SUMMARY

First International Multidisciplinary Forum on New Drugs

EMCDDA - Lisbon, Portugal

I. Summary

The new drugs phenomenon has gone through a period of dynamic change in recent years and new psychoactive substances are becoming widely available at an unprecedented pace. It is therefore particularly timely to be holding the First international multidisciplinary forum on new drugs.

The rate at which this area is developing is reflected, not only in the increased number of substances appearing on the market, but also in their diversity. Furthermore, it is evident in changes in the way that these substances — often referred to as ‘legal highs’ — are now being produced, distributed and marketed. These developments pose a serious challenge to current approaches to how we monitor, assess the risk of, respond to, and potentially control, new psychoactive substances.

The purpose of the forum was to take stock of the current state of the art in this area and identify common anchor points that can inform our future actions. In discussions, the delegates described how this phenomenon had developed over the last 10 years and explored, through case studies, differing national experiences.

The programme focused on early-warning systems as well as responses to new drugs, such as risk assessments, controls and options for prevention and treatment.

The forum proposed

• audit the state of play and provide a global overview on new drugs and ‘legal highs’;
• identify key issues, commonalities and differences in the experience of, and response to, this phenomenon;
• anticipate future challenges; and
• begin to chart a comprehensive vision for the future as to how these substances will impact on drug use, responses and policies.

The forum was organised in conjunction with the 11th Annual meeting of the Reitox early-warning system (EWS) network. The EWS provides EU Member States with an information exchange mechanism for reporting on the emergence of new psychoactive substances. It is a key element in the European fast-track system for assessing and responding to new drugs.
Participants

The forum was an expert meeting, by invitation only, with a target audience of around 100 invited participants. The event will brought together, for the first time, key European and international experts in the field of new psychoactive substances. In so doing, it was created a forum to discuss the latest developments regarding new drugs and to identify the challenges that need to be overcome.

Participants had included representatives of the Reitox national focal points from the 30 EMCDDA member countries — 27 EU Member States, Croatia, Turkey and Norway — as well as from the European Commission, Europol and the European Medicines Agency. Also invited are experts from: Australia, Belarus, Canada, Hong Kong SAR (Special Administrative Region), Israel, Japan, New Zealand, Russia, Switzerland, Ukraine and the United States.

The participants were selected for their technical expertise and research in the field of new psychoactive substances. They included: epidemiologists; forensic scientists; clinicians; law-enforcement experts concerned with new drugs; as well as technical staff from EU and international institutions.

Themes

The forum was organised around six thematic sessions:

- **Global review: perspectives on a dynamic phenomenon** — the appearance and use of new drugs and responses (e.g. risk assessment, control, prevention, treatment)
- **Understanding the evidence: forensic science, a key component** — forensic data as a foundation for identification and response
- **Epidemiology: auditing current capacity and identifying future priorities** — the epidemiological challenges of tracking a moving target
- **Making the most of the evidence: early warning** — multidisciplinary early-warning systems (models, rationale and function)
- **Defining a balanced response agenda** — risk assessment: final destination or point of departure?
- **A comprehensive vision for the future** — conclusions
### II. New drugs by country

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Vicodin
Opioid analgesics

"Spice"/K2
Synthetic Cannabinoids

"Bath Salts"
MDPV
4-Methyemietacine

III. Relevant comments of the experts

In Israel cathinone is the most popular synthetic drug, even more than amphetamines and methamphetamines. In order to avoid control systems, chemical products are usually altered from their original formula, when specific substances begin to being controlled. Those working in illegal trade of synthetic drugs have the capacity of alter a drug on the same week when it´s being under legal control.

In the Netherlands forensic laboratories, interviews with consumers and with groups of experts about new drugs are of high importance. Forensic analyses have reported that amphetamines pills present a high level of caffeine. In the same way, it has been reported that cocaine has a high level of levamisole, changes in new drugs trade are usually due to control enforced by law, and those changes use to have significant effects on people´s health. Because of this it is important a monitoring of new drugs in real time. Most of the European countries report this kind of information twice a year. Forensic laboratories are key to this work with information about new drugs appearing and chemical composition of substances in the market. With annual and biannual facts monitored and registered, trends on new drugs appearing or changes in chemical compositions of current drugs could be widespread known. The Netherlands have trends of the last 10 years of chemical composition of cocaine, ecstasy, amphetamines, among others. Those changes are important to users, since a different chemical composition could mean serious health problems for those using these drugs.

In Canada products containing Salvia are not allowed. Salvia is not a controlled product and is not included in United Nations list. In 2008-2009 school survey 4.9% of Canadian students reported having used salvia the last year.
From the United Kingdom it is emphasized the importance of surveys through the Internet in order to obtain information about new drugs. Mephedrone is one of the most consumed drugs in the United Kingdom.

Spain reports new drugs use from information of school surveys. The school survey has included a unit called “New drugs”. There is a list of substances in that unit that has been previously tested through other kind of survey. Among the most consumed new drugs in Spain Ketamine and Spice are mentioned, with prevalences of the last year close to 1%. Ketamine and hallucinogenic (“magic”) mushrooms are the most available drugs, according to students. Nexus is mentioned as the new drug of less availability.

Through a study among 18-24 years old youth in the framework of a prevention programme on new drugs in European countries, there were identified more than 450 new components and combinations of drugs. The presence of uncountable new drugs in the Web was identified as well. Results of such study are spread through social networks sites. Virtual seminars for professionals are realized and information is sent via smartphones. Interactive games are a useful way to hand out information. This programme teaches young people about the good use of creativity.

IV. Recommendations

It is necessary a development of early alert and monitoring systems efficient and comprehensive enough for new drugs detection. These should include periodical development of forensic and epidemiological studies as well as information spreading at least twice a year.

In the general epidemiological studies there is a need of an unit about new drugs, according to information from other sources of more specific information. New drugs lists should include individual names and not drugs groups.

Forensic studies should be realized annually, and new drugs trends as well as chemical composition of those widely known should be registered.

Among most mentioned drugs there are mephedrone, synthetic cannabinoids, salvia, ketamine, piperazine and BZP.
ANNEX

Specific information about new drugs

N-BENZYLPIPERAZINE
(Street Names: BZP, A2, Legal E or Legal X)

BZP is used as an intermediate in chemical synthesis. It has no known medical use. N-Benzylpiperazine (BZP) was first synthesized in 1944 as a potential antiparasitic agent. It was subsequently shown to possess antidepressant activity and amphetamine-like effects, but was not developed for marketing. The amphetamine-like effects of BZP attracted the attention of drug abusers. Since 1996, BZP has been abused by drug abusers; as evidenced by the encounters of this substance by law enforcement officials in various states and the District of Columbia. The Drug Enforcement Administration (DEA) placed BZP in schedule I of the Controlled Substances Act (CSA) because of its high abuse potential and lack of accepted medical use or safety.

Both animal studies and human clinical studies have demonstrated that the pharmacological effects of BZP are qualitatively similar to those of amphetamine. BZP has been reported to be similar to amphetamine in its effects on chemical transmission in brain. BZP fully mimics discriminative stimulus effects of amphetamine in animals. Subjective effects of BZP were amphetamine-like in drug-naive volunteers and in volunteers with a history of stimulant dependence. BZP acts as a stimulant in humans and produces euphoria and cardiovascular effects, namely increases in heart rate and systolic blood pressure. BZP is about 10 times less potent than amphetamine in producing these effects in subjects with histories of amphetamine dependence. Experimental studies demonstrate that the abuse, dependence potential, pharmacology and toxicology of BZP are similar to those of amphetamine. Public health risks of BZP are similar to those of amphetamine.

BZP is often abused in combination with 1-[3-(trifluoro-methyl)phenyl]piperazine (TFMPP), a noncontrolled substance. This combination has been promoted to the youth population as a substitute for MDMA at raves (all-night dance parties). However, there are no scientific studies indicating this combination produces MDMA-like behavioral effects. BZP may also be abused alone for its stimulant effects. BZP is generally administered orally as either powder or tablets and capsules. Other routes of administration included smoking and snorting. In 2001, a report from University in Zurich, Switzerland described the death of a young female which was attributed to the combined use of BZP and MDMA. Youth and young adults are the main abusers of BZP.

According to the System to Retrieve Information from Drug Evidence (STRIDE) and the National Forensic Laboratory Information System (NFLIS), BZP seizures increased substantially in the past six years. The largest increases occurred after 2006. In 2004, law enforcement officials submitted 48 drug items/exhibits to federal, state and local...
forensic laboratories identified as BZP. The number of BZP items/exhibits increased from 437 in 2007 to 6,088 in 2008. BZP items/exhibits submitted to forensic laboratories increased 127% from 6,088 in 2008 to 13,822 in 2009.

Illicit distributions occur through smuggling of bulk powder through drug trafficking organizations with connections to oversea sources of supply. The bulk powder is then processed into capsules and tablet. BZP is encountered as pink, white, off-white, purple, orange, tan, and mottle orange-brown tablets. These tablets bear imprints commonly seen on MDMA tablets such as housefly, crown, heart, butterfly, smiley face or bull's head logos and are often sold as “ecstasy.” BZP has been found in powder or liquid form which is packaged in small convenience sizes and sold on the Internet.

BZP was temporarily placed into schedule I of the CSA on September 20, 2002 (67 FR 59161). On March 18, 2004, the DEA published a Final Rule in the Federal Register permanently placing BZP in schedule I. Several states have placed BZP in schedule I: Iowa, Tennessee, Wyoming, Mississippi, Louisiana, Idaho, Colorado, Illinois, Indiana, Kansas, Missouri, Oklahoma and Nebraska.

Source: U.S. Department of Justice

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**Synthetic Cannabinoid**

The chemist who designed (and lent his initials to) JWH-18, John W Huffman, an organic chemist at Clemson University in South Carolina, told *Chemistry World* that his goal had been to make a simple compound to study structure-receptor relationships. The compound interacts with both cannabis receptors. The first batch was actually made by an undergraduate student working under a post-doc.

The synthetic substance, JWH-018, a cannabinoid receptor agonist from the aminoalkylindole family, has been found in herbal mixtures sold legally under various 'spice' names, such as Spice Gold and Spice Yucatan Fire. The mixture is sold as
incense, but is smoked to get high. JWH-018 is four to five times more potent than tetrahydrocannabinol, more commonly known as THC, which is the main psychoactive substance in cannabis.

JWH-018 has not been licensed anywhere in the world for medical applications and little is known about the effect on humans, as not even pre-clinical studies have been to determine potential toxicity.

Other synthetic cannabinoids found in herbal products are:

- CP-47,497 and Cannabicyclohexanol (CP-47,497 C8 homologue)
- HU-210\[(6aR,10aR)-9-(hydroxymethyl)-6,6-dimethyl-3-(2-methyl octan-2-yl)-6a,7,10,10a-tetrahydrobenzo[c]chromen-1-ol]\][Purported Ingredient of “Spice”]
- HU-211(dexanabinol,(6aS,10aS)-9-(hydroxymethyl)-6,6-dimethyl-3-(2-methyl octan-2-yl)-6a,7,10,10a-tetrahydrobenzo[c]chromen-1-ol][Purported Ingredient of “Spice”]

Sources:
- Royal Society of Chemistry (http://www.rsc.org/chemistryworld/News/2009/January/15010901.asp)
- U.S. Department of Justice (http://www.deadiversion.usdoj.gov/drugs_concern/spice/index.html)

Cathinone / Catinonas / KHAT
(Street Names: Khat, Qat, Kat, Chat, Miraa, Quaadka)

Khat, *Catha edulis*, is a flowering shrub native to East Africa and the Arabian-Peninsula. Khat refers to the leaves and young shoot of *Catha edulis*. It has been widely used since the thirteenth century as a recreational drug by the indigenous people of East Africa, the Arabian Peninsula and throughout the Middle East.

Khat contains two central nervous system (CNS) stimulants, namely cathinone and cathine. Cathinone (alpha-aminopriopiophenone), which is the principal active stimulant, is structurally similar to d-amphetamine and almost as potent as a CNS stimulant.
Cathine, also called d-norpseudoephedrine, is about 10 times less potent than cathinone as a CNS stimulant.

Cathinone levels are highest in the freshly cut khat plant. Once cut, levels of cathinone start declining. Cooling the plant material will reduce the rate of decline in cathinone levels such that detectable levels may be found at least out to 10 days post cutting. Over the last few years, exhibits of dried or dehydrated khat have been encountered. In these samples, cathinone may be detected for many months or even years. Cathine remains stable in khat after the plant has been cut.

Khat produces amphetamine-like effects. They include: euphoria, a feeling of increased alertness and energy, hyperactivity, anorexia, and lack of fatigue. The users also feel relaxed and talkative. Sympathomimetic effects may include elevated blood pressure, dilated pupils, hyperthermia, arrhythmias, and increased respiration. The effects of khat usually last between 90 minutes and 3 hours. After-effects of khat use have been reported as lack of concentration, numbness and insomnia.

Khat abuse leads to psychological dependence. Chronic abuse of khat can lead to behavioral changes and impairment of mental health. Clinical manifestations include manic behavior with grandiose delusions, violence, suicidal depression, or schizophreniform psychosis characterized by paranoid delusions. Chronic abuse can also produce physical exhaustion, anorexia, periodontal disease and disturbances of the gastrointestinal system.

Khat is abused for its stimulant and euphoric effects. Most often the fresh leaves and shoots of the khat shrub are chewed, and then retained in the cheek and chewed intermittently until all the juices are extracted. To counter the bitter taste of the plant, copious amounts of water or sweet soda are drank. Dried khat can be made into tea or a chewable paste. Rarely other modes of self-administration include smoking or sprinkling on food.

Cathinone and cathine are in Schedules I and IV, respectively, of the Controlled Substances Act. Missouri placed khat in schedule I of state law. California placed khat in schedule II of state law.

Source: U.S. Department of Justice (http://www.deadiversion.usdoj.gov/drugs_concern/khat.htm)

**Levamisole**

The Substance Abuse and Mental Health Services Administration (SAMHSA) is alerting medical professionals, substance abuse treatment centers and other public health authorities about the risk that substantial levels of cocaine may be adulterated with levamisole – a veterinary anti-parasitic drug. There have been approximately 20 confirmed or probable cases of agranulocytosis (a serious, sometimes fatal blood disorder), including
two deaths, associated with cocaine adulterated with levamisole. The number of reported cases is expected to increase as information about cocaine adulterated with levamisole is disseminated.

Levamisole is used in veterinary medicine and is currently approved for use in cattle, sheep and swine as an anti-parasitic agent. Although it was once used in human medicine in the past for treating autoimmune diseases and cancer, it is no longer an approved drug for human use.

Ingesting cocaine mixed with levamisole can seriously reduce a person's white blood cells, suppressing immune function and the body's ability to fight off even minor infections. People who snort, smoke, or inject crack or powder cocaine contaminated by levamisole can experience overwhelming, rapidly-developing, life threatening infections.

According to the Drug Enforcement Administration and State testing laboratories, the percentage of cocaine specimens containing levamisole has increased steadily since 2002, with levamisole now found in over 70 percent of the illicit cocaine analyzed in July. In addition, a recent analysis in Seattle, Washington found that almost 80 percent of the individuals who test positive for cocaine also test positive for levamisole.

Source: SAMHSA (http://www.samhsa.gov/newsroom/advisories/090921vet5101.aspx)

Ketamine
(Street Names: Special K, "K", Kit Kat, Cat Valium)

Ketamine is a dissociative anesthetic that has gained popularity as a drug of abuse. On the street, it is commonly known as "K" or "Special K." Other street names include Cat Valium, Super Acid, Special La Coke, Purple, Jet (Texas), and Vitamin K. Slang for experiences related to ketamine or effects of ketamine include: "k-land" (refers to a mellow & colorful experience), "K-hole" (refers to the out-of-body, near death experience), "baby food" (users sink in to blissful, infantile inertia), and "God" (users are convinced that they have met their maker).

Since the 1970s, ketamine has been marketed in the United States as an injectable short-acting anesthetic for use in humans and animals. It is imported into the United States and formulated into dosage forms for distribution under the trade names Ketalar, Ketaset, Ketajet, Ketavet, Vetamine, Vetaket, and Ketamine Hydrochloride Injection.

Ketamine distorts perceptions of sight and sound and makes the user feel disconnected and not in control. A "Special K" trip is touted as better than that of LSD or PCP because its hallucinatory effects are relatively short in duration, lasting approximately 30 to 60 minutes as opposed to several hours.
Ketamine powder is usually snorted, mixed in drinks or smoked. Liquid ketamine is injected, applied on a smokeable material or consumed in drinks. Most abusers of ketamine take small lines or "bumps" for a mild, dreamy effect. A dose of 100 mg is usually enough to enter a "k-hole" experience. A dose is referred to as a "bump."

On August 12, 1999, ketamine became a schedule III non-narcotic substance under the Controlled Substances Act.

Source: U.S. Department of Justice
(http://www.deadiversion.usdoj.gov/drugs_concern/ketamine/ketamine.htm)

4-methylmethcathinone / 4-MMC / Mefedrona
(Street Names: Mephedrone, 4-MMC, meow meow, m-CAT, bounce, bubbles, mad cow)

4-Methylmethcathinone (mephedrone) is a designer drug of the phenethylamine class and shares substantial structural similarities with methcathinone (Schedule I). Evidence of mephedrone use and associated toxicity has been increasing, in 2009 and 2010, particularly in the United Kingdom and other European countries. To date, one confirmed and several suspected deaths related to mephedrone have been reported by Europol-EMCDDA Joint report on mephedrone 2010. In recent years, law enforcement agencies have documented seizures (Oregon, Illinois and Alabama) associated with mephedrone in the United States.

Structure-activity relationship studies allow to predict that the pharmacology of mephedrone is similar to methcathinone as well as other substances of phenethylamine chemical class. The compounds having similar structure (e.g., methamphetamine, methylone, 3,4-methylenedioxymethamphetamine, cathinone and methcathinone) have been used to assess the pharmacological profile of mephedrone. This class of compounds is known to produce central nervous system stimulation, psychoactivity and hallucinations.

The adverse health effects caused by mephedrone are broadly similar to those seen with other stimulant drugs. Adverse effects produced by phenethylamines are increased heart rate, chest pain, agitation, irritability, dizziness, delusions, nose bleeding, nausea and vomiting. Consistent with the above discussion, mephedrone was reported to produce agitation, dilated pupils, increased heart rate and blood pressure in a 22-year-old man who used it for recreational purpose.
It is predominantly used by youth population (15-24 years), higher in males than females, from urban areas, who frequent clubs, discos and dance events. Mephedrone is sold over the internet and is promoted as a “research chemical”, “bath salts” or “plant food.”

Mephedrone is not scheduled under Controlled Substance Act (CSA). However, it can be considered an analogue of methcathinone (schedule I substance) under the analogue provision of the CSA (Title 21 United States Code 813). Therefore, law enforcement cases involving mephedrone can be prosecuted under the Federal Analog Act of the CSA.


**Bath Salts**

There’s a new designer drug that’s raising alarm with authorities around the country. It's referred to as "bath salts," but it's really a dangerous stimulant with effects akin to cocaine or meth. "Bath Salts", the newest fad to hit the shelves (virtual and real), is the latest addition to a growing list of items that young people can obtain to get high. The synthetic powder is sold legally online and in drug paraphernalia stores under a variety of names, such as "Ivory Wave," "Purple Wave," "Red Dove," "Blue Silk," "Zoom," "Bloom," "Cloud Nine," "Ocean Snow," "Lunar Wave," "Vanilla Sky," "White Lightning," "Scarface," and "Hurricane Charlie." Because these products are relatively new to the drug abuse scene, our knowledge about their precise chemical composition and short- and long-term effects is limited, yet the information we do have is worrisome and warrants a proactive stance to understand and minimize any potential dangers to the health of the public.

These products often contain various amphetamine-like chemicals, such as methylenedioxypyrovalerone (MPDV), mephedrone and pyrovalerone. These drugs are typically administered orally, by inhalation, or by injection, with the worst outcomes apparently associated with snorting or intravenous administration.

Methylenedioxypyrovalerone (MDPV) is a designer drug of the phenethylamine class. MDPV is structurally related to cathinone, an active alkaloid found in the khat plant, methamphetamine, and methylenedioxymethamphetamine (MDMA). MDPV is a central nervous system (CNS) stimulant and it was first seized in Germany in 2007. The abuse of MDPV is increasing, particularly in Europe and Australia. MDPV has been identified in products called “bath salts” which are sold on websites based in Europe. MDPV is not approved for medical use in the United States.

Mephedrone is of particular concern because, according to the United Kingdom experience, it presents a high risk for overdose. These chemicals act in the brain like stimulant drugs (indeed they are sometimes touted as cocaine substitutes); thus they present a high abuse and addiction liability. Consistent with this notion, these products have been reported to trigger intense cravings not unlike those experienced by
methamphetamine users, and clinical reports from other countries appear to corroborate their addictiveness. They can also confer a high risk for other medical adverse effects. Some of these may be linked to the fact that, beyond their known psychoactive ingredients, the contents of "bath salts" are largely unknown, which makes the practice of abusing them, by any route, that much more dangerous.

Unfortunately, "bath salts" have already been linked to an alarming number of ER visits across the country. Doctors and clinicians at U.S. poison centers have indicated that ingesting or snorting "bath salts" containing synthetic stimulants can cause chest pains, increased blood pressure, increased heart rate, agitation, hallucinations, extreme paranoia, and delusions. It is noteworthy that, even though we are barely two months into 2011, there have been 251 calls related to "bath salts" to poison control centers so far this year. This number already exceeds the 236 calls received by poison control centers for all of 2010. In response to this emerging threat, several states, including Hawaii, Michigan, Louisiana, Kentucky, and North Dakota, have introduced legislation to ban these products, which are incidentally labeled as "not fit for human consumption." In addition, several counties, cities, and local municipalities have also taken action to ban these products.

Source: NIDA and U.S. Department of Justice.  
(http://www.nida.nih.gov/about/welcome/MessageBathSalts211.html)  
(http://www.deadiversion.usdoj.gov/drugs_concern/mdpv.pdf)

Salvia Divinorum and Salvinorin A  
(Street Names: Maria Pastora, Sage of the Seers, Diviner’s Sage, Salvia, Sally-D, Magic Mint)

Salvia divinorum is a perennial herb in the mint family native to certain areas of the Sierra Mazateca region of Oaxaca, Mexico. The plant, which can grow to over three feet in height, has large green leaves, hollow square stems and white flowers with purple calyces, can also be grown successfully outside of this region. Salvia divinorum has been used by the Mazatec Indians for its ritual divination and healing. The active constituent of Salvia divinorum has been identified as salvinorin A. Currently, neither Salvia divinorum nor any of its constituents, including salvinorin A, are controlled under the federal Controlled Substances Act (CSA).

Several studies have reported the effects of using either plant material or salvinorin A. Psychic effects include perceptions of bright lights, vivid colors and shapes, as well as body movements and body or object distortions. Other effects include dysphoria, uncontrolled laughter, a sense of loss of body, overlapping realities, and hallucinations (seeing objects that are not present). Adverse physical effects may include incoordination, dizziness, and slurred speech.

Scientific studies show that salvinorin A is a potent and selective kappa opioid receptor agonist. Other drugs that act at the kappa opioid receptor also produce hallucinogenic
effects and dysphoria similar to that produced by salvinorin A. Salvinorin A does not activate the serotonin 2A receptor, which mediates the effects of other schedule I hallucinogens. Salvinorin A and *Salvia divinorum* products are abused for their ability to evoke hallucinogenic effects, which, in general, are similar to those of other scheduled hallucinogenic substances.

*Salvia divinorum* is grown domestically and imported from Mexico and Central and South America. The Internet is used for the promotion and distribution of *Salvia divinorum*. It is sold as seeds, plant cuttings, whole plants, fresh and dried leaves, extract-enhanced leaves of various strengths (e.g., 5x, 10x, 20x, 30x), and liquid extracts purported to contain salvinorin A. These products are also sold at local shops (e.g., head shops and tobacco shops).

Salvinorin A and/or *Salvia divinorum* have been placed under regulatory controls in Australia, Belgium, Denmark, Estonia, Finland, Italy, Japan, Spain, and Sweden. As of September 2010, 24 states in the United States have enacted legislation placing regulatory controls on *Salvia divinorum* and/or salvinorin A.

Source: U.S. Department of Justice.  
([http://www.deadiversion.usdoj.gov/drugs_concern/salvia_d.pdf](http://www.deadiversion.usdoj.gov/drugs_concern/salvia_d.pdf))
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