European Monitoring Centre
for Drugs and Drug Addiction

RISK ASSESSMENTS 14

ISSN 1725-4493

MDPV

Report on the risk assessment of 1-(1,3-benzodioxol-5-yl)-2-(pyrrolidin-1-yl) pentan-1-one (3,4-methylenedioxypyrovalerone, MDPV) in the framework of the Council Decision on new psychoactive substances

About this series

EMCDDA Risk Assessments are publications examining the health and social risks of individual new psychoactive substances.

The Risk Assessment Report consists of an analysis of the scientific and law enforcement information available on the new psychoactive substance under scrutiny and the implications of placing it under control. It is the outcome of a meeting convened under the auspices of the EMCDDA Scientific Committee.

This process is part of a three-step procedure involving information exchange/early warning, risk assessment and decision-making in the framework of Council Decision 2005/387/JHA.

Contents

Acknowledgements

The EMCDDA would like to thank the following for their contribution in producing this publication:

- the members of the extended Scientific Committee of the EMCDDA; the advisers to the Scientific Committee and the invited external experts who took part in the risk assessment meeting;
- the Early Warning System (EWS) correspondents of the Reitox national focal points (NFPs) and experts from their national EWS networks;
- the services within each Member State that collected the raw data for the risk assessment;
- Europol, the European Medicines Agency (EMA) and the European Commission;
- Dr Paul Dargan, Dr David Wood and Ms Alison Dines for preparing the technical review on the pharmacotoxicological, sociological and criminological evidence and public health risks of MDPV;
- Dr Simon Brandt for contributing to specific sections of the technical review on MDPV;
- EMCDDA colleagues: Paul Griffiths, Anabela Almeida, Isabelle Giraudon and Katarzyna Natoniewska, who managed the production of the publication.

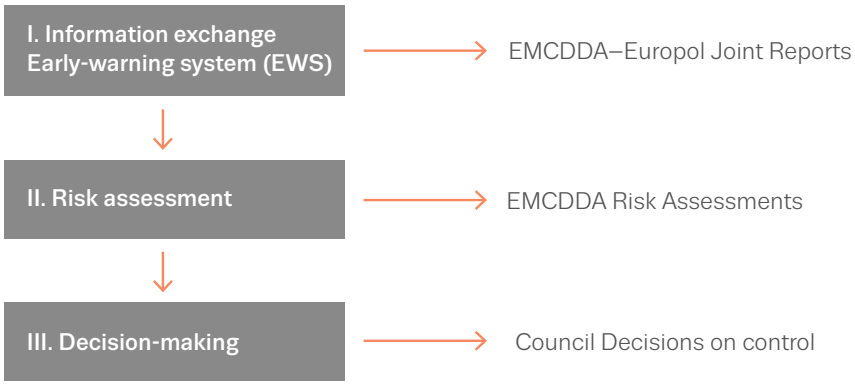
EMCDDA project leaders: Andrew Cunningham, Michael Evans-Brown, Ana Gallegos and Roumen Sedefov

EMCDDA actions on monitoring and responding to new drugs

The EMCDDA has been assigned a key role in the detection and assessment of new drugs in the European Union under the terms of a Council Decision 2005/387/JHA on the information exchange, risk-assessment and control of new psychoactive substances. It establishes a mechanism for the rapid exchange of information on new psychoactive substances and provides for an assessment of the risks associated with them in order to permit the measures applicable in the Member States for the control of narcotic and psychotropic substances to be applied also to new psychoactive substances.

The three-step process involves information exchange/early warning, risk assessment and decision-making (see below). More detailed information can be found in the section 'Action on new drugs' of the EMCDDA's website: www.emcdda.europa.eu/activities/action-on-new-drugs

Council Decision 2005/387/JHA of 10 May 2005 on the information exchange, risk-assessment and control of new psychoactive substances



EMCDDA–Europol Joint Report on MDPV (3,4-methylenedioxypyrovalerone) — a summary

EMCDDA–Europol Joint Report on a new psychoactive substance: 3,4-methylenedioxypyrovalerone — in accordance with Article 5 of Council Decision 2005/387/JHA on the information exchange, risk assessment and control of new psychoactive substances

At the end of September 2013, the EMCDDA and Europol examined the available information on a new psychoactive substance 3,4-methylenedioxypyrovalerone, commonly known by the abbreviation 'MDPV', through a joint assessment based upon the following criteria: (1) the amount of the material seized; (2) evidence of organised crime involvement; (3) evidence of international trafficking; (4) analogy with better-studied compounds; (5) evidence of the potential for further (rapid) spread; and (6) evidence of cases of serious intoxication or fatalities.

The EMCDDA and Europol agreed that the information available on MDPV satisfied criteria 1, 2, 3, 4 and 6. The two organisations therefore concluded that sufficient information has been accumulated to merit the production of a Joint Report on MDPV as stipulated by Article 5.1 of the Decision. Accordingly, the NFPs, the Europol national units (ENUs), the EMA and the World Health Organization (WHO) were formally asked to provide the relevant information within six weeks from the date of the request, i.e. by 18 November 2013.

The resulting Joint Report on MDPV was submitted to the Council, the Commission and the EMA on 16 December 2013. The report concluded that the health and social risks, caused by the use of, the manufacture of, and traffic in MDPV, as well as the involvement of organised crime and possible consequences of control measures, could be thoroughly assessed through a risk assessment procedure as foreseen by Article 6 of Council Decision 2005/387/JHA.

The full text of the Joint Report can be found at:

www.emcdda.europa.eu/publications/joint-report/MDPV

Risk Assessment Report of a new psychoactive substance: 1-(1,3-benzodioxol-5-yl)-2-(pyrrolidin-1-yl)pentan-1-one (3,4-methylenedioxy-pyrovalerone, MDPV)

Introduction

This Risk Assessment Report presents the summary findings and conclusions of the risk assessment carried out by the extended Scientific Committee of the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) on the new psychoactive substance 1-(1,3-benzodioxol-5-yl)-2-(pyrrolidin-1-yl)pentan-1-one, commonly called 3,4-methylenedioxy-pyrovalerone (MDPV). The report has been prepared and drafted in accordance with the conceptual framework and the procedure set out in the *Risk assessment of new psychoactive substances: operating guidelines* ([1]). It is written as a stand-alone document that presents a summary of the information considered during the detailed analysis of the scientific and law enforcement data available at this time. The conclusion of the report summarises the main issues addressed and reflects the opinions held by the members of the Scientific Committee. A list of the information resources considered by the Scientific Committee, including a detailed Technical report on MDPV, is provided below.

The risk assessment has been undertaken in compliance with Article 6 of Council Decision 2005/387/JHA of 10 May 2005 on the information exchange, risk assessment and control of new psychoactive substances ([2]) (hereafter the 'Council Decision'). The Council Decision established a mechanism for the rapid exchange of information on new psychoactive substances (hereafter 'Early Warning System' ([3])) that may pose a threat to public health and create social problems, including the involvement of organised crime. The Council Decision therefore allows the institutions of the European Union and the Member States to act on all new narcotic and psychotropic substances ([4]) that appear on the European Union drug market. The Council Decision also provides for an assessment of the risks associated with these new psychoactive substances so that, if necessary, control measures can be applied in the Member States ([5]).

MDPV was first identified in a seizure made by Finnish customs authorities in November 2008, and Finland formally notified the Early Warning System in December 2008. Following an assessment of the available information on MDPV, and in accordance with Article 5 of the Council Decision, on 16 December 2013 the EMCDDA and Europol submitted a Joint Report on MDPV to the Council of the European Union, the European Commission and the European Medicines Agency (EMA) ([6]).Taking into account the conclusion of the Joint Report, and in accordance with Article 6 of the Council Decision, on 29 January 2014 the Council formally requested that 'the risk assessment should be carried out by the extended Scientific Committee of the EMCDDA and be submitted to the Commission and the Council within 12 weeks from the date of this notification'.

In accordance with Article 6.2, the meeting to assess the risks of MDPV was convened under the auspices of the Scientific Committee of the EMCDDA with the participation of five additional experts designated by the Director of the EMCDDA,

([1]) EMCDDA (2010), *Risk assessment of new psychoactive substances: operating guidelines*, Publications Office of the European Union, Luxembourg.
([2]) OJ L 127, 20.5.2005, p. 32.
([3]) The information exchange mechanism laid down by the Council Decision is operationalised as the European Union Early Warning System on New Psychoactive Substances ('Early Warning System'). It is operated by the EMCDDA and Europol in partnership with the Reitox national focal points in the Member States, the European Commission and the European Medicines Agency.
([4]) According to the definition provided by the Council Decision, 'new psychoactive substance' means a new narcotic drug or a new psychotropic drug in pure form or in a preparation; 'new narcotic drug' means a substance in pure form or in a preparation that has not been scheduled under the 1961 United Nations Single Convention on Narcotic Drugs, and that may pose a threat to public health comparable to the substances listed in Schedules I, II or IV; 'new psychotropic drug' means a substance in pure form or in a preparation that has not been scheduled under the 1971 United Nations Convention on Psychotropic Substances, and that may pose a threat to public health comparable to the substances listed in Schedules I, II, III or IV.
([5]) In compliance with the provisions of the 1961 United Nations Single Convention on Narcotic Drugs and the 1971 United Nations Convention on Psychotropic Substances.
([6]) EMCDDA and Europol (2014), *EMCDDA–Europol Joint Report on a new psychoactive substance: MDPV (3,4-methylenedioxypyrovalerone)*, Lisbon.

acting on the advice of the Chairperson of the Scientific Committee, chosen from a panel proposed by Member States and approved by the Management Board of the EMCDDA. The additional experts were from scientific fields that were either not represented, or not sufficiently represented, on the Scientific Committee, and whose contribution was necessary for a balanced and adequate assessment of the possible risks of MDPV, including health and social risks. Furthermore, two experts from the Commission, one expert from Europol and one expert from the EMA participated in the risk assessment. The meeting took place on 1 and 2 April 2014 at the EMCDDA in Lisbon. The risk assessment was carried out on the basis of information provided to the Scientific Committee by the Member States, the EMCDDA, Europol and the EMA. A list of the extended Scientific Committee and the other participants attending the risk assessment meeting is included at the end of this publication.

The extended Scientific Committee considered the following information resources during the risk assessment:

(i) Technical report on 1-(1,3-benzodioxol-5-yl)-2-(pyrrolidin-1-yl)pentan-1-one (MDPV) (Annex 1);
(ii) *EMCDDA–Europol Joint Report on a new psychoactive substance: MDPV (3,4-methylenedioxypyrovalerone)*;
(iii) scientific articles, official reports and grey literature, and Internet drug discussion forums and related websites (hereafter, 'user websites');
(iv) data from EMCDDA monitoring of Internet suppliers (which typically appear to be manufacturers and/or wholesalers) and retailers selling MDPV;
(v) *Risk assessment of new psychoactive substances: operating guidelines*; and,
(vi) Council Decision 2005/387/JHA of 10 May 2005 on the information exchange, risk assessment and control of new psychoactive substances.

Finally, it is important to note that this Risk Assessment Report contains a discussion of the available information on non-fatal intoxications and deaths associated with MDPV. Such information is critical to the identification of emerging toxicological problems associated with new psychoactive substances within the European Union. In this context, it is important to recognise that the capacity to detect, identify and report these events differs both within and between the Member States. Some Member States have introduced programmes in the past few years to strengthen these capacities. As a result, more information is available; however, it is likely that serious adverse events remain under-detected.

Physical, chemical and pharmacological description of MDPV and its mechanism of action, including its medical value

MDPV is a ring-substituted methylenedioxy analogue of the synthetic stimulant pyrovalerone, which is in turn an analogue of the naturally occurring chemical cathinone ([7]). The systematic (International Union of Pure and Applied Chemistry, IUPAC) name for MDPV is *(RS)*-1-(1,3-benzodioxol-5-yl)-2-(pyrrolidin-1-yl)pentan-1-one. Both pyrovalerone and cathinone are controlled under the 1971 United Nations Convention on Psychotropic Substances. MDPV contains one asymmetric carbon atom and is thus a chiral molecule (Figure 1). So far, only the racemic mixture of the 1:1 ratio of the two possible enantiomers has been characterised.

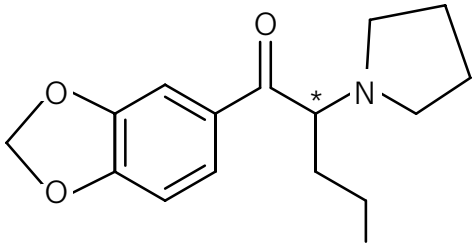
MDPV is one of over fifty synthetic cathinones that have been reported to the Early Warning System by the Member States; other examples include mephedrone (4-MMC) ([8]) and methylone (bk-MDMA).

The Chemical Abstract Service (CAS) Registry Number for MDPV (base) is 687603-66-3 and the molecular formula is $C_{16}H_{21}NO_3$, equating to a molecular weight of 275.343 g/mol.

The free base form of MDPV has been described as being a brown or yellow-green amorphous powder, whilst the hydrochloride salt form is white but has also been described as white-tan coloured powder.

MDPV is typically supplied as a powder; there are also reports of its supply in tablet, capsule and liquid form. MDPV is

FIGURE 1
The molecular structure, formula, weight and monoisotopic mass of MDPV



Molecular formula: $C_{16}H_{21}NO_3$
Molecular weight: 275.3429
Monoisotopic mass: 275.152

([7]) Cathinone is the principal active stimulant found in the khat plant (*Catha edulis*).
([8]) Mephedrone was subject to risk assessment at the European Union level in 2010 and subsequently subject to control measures within the Member States.

soluble in water and the powder can be dissolved for oral use or intravenous and subcutaneous injection.

The detection of MDPV is straightforward, using a range of analytical techniques. Methods have been developed for MDPV and some of its metabolites using gas chromatography coupled with ion trap mass spectrometry (GC-IT-MS), ultra high-pressure liquid chromatography-tandem mass spectrometry (LC-MS/MS), ultra performance liquid-chromatography coupled with quadrupole time-of-flight mass spectrometry (UPLC-QTOF-MS) and Raman spectroscopy coupled with high-performance liquid chromatography (HPLC). MDPV has been reported to cause false-positive phencyclidine immunoassay results in urine samples.

The tentative 'common doses' of MDPV reported by users by route of administration are: 5–11 mg (insufflation); 8–15 mg (oral); and 6–12 mg (rectal). The onset of desired effects is typically seen within 5–30 minutes, with desired effects lasting 2–7 hours for the common routes of administration (oral and nasal). In addition, there is evidence from non-fatal intoxications and deaths reported to the Early Warning System by the Member States, studies published in the literature, and self-reported experiences on user websites and needle exchange programmes that MDPV is injected by some users, including problem drug users.

MDPV selectively inhibits catecholamine uptake (dopamine transporter (DAT) and norepinephrine transporter (NET)), while serotonin uptake is significantly less affected. The effects of MDPV appear to be longer lasting than cocaine in animal models; information provided in clinical case reports ([9]) appear to be consistent with these findings. The subcutaneous LD_{50} value for MDPV in the mouse is 175 mg/kg.

The main phase I metabolic steps identified in both the rat *in vivo* and human *in vitro* studies included demethylation followed by methylation, aromatic and side chain hydroxylation and oxidation of the pyrrolidine ring to the corresponding lactam and ring opening to the corresponding carboxylic acid. No data are available on the biological activity of these metabolites.

MDPV was patented as a central nervous system stimulant in the mid-1960s. Currently, MDPV is available as an analytical reference material and is used in scientific research investigating its chemistry, pharmacology and toxicology as a result of its emergence on the drug market. There are currently no known uses of MDPV as an industrial, agricultural or cosmetic compound. According to information provided by the EMA, there is no known human or veterinary medical use of MDPV in the European Union. There is no marketing authorisation (existing, on-going or suspended) for MDPV at the European Union level or in the Member States that responded to the information request by the EMA that was launched under Article 5 of the Council Decision. There is no information to suggest that MDPV is used in the manufacture of a medicinal product in the European Union. However, it should be noted that there is no European Union database on the synthetic routes of all registered medicinal products.

([9]) The term 'clinical case reports' is used to denote both clinical case reports and case series published in the scientific literature.

Chemical precursors that are used for the manufacture of MDPV

The synthesis of MDPV is described in (now expired) patents from the 1960s that were granted in France, Germany, the United Kingdom and the United States. They describe the precursor 1-(1,3-benzodioxol-5-yl)pentan-1-one being α-brominated to form a 2-bromopentan-1-one intermediate. Reaction of the intermediate with pyrrolidine yields MDPV, which is then converted into the hydrochloride salt. The ketone precursor may be obtained from a number of starting materials, including 1,3-benzodioxole, although several alternative routes can be used.

Currently no information regarding manufacturing sites, the chemical precursors or the synthetic routes used for MDPV has been detected on the drug market.

Analysis of seized products has found MDPV on its own, and also in combination with active pharmaceutical ingredients (e.g. lidocaine, procaine, piracetam, trimethoprim and diltiazem) and/or other psychoactive substances (e.g. cocaine, ketamine, methamphetamine, TFMPP, BZP, mephedrone, methylone, 4-MEC, MDPBP, alpha-PVP and synthetic cannabinoid receptor agonists).

Health risks associated with MDPV

Individual health risks

The assessment of individual health risks includes a consideration of the acute and chronic toxicity of MDPV, its dependence potential and its similarities to and differences from other chemically related substances.

As noted, information on the acute toxicity associated with MDPV is not collected uniformly across the European Union. It is important to note, when interpreting the information from non-fatal intoxications and deaths reported by the Member States and from clinical case reports and user websites, that individuals may have used other pharmacologically active substances in addition to MDPV. The presence of other substances may account for some of the reported effects.

Information obtained from a series of studies carried out *in vitro* and *in vivo* in animal models suggests that the psychopharmacological (behavioural) profile observed for MDPV is similar to cocaine and methamphetamine. However, it appears that MDPV is more potent and longer lasting. Clinical case reports appear to be consistent with these findings. A key pharmacological mechanism of MDPV includes catecholamine-selective transporter blockage. Compared to cocaine, MDPV was shown to be 50-fold more potent at DAT, 10-fold more potent at NET, and 10-fold less potent at SERT (serotonin transporter). In addition, it is clear that MDPV does not act as a substrate. Consistent with the *in vitro* data, *in vivo* microdialysis studies in rats found that MDPV increased extracellular concentrations of dopamine in the nucleus accumbens and that it was 10-fold more potent than cocaine. Furthermore, MDPV was also found to be 10 time more potent in its ability to induce locomotor activation, tachycardia and hypertension. The observation of hyperpyrexia in animals varies with ambient temperature, which warrants further study.

There are no data on the interactions between MDPV and other drugs and medicinal products (including oral contraceptives). Investigations with recombinant human cytochrome P450 isoenzymes (CYPs) revealed that CYP 2C19, CYP 2D6 and CYP 1A2 were important isoforms involved in metabolism, which may be relevant when considering polymorphisms and the potential for drug–drug interactions that involve the same subtypes (e.g. CYP 2C19/10/9: fluoxetine, carbamazepine, moclobemide; CYP 2D6: tramadol, fluoxetine, haloperidol, diltiazem, citalopram; CYP1A2: caffeine, diazepam, cannabis, olanzapine).

A total of 525 non-fatal intoxications associated with MDPV have been reported to the Early Warning System by eight Member States: Belgium (two cases), France (19), Germany (six), Greece (two), Ireland (one), Italy (three), Slovakia (five) and Sweden (487). Of these cases, 110 have been analytically confirmed, with MDPV being confirmed in biological samples in all but one case. These cases are from: Belgium (two cases), France (four), Greece (one), Ireland (one involving analysis of the substance taken), Italy (three) and Sweden (99). In 13 of the cases, no other substances were reported. In addition, there are 77 European ([10]) and 89 non-European clinical case reports associated with MDPV use that include analytical confirmation of the substance in biological samples.

Data from these reports and information from self-reported experiences on user websites suggest that individuals typically present with features similar to those seen with other stimulant drugs such as cocaine, amphetamines and mephedrone. These features include tachycardia, hypertension, convulsions, insomnia, nausea, stomach cramps, sweating, headache, reduced appetite, dilated pupils, dizziness, breathing problems, depression, confusion, agitation, aggression, severe and prolonged anxiety attacks, auditory and visual hallucinations, violent outbursts and paranoid psychosis. In addition, there are reports of more severe toxicity including hyperpyrexia, rhabdomyolysis, acute kidney injury and stroke.

Since experience on the toxicological profile of MDPV is limited, it is difficult to be sure that rare, but clinically significant, severe effects are not associated with its use.

A total of 108 deaths in which MDPV has been detected in post-mortem biological samples and/or implicated in the cause of death were reported to the Early Warning System by eight Member States and Norway between September 2009 and August 2013: Austria (one death), Finland (40), France (one), Hungary (one), Ireland (eight), Poland (three), Sweden (21), United Kingdom (32) and Norway (one). In addition, deaths have been reported in the scientific literature that occurred within the European Union (17 deaths) ([11]) and elsewhere, including the United States (33) and Japan (one). It should be noted that in some of these deaths it is likely that other drugs and/or other medical conditions or trauma may have contributed to and/or been responsible for death.

No published animal or human studies have investigated the potential for neurotoxicity, reproductive toxicity, genotoxicity and carcinogenic potential of MDPV use. There are three clinical case reports of individuals who developed medium-term to long-term consequences (renal failure requiring haemodialysis (two cases) and stroke (one)), secondary to complications of the acute adverse health effects of MDPV.

([10]) There is a possibility that some of the non-fatal intoxications published in the scientific literature that have occurred within the European Union might be the same as some of the non-fatal intoxications reported to the Early Warning System by the Member States.

([11]) There is a possibility that some of the deaths published in the scientific literature that have occurred within the European Union might be the same as some of the deaths reported to the Early Warning System by the Member States.

A number of animal studies have investigated the abuse potential of MDPV using models involving self-administration, intracranial self-stimulation, discrimination, substitution and conditioned taste-aversion. These studies suggest that MDPV has rewarding and hedonic properties similar to methamphetamine; it is also self-administered, including dose escalation. There have been no studies investigating the abuse liability and dependence potential of MDPV in humans. There are published reports in the scientific literature of individuals with suspected dependency on MDPV.

There is no information on the psychosocial consequences of chronic MDPV use, such as the effects on psychological development and the interaction with the social environment.

Public health risks

The public health risks associated with MDPV may be categorised in terms of: patterns of use (extent, frequency, route of administration, etc.); availability and quality of the drug; information, availability and levels of knowledge amongst users; and negative health consequences.

Reports have been received by the Early Warning System of detections of MDPV in 27 Member states, Norway and Turkey since 2008. There is limited information available on the quality and purity of MDPV available to users.

In some cases MDPV is being sold and used as a substance in its own right, and has also been detected in combination with other psychoactive substances. Similar to other drugs, users may combine MDPV with other substances (stimulants, hallucinogens and/or depressants including alcohol). However, some users have taken MDPV unknowingly along with or instead of other substances, particularly when they may have intended to use other stimulant drugs. Therefore it is likely that information related to the use of MDPV is under-reported.

There appear to be no co-ordinated national or European population surveys examining MDPV use. The only European data is available from non-representative studies. One non-representative Internet survey in 2010/11 of clubbers in the United Kingdom reported lifetime and last year use of 4.4 % and 3.0 % respectively. The total number of respondents was not reported.

MDPV is available to users from Internet suppliers and retailers, bricks and mortar head shops and street-level drug dealers. EMCDDA monitoring of Internet suppliers and retailers selling MDPV (conducted in the month prior to the risk assessment) identified more than twenty companies, which may be based within the European Union and China, offering up to multi-kilogram quantities of the substance.

There are limited data available on the characteristics and behaviour of users; however, it is likely that they will be similar to those using other stimulant drugs. There is no data available on context-related risks for MDPV users.

The injection of MDPV by problem drug users has been reported in a number of countries, including Hungary, Finland and Romania. In a study from Hungary, 183 clients of a needle exchange programme agreed to report their drug using habits. The study found that during 2011 changes occurred in the nature of primary injected substances: amphetamine was cited as the primary injected substance by 45.9 % of the respondents and MDPV by 48.1 %. Almost half of the former amphetamine injectors had switched to MDPV (64 people, 45.1 %) as had 10 (41.7 %) of the former heroin injectors and 11 (78.6 %) of those using other substances (cocaine and mephedrone). Injecting MDPV carries public health risks of bacterial infections and transmission of blood-borne viruses such as human immunodeficiency virus, hepatitis C virus and hepatitis B virus.

Social risks associated with MDPV

There is limited information on the social risks associated with MDPV. There is no information on whether the use of MDPV affects education or career, family or other personal or social relationships, including marginalisation. However, in some countries, marginalised problem drug users have used MDPV.

Although there are no relevant studies, it may be assumed that the acute behavioural effects of MDPV on operating machinery and driving are similar to those caused by other stimulant substances.

The detection of MDPV has been reported in biological samples other than non-fatal intoxications and deaths from 2009 onwards. These cases relate to fatal and non-fatal road traffic accidents, driving under the influence of drugs (DUID) and/or other petty crimes in Finland (519 cases), Germany (two), Sweden (fourteen) and the United Kingdom (one). In addition, studies have demonstrated that MDPV was detected in 0.2 % and approximately 5 % of DUID samples analysed in Denmark and Finland, respectively. In the majority of these cases other substances, such as amphetamines or benzodiazepines, were also detected. The available information does not permit comment on the extent of driving impairment.

There are healthcare costs associated with the treatment of acute MDPV toxicity presenting to hospitals. Most of these cases involve short assessments within the emergency department; however, a minority have had more prolonged clinical features over a few days and/or have required admission to critical care. In addition, some individuals have also required admission to psychiatric facilities due to on-going symptoms.

Severe agitation, aggression and violence are not uncommon in MDPV users, which appears to be a more pronounced feature than is normally observed with other classical stimulant drugs.

Information on the level of involvement of organised crime, seizures and/or detections by the authorities, and the manufacture of MDPV

There is no evidence available regarding the involvement of organised crime in the production and wholesale trafficking of MDPV. Bulk quantities of MDPV are being offered for sale from companies trading on the Internet. However, in the context of its widespread control, MDPV continues to be sold on the illicit market and multi-kilogram seizures continue to be reported. There have been reports of tablets with markings that would normally be associated with other recreational drugs (e.g. 'ecstasy'). There are some indications that suggest a degree of organisation in the tableting and distribution of this substance in the European Union.

MDPV has been found in combination with a range of new psychoactive substances and/or classical recreational drugs. It is not possible to determine whether this adulteration was intentional or not.

Information on any assessment of MDPV in the United Nations system

The World Health Organization is the specialised agency of the United Nations designated for the evaluation of the medical, scientific and public health aspects of psychoactive substances under the 1961 United Nations Single Convention on Narcotic Drugs, and the 1971 United Nations Convention on Psychotropic Substances.

The World Health Organization informed the EMCDDA that MDPV would be subject to evaluation at the 36th meeting of the Expert Committee on Drug Dependence, held in June 2014.

Article 7.1 of Council Decision states:

'*No risk assessment shall be carried out in the absence of a Europol/EMCDDA Joint Report. Nor shall a risk assessment be carried out where the new psychoactive substance concerned is at an advanced stage of assessment within the United Nations system, namely once the WHO Expert Committee on Drug Dependence has published its critical review together with a written recommendation, except where there is significant new information that is relevant in the framework of this Decision.*'

The risk assessment has been carried out on the understanding that MDPV is not at an advanced stage of assessment within the United Nations system.

Description of the control measures that are applicable to MDPV in the Member States

MDPV is not listed for control in the 1961 United Nations Single Convention on Narcotic Drugs or in the 1971 United Nations Convention on Psychotropic Substances (together 'UN drug conventions').

Twenty-one Member States (Belgium, Bulgaria, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, France, Germany, Hungary, Ireland, Finland, Italy, Latvia, Lithuania, Luxembourg, Poland, Slovakia, Slovenia, Sweden and the United Kingdom), Turkey and Norway control MDPV under legislation by virtue of their obligations under the UN drug conventions.

Seven Member States (Austria, Greece, Malta, the Netherlands, Portugal, Romania and Spain) do not control MDPV by virtue of their obligations under the UN drug conventions.

Of these seven Member States, four of them (Austria, the Netherlands, Portugal and Romania) use other legislative measures to control MDPV. In Austria it is controlled under the generic definition within the New Psychoactive Substances Act. The Netherlands uses its medicines legislation to control MDPV. In Portugal it is listed as controlled under Decree-Law 54/2013. In Romania the Law 194/2011 subjects to control

any psychoactive substance that qualifies by conforming to certain criteria (all substances with psychoactive potential are subject to control until proven harmless by a special designated commission).

Options for control and the possible consequences of the control measures

Under Article 9.1 of the Council Decision, the option for control that is available is for the Member States to submit the new psychoactive substance MDPV to control measures and criminal penalties, as provided for under their legislation, by virtue of their obligations under the UN drug conventions. There are no studies on the possible consequences of such control measures on MDPV. If this option of control is pursued, the Committee considers that the following consequences are possible. Some of these may apply to any new psychoactive substance.

- MDPV is controlled in 21 Member States under legislation by virtue of their obligations under the UN drug conventions. Should a decision be made to submit MDPV to control measures it would be expected to further facilitate the detection, seizure and monitoring of MDPV related to its unlawful manufacture, distribution and use by facilitating cooperation between the judicial authorities and law enforcement agencies across the European Union. However, this may have little impact on the manufacturers and suppliers based outside the European Union.
- A positive health consequence that may result from this control is the benefit brought about by the presumed reduction of availability and use.
- This control option would imply additional costs to some countries. Such costs may include the criminal justice system, encompassing forensic services, law enforcement and the courts.
- In some countries this control option could lead to replacement with other (established or new) psychoactive substances, which may in themselves have public health consequences.
- It is not possible to gauge to what extent this control is likely to impact on current and future research by research/academic institutes, pharmaceutical or chemical industries.
- In some countries this control option could create an illicit drug market in MDPV with increased risk of associated criminal activity, including organised crime.

In order to examine the consequences of control, the Committee wishes to note that should this option be pursued it will be important to monitor for the presence of MDPV on the market post-control.

Aside from the option for control under those stipulated in Article 9.1 of the Council Decision, other options for control may be available to Member States. These may include medicines legislation or restricting the importation and supply of the substance using other legislative options.

Conclusion

MDPV is a ring-substituted synthetic derivative of cathinone chemically related to pyrovalerone, both of which are subject to control under the 1971 United Nations Convention on Psychotropic Substances. MDPV has potent cocaine-like stimulant properties. It was first identified in a seizure made by Finnish customs authorities in November 2008, and Finland formally notified the Early Warning System in December 2008. MDPV is found mostly as a powder, but tablets and liquid forms have also been encountered. MDPV has been sold by Internet suppliers and retailers, in bricks and mortar head shops and by street-level drug dealers. Analysis of seized products has found MDPV on its own and in combination with other pharmacologically active substances, including psychoactive drugs.

MDPV has been reported in seizures in 27 Member states, Norway and Turkey. EMCDDA monitoring of Internet suppliers and retailers selling MDPV has identified more than twenty companies that may be based within the European Union and China, offering up to multi-kilogram quantities of the substance.

There are no systematic data at national level in Europe on the prevalence of use of MDPV. The only European data are available from non-representative studies. There are limited data available on the characteristics and behaviour of users; however, it is likely that these will be similar to those using other stimulant drugs. Routes of administration include nasal insufflation, inhalation, oral and rectal administration and injection.

MDPV selectively inhibits the uptake of dopamine and norepinephrine, while it does not act as a substrate. In addition, serotonin uptake is significantly less affected. The effects of MDPV appear to be more potent and longer lasting than cocaine in animal models, in addition clinical case reports appear to be consistent with laboratory findings.

A total of 525 non-fatal intoxications associated with MDPV have been reported by eight Member States. Key adverse

effects associated with MDPV intoxication frequently reported in clinical case reports include: paranoid psychosis, hypertension, tachycardia, diaphoresis, severe agitation, auditory and visual hallucinations, profound anxiety, hyperthermia, violent outbursts and multiple organ dysfunction.

Data from animal studies and clinical case reports indicate that MDPV shows reinforcing effects with high abuse liability.

There have been a total of 108 deaths associated with MDPV reported by eight Member states and Norway in which MDPV has been detected in biological samples and/or implicated in the cause of death. In many of these cases it is not possible to determine the role of MDPV in the death. There are no data on the potential for reproductive toxicity, genotoxicity and carcinogenic potential associated with the use of MDPV.

There is very limited information available on the social consequences of MDPV use. However, some countries have reported the use of MDPV by marginalised groups, such as injecting drug users.

Although MDPV has been seized on a multi-kilogram scale in Member States, detailed information on the involvement of organised crime with MDPV is not available. There are indications that suggest some degree of organisation in the tableting and distribution of MDPV within the European Union. There is no information to suggest that MDPV is currently manufactured in any of the Member States. The chemical precursors and the synthetic routes used to manufacture the MDPV detected in the Member States are unknown.

MDPV has no established or acknowledged medical value or use (human or veterinary) in the European Union. There are no indications that MDPV may be used for any legitimate purpose other than in analytical reference materials and in scientific research.

MDPV is not listed for control in the 1961 United Nations Single Convention on Narcotic Drugs or in the 1971 United Nations Convention on Psychotropic Substances. MDPV is currently undergoing assessment by the United Nations system. Twenty-one Member States, Turkey and Norway control MDPV under legislation by virtue of their obligations under the UN drug conventions; four Member States use other legislative measures to control MDPV.

Many of the questions posed by the lack of evidence on the health and social risks of MDPV, as for any new psychoactive substance, could be answered through further research. Areas where additional information is important include: receptor binding and functional activity studies; metabolic pathway studies; behavioural studies; clinical patterns of acute and chronic toxicity in humans; the potential interaction between MDPV and other substances (in particular those that affect the monoaminergic system); prevalence and patterns of use (including targeted studies that examine user groups and risk behaviours); market studies; chemical profiling studies; studies on the abuse liability and dependence potential; and, studies on the social risks associated with its use.

The Committee notes that many Member States have measures in place to control MDPV. Should a decision be made to submit MDPV to control measures this would be expected to further facilitate the detection, seizure and monitoring of MDPV related to its unlawful manufacture, distribution and use by facilitating cooperation between the judicial authorities and law enforcement agencies within the European Union. This has a potential positive consequence in terms of reducing availability and therefore the adverse health and social consequences arising from the use of MDPV. It is important, however, to anticipate and minimise where possible any potential negative consequences of control. Control measures could extend an illegal market in MDPV, with the associated risk of criminal activity. The implementation of control measures may also lead to the criminalisation of those who continue to use this substance, with the possible attendant risks of socio-economic stigmatisation and marginalisation. Finally, control should not inhibit the gathering and dissemination of accurate information on MDPV to users and to relevant professionals.

ANNEX 1
Technical report on 1-(1,3-benzodioxol-5-yl)-2-(pyrrolidin-1-yl)pentan-1-one (3,4-methylenedioxypyrovalerone, MDPV)

This Technical report was prepared under EMCDDA contract and, while the scientific data presented has been verified to the extent possible, it has not been formally edited by the EMCDDA. The Risk Assessment Report of 1-(1,3-benzodioxol-5-yl)-2-(pyrrolidin-1-yl)pentan-1-one (3,4-methylenedioxy-pyrovalerone, MDPV), to which this report is annexed was produced by the Scientific Committee of the EMCDDA and shall be regarded as the authoritative document.

Suggested citation: *Technical report on 1-(1,3-benzodioxol-5-yl)-2-(pyrrolidin-1-yl)pentan-1-one (3,4-methylenedioxy-pyrovalerone, MDPV))*, EMCDDA, Lisbon, April 2014.

The full text of the Technical report on 1-(1,3-benzodioxol-5-yl)-2-(pyrrolidin-1-yl)pentan-1-one (3,4-methylenedioxypyro-valerone, MDPV) can be accessed under the following link: www.emcdda.europa.eu/publications/risk-assessment/MDPV/annex1

Tables on non-fatal intoxications and deaths, in which MDPV was analytically confirmed, have been extracted from the Technical report and are presented in the following pages.

TABLE 6 FROM THE TECHNICAL REPORT

Non-fatal intoxications in which MDPV has been detected in biological samples and that were reported to the EU Early Warning System by the Member States

Country	Date	Sample type	MDPV result	Results for other substances	Notes
Belgium	Aug 2011 (F, 31)	Urine	+	cocaine (+) amphetamines (+)	First time MDPV use. Drug taken orally. Clinical features included hallucinations and severe psychosis, paranoia, visual and auditory hallucinations, aggressiveness, hypertension and tachycardia. Treated with antipsychotics and admitted to a psychiatric ward. Status normal after 3-4 days.
Belgium	Aug 2011 (M, 34)	Urine	+	cocaine (+) amphetamines (+)	First time MDPV use. Drug taken orally. Clinical features included hallucinations and severe psychosis, paranoia, visual and auditory hallucinations, aggressiveness, hypertension and tachycardia. Treated with antipsychotics and admitted to a psychiatric ward. Status normal after 3-4 days. This case is related to the case described above.
France	Date not specified (M, 27)	Not specified	+	pyrovalerone (+) cannabis (+)	Brought to the Emergency Department by the police. Clinical features included delirium, hallucinations, rhabdomyolysis, tachycardia, hypotension, agitation, acute renal failure. Man brought in to the emergency by the police.
France	Date not specified (M, 25)	Blood	366 ng/mL	methylone (4400 ng/mL)	Clinical features included tachycardia, mydriasis, hypertension, agitation, profuse sweating, trembling, scarification, rhabdomyolysis, paranoid psychosis, aggression. Route of administration: inhaled and oral, dose 10g. Bought on the internet. In combination with methylone. Forced hospitalization.
France	Date not specified (M, 22)	Hair	+	alcohol (+) cannabis (+)	Nasal insufflation. Clinical features: mydriasis, paranoid psychosis. Duration of effects: 2 days.
France	Date not specified	Not specified	+	4-MEC	MDPV injected. Patient had abnormal movements, trismus, profuse sweating, visual disorders, insomnia, anorexia and vertigo. He also reported dysuria which lasted 24 hours; no further details were specified.
Greece	2013 (M, 47)	Urine	+	+ ATS immunoassay - other immunoassays (MDPV only confirmed by GC-MS)	Sudden loss of consciousness after ingestion of MDPV bought from the Internet. Patient required urgent intubation and was admitted to the Intensive Care Unit due to multi-organ failure (hepatic impairment, rhabdomyolysis and renal insufficiency). The patient was in ICU for one week and required kidney dialysis for two weeks after discharge.
Italy	Aug 2011 (M, 20)	Urine	4 mg/L	butylone (+)	On admission, the patient was very agitated with tachycardia (Fc 115 bpm). He reported having consumed cannabis, alcohol and 3 white capsules. He was treated with benzodiazepine and discharged two days later.
Italy	Oct 2012 (M, 38)	Blood Urine	12 mg/L (blood) 17 mg/L (urine)	Urine: ketamine (-) atropine (-) scopolamine (-) levamisole (-) mephedrone (-) butylone (-) 4-methylethcathinone (-) methoxetamine (-) APB (1) isomers (-) 4-fluoroamphetamine (-) MDAI (2) (-)	The patient was admitted to the emergency department and reported nasal insufflation of ecstasy and synthetic drugs generally named as "mefre, crystal and energy". Clinical features included agitation, tachycardia (105 bpm), distress, psychosis, visual and auditory hallucinations. During the first 24 hours, the patient was treated with fluids, benzodiazepines and haloperidol and transferred to a psychiatric ward.

(1) (Aminopropyl)benzofuran.
(2) 3,4-Methylenedioxyaminoindane.

Country	Date	Sample type	MDPV result	Results for other substances	Notes
Italy	Oct 2012 (M, 27)	Urine	On admission: 55 µg/L Three days after admission: 35 µg/L	On admission: alprazolam (113.79 µg/L) hydroxyalprazolam (103.59 µg/L) 3 days after admission: chlordiazepoxide (13.03 µg/L) nordiazepam (61.55 µg/L) oxazepam (114.99 µg/L) diazepam (1.26 µg/L) temazepam (169.90 µg/L) alprazolam (10.43 µg/L) alpha-hydroxyalprazolam (13.45 µg/L)	On arrival in the emergency department the patient reported having using MDPV intravenously, for the last 3-4 days together with benzodiazepines to counteract the excitatory effect of MDPV. Clinical features included psychomotor agitation, confusion and anxiety. Anamnestic information from the patient revealed previous use of pentedrone and 3-methylmethcathinone, the patient had abandoned these for decreased interest in these substances. Three days after admission, the patient had a second urine analysis, and reported having continued his use of MDPV. The MDPV was purchased via Internet and marketed as "bath salts".
Sweden	Jan–Sep 2012	Blood Urine	+	Result for other substances was positive for 15/17 cases with severe symptoms. Benzodiazepines (7) were the most frequently identified substances. Medicines included buprenorphine, tramadol and fentanyl.	From a total of 86 cases, in 17 cases the clinical features were severe (Poisoning Severity Score - PSS 3) and consisted of extreme agitation, psychosis, hyperthermia, tachycardia, hypertension, myocardial infarction, rhabdomyolysis and renal failure. "A few" patients needed therapy with sedatives for several days due to prolonged symptoms. [Bäckberg et al., 2013]
Sweden	Apr–May 2012	Not specified	+	None reported	Twelve of the 13 cases described were classified as chronic drug users with >60% noted to be HCV-positive. [Lindeman et al., 2013]

TABLE 7 FROM THE TECHNICAL REPORT

Deaths reported to the EU Early Warning System and included in the Annex to the EMCDDA Joint Report on MDPV

Case number	Country	Date	Biological sample	MDPV result	Results of toxicological analysis for other substances	Notes
1	**Austria**	Jan 2012 (M)	Not specified	+	butylone (+) methylone (+) 4-methylethcathinone (+) cocaine (+)	Butylone (bk-MBDB) overdose in combination with methylone, 4-methylethcathinone and cocaine.
2	**Finland***	Sep 2009	Urine Blood	+ (urine)	Blood: olanzapine (0.7 mg/L) methadone (0.4 mg/L) chlorprothixen (0.1 mg/L) diazepam (0.03 mg/L) amphetamine (8.4 mg/L)	Accidental death, poisoning by narcotics.
3	**Finland**	Sep 2009	Blood	40 mg/mL	ethanol (1.5 g/kg) buprenorphine (0.001 mg/L)	Accidental death, poisoning by narcotics.
4	**Finland**	Oct 2009	Blood	+	diazepam (0.1 mg/L) temazepam (0.3 mg/L) morphine (0.6 mg/L) amphetamine (0.88 mg/L) THC ([1]) (<LOQ)	Accidental death, poisoning by drugs or medicaments.
5	**Finland**	Oct 2009	Urine Blood	+ (urine)	Blood: alprazolam (0.1 mg/L) tramadol (1.4 mg/L) methadone (0.2 mg/L) diazepam (0.02 mg/L)	Accidental death, poisoning by drugs or medicaments.
6	**Finland**	Oct 2009	Blood	840 mg/mL (estimated value)	levomepromazine (2.4 mg/L) trimipramine (0.3 mg/L) oxycodone (2.2 mg/L)	Suicide, poisoning by drugs or medicaments.
7	**Finland**	Oct 2009	Urine Blood	+ (urine)	Blood: zolpidem (0.4 mg/L) citalopram (0.9 mg/L) oxazepam (1.7 mg/L) olanzapine (0.2 mg/L) propranolol (2.1 mg/L)	Suicide, propranolol poisoning.
8	**Finland**	Feb 2010	Blood	4800 mg/mL	Blood: morphine (0.08 mg/L) amphetamine (1.6 mg/L)	Homicide, multiple injuries of neck.
9	**Finland**	Feb 2010	Urine	+	temazepam (0.9 mg/L) diazepam (0.4 mg/L) amphetamine (7.3 mg/L)	Suicide, hanging.
10	**Finland**	Feb 2010	Blood	1800 mg/mL	methadone (1.3 mg/L) temazepam (0.3 mg/L) diazepam (0.1 mg/L) amphetamine (0.06 mg/L) buprenorphine (0.0044 mg/L)	Accidental death, poisoning by drugs or medicaments.
11	**Finland**	Feb 2010	Urine Blood	+ (urine)	Blood: tramadol (5.3 mg/L) valproate (19 mg/L) THC ([1]) (0.0061 mg/L)	Accidental death, poisoning by drugs or medicaments.
12	**Finland**	Feb 2010	Blood	70 mg/mL	ethanol (0.22 g/kg) amphetamine (0.16 mg/L)	Accidental death, Injury of thoracic aorta.
13	**Finland**	Feb 2010	Blood	+	metoclopramide (0.3 mg/L) diazepam (0.1 mg/L) oxycodone (0.13 mg/L)	Accidental death, poisoning by drugs or medicaments.
14	**Finland**	Feb 2010	Blood	+	None reported	Disease, infective myocarditis.

([1]) Δ9-tetrahydrocannabinol, the main psychoactive substance in cannabis.

Case number	Country	Date	Biological sample	MDPV result	Results of toxicological analysis for other substances	Notes
15	**Finland**	Mar 2010	Blood	1200 mg/mL	ethanol (1.3 g/kg) venlafaxine (8.7 mg/L) levomepromazine (0.4 mg/L) mirtazapine (0.3 mg/L) nordiazepam (0.05 mg/L) codeine (0.53 mg/L) buprenorphine)0.0032 mg/L)	Accidental death, poisoning by drugs or medicaments.
16	**Finland**	Mar 2010	Blood	+	ethanol (0.36 g/kg) venlafaxine (0.9 mg/L) alprazolam (0.05 mg/L) diazepam (0.34 mg/L) buprenorphine (0.0076 mg/L)	Accidental death, poisoning by drugs or medicaments.
17	**Finland**	Apr 2010	Blood	60 mg/mL	oxazepam (0.46 mg/L) temazepam (0.096 mg/L) nordiazepam (0.024 mg/L) amphetamine (0.11 mg/L) buprenorphine (0.70 mg/L)	Accidental death, poisoning by drugs or medicaments.
18	**Finland**	Jun 2010	Liver Muscle	+ (liver)	Muscle: ethanol (0.51 g/kg)	Suicide, hanging.
19	**Finland**	Jun 2010	Blood	40 mg/mL	nordiazapam (0.12 mg/L) morphine (0.15 mg/L) codeine (0.02 mg/L) amphetamine (0.20 mg/L) oxycodone (<LOQ) THC (1) (+)	Accidental death, poisoning by narcotics.
20	**Finland**	Sep 2010	Blood	20 mg/mL	methadone (0.3 mg/L) temazepam (0.13 mg/L) oxazepam (0.15 mg/L) nordiazepam (0.026 mg/L) amphetamine (+)	Accidental death, poisoning by narcotics.
21	**Finland**	Oct 2010	Blood	530 mg/mL	diazepam (0.033 mg/L) DPMP (2) (+) methylone (+)	Accidental death, poisoning by narcotics.
22	**Finland**	Feb 2011	Hair Blood	+ (hair)	Blood: amitriptyline (4.3 mg/L) hydroxyzine (1.1 mg/L) citalopram (0.7 mg/L) perfenazine (0.21 mg/L)	Suicide, poisoning by drugs or medicaments.
23	**Finland**	Feb 2011	Urine Blood	+ (urine)	Blood: alprazolam (0.018 mg/L) methadone (0.4 mg/L) diazepam (0.13 mg/L)	Disease, other and unspecified cirrhosis of liver.
24	**Finland**	Apr 2011	Blood	+	alprazolam (0.44 mg/L) clonaxepam (0.12 mg/L) amphetamine (0.42 mg/L) buprenorphine (0.00042 mg/L)	Suicide, crushing injury of skull.
25	**Finland**	May 2011	Hair Blood	+ (hair)	Coronary blood: temazepam (1.1 mg/L) quetiapine (0.3 mg/L) methadone (0.2 mg/L) diazepam (0.029 mg/L)	Accidental death, poisoning by drugs.
26	**Finland**	May 2011	Hair Liver	+ (hair)	Liver: temazepam (+) methadone (+) quetiapine (+)	Accidental death, poisoning by drugs. This case has a connection to case 25. The two deceased were found together.
27	**Finland**	May 2011	Blood	110 mg/mL	nordiazepam (0.20 mg/L)	Suicide, toxic effect of carbon monoxide (COHb (3) 71 %).

(2) (Diphenylmethyl)piperidine.
(3) Carboxyhaemoglobin.

Case number	Country	Date	Biological sample	MDPV result	Results of toxicological analysis for other substances	Notes
28	**Finland**	Jun 2011	Urine	+	diazepam (0.30 mg/L) buprenorphine (0.0037 mg/L) alprazolam (+) clonazepam (+)	Suicide, crushing injuries involving other combinations of body regions.
29	**Finland**	Jul 2011	Blood	30 mg/mL	methadone (0.6 mg/L) temazepam 0.22 mg/L) diazepam (0.15 mg/L) buprenorphine (0.0017 mg/L)	Accidental death, poisoning by drugs or medicaments.
30	**Finland**	Oct 2011	Blood	170 mg/mL	2,3-DMMC ([4]) (0.01 mg/L) amphetamine (1.8 mg/L)	Accidental death, poisoning by narcotics.
31	**Finland**	Oct 2011	Blood	190 mg/mL	methadone (1.1 mg/L) mirtazapine (0.07 mg/L) oxazepam (0.077 mg/L) amphetamine (0.24 mg/L) pregabalin (3.7 mg/L)	Accidental death, poisoning by drugs or medicaments.
32	**Finland**	Jan 2012	Hair	+	buprenorphine (+) verapamil (+) propofol (+) diazepam (+)	Accidental death, poisoning by narcotics.
33	**Finland**	Apr 2012	Blood	130 mg/mL	fentanyl (0.0097 mg/L) clonazepam (0.005 mg/L)	Accidental death, poisoning by narcotics.
34	**Finland**	Jul 2012	Blood	1700 mg/mL	olanzapine (0.3 mg/L) alprazolam (0.005 mg/L) GHB ([5]) (1500 mg/L)	Accidental death, poisoning by narcotics.
35	**Finland**	Jul 2012	Blood	80 mg/mL	ethanol (0.23 g/kg) isopropylalcohol (0.1 g/kg) diazepam (0.048 mg/L) buprenorphine (0.0079 mg/L)	Accidental death, poisoning by narcotics.
36	**Finland**	Jul 2012	Blood Vitreous humor	590 mg/mL (blood)	Blood: α-PVP ([6]) (0.60 mg/L) amphetamine (1.6 mg/L) Vitreous humor: ketamine (+)	Accidental death, multiple fractures of ribs.
37	**Finland**	Nov 2012	Urine Blood	+ (urine)	Blood: diazepam (0.064 mg/L) buprenorphine (0.00066 mg/L) pregabalin (4.4 mg/L) amphetamine (< LOQ)	Disease, intoxication -psychoactive substances.
38	**Finland**	Dec 2012	Blood	30 mg/mL	doxepine (1.5 mg/L) citalopram (1.9 mg/L) quetiapine (1.3 mg/L) α-PVP (0.070 mg/L) buprenorphine (0.029 mg/L) temazepam (<LOQ)	Suicide, doxepin poisoning.
39	**Finland**	Jan 2013	Urine	+	ethanol (1.6 g/kg) alprazolam (0.005 g/L) diazepam (0.45 g/L) codeine (0.15 g/L) buprenorphine)0.0006 g/L)	Cause of death not yet registered.
40	**Finland**	Apr 2013	Blood	30 mg/mL	trimethoprim (1.6 mg/L)	Cause of death not yet registered.
41	**Finland**	Aug 2013	Urine	+	alprazolam (0.044 mg/L) diazepam (0.092 mg/L) THC ([7]) (0.0051 mg/L) buprenorphine (0.0012 mg/L) fentanyl (0.0082 mg/L) pregabalin (4.0 mg/L)	Cause of death not yet registered.

([4]) 2,3-dimethylmethcathinone.
([5]) Gammahydroxybutyrate.
([6]) α-Pyrrolidinovalerophenone.
([7]) Δ9-tetrahydrocannabinol, the main psychoactive substance in cannabis.

Case number	Country	Date	Biological sample	MDPV result	Results of toxicological analysis for other substances	Notes
42	**France**	Oct 2012	Blood Urine	106 µg/L (blood) 760 µg/L (urine)	PVP (40 µg/L in blood) (295 µg/L in urine) pentedrone (33 µg/L in blood) (110 µg/L in urine) hydroxyzine (194 µg/L in blood) nordazepam (47 µg/L in blood) oxazepam (8 µg/L in blood) cannabinoic acid (15.7 µg/L in blood) ethanol (0.3 g/L in blood)	Cause of death was drowning.
43	**Hungary**	Nov 2011	Not specified	+	Not reported	Noted to be in 'Indirect death' (f. e. fatal traffic accidents).
44-47	**Ireland**	Jan 2010 – Dec 2011	Not specified	+	Not reported	'Drug implicated in the cause of death by coroner'.
48-51	**Ireland**	Jan 2012 – Dec 2012	Not specified	+	Not reported	MDPV 'Not necessarily implicated in the cause of death' (by coroner).
52	**Norway**	2012	Blood	+	None reported	Cause of death not reported.
53	**Poland**	Sep 2010	Blood	430 ng/mL	ephedrine (324 ng/mL)	Cause of death: 'metabolic dysfunction' caused by MDPV.
54	**Poland**	2011	Blood	38 ng/mL	buphedrone (127 ng/mL)	Indirect death: car accident. During inspection of the deceased driver, the police revealed packages of white powders, with the names Ivory Speed and Exclusive Dust and a note 'collector's product for field stone rinsing' [Adamowicz et al., 2013].
55	**Poland**	2011	Blood	17 ng/mL	clonazepam (1.2 ng/mL) 7-aminoclonazepam (96 ng/mL)	Death after a night of partying, a witness testified that the man had taken a product called Speedway. The autopsy showed emaciation, external hydrocephalus and atherosclerosis. Deceased with a history of drug addiction, HIV+ [Adamowicz et. all 2013].
56-58	**Sweden**	2010	Not specified	+	None reported	3 cases The deaths were intoxications involving several substances (not further described).
59-61	**Sweden**	2011	Not specified	+	None reported	3 cases None of the 3 deaths related only to MDPV.
62-70	**Sweden**	2012	Not specified	+	None reported	9 cases There were several accidents, death by hanging and intoxications with several drugs (not further described).
71-76	**Sweden**	2013	Not specified	+	None reported	6 cases There was one car accident and intoxications with several drugs (not further described).

Case number	Country	Date	Biological sample	MDPV result	Results of toxicological analysis for other substances	Notes
77-78	**United Kingdom**	Jan–Dec 2010	Blood Urine	+	Case 1 fluoromethcathinone (+) mirtazapine(+) olanzapine (+) amphetamine (+) Case 2 fluoromethcathinone (+) ibuprofen(+)	2 cases Case 1 – hit by train Case 2 – bag over head
79-81	**United Kingdom**	Jan–Dec 2011	Blood Urine	+	Case 1 ketamine (+) Case 2 quetiapine (+) Case 3 fluoromethcathinone (+) MDMA ([8]) (+) methylone (+) MDAI ([9]) (+) 5-IAI ([10]) (+) methoxetamine (+) AMT ([11]) (+)	3 cases Case 1 – hanging Case 2 – no circumstances reported Case 3 – found at home
82-91	**United Kingdom** **	Jan–Dec 2012	Blood Urine	+	None reported	11 cases 6 cases of hanging 1 case murder victim 1 case murder suspect 2 cases found dead at home 1 case found in a canal 1 case found dead in a car (carbon monoxide poisoning) (One of the cases is a duplicate, although it is not certain which one, hence this group is counted as 11 cases – see death 99)
92	**United Kingdom**	Jan–Dec 2013	Blood Urine	+	methadone (+) morphine (+) mirtazapine (+) diazepam (+) zopiclone (+) codeine (+)	Methadone intoxication.
93	**United Kingdom**	Jan 2010 (M, 57)	Blood	0.01 mg/L	N-desalkyl-4-methylmethcathinone (+)	Coronary artery disease in the presence of MDPV. Coroner's verdict: open verdict/ unascertained.
94	**United Kingdom**	Feb 2010 (M, 34)	Blood Gastric	+ (blood)	fentanyl (24 ng/mL in blood) (37 µg in gastric sample) cannabis (+)	Fentanyl toxicity implicated. Coroner's verdict: open verdict/ unascertained.

([8]) Methylenedioxymethylamphetamine (commonly known as 'ecstasy').
([9]) 3,4-Methylenedioxyaminoindane.
([10]) 5-Iodoaminoindane.
([11]) Alpha-methyltryptamine.
([12]) Δ9-tetrahydrocannabinolic acid, a breakdown product of Δ9-tetrahydrocannabinol, the main psychoactive substance in cannabis.
([13]) Gammabutyrolactone.

Case number	Country	Date	Biological sample	MDPV result	Results of toxicological analysis for other substances	Notes
96	**United Kingdom**	Jul 2010 (M, 26)	Blood Gastric	+ (blood) + (gastric)	pyrovalerone (+ in blood) (+ in gastric sample) THC-acid ([12]) (+ in blood) lignocaine (+ in antemortem blood) amiodarone (+ blood, therapeutic use suspected)	Cause of hypovolaemic shock, laceration of left forearm associated with partial transection of cephalic vein. Toxic effects of pyrovalerone and MDPV. Coroner's verdict accidental / misadventure.
97	**United Kingdom**	Apr 2010 (F, 45)	Blood	+	+) GBL ([13]) (+) methylone (+)	Mixed drug toxicity. Implicated: methedrone, GBL and methylone. Cause of death non-dependent abuse of drugs. Coroner's verdict: open verdict/ unascertained.
98	**United Kingdom** **	Nov 2010 (F, 29)	Blood Urine	<LOD (blood) + (urine)	alcohol (63 mg/100mL in blood) (118 mg/100mL in urine) mephedrone (<LOD ([14]) in matrix unknown) cocaine (+ in urine) levamisole (+ in urine) quinine (+ in urine)	Multiple injuries. Had taken a variety of substances and alcohol. Coroner's verdict: suicide. Implicated drugs alcohol, mephedrone and MDPV.
99	**United Kingdom**	Jun 2010 (M, 39)	Blood	0.13µg/L	alcohol (175 mg/100mL) citalopram (0.12 mg/L) diazepam (85 µg/L) temazepam (99 µg/L)	Carbon monoxide poisoning, alcoholic liver disease. Implicated- 4-fluoromethcathinone and mephedrone Coroner's verdict: suicide.
100	**United Kingdom**	Apr 2010 (M, 29)	Blood Urine	0.11 mg/L	4-fluoromethcathinone (0.21 mg/L in blood) (23.62 mg/mL in urine mephedrone (<0.05 mg/L in urine) ibuprofen (+ blood)	Asphyxia. Implicated: 4-fluoromethcathinone and mephedrone. Coroner's verdict: accidental/ misadventure.
101	**United Kingdom**	Jun 2010 (M, 38)	Blood Urine	0.41 mg/L (blood) 0.75 mg/L (urine)	amphetamine (+ blood) mephedrone (0.05 mg/L in blood) (0.05 mg/L in urine) 4-fluoromethcathinone (0.55 mg/L in blood) (6.51 mg/L in urine)	Cardiac arrest caused by either multiple drug toxicity or excited delirium. Coroner's verdict: accidental/ misadventure.
102	**United Kingdom**	Jun 2010 (M, 33)	Unspecified	1.5 mg/L	alcohol (57 mg/100 mL) benzodiazepine (7.4 mg/L) TFMPP ([15]) (1.9 mg/L) lignocaine (+)	Cause of death unascertained. Coroner's verdict: open verdict/ unascertained.
103	**United Kingdom**	Feb 2011 (M, 37)	Blood Nasal swab	+ (blood) + (nasal swab) both low level	amphetamine (0.04 µg/mL in blood) (+ on nasal swab) lignocaine (+ on nasal swab) benzocaine (+ on nasal swab) sertraline (+ in blood) diazepam (+ in blood)	Hanging. Coroner's verdict: open verdict/ unascertained.

([14]) Limit of detection – the lowest amount that can be detected by the method used.
([15]) Trifluoromethylphenylpiperazine.
([16]) Methylenedioxymethylamphetamine (commonly known as 'ecstasy').
([17]) 3,4-Methylenedioxy-α-pyrrolidinobutyrophenone.

Case number	Country	Date	Biological sample	MDPV result	Results of toxicological analysis for other substances	Notes
104	**United Kingdom**	Apr 2011 (M, 24)	Blood	1.63 mg/L	MDMA ([16]) (7460 µg/L) cocaine (929 µg/L) benzoylecgonine (1.89 mg/L) mephedrone (0.17 mg/mL) diazepam (3284 µg/L) nordiazepam (1138 µg/L)	Drowning and multiple drug overdose. Implicated- MDMA, cocaine and mephedrone. Coroner's verdict: accidental/ misadventure.
105	**United Kingdom** **	May 2011 (M, 53)	Blood Urine	+	MDPBP ([17]) (1.55 mg/l in blood), (94.2 mg/l in urine) pentylone (0.34 mg/l in blood) (29.4 mg/l in urine) mephedrone (+ in matrix unknown) cocaine (+ in urine)	Cause of death: ischemic heart disease and illicit use of cathinones. Implicated drugs: mephedrone, MDPBP and pentylone. Coroner's verdict accidental/ misadventure.
106	**United Kingdom**	Dec 2011 (M, 56)	Not specified	+	MDMA ([16]) (+) cocaine (+) cathinone (+)	MDMA, cocaine, MDPV and methylmethcathinone toxicity. Implicated: ecstasy, cocaine and cathinones. Coroner's verdict: open verdict/ unascertained.
107	**United Kingdom**	Aug 2011 (M, 27)	Unspecified	+	None reported	MDPV and heart attack. Coroner's verdict: open verdict/ unascertained.
108	**United Kingdom** **	Apr 2012 (M, 31)	Blood	<0.1 mg/L	AMT ([18]) (0.89 mg/L)	Cause of death cardiac failure, MDPV and AMT drug toxicity plus left ventricular hypertrophy and obesity. Coroners' verdict: accidental/ misadventure.

Notes:
In this table LOD is the limit of detection and LOQ is the limit of quantification.
* All cases in Finland are from a medico-legal source and include suspect and unnatural deaths, non-related to poisoning.
** The United Kingdom reported data on fatal intoxications from two separate sources, ROAR Forensics and the national programme for Substance Abuse Deaths (np-SAD). It should be noted that based on case specific details, case 108 is believed to be a duplicate of one of the cases reported in the aggregated data from 2012 and has been counted once only.

([18]) Alpha-methyltryptamine.

Council Decision

COUNCIL IMPLEMENTING DECISION of 25 September 2014 on subjecting 4-iodo-2,5-dimethoxy-N-(2-methoxybenzyl)phenethylamine (25I-NBOMe), 3,4-dichloro-N-[[1-(dimethylamino)cyclohexyl]methyl]benzamide (AH-7921), 3,4-methylenedioxypyrovalerone (MDPV) and 2-(3-methoxyphenyl)-2-(ethylamino)cyclohexanone (methoxetamine) to control measures (2014/688/EU)

THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Council Decision 2005/387/JHA of 10 May 2005 on the information exchange, risk-assessment and control of new psychoactive substances ([1]), and in particular Article 8(3) thereof,

Having regard to the proposal from the European Commission,

Whereas:

(1) Risk assessment reports on the new psychoactive substances 4-iodo-2,5-dimethoxy-N-(2-methoxybenzyl) phenethylamine (25I-NBOMe), 3,4-dichloro-N-[[1-(dimethylamino) cyclohexyl]methyl]benzamide (AH-7921), 3,4-methylenedioxypyrovalerone (MDPV) and 2-(3-methoxyphenyl)-2-(ethylamino)cyclohexanone (methoxetamine) were drawn up in compliance with Decision 2005/387/JHA by a special session of the extended Scientific Committee of the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), and were subsequently submitted to the Commission and to the Council on 23 April 2014.

(2) 25I-NBOMe, AH-7921, MDPV and methoxetamine had not been under assessment at the United Nations' level by the time the risk assessment was requested at Union level, but they were evaluated in June 2014 by the Expert Committee on Drug Dependence of the World Health Organization.

(3) 25I-NBOMe, AH-7921, MDPV and methoxetamine have no established or acknowledged medical use (human or veterinary). Apart from their use in analytical reference materials, and in scientific research investigating their chemistry, pharmacology and toxicology as a result of their emergence on the drug market — and, in the case of 25I-NBOMe, also in the field of neurochemistry — there is no indication that they are being used for other purposes.

(4) 25I-NBOMe is a potent synthetic derivative of 2,5-dimethoxy-4-iodophenethylamine (2C-I), a classical serotonergic hallucinogen, which was subject to risk assessment and to control measures and criminal sanctions at Union level from 2003 by Council Decision 2003/847/JHA ([2]).

(5) The specific physical effects of 25I-NBOMe are difficult to determine because there are no published studies assessing its acute and chronic toxicity, its psychological and behavioural effects, and dependence potential, and because of the limited information and data available.

([1]) OJ L 127, 20.5.2005, p. 32.
([2]) Council Decision 2003/847/JHA of 27 November 2003 concerning control measures and criminal sanctions in respect of the new synthetic drugs 2C-I, 2C-T-2, 2C-T-7 and TMA-2 (OJ L 321, 6.12.2003, p. 64).

Clinical observations of individuals who have used this substance suggest that it has hallucinogenic effects and has the potential for inducing severe agitation, confusion, intense auditory and visual hallucinations, aggression, violent accidents and self-induced trauma.

(6) There have been four deaths associated with 25I-NBOMe registered in three Member States. Severe toxicity associated with its use has been reported in four Member States, which notified 32 non-fatal intoxications. If this new psychoactive substance were to become more widely available and used, the implications for individual and public health could be significant. There is no information available on the social risks associated with 25I-NBOMe.

(7) 22 Member States and Norway have reported to the EMCDDA and European Police Office (Europol) that they detected 25I-NBOMe. No prevalence data is available on the use of 25I-NBOMe, but the limited information that exists suggests that it may be consumed in a wide range of settings, such as at home, in bars, nightclubs and at music festivals.

(8) 25I-NBOMe is openly marketed and sold on the internet as a 'research chemical' and information from seizures, collected samples, user websites and internet retailers suggests that it is being sold as a drug in its own right and also marketed as a 'legal' replacement for LSD. EMCDDA identified more than 15 internet retailers selling this substance, who may be based within the Union and China.

(9) The risk assessment report reveals that there is limited scientific evidence available on 25I-NBOMe and points out that further research would be needed to determine the health and social risks that it poses. However, the available evidence and information provides sufficient ground for subjecting 25I-NBOMe to control measures across the Union. As a result of the health risks that it poses, as documented by its detection in several reported fatalities, of the fact that users may unknowingly consume it and of the lack of medical value or use of the substance, 25I-NBOMe should be subjected to control measures across the Union.

(10) Since six Member States control 25I-NBOMe under national legislation complying with the obligations of the 1971 United Nations Convention on Psychotropic Substances, and seven Member States use other legislative measures to control it, subjecting this substance to control measures across the Union would help avoid the emergence of obstacles to cross-border law enforcement and judicial cooperation, and would help protect against the risks that its availability and use can pose.

(11) AH-7921 is a structurally atypical synthetic opioid analgesic commonly known by internet suppliers, user websites and media as 'doxylam'. It can be easily confused with 'doxylamine', an antihistaminic medicine with sedative-hypnotic properties, which could lead to unintentional overdoses.

(12) The specific physical effects of AH-7921 are difficult to determine because there are no published studies assessing its acute and chronic toxicity, its psychological, behavioural effects, and dependence potential, as well as the limited information and data available. Based on user reports, the effects of AH-7921 appear to resemble those of classical opioids with the feeling of mild euphoria, itchiness and relaxation; nausea appears to be a typical adverse effect. In addition to self-experimentation with AH-7921, as well as 'recreational use', some of the users report self-medicating with this new drug to relieve pain, others to alleviate withdrawal symptoms due to cessation of the use of other opioids. This may indicate a potential of AH-7921 to spread among the injecting opioid population.

(13) There is no prevalence data on the use of AH-7921, but the information available suggests that it is not widely used, and that when it is used, that use is in the home environment.

(14) 15 fatalities were recorded in three Member States between December 2012 and September 2013 where AH-7921, alone or in combination with other substances, was detected in post-mortem samples. While it is not possible to determine with certainty the role of AH-7921 in all of those fatalities, in some cases it has been specifically noted in the cause of death. One Member State reported six non-fatal intoxications associated with AH-7921. If this new psychoactive substance were to become more widely available and used, the implications for individual and public health could be significant. There is no information available on the social risks associated with AH-7921.

(15) The risk assessment report reveals that there is limited scientific evidence available on AH-7921 and points out that further research would be needed to determine the health and social risks that it poses. However, the available evidence and information provides sufficient ground for subjecting AH-7921 to control measures across the Union. As a result of the health risks that it poses, as documented by its detection in several reported fatalities, of the fact that users may unknowingly consume it, and of the lack of medical value or use of the substance, AH-7921 should be subjected to control measures across the Union.

(16) Since one Member State controls AH-7921 under national legislation complying with the obligations of the 1971 United Nations Convention on Psychotropic Substances and five Member States use other legislative measures to control it, subjecting this substance to control measures across the Union would help avoid the emergence of obstacles in cross-border law enforcement and judicial cooperation, and would help protect against the risks that its availability and use can pose.

(17) MDPV is a ring-substituted synthetic derivative of cathinone chemically related to pyrovalerone, which are both subject to control under the 1971 United Nations Convention on Psychotropic Substances.

(18) Information on the chronic and acute toxicity associated with MDPV, as well as on psychological and behavioural effects, and on dependence potential, is not collected uniformly across the Union. Information from published studies, confirmed by clinical cases, suggests that the psychopharmacological profile observed for MDPV is similar to that for cocaine and methamphetamine, albeit more potent and longer lasting. Furthermore, MDPV was found to be 10 times more potent in its ability to induce locomotor activation, tachycardia and hypertension.

(19) Users' websites indicate that its acute toxicity can provoke adverse effects on humans, similar to those associated with other stimulants. These include paranoid psychosis, tachycardia, hypertension, diaphoresis, breathing problems, severe agitation, auditory and visual hallucinations, profound anxiety, hyperthermia, violent outbursts and multiple organ dysfunctions.

(20) 108 fatalities were registered in eight Member States and Norway between September 2009 and August 2013, where MDPV has been detected in post-mortem biological samples or implicated in the cause of death. A total of 525 non-fatal intoxications associated with MDPV have been reported by eight Member States. If this new psychoactive substance were to become more widely available and used, the implications for individual and public health could be significant.

(21) The detection of MDPV has also been reported in biological samples related to fatal and non-fatal road traffic accidents, or driving under the influence of drugs, in four Member States since 2009.

(22) MDPV has been present in the Union drug market since November 2008 and 27 Member States, Norway and Turkey reported multi-kilogram seizures of the substance. MDPV is being sold as a substance in its own right, but it has also been detected in combination with other substances. It is widely available from internet suppliers and retailers, 'head shops' and street-level dealers. There are some indications that suggest a degree of organisation in the tableting and distribution of this substance in the Union.

(23) The risk assessment report reveals that further research would be needed to determine the health and social risks posed by MDPV. However, the available evidence and information provides sufficient ground for subjecting MDPV to control measures across the Union. As a result of the health risks that it poses, as documented by its detection in several reported fatalities, of the fact that users may unknowingly consume it, and of the lack of medical value or use of the substance, MDPV should be subjected to control measures across the Union.

(24) Since 21 Member States control MDPV under national legislation complying with the obligations of the 1971 United Nations Convention on Psychotropic Substances and four Member States use other legislative measures to control it, subjecting this substance to control measures across the Union would help avoid the emergence of obstacles in cross-border law enforcement and judicial cooperation, and would protect against the risks that its availability and use can pose.

(25) Methoxetamine is an arylcyclohexylamine substance which is chemically similar to ketamine and the internationally controlled substance phencyclidine (PCP). Like ketamine and PCP, it has dissociative properties.

(26) There are no studies assessing the chronic and acute toxicity associated with methoxetamine, as well as its psychological and behavioural effects, and dependence potential. Self-reported experiences from user websites suggest adverse effects similar to ketamine intoxication. These include nausea and severe vomiting, difficulty in breathing, seizures, disorientation, anxiety, catatonia, aggression, hallucination, paranoia and psychosis. In addition, acute methoxetamine intoxications may include stimulant effects (agitation, tachycardia and hypertension) and cerebral features, which are not expectable with acute ketamine intoxication.

(27) Twenty deaths associated with methoxetamine were reported by six Member States that detected the substance in post-mortem samples. Used alone or in combination with other substances, methoxetamine was detected in 20 non-fatal intoxications reported by five Member States. If this new psychoactive substance were to become more widely available and used, the implications for individual and public health could be significant.

(28) 23 Member States, Turkey and Norway have reported that they detected methoxetamine, since November 2010. Information suggests that it is sold and used as a substance in its own right, but it is also sold as a 'legal' replacement for ketamine by internet retailers, 'head shops' and street-level drug dealers.

(29) Multi-kilogram quantities in powder form were seized within the Union, but there is no information on the possible involvement of organised crime. The manufacture of methoxetamine does not require sophisticated equipment.

(30) Prevalence data are limited to non-representative studies in two Member States. Those studies suggest that the prevalence of the use of methoxetamine is lower than that

of ketamine. The available information suggests that it may be consumed in a wide range of settings, including at home, in bars, nightclubs and at music festivals.

(31) The risk assessment report reveals that further research would be needed to determine the health and social risks posed by methoxetamine. However, the available evidence and information provides sufficient grounds for subjecting methoxetamine to control measures across the Union. As a result of the health risks that it poses, as documented by its detection in several reported fatalities, of the fact that users may unknowingly consume it, and of the lack of medical value or use, methoxetamine should be subjected to control measures across the Union.

(32) Since nine Member States control methoxetamine under national legislation complying with the obligations of the 1971 United Nations Convention on Psychotropic Substances and nine Member States use other legislative measures to control it, subjecting this substance to control measures across the Union would help avoid the emergence of obstacles in cross-border law enforcement and judicial cooperation, and would protect against the risks that its availability and use can pose.

(33) Decision 2005/387/JHA reserves to the Council implementing powers with a view to giving a quick and expertise-based response at the Union level to the emergence of new psychoactive substances detected and reported by the Member States, by submitting those substances to control measures across the Union. As the conditions and procedure for triggering the exercise of such implementing powers have been met, an implementing decision should be adopted in order to put 25I-NBOMe, AH-7921, MDPV and methoxetamine under control across the Union,

HAS ADOPTED THIS DECISION:

Article 1

The following new psychoactive substances shall be subjected to control measures across the Union:

(a) 4-iodo-2,5-dimethoxy-N-(2-methoxybenzyl) phenethylamine(25I-NBOMe);
(b) 3,4-dichloro-N-[[1-dimethylamino) cyclohexyl]methyl] benzamide (AH-7921);
(c) 3,4-methylenedioxypyrovalerone (MDPV);
(d) 2-(3-methoxyphenyl)-2-(ethylamino)cyclohexanone (methoxetamine).

Article 2

By 2 October 2015, Member States shall subject in accordance with their national legislation, the new psychoactive substances referred to in Article 1 to control measures and criminal penalties, as provided for under their legislation complying with their obligations under the 1971 United Nations Convention on Psychotropic Substances.

Article 3

This Decision shall enter into force on the twentieth day following that of its publication in the *Official Journal of the European Union*.

Done at Brussels, 25 September 2014.

For the Council
The President
F. Guidi

Participants of the risk assessment meeting, 2 April 2014

Scientific Committee members

- **Dr Anne-Line Bretteville Jensen,** Norwegian Institute for Alcohol and Drug Research, Oslo
- **Prof. Dr Gerhard Bühringer,** Addiction Research Unit, Dep. of Clinical Psychology and Psychotherapy, Technische Universität Dresden, Institut für Therapieforschung (IFT), Munich, Vice-Chair of the Scientific Committee
- **Dr Catherine Comiskey,** Director, Centre for Practice and Healthcare Innovation, Trinity College Dublin, School of Nursing and Midwifery, Dublin
- **Dr Paul Dargan,** Clinical Toxicology, St Thomas' Hospital, Guy's and St Thomas' NHS Foundation Trust, London
- **Prof. Gabriele Fischer,** Medical University Vienna, Center of Public Health, Department of Psychiatry and Psychotherapy, Vienna
- **Prof. Dr Matthew Hickman,** Social Medicine, Bristol
- **Prof. Letizia Paoli,** LINC, Leuven Institute of Criminology, University of Leuven Faculty of Law, Leuven
- **Dr Fernando Rodriguez de Fonseca,** Fundación IMABIS, Hospital Carlos Haya, Málaga
- **Prof. Dr Brice De Ruyver,** Department of Criminal Law and Criminology, Faculty of Law, Universiteit Gent

Advisers to the Scientific Committee

- **Dr Peter Blanckaert,** Belgian Early Warning System on Drugs, DO Public Health and Surveillance, Substance use and related disorders (SURD), Brussels
- **Dr Simon Brandt,** School of Pharmacy and Biomolecular Sciences, Liverpool John Moores University, Liverpool
- **Prof. Desmond Corrigan,** The School of Pharmacy and Pharmaceutical Sciences, Trinity College, Dublin
- **Prof. Gaetano Di Chiara,** Cagliari University, Biomedical Sciences Department, Cagliari
- **Dr Dariusz Zuba,** Institute of Forensic Research, Kraków

Representatives of the institutions

European Commission

- **Elsa Maia,** Anti-Drugs Policy Unit, European Commission, Brussels
- **Fabiano Reniero,** Joint Research Centre, Institute for Health and Consumer Protection (IHCP), Brussels

European Medicines Agency (EMA)

- **Jean-Marc Vidal,** Scientific Support and Projects, Non-clinical Safety, Human Medicines Evaluation Division, London

Europol

- **Daniel Dudek,** Project SYNERGY, Europol, The Hague

EMCDDA

- **Paul Griffiths,** Scientific Director, EMCDDA, Lisbon
- **Roumen Sedefov,** Head of unit, Supply reduction and new trends unit, EMCDDA, Lisbon

Invited external experts

- **Dr Simon Elliott,** (ROAR) Forensics Ltd, Worcestershire
- **Dr István Ujváry,** Budapest University of Technology and Economics, Budapest
- **Dr David Wood,** Clinical Toxicology, St Thomas' Hospital, Guy's and St Thomas' NHS Foundation Trust, London

EMCDDA staff present

- **Ana Gallegos,** Head of Sector, Action on new drugs, Supply reduction and new trends unit
- **Andrew Cunningham,** Scientific analyst, Action on new drugs, Supply reduction and new trends unit
- **Michael Evans-Brown,** Scientific analyst, Action on new drugs, Supply reduction and new trends unit
- **Anabela Almeida,** Project assistant, Action on new drugs, Supply reduction and new trends unit
- **Isabelle Giraudon,** Scientific analyst, Health consequences, Prevalence, consequences and data management unit

TD-AK-14-003-EN-N

Recommended citation:

European Monitoring Centre for Drugs and Drug Addiction (2014), *Report on the risk assessment of 1-(1,3-benzodioxol-5-yl)-2-(pyrrolidin-1-yl)pentan-1-one (3,4-methylenedioxypyrovalerone, MDPV) in the framework of the Council Decision on new psychoactive substances*, Risk Assessments, Publications Office of the European Union, Luxembourg.

About the EMCDDA

The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) is the central source and confirmed authority on drug-related issues in Europe. For over 20 years, it has been collecting, analysing and disseminating scientifically sound information on drugs and drug addiction and their consequences, providing its audiences with an evidence-based picture of the drug phenomenon at European level.

The EMCDDA's publications are a prime source of information for a wide range of audiences including: policymakers and their advisors; professionals and researchers working in the drugs field; and, more broadly, the media and general public. Based in Lisbon, the EMCDDA is one of the decentralised agencies of the European Union.

Related publications and websites

EMCDDA

- Risk assessment of new psychoactive substances — operating guidelines, 2010

EMCDDA and Europol

- EMCDDA–Europol Joint Report on a new psychoactive substance: MDPV, 2014
- EMCDDA–Europol 2013 Annual Report on the implementation of Council Decision 2005/387/JHA, 2014
- EMCDDA–Europol Early-warning system on new psychoactive substances — operating guidelines, 2007

These and all other EMCDDA publications are available from emcdda.europa.eu/publications

- EMCDDA Action on new drugs website: www.emcdda.europa.eu/drug-situation/new-drugs

Luxembourg: Publications Office of the European Union
doi: 10.2810/57789 | ISBN 978-92-9168-749-7

This publication is only available in electronic format.

EMCDDA, Praça Europa 1, Cais do Sodré, 1249-289 Lisbon, Portugal
Tel. (351) 211 21 02 00 | info@emcdda.europa.eu
emcdda.europa.eu | twitter.com/emcdda | facebook.com/emcdda

Publications Office