopram in specimens from the decedent.

23. The Michigan Department of Community Health reported the death of an individual from MDPV. Marijuana and other prescriptions drugs (venlafaxine and desmethylvenlafaxine) were also detected. Autopsy results revealed MDPV toxicity to be the primary factor contributing to death (MMWR, 2011).

24. A police report described the death of a 23-year-old male suspected of using methylone. The decedent was walking in and out of traffic and acting belligerently. The decedent was detained by law enforcement and transported to the hospital. The decedent had a high temperature and subsequently went into respiratory failure. After several attempts by medical personnel to stabilize the decedent, he died. The medical examiner listed the cause of death as intoxication by methylone.

Drug Screens

25. Redwood Toxicology Laboratory screened over 2,000 urine samples for 14 designer stimulants: amphetamines (MDA, MDMA, MDEA, MBDB), cathinones (methylone, ethylone, butylone, cathinone, methcathinone, MDPV, mephedrone) and designer piperazines (BZP, TFMPP and mCPP). They detected 6 out of 14 designer stimulants in these samples. MDPV (88%) and methylone (21%) were the most common substances detected. The other substances detected were mephedrone, butylone, TFMPP, and BZP (Rana et al., 2011).

26. Drug courts analyze specimens from participants for new and existing drugs of abuse. Drug court reports have identified synthetic cathinones in specimens submitted for testing by drug court participants. Drug Court reports have identified mephedrone, methylone, MDPV and butylone in specimens submitted for testing by drug court participants. Of the 18 drug court reports received, mephedrone was the most common substance detected and MDPV was the second most common substance detected.

Driving while Under the Influence of Drugs (DUIDs)

27. Urine samples from drivers in Ohio suspected of DUIDs have tested positive for MDPV. In one DUID case, a 31-year-old female hit three parked cars in different locations and was unaware that she hit anything. MDPV was confirmed in blood specimen; benzoylecmethylecgonine (a metabolite of cocaine) and fluoxetine were also detected. In another case, a 37-year-old male died when he collided head on with a passenger van. Samples from the decedent tested positive for THC, MDPV, and methylone.

28. Urine samples from drivers in Maine suspected of DUIDs have tested positive for MDPV. MDPV was confirmed in the urine of five individuals suspected of DUIDs.

Other substances detected in some specimens were THC, buprenorphine, cocaine, tramadol, mirtazepine, gabapentine, and lorazepam.