European Monitoring Centre
for Drugs and Drug Addiction

EUROPOL

EMCDDA–Europol Joint Report on a new psychoactive substance: MDPV (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

Contents

1. Introduction 3

2. Information collection process 3

The EMA and the twenty-four Member States (), Iceland and Norway replied to the EMA's request in this regard. 5

3. Information required by Article 5.2 of the Decision 5

3.1 Chemical and physical description, including the names under which the new psychoactive substance is known — Article 5.2(a) of the Decision 6

3.2 Information on the frequency, circumstances and/or quantities in which a new psychoactive substance is encountered, and information on the means and methods of manufacture of the new psychoactive substance — Article 5.2(b) of the Decision 8

3.2.1 Information provided to Europol 8

3.2.2 Information provided to the EMCDDA 12

3.4 A first indication of the risks associated with the new psychoactive substance, including the health and social risks, and of the characteristics of users — Article 5.2(d) of the Decision 15

3.4.1 First indication of health risks 16

3.4.2 Characteristics of users 16

3.5 Information on whether or not the new substance is currently under assessment, or has been under assessment, by the UN system — Article 5.2(e) of the Decision 26

3.6 The date of notification on the Reporting Form of the new psychoactive substance to the EMCDDA or to Europol — Article 5.2(f) of the Decision 26

3.7 Information on whether or not the new psychoactive substance is already subject to control measures at national level in a Member State — Article 5.2(g) of the Decision 27

3.8 Further information — Article 5.2(h) of the Decision 28

3.8.1 The chemical precursors that are known to have been used for the manufacture of the substance 28

3.8.2 The mode and scope of the established or expected use of the new substance 28

3.8.3 Other use of the new psychoactive substance and the extent of such use, the risks associated with this use of the new psychoactive substance, including the health and social risks 28

4. Information from the EMA as requested by Article 5.3 of the Decision 30

4.1 Marketing authorisation 30

4.2 Application for a marketing authorisation 30

4.3 Suspended marketing authorisation 30

5. Conclusions 30

References 32

Annex 1: Images of MDPV from seizures and collected samples 35

Annex 2: Table of non-fatal intoxications and deaths where MDPV has been analytically confirmed in biological samples 38

1. Introduction

Article 5.1 of Council Decision 2005/387/JHA ([1]) (hereinafter referred to as the 'Decision') stipulates that '*Where Europol and the EMCDDA, or the Council, acting by a majority of its members, consider that the information provided by the Member State on a new psychoactive substance merits the collection of further information, this information shall be collated and presented by Europol and the EMCDDA in the form of a Joint Report (hereinafter the 'Joint Report').*' The Joint Report shall be submitted to the Council, the European Medicines Agency (EMA) and the Commission.

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 collected on MDPV satisfied criteria 1, 2, 3, 4 and 6. The two organisations therefore concluded that sufficient information had been accumulated to merit the production of a Joint Report on MDPV as stipulated by Article 5.1 of the Decision.

2. Information collection process

In compliance with the provisions of the Decision, on 7 October 2013 the EMCDDA and Europol launched a procedure for the collection of information on MDPV, in order to prepare the Joint Report. The information was collected mainly through the Reitox National Focal Points in the Member States, Turkey and Norway as well as the Europol National Units. In addition, the EMA collected information through the national competent authorities responsible for human and veterinary medicinal

([1]) OJ L 127, 20.5.2005, p. 32.

products in the Member States as well as in Norway and Iceland. The information collection process was largely concluded by 18 November 2013; additional information and clarifications from some countries were received up to four weeks after this date.

Europol asked the Europol National Units to provide information on:

- the level of production of MDPV in their country;
- the level of distribution of MDPV in their country;
- the level of trafficking of MDPV in their country, both for internal, transit or export purposes;
- the number of seizures of MDPV in their country, the total amount of the seizures, country of origin, details on the physical forms (including photos);
- the role of organised crime, or criminal groups, in the production, distribution and trafficking of MDPV in their country; and,
- any known aspect of violence and/or money laundering relating to the production and trafficking of MDPV.

Europol received responses from 15 Member States.

According to Article 5.3 of the Decision, the EMA asked the national competent authorities responsible for human and veterinary medicinal products in the Member States as well as in Norway and Iceland to provide information on whether:

- the new psychoactive substance MDPV has obtained a marketing authorisation;
- the new psychoactive substance MDPV is the subject of an application for a marketing authorisation; and,
- a marketing authorisation that had been granted in respect of the new psychoactive substance MDPV has been suspended.

Twenty-five Member States ([2]), Norway and Iceland replied to the EMA's request. The EMA also provided information as relevant to the central authorisation procedure.

Furthermore, in anticipation of Article 7.3 of the Decision in relation to the manufacturing of medicinal products in the European Union, the EMA also requested whether the new psychoactive substance MDPV is used to manufacture a medicinal product:

([2]) Austria, Belgium, Croatia, Cyprus, Czech Republic, Denmark, Estonia, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom.

- which has been granted a marketing authorisation;
- for which an application has been made for a marketing authorisation; and,
- for which a marketing authorisation has been suspended by a competent authority.

Twenty-four Member States ([3]), Norway and Iceland replied to the EMA's request. The EMA also provided information as relevant to the central authorisation procedure.

The EMCDDA collected data through:

1. a structured questionnaire from the Reitox national focal points. The EMCDDA received replies from 28 Member States as well as Norway and Turkey;
2. data previously provided to the EU Early warning system in EMCDDA-Europol Reporting forms, EWS Progress and Final Reports;
3. a specific information request to the World Health Organization on whether or not MDPV is under assessment by the United Nations system (see section 3.5); and,
4. a structured search of the scientific literature and of relevant Internet sites.

Thus, information included in sections 3.2.1 and 3.3 of the Joint Report was provided by Europol, while the EMCDDA provided information included in sections 3.1, 3.2.2, 3.4, 3.5, 3.6, 3.7, 3.8.1, 3.8.2 and 3.8.3 (in part). The information included in sections 3.8.3 (in part), 4.1, 4.2 and 4.3 was provided by the EMA. The conclusion of the Joint Report were prepared and agreed by the two organisations responsible — the EMCDDA and Europol. Further details of the seizures and collected samples (including images where available) reported to the EMCDDA are provided in Annex 1. The details of deaths associated with MDPV that have been reported to the EMCDDA are provided in Annex 2.

3. Information required by Article 5.2 of the Decision

The order and titles of subsections 3.1 to 3.8 and section 4 below are as they appear in Article 5.2(a) to (h) and Article 5.3(a) to (c) of the Decision; all sections are cross-referenced with those set down in the Decision.

([3]) Austria, Belgium, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom.

3.1 Chemical and physical description, including the names under which the new psychoactive substance is known — Article 5.2(a) of the Decision

Chemical description and names

MDPV is a synthetic derivative of the naturally occurring substance cathinone, one of the psychoactive principles in khat (*Catha edulis* Forsk). All monitored synthetic cathinone derivatives are either *N*-alkylated or the nitrogen atom is part of a pyrrolidine ring, which is the case with MDPV. Most of the cathinone derivatives are also ring-substituted and MDPV contains the 3,4-methylenedioxy substitution pattern on the phenyl ring which is observed in other illicit drugs such as MDMA (3,4-methylenedioxymethamphetamine).

Pyrrolidine derivatives, such as MDPV, can be regarded as a subset of cathinone derivatives sharing the same structural skeleton as pyrovalerone (Figure 1). Other examples in this group are 1-phenyl-2-(1-pyrrolidinyl)-1-pentanone (α-PVP) and 4-methyl-α-pyrrolidinobutyrophenone (MPBP).

MDPV is the common name for 3,4-methylanedioxypyrovalerone. The systematic chemical name is: (*RS*)-1-(benzo[d][1,3]dioxol-5-yl)-2-(pyrrolidin-1-yl)pentan-1-one.

Additional chemical synonyms reported are:

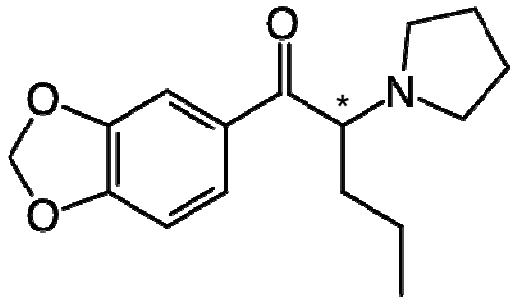
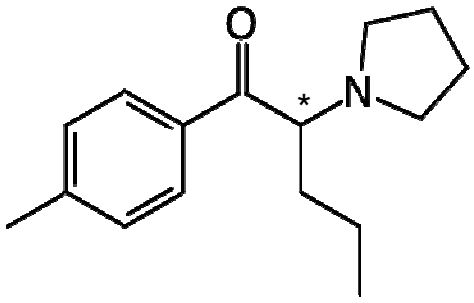
1-(3,4-methylenedioxyphenyl)-2-pyrrolidinyl-pentan-1-one;
1-(3,4-methylenedioxy-phenyl)-2-pyrrolidin-1-yl-pentan-1-one;
1-(benzo[d][1,3]dioxol-5-yl)-2-(pyrrolidin-1-yl)pentan-1-one;
1-(1,3-benzodioxol-5-yl)-2-(pyrrolidin-1-yl)pentan-1-one;
1-(1,3-benzodioxol-5-yl)-2-(1-pyrrolidinyl)-1-pentanone;
(*RS*)-[1-(3,4-metyleenidioksifenyyli)-2-(1-pyrrolidinyyli)-1-pentanoni)] (Finnish).

Common names or codenames that have also been reported are: MDPK and metyleenidioksipyrovaleroni (Finnish).

The following street names have also been reported: MDPK, Magic, Super coke, Peevee, New Ivory Wave, Kannibaldrogen, Apdamm, Aakkoset (meaning alphabet in Finnish), Bath salt, MP, MP4 and MP3.

Finally, the following ‘legal high’ product names have been associated with MDPV: ‘Mojo’, ‘Yellow Submarine’, ‘Ivory Wave’, ‘Vanilla sky’, ‘NRG-3’, ‘Flower magic’, ‘Gumi cucoriedka’, ‘Kamikadze’, ‘Xtacy’, ‘Ivory wave’, ‘Extreme star dust’, ‘Hurricane Charlie’, ‘Dogs bollix’, ‘Doves red’, ‘Doves ultra’, ‘Sextasy’, ‘Orange orbits’, ‘Stardust’, ‘Blow’, ‘Recharge’, ‘Charge+’, ‘Lucky’, ‘Generation 2012’, ‘EL PADRINO’ (translation: the Godfather), ‘Coco Jumbo’, ‘Cherry Coco Jumbo’, ‘SUNRISE’, ‘TECHNO’, ‘Greenway Speedway’, ‘DANA’, ‘OLGA’, ‘LENA’, ‘EVA’, ‘CLARA’, ‘MARKETA’ and ‘JANA’.

Figure 1. Molecular structure, weight and monoisotopic mass of MDPV. The molecular structure for pyrovalerone is provided for comparison (* denotes the chiral centre).

<table>
<tr><td>  </td><td>  </td></tr>
<tr><td>MDPV</td><td>pyrovalerone</td></tr>
<tr><td>Molecular formula: $C_{16}H_{21}NO_3$

Molecular weight: 275.3429

Monoisotopic mass: 275.152</td><td></td></tr>
</table>

Chemical Abstract Service registry numbers (CAS RN)

687603-66-3	free base
24622-62-6	hydrochloride salt
1388142-27-5	*R*-enantiomer base
1388142-28-6	*S*-enantiomer base
1246912-12-8	deuterated (D_8) base
1246820-09-6	deuterated (D_8) hydrochloride salt

The REACH registered substances database hosted by the European Chemicals Agency (ECHA) was searched using the CAS registry numbers listed above. The search returned no results.

Physical description

The free base form of MDPV has been described to be a brown or yellow-green amorphous powder. The hydrochloride salt form is described as a white-tan crystalline hygroscopic powder with a melting point of 238–239°C.

Reports from seizures and collected samples have noted the presence of MDPV in: powders, powder-filled capsules, tablets, blotters (small paper doses for sublingual/buccal administration), liquids, vegetable material, and, in residues on injecting equipment.

A more detailed description of MDPV seizures and collected samples encountered can be found in subsections 3.2.1 and 3.2.2 below.

3.2 Information on the frequency, circumstances and/or quantities in which a new psychoactive substance is encountered, and information on the means and methods of manufacture of the new psychoactive substance — Article 5.2(b) of the Decision

3.2.1 Information provided to Europol

Europol received replies from 15 Member States: Belgium, Bulgaria, Croatia, Cyprus, Denmark, Estonia, Finland, Hungary, Italy, Latvia, Lithuania, Luxembourg, Poland, Slovakia and Slovenia. Of these, four countries had no data relating to MDPV: Cyprus, Latvia, Luxembourg and Slovenia. The remaining 11 countries: Belgium, Bulgaria, Croatia, Estonia, Finland, Germany, Hungary, Italy, Lithuania, Poland and Slovakia reported the following information.

The level of production, distribution and trafficking

Belgium reported that in 2013 there were, so far eight cases in total, where MDPV was sent from China and entered Belgium en-route to third countries. The final destinations in these cases were: Italy (3 cases), the Netherlands (3) and the United Kingdom (2). The seized MDPV destined for Italy ranged from 18 grams to 510 g. On two occasions the substance was labelled as 'ULTRAVIOLET AB' (18 grams and 510 grams) and as 'LITHOPHONE' (100 grams) on the remaining occasion. The MDPV ordered by consumers in the Netherlands was labelled as 'SODIUM ALGINATE', with the following quantities seized: 1516 grams, 1521 grams and 2022 grams. In one of the two cases when MDPV was destined for the United Kingdom market (which weighed 260 grams in each case), the seized substance was labelled as 'HETASTARCH'.

Bulgaria reported that Customs have reported 12 seizures of MDPV made between July 2010 and March 2012. All seizures took place at Sofia Airport, when the substance was sent to Bulgaria (in the majority of cases) from: China, Spain, Portugal, the United Kingdom or the Netherlands. One case was reported which involved almost 5000 small packages of MDPV being sent to Poland via Hungary. In these 12 seizures 5267 grams and 300 tablets of MDPV were seized. In some cases MDPV powder was mixed with caffeine and lidocaine. MDPV tablets had a pink colour, elliptic shape and were packed in small packages (containing 2 tablets each) bearing label: 'DOVES RED'. MDPV in powder form was identified in small packages

bearing different labels, for example, ‘IVORY WAVE’, ‘MOJO’, ‘FLOWER MAGIC POWDER’ and ‘LOAD’.

In addition, the Bulgarian authorities reported that currently the Research Institute of Forensic Sciences and Criminology of the Ministry of the Interior has recorded 19 cases related to MDPV seizures. In some of these cases MDPV was destined to smart shops located in nearby resorts at the Black Sea.

Croatia provided information that MDPV was detected in 10 cases (14 grams in total).

Estonia reported one seizure of MDPV (1.68 grams), made by Customs in incoming mail from the United Kingdom. In this case, MDPV was mixed with alpha-PVP and pentedrone.

Finland reported that a few years ago, the number of seizures of MDPV was higher. Since the substance was classified as a controlled substance, the number of seizures declined. According to data provided by Finland, there were eight incidents where MDPV was seized in powder form (63.5 grams in total). There is also information that MDPV was identified in 11 blood samples (no further details were provided to Europol).

The German contribution to Europol mentioned two significant investigations during which seizures of MDPV were recorded.

The first investigation was conducted between September 2011 and March 2013. It was focused on distribution of new psychoactive substances sold via the Internet as so-called ‘legal high’ products. During house searches made in March 2013, 5524 products containing new psychoactive substances (NPS) were seized. Moreover during further mail confiscation another 3999 NPS products were seized. Among these, the following products contained MDPV:

10 packages (1 gram each) of the ‘bath salt’ named ‘Charlie Sheen’;
11 packages (1 gram each) of the ‘bath salt’ named ‘Mojo’;
20 capsules (0.5 grams each).

Further analysis revealed that more than 4000 customers from Germany and foreign countries had used this now disrupted network. The NPS products were ordered by wholesalers in Belgium, the Netherlands, the Czech Republic, Portugal and Belize.

The second investigation involved online vendors who were involved in supplying MDPV and methoxetamine. In the framework of this investigation, 30 kilograms of different NPS products were seized. Amongst others the following seizures of MDPV were identified:

4 packages (1 gram each) of the ‘bath salt’ named ‘highway’;

6.29 grams of a white powder labelled as '4-FMP';

13.58 grams of a white powder labelled as 'MDPV';

0.94 grams of a white powder labelled as 'ECKO', mixed with caffeine;

a total of 90 grams of a white powder with different labelling: 'MDPV', 'methylone', '4-FA', with a purity of 73 %;

a total of 2.568 grams of a white powder with different labelling: 'MDMAI', 'MPPP', 'Dimethocaine', 'Alpha PPP', with a purity of 81 %;

1.431 grams of a white and beige powder with different labelling: 'Synthacain', 'Charge+', 'Dimethocaine', 'R-MMC', 'Dichloropan', without labelling; with a purity of 62 %;

1 gram of a white powder labelled as 'Alpha-PPP';

14 grams of a white powder labelled as 'Alpha-PVP';

30 grams of a brown powder;

61 packages of the so called 'legal high' product named 'Brutal powder', mixed with caffeine and lidocaine;

10 grams of a white powder labelled as 'Dichloropan';

28 grams of a white powder labelled as 'Dimethocaine';

24 grams of green tablets, also containing caffeine;

78 grams of green tablets 'Benzo F'; also containing caffeine;

6 grams of a white powder labelled as 'Synthacain';

20 packages of the 'bath salt' named 'Tony Montana' ([4]), also containing caffeine and lidocaine.

Data provided by Germany concerning MDPV seizures were recorded from February 2011 and November 2013. There has been huge number of seizures where MDPV was detected. Bearing in mind the number of seizures and level of distribution it can be concluded that market for the MDPV has been rising during the last years. German authorities assume that the number of unreported cases, in relation to MDPV is high. In the majority of cases MDPV was identified in so called 'legal high' products, with different labelling: 'Mojo', 'Mitseez', 'Buzz Powder', 'Sweed', 'Ivory Wave', 'J White Powder Cleaner', 'wakup', 'Yellow Submarine', 'XXX', 'Buty', 'Lionheart', 'Rush Hour', 'Lets play crack inside', 'Charlie Sheen', 'All Day, All Night – What the fuck', 'Highway', 'ECKO', 'Brutal Powder', 'Sextacy', 'Insomnia' and 'Ultra Charge'.

In most of these cases, MDPV was identified as main active ingredient mixed with other new psychoactive substances and/or adulterants like: 4-MEC, flephedrone, butylone, MDPBP, TFMPP, 3-FMC, MXE, 2C-E, para-fluoramphetamine, AM-2201, pentedrone and/or lidocaine, caffeine, starch, taurine, mannitol and benzocaine.

The seizures of MDPV ranged from 0.02 grams (March 2012) to 1 kilogram (January 2013 – 2 x 500 grams).

([4]) 'Tony Montana' is the name of Al Pacino's character in the 1983 film 'Scarface', directed by Brian de Palma, which tells the story of a Cuban refugee who becomes a drug kingpin in the cocaine trade in Miami, USA.

In Hungary, the increase in availability, use and distribution of MDPV led the Ministry of Justice to propose an amendment to the Act on Drugs which then placed MDPV as a Class A drug. The Hungarian Europol Liaison Officer reported that MDPV has been seized in tablet and powder form in 2009 and 2010 respectively.

Seizures of MDPV tablets have risen from 551 tablets in 2009 (6 cases) to 8522 tablets in 2012 (9 cases). Seizures of powder have evolved from 133 grams in 2010 to 9579 grams in 2010 and to 5730 grams in 2012. In 2013 the seizures of MDPV (both tablets and powder form) have been noted to have dropped significantly.

Italy reported a limited number of seizures of MDPV. There were three seizures of MDPV (in total, 307.6 grams) made in the provinces of Roma, Milano and Taranto (September – October 2013). The involvement of Italian citizens has been reported in these cases.

Lithuania reported four seizures of MDPV made in 2012, totalling 1.326 grams.

In Poland, MDPV was seized as powder in quantities ranging from 0.11 grams to 525 grams. This is the largest seizure, which was made in April 2013, when the substance was sent from China (ordered via: www.sensearomatic.com) to Poland by shipping company FedEx.

Slovakia reported 24 cases where MDPV was seized as a powder (different colours). In a significant majority of cases, the substance was seized in small packages labelled with different names: 'Long Play' (8 cases); 'Beep beep' (8); 'Speed way' (1); 'Popeyes Sniff' (1) and 'LP' (1). In almost all cases, MDPV was identified in a mixture with other new psychoactive substances such as: 2-DPMP ([5]) and buphedrone (majority), MABP, bk-MDMA and ethcathinone. Seizures of MDPV weighed between 0.218 grams and 53.315 grams.

The Slovakian Financial Administration reported a case focused on a smart shop (Euphoria Shop Ltd.), which distributed goods called 'Aromatic herbs and imitations of spa salts'. The Forensic Institute revealed that the products contained MDPV. The distribution of goods took place via branches in six cities in Slovakia. In June 2012, during searches made in these branches and in the house of a suspect, a total amount of 19,562 packages containing MDPV were seized. In addition, 5 plastic bags with crystalline white powder were seized (20 grams, 80 grams, 300 grams, 800 grams, 1 kilogram) and EUR 6191 in cash.

In addition, Slovakia reported a seizure of 10 kilograms of MDPV powder seized by Customs officers of Airport Financial Administration (no other details provided).

According to Slovakian authorities, imports are ordered via the Internet and then delivered from China to Slovakia by mail order (DHL, TNT, FedEx, etc.).

([5]) 2-(Diphenylmethyl)piperidine

No reports were received that indicated licit or illicit production of MDPV in any of these countries.

3.2.2 Information provided to the EMCDDA

According to reports to the EMCDDA, MDPV has been present on the EU drugs market since 2008 and subsequently a large volume of data has been collected during this period, of which a summary is presented below.

Twenty-seven Member States (all Member States with the exception of Luxembourg) and Norway and Turkey reported detections of MDPV ([6]).

Seizures

Twenty-seven Member States (all Member States with the exception of Luxembourg), Norway and Turkey have reported seizures ([7]) of MDPV to the EMCDDA. In excess of 5500 seizures have been reported with two countries reporting more than 1000 seizures each: the United Kingdom (1704) and Finland (1340). A further four countries reported more than 100 seizures: Hungary (599), Poland (401), Ireland (242) and Spain (176).

MDPV has typically been seized in powder form (reported by all countries where MDPV was detected). Some countries also reported seizures of tablets or powder-filled capsules (Finland, France, Germany, Hungary, Italy, Lithuania, the Netherlands, Norway, Poland, Portugal, Romania, Spain, Sweden, and the United Kingdom). Six countries (Denmark, Finland, France, Latvia, Sweden, and the United Kingdom) have seized liquids containing MDPV. Finland and Poland each reported a single seizure of paper doses (also known as a 'blotters'), i.e. small pieces of paper impregnated with MDPV for sublingual/buccal administration. The Polish blotters (4 in total) had an image of Bugs Bunny on them and also contained 2-DPMP, ethylphenidate and the nootropic substance piracetam. Hungary also reported two cases where MDPV was present as 'powder on herb' and Poland reported a seizure of a 'legal high' product labelled as 'Greenway Speedway', which contained vegetable material with MDPV present. Indeed, MDPV has often been found as an ingredient in so-called 'legal high' products, often in combination with other substances. Several countries have described these as 'bath salts', a term frequently used to describe 'legal high'

([6]) 'Detections' is an all-encompassing term and may include seizures and/or collected and/or biological samples. Seizure means a substance available (seized) through law enforcement activities (police, customs, border guards, etc.). Collected samples are those that are actively collected by drug monitoring systems (such as test purchases) for monitoring and research purposes. Biological samples are those from human body fluids (urine, blood, etc.) and/or specimens (tissues, hair, etc.)

([7]) Many 'seizures' relate to individual case-level data, however, some data provided to the EMCDDA are aggregated at the country level. Some of the data from the United Kingdom are reported as 'records', where several records may come from the same case. Data is drawn from the Joint Report questionnaires and data provided in the bi-annual data gathering (EWS progress and final reports) and from individual Reporting forms submitted on an ad hoc basis.

products. Several of these products carry names that are associated with or similar to street-names used for cocaine, amphetamine or 'ecstasy' (MDMA). Other substances found along with MDPV in the same preparation include a wide range of new psychoactive substances (predominantly cathinones, but also phenethylamines, piperazines, synthetic cannabinoid receptor agonists and a range of other substances), adulterants such as benzocaine, lidocaine and caffeine and in a smaller number of cases, with substances that are internationally controlled or controlled at EU-level.

Where information has been provided, quantities of powder for single seizures ranged from 0.02 grams (Germany and Poland) to 5 kilograms (Czech Republic). Hungary reported a seizure of 300 yellow tablets bearing a heart logo and a separate seizure of two white tablets bearing markings resembling the Louis Vuitton 'LV' logo ([8]). Norway reported a seizure of 98 purple tablets bearing a spaceship/rocket logo. These tablet findings may suggest that MDPV is being sold as 'ecstasy'. There were also unmarked tablets reported in a variety of colours including white, grey, pink, reddish and green, although many of these were associated with 'legal high' products. A selection of images is provided in Annex 1.

More than 4500 individual MDPV powder cases have been reported, amounting to an excess of 200 kilograms of seized MDPV. The vast majority of these are small cases, however, 45 of these cases (reported by the Czech Republic, Finland, France, Hungary, Latvia, the Netherlands, Spain and Sweden) were in excess of 500 grams accounting for more than approximately one third of the total weight of powder seized. In 2011, for example, Customs authorities in Hungary made 7 separate seizures of MDPV powder amounting to approximately 14.5 kilograms. Belgium, the Czech Republic, Germany and Lithuania provided information that MDPV seized by customs authorities had been sent from China. No other non-EU countries were identified in the reports, although two Member States reported the interception of packages sent from another Member State. Several countries reported MDPV in powders contained in 'legal high' products with names such as Charlie Sheen, synthacaine or speedway pro (a full list of names is provided in Section 3.1 above).

There were over 500 cases involving MDPV tablets or capsules, containing approximately 30,000 tablets in total. Several countries reported tablets containing MDPV in branded 'legal high' products with names such as 'Yellow submarine', 'Doves red' and 'Mind candy' (a full list of names is provided in Section 3.1 above).

Biological samples

Eleven countries reported detections of MDPV in biological samples, including:

([8]) It is common to find markings on tablets sold as 'ecstasy' including those of popular cultural and iconic brands often having an association with quality. Louis Vuitton is a French fashion label.

- a total of 99 deaths: Finland (40 deaths), United Kingdom (32), Sweden (21), Poland (3), Austria, France and Norway (1) – see section 3.4.1 and Annex 2 for further details

- 107 analytically confirmed non-fatal intoxications: Sweden (99 cases), France (3), Italy (3) and Belgium (2)

- detections related to cases of suspicion of driving under the influence of drugs (Finland (514 in the period 2009-2013), Poland (1)); driving under the influence of drugs and other crimes (Norway (9), United Kingdom (1)); drug testing (Poland (1)); as well as unspecified detections in biological samples (Sweden (842), Hungary (387), United Kingdom (6) and Norway (6))

Collected samples

In addition to the detections of MDPV in seizures and biological samples, ten Member States (Austria, Cyprus, Denmark, France, Ireland, Italy, the Netherlands, Poland, Slovakia and the United Kingdom) also reported collected samples.

In Austria, 32 samples of powder were collected and analysed as part of the 'pill'-testing project run by 'ChEckiT!' between 2010 and 2013. The samples were sold as mephedrone, cocaine, MDPV and speed. In two cases, amphetamine and caffeine or bk-MBDB ([9]) were also detected.

France reported nine samples of powder collected from different venues. Where quantitative information is available, the weight ranged from 0.1 to 0.5 grams. In two of the samples alpha-PVP and pentedrone were also detected; in the other sample alpha-PVP and caffeine were detected. In one of the cases the sample was sold as cocaine.

In Ireland, MDPV was identified in products collected from headshops branded 'Hurricane Charlie', 'Dogs Bollix', 'Doves Red', 'Doves Ultra', 'Ivory Wave', 'Sextasy', 'Orange Orbits' and 'Stardust'.

In the Netherlands, the Drugs Information and Monitoring System (DIMS) detected MDPV in 27 samples (11 in 2010, 9 in 2012 and 7 in 2013). Where information is provided, the samples were sold at consumer level as sold as MDPV (1 sample), cocaine (3), synthetic cocaine (2), 'moji' (1), 6-APB ([10]) (2), 5-APB ([11]) (1) and 'meferon' (2).

Poland reported 887 cases of branded products containing up to 500mg of MDPV mostly in powder form, as well as in tablets and capsules. Other substances detected in these samples are other synthetic cathinones (naphyrone, methedrone,

([9]) 2-Methylamino-1-(3,4-methylenedioxyphenyl)butan-1-one, also known as butylone.
([10]) 6-(aminopropyl)benzofuran.
([11]) 5-(aminopropyl)benzofuran.

buphedrone, pentedrone methylone, 4-MEC, FMC, MDPBP, butylone, BMDP), phenethylamines (pFPP, fluoroamphetamine, 2C-E), synthetic cannabinoids (RCS-4, JWH-122, JWH-081), TFMPP, 5-HTP, creatine, lidocaine, and caffeine.

Slovakia reported a total of 304 collected samples; some of them were offered through online shops (i.e. www.euphoriashop.sk, www.hypnotic.sk) under a variety of names including 'Beep Beep', 'Long Play', 'Popeyes Sniff', 'Speed Way', etc. Other substances often detected in the samples include the synthetic cathinones buphedrone, N-ethylcathinone and methylone; 2-DPMP and piracetam.

A small number of collected samples were reported by Cyprus, Denmark, Italy and the United Kingdom. In 2010, Cyprus reported MDPV in two samples of a product of 500 mg labelled 'Ivory wave'. Denmark reported three samples of powder in 2013. Italy reported a sample of 0.5 grams of white powder purchased from the Internet and branded 'Ivory wave'. On the label at the back of the package, ingredients listed were 'water softening agents, Epsom salts, sodium bicarbonate, sodium chloride, amino acid blends, and naturally occurring trace elements and minerals'. No other substances in addition to MDPV were detected. The United Kingdom reported a sample of 33 grams of MDPV powder purchased from an Internet retailer (http://www.chembay.co.uk) in December 2008.

Further details of these collected samples, including information on the product labels, are provided in Annex 1.

3.3 Information on the involvement of organised crime in the manufacture or trafficking of the new psychoactive substance — Article 5.2(c) of the Decision

According to German authorities there are no links to suggest the involvement of organised crime groups in the production, trafficking and/or distribution of MDPV. It should be borne in mind that easy access to substances in and outside of the European Union (also in big amounts) via Internet shops indicates at least a certain level of organisation.

In addition, the interest and presence of organised crime groups in the phenomenon of new psychoactive substances can be easily concluded from enormous attainable financial profits they can obtain from this type of criminal activities.

Money laundering aspects

No information was received on money laundering in connection with the production and/or trafficking of MDPV.

Violence in connection with production, wholesale and distribution

No information was received on incidents of violence in connection with the production, wholesale and/or trafficking of MDPV.

3.4 A first indication of the risks associated with the new psychoactive substance, including the health and social risks, and of the characteristics of users — Article 5.2(d) of the Decision

3.4.1 First indication of health risks

Up to 107 non-fatal intoxications and 99 deaths, analytically confirmed to be associated with MDPV were reported by Austria, Belgium, Finland, France, Italy, Poland, Sweden, the United Kingdom and Norway. In addition, Germany, Greece, Hungary, Ireland and Slokavia reported further cases which have not been described below due to their non-confirmed status.

Non-fatal intoxications

Belgium reported two analytically confirmed linked non-fatal intoxications in which the patients presented were stimulated, hypertensive and tachycardic. Traces of cocaine and amphetamines were also detected in urine samples (not quantified). They both reported visual and auditory hallucinations and severe psychosis, paranoia and were aggressive. They were treated with antipsychotics and their status returned to normal after 3-4 days.

France reported three analytically confirmed non-fatal intoxication cases. In one case, a man was brought in to the emergency department by the police. In this case, delirium syndrome was reported, including hallucinations as well as rhabdomyolysis, tachycardia, hypotension, agitation, logorrhea and acute renal failure. The MDPV metabolite, pyrovalerone and cannabis were also detected in this case. In the second case, which was a 'forced hospitalisation', paranoid psychosis and aggression were noted. The symptoms reported were tachycardia, mydriasis, hypertension, agitation, profuse sweating, trembling, scarification and rhabdomyolysis. In this case, the route of administration was nasal and oral and the MDPV had been bought on the Internet. Methylone (4400 ng/ml) was also detected in this case. In the last case, where the detection of MDPV was in a sample of hair, the patient had also bought MDPV via the Internet and the route of administration was nasal. Symptoms reported were mydriasis and paranoid psychosis. Cannabis and alcohol were also detected in this case.

Italy reported three analytically confirmed non-fatal intoxications. The first was from August 2011 when a 20 year old male was admitted to hospital very agitated with tachycardia (HR ([12]) 115 bpm). He reported having consumed cannabis, alcohol and three white capsules. MDPV was found in urine (14 mg/L) and butylone was also present (concentration not provided). The patient was treated with benzodiazepines

([12]) Heart rate

and discharged two days later. The second case was from October 2012 and involved a 38 years old male who presented at the emergency department with agitation, mild tachycardia (HR 105 bpm), distress and psychotic symptoms. He also reported visual and auditory hallucinations. He reported to have taken ecstasy and synthetic drugs generally named as 'mefre, crystal and energy' by nasal insufflation. MDPV was detected in blood (12 mg/L) and urine (17 mg/L). Urine screening of ketamine, atropine, scopolamine, levamisole, mephedrone, butylone, 4-MEC, methoxetamine, APB ([13]) (isomers), 4-FA ([14]), and MDAI ([15]), resulted negative. The final case also occurred in October 2012 and involved a 27 years old male who presented at the emergency department. His father had found him in a state of agitation, confusion and anxiety. The patient reported having taken MDPV by intravenous injection for the last 3-4 days together with benzodiazepines to counteract the excitatory effect of MDPV. The MDPV had been purchased from the Internet as a 'bath salt'. Analysis of the patient's urine revealed MDPV (55 µg/L), alprazolam (113.79 µg/L) and hydroxyalprazolam (103.59 µg/L). Three days after admission, the patient returned to the hospital for a second urine analyses, as requested by sanitary authorities. The patient reported continuing his use of MDPV and this was confirmed by the detection of MDPV in urine at a concentration of 35 µg/L. The analyses also found 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) and alpha-hydroxyalprazolam (13.45 µg/L).

Sweden reported 459 non-fatal intoxications between 2007 and 2013 as follows: 2007 (1 case), 2008 (4), 2009 (15), 2010 (47), 2011 (32), 2012 (194) and 2013 (166). Of these, between 86 and 99 cases are known to be analytically confirmed ([16]). Two literature sources which describe a total of 99 non-fatal intoxications have been used for the purposes of describing the health risks. In the first report (Lindeman, et al., 2013), cases of stimulant toxicity were studied from one hospital in Sweden covering April-May for three consecutive years (2010 to May 2012). In April-May 2012 the number of patients with stimulant toxicity was 45 and 17 of these cases were examined toxicologically. Thirteen of these tested positive for MDPV and 12 of these were classified as chronic drug users with >60% noted to be HCV (Hepatitis C virus) positive. The second study (Bäckberg et al., 2013) focussed on the results of the STRIDA project which monitors trends in acute poisonings with novel recreational drugs in Sweden. The study summarises the results for the first 9 months in 2012 when MDPV was detected in 86 out of 321 samples. In 17 cases the symptoms were severe (Poisoning Severity Score - PSS 3 (Persson et al, 1998)) 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. It was noted by the authors

([13]) (Aminopropyl)benzofuran
([14]) 4-Fluoroamphetamine
([15]) 3,4-Methylenedioxyaminoindane
([16]) There is a potential that there may be an overlap of some cases reported by Lindeman et al., 2013 and the cases reported by Bäckberg et al., 2013

that among people that come to medical attention, the incidence of severe poisonings (PSS 3) was highest for MDPV.

Deaths

There were 99 deaths associated with MDPV that were analytically confirmed. These were reported by Austria (1), Finland (40), France (1), Poland (3), Sweden (21) the United Kingdom (32) and Norway (1) ([17]).

Austria

Austria reported one death which occurred in January 2012. The case involved a 'young man' who died from butylone (bk-MBDB) overdose in combination with MDPV, methylone and 4-MEC. No further details were provided.

Finland

Finland reported 40 deaths which occurred between September 2009 and August 2013. The cases were all analytically confirmed and where the concentration of MDPV was reported (20 cases) it ranged from 20-4800 mg/mL in blood; in all but one case, up to seven other substances were detected. In fourteen cases, five or more substances were detected in addition to MDPV. The most frequently encountered other substances detected were diazepam (22 cases), amphetamine (14), buprenorphine (14), temazepam (9), alprazolam (8), ethanol (7), morphine (3) and pregabalin (3). Causes of death reported were accidental poisoning (22 cases), suicidal poisoning (4), suicide resulting from crushing injuries (2), suicide by hanging (2), suicide by carbon monoxide poisoning (1), unspecified intoxication (1), unspecified death and cirrhosis of liver (1), accidental injury to thoracic aorta (1), accidental death due to multiple rib fractures (1), infective myocarditis disease (1) and homicide (1). The cause of death was not yet registered in three cases.

France

France reported one death that occurred in October 2012. The cause of death was drowning. MDPV was present at a concentration of 106 µg/L (blood) and 760 µg/L (urine). Other drugs detected were PVP ([18]) (blood 40 µg/L; urine 295 µg/L), pentedrone (blood 33 µg/L; urine 110 µg/L), hydroxyzine (blood 194 µg/L), nordiazepam (blood 47 µg/L), oxazepam (blood 8 µg/L), cannabinoic acid (blood 15.7 µg/L) and ethanol (blood 0.3 g/L). No further details were provided.

Poland

([17]) Hungary reported two indirect deaths which occurred in November 2011. No further details were provided and it is not known if these cases are analytically confirmed.

([18]) Pyrrolidinovalerophenone

Poland reported three deaths associated with MDPV. The first death was in September 2010 and the reported cause of death was 'metabolic dysfunction' caused by MDPV. The concentration of MDPV determined in blood was 430 ng/mL and ephedrine was also detected at a concentration of 324 ng/mL. No further details were available. The second and third cases were reported from 2011. One of the cases involved a road traffic collision where one driver suffered severe injuries, resulting in his death. During the police investigation, packages of white powders, called 'Ivory Speed' and 'Exclusive Dust' were found (Adamowicz et al., 2013). MDPV was detected in blood at a concentration of 38 ng/mL and buphedrone was also detected at a concentration of 127 ng/mL. The third case involved a man with a history of drug addiction who was found unresponsive after a night of partying. A witness reported that he had taken a product called 'Speedway' while at the party. The post mortem examination showed emaciation, external hydrocephalus and atherosclerosis. The man also suffered from human immunodeficiency virus (HIV) infection (Adamowicz et al., 2013). MDPV was detected in blood at a concentration of 17 ng/mL and in addition clonazepam (1.2 ng/mL) and 7-aminoclonazepam (96 ng/mL) were also detected.

Sweden

Sweden reported twenty-one deaths: 3 in 2010, 3 in 2011, 9 in 2012 and 6 in 2013. Brief comments were reported as follows: in 2010 the deaths were intoxications involving several substances (not further described); in 2011 none of the three deaths related only to MDPV; in 2012 there were several accidents, death by hanging and intoxications with several drugs (not further described); and in 2013 there was one car accident and intoxications with several drugs (not further described).

United Kingdom

The United Kingdom reported 32 deaths that occurred between January 2010 and an unspecified date in 2013 (12 in 2010, 8 in 2011, 12 in 2012 and 1 in 2013).

Where reported, the causes of death were noted to be hanging (7 cases), cardiac-related causes ([19]) (5), drug toxicity (4), drowning (2), carbon monoxide poisoning (2), asphyxia (1), multiple injuries (suicide) (2), hypovolemic shock due to laceration of left forearm associated with partial transection of cephalic vein (1). In the remaining cases the cause was either unascertained or not specified. In the cases of drug toxicity, MDPV was normally present with other drugs. Where reported, the most common other substances present were mephedrone (9 cases), 4-fluoromethcathinone (7), cocaine (4), amphetamine (4) and MDMA (3), although a range of other controlled drugs and medicines were also detected. MDPV was not

([19]) Specifically: heart attack (1 case), cardiac arrest (1), cardiac failure (1), coronary artery disease (1) and ischemic heart disease (1).

the sole cause noted in any of the cases and was specifically implicated as a contributory factor in nine of the cases.

Norway

Norway reported one death in 2012 in which MDPV was detected during the toxicological examination of blood. The cause of death in this case was not reported and no further information was provided.

Pharmacology and mode of action

Work by Baumann et al., (2013a) provides a systematic evaluation of the pharmacology and mode of action of MDPV using *in vitro* and *in vivo* studies in rodents ([20]). *In vitro* data shows that MDPV acts as a potent catecholamine-selective (dopamine and noradrenaline) transporter blocker (Table 1); sharing some similarities with the structurally related compound pyrovalerone. Compared to cocaine, MDPV is 50-fold more potent at DAT (dopamine transporter), 10-fold more potent at NET (norepinephrine transporter), and 10-fold less potent at SERT (serotonin transporter) (Baumann et al., 2013a). In addition the data also showed that MDPV does not act as a transporter substrate. Consistent with the *in vitro* data, *in vivo* microdialysis studies in rats found that MPDV increased extracellular concentrations of dopamine in the nucleus accumbens and was 10-fold more potent than cocaine; while *in vivo* locomotor activity testing (stereotypy and forward locomotion) and assessment of cardiovascular parameters (heart rate and blood pressure) found that MPDV is at least 10-fold more potent than cocaine in inducing locomotor activation, tachycardia and hypertension. The authors concluded that the 'potent blockade of dopamine uptake caused by MDPV predicts that the drug has a high risk for abuse, whereas the potent blockade of norepinephrine uptake portends dangerous cardiovascular stimulation' (Baumann et al., 2013a).

Simmler et al., (2012) using a human *in vitro* model assessed the blood-brain permeability of MDPV. They reported that MDPV exhibited particularly high blood-brain barrier permeability as compared to other synthetic cathinones (with the exception of mephedrone) as well as reference compounds such as MDMA and amphetamine. In addition they reported that the data for MDPV was consistent with active transport across the blood-brain barrier. The authors concluded that the potency of MDPV at the DAT and NET and high blood–brain barrier permeability could 'result in high sympathomimetic toxicity and risk of addiction in humans'.

No studies were identified that have examined the pharmacology and mode of action of MDPV in humans.

Meyer et al., (2010) and Strano-Rossi et al., (2010) provide data on the possible metabolites and metabolic pathways for MDPV *in vitro* using rat and/or human urine and human liver microsomes.

([20]) See also: Gregg and Rawls (2013); Huang et al., (2012);

Table 1. Transporter-mediated inhibition of uptake and stimulation of release in rat brain synaptosomes. Values are given as nM ± S.E.M. for N=3–4 experiments per drug. E_{max}% refers to percentage of maximal release response. Key: "—" indicate that compounds failed to elicit >30% of the maximal response and therefore compounds are considered inactive in the release assay. Modified from Baumann et al., (2013a,b).

Compound	DAT uptake IC_{50} (nM ± S.E.M.)	NET uptake IC_{50} (nM ± S.E.M.)	SERT uptake IC_{50} (nM ± S.E.M.)	DAT release EC_{50} (nM ± S.E.M.) [Emax %]	NET release EC_{50} (nM ± S.E.M.) [Emax %]	SERT release EC_{50} (nM ± S.E.M.) [Emax %]
MDPV	4.1 ± 0.5	26 ± 8	3349 ± 305	—	—	—
Cocaine	211 ± 19	292 ± 34	313 ± 17	—	—	—
Mephedrone	762 ± 79	487 ± 66	422 ± 26	51 ± 5 [102 ± 2]	58 ± 11 [99 ± 4]	122 ± 10 [101 ± 1]
Methylone	1232 ± 133	1031 ± 162	1017 ± 59	117 ± 12 [96 ± 1]	140 ± 17 [94 ± 2]	234 ± 35 [98 ± 2]
MDMA	1009 ± 39	450 ± 30	125 ± 11	42 ± 2 [100 ± 4]	53 ± 7 [95 ± 2]	39 ± 5 [103 ± 4]
Amphetamine	93 ± 17	67 ± 16	3418 ± 314	5.8 ± 0.4 [102 ± 1]	6.6 ± 0.7 [92 ± 1]	698 ± 71 [97 ± 2]

Toxicology

See 'Pharmacology and mode of action' (above) for an overview of some of the *in vitro* and *in vivo* animal data that is relevant to the toxicity of MDPV in humans.

Simmler et al., (2013) examined the cytotoxicity of MDPV *in vitro* using a cell membrane integrity assay which measures the release of adenylate kinase from damaged cells. MDPV did not show apparent cytotoxicity at concentrations of 10 and 100 µM after 4 h of incubation at 37°C. No studies were identified that have examined the toxicity of MDPV in humans.

The clinical features of acute toxicity associated with MDPV use as reported by the Member States are provided in section 3.4.1 'Non-fatal intoxications' and 'Deaths' as well as in Annex 2. These include a number of analytically confirmed cases. Case reports/series of intoxications where MDPV was analytical confirmed report similar findings (Spiller et al., 2011).

Methods for the toxicological screening of MDPV in urine have been reported by Strano-Rossi et al., (2010) and in blood by Marinetti and Antonides (2013).

Dependence and abuse potential

A review by Gregg and Rawls (2013) provides an overview of the *in vivo* animal behavioural pharmacology studies relevant to the possible abuse potential of MPDV

in humans ([21]). They note that in rats the administration of MDPV both lowered intracranial self-stimulation thresholds and led to self-administration across multiple doses; while in a progressive-ratio model of reinforcement, higher doses of MDPV produced the highest breakpoints (Aarde et al., 2013; Watterson et al., 2012). In addition, dose-substitution studies suggested that MDPV possessed greater potency and efficacy than methamphetamine; with escalation studies showing that MDPV increases drug intake at similar doses to those observed with methamphetamine (Watterson et al., 2012). Finally they note that studies in mice undertaken by Fantegrossi et al., (2013) found that MDPV discriminates from saline and fully substitutes for MDMA and methamphetamine.

The findings reviewed by Gregg and Rawls (2013) are supported by the work of Baumann et al., (2013) which are discussed in the section on 'Pharmacology and mode of action (above). They note that based on the 'potent and efficacious actions of MDPV on extracellular dopamine and motor activity' shown in their study suggests that MDPV has a high potential for abuse. In addition, they suggest that given that MDPV has weak effect on SERT this may further enhance the reinforcing effects of the drug given that studies have shown that elevations in synaptic serotonin can dampen the stimulant effects mediated by dopamine (Baumann et al., 2011; Wee et al., 2005). No studies were identified that have examined the dependence and abuse potential of MDPV in humans.

3.4.2 Characteristics of users

The section below includes a discussion of the characteristics of users which includes information from self-reported use from Internet drug discussion forums and related websites (hereafter 'user websites'). As such it is important to note that it is not possible to confirm the specific substance(s) used, nor the purity, dose, etc. Analysis of products containing new psychoactive substances that are sold on the drug market have shown that the composition can differ between that claimed by the retailer, as well as differ over different geographical areas and time. Similar caveats apply to these types of information that have been provided in case reports/series unless biological and collected samples were taken and subjected to toxicological and forensic analysis. In addition, the information provided by patients in case reports/series as well as that provided on user websites should be regarded as illustrative only and not taken as representative of users of MDPV in general. Finally, information from seizures, collected samples and user websites suggest that MDPV has been commonly sold as a 'legal' replacement for cocaine, amphetamine or 'ecstasy' (MDMA). There is also information to suggest that MDPV has been sold directly on the illicit drug market as cocaine, amphetamine and MDMA, as well as mephedrone. In these cases, users may be unaware that they are consuming MDPV. Additional research is required in order to examine to what extent the characteristics of MDPV users reflect those who use other stimulant drugs.

Route of administration, dose and drug regimens

([21]) See also Watterson et al., (2013).

Information provided by the Member States, as well as from case reports/series and user websites suggests the routes of administration for MDPV were mainly nasal (insufflation/sniffing) and oral (swallowing) or intravenous injection. Two countries reported that MDPV was detected in paper blotters and therefore buccal or sublingual administration may also occur. Furthermore, two countries reported the presence of MDPV in vegetable material, and this product would most probably be smoked. Information from user websites suggests that rectal administration may also be a route used.

Information from case reports/series and user websites suggest a range of doses are used that may depend on the route of administration. The Erowid user website includes a range of tentative 'common doses' for three routes of administration: insufflation 5-11 mg; oral 8-15 mg; rectal 6-12 mg (Erowid, 2013a). One case report noted that MDPV produces psychoactive effects with as little as 3 to 5 mg, depending on its route of administration, and the average dose is approximately 5 to 20 mg. This report goes on to say that repeated dosing is common to avoid unpleasant come-down being described with large single doses (Ross et al., 2012).

France also reported cases identified on the basis of interviews with patients. For one of these cases, the patient reported suffering malaise, tetany, language disorders and respiratory distress after taking MDPV by injection. Another patient suffered abnormal movements, trismus, profuse sweating, visual disorders, insomnia, anorexia, dysuria, vertigo and dysuria for 24 hours after he had injected the drug. He also reported having taken 4-MEC. Another patient suffered agitation, confusion and had attempted suicide after injecting the drug. He also reported taking MDMA and 'cathinone' as well. In addition, other symptoms reported included reduced appetite and weight loss, insomnia, loss of focus, absences, paranoia, sensation of cold and sensation of electrical discharge in heels by patients who had taken MDPV intransally. The drug had been bought on the internet. A range of other effects were also noted, such as insomnia, psychomotor agitation (experienced for three days by an injecting user); anxiety, intellectual stimulation, obsession to consume MDPV, withdrawal symptoms, fatigue, sleep disorder and pain at the site of injection; chest pain, accelerated heart rate and sensation of warmth (injecting user); agitation, facial erythrosis, dryness of the mucous and anxiety for 5 days for a patient with intranasal use. Two others reported sexual stimulation and increased sociability.

Two studies are available that report the injection of MDPV, although its injection is documented in other countries, such as France, Romania and Finland. In the first study, 183 clients of a needle exchange programme in Hungary agreed to report their drug using habits (Csák et al., 2013). This 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 persons, 45.1%) as had 10 (41.7%) of the former heroin injectors and 11 (78.6%) of those using other substances (cocaine and mephedrone). The second study (Lindeman, et al., 2013), also mentioned in Section 3.4.1, was initiated due to a sharp rise in the

number of enquiries to the Swedish Poisons Information Centre regarding intoxications with MDPV. Of particular note is that of the patients with confirmed or suspected MDPV consumption, 95% were classified as chronic drug users and > 60% were reported as positive for hepatitis virus C.

Information from user websites suggest that MDPV may be used on its own as well as in combination with other new psychoactive substances, controlled drugs and/or prescription medication (Erowid, 2013b; Drugs Forum, 2013). In most of the cases of non-fatal intoxications and deaths reported by the Member States other new psychoactive substances and/or controlled drugs were detected in biological samples (Section 3.4.1 and Annex 2).

Subjective effects

No studies were identified that have examined the subjective effects of MDPV in humans; information is largely limited to that provided in case reports/series (see 'non-fatal intoxications' and section above) and self-reported experiences from user websites. Table 2 provides an overview of self-reported duration of effects when MDPV is taken by the oral and insufflated routes as reported by Erowid (2013c). Table 3 provides an overview of subjective effects of MDPV as reported by Erowid (2013c). In both cases, the information was collated from users, research, and other resources. No further details were provided on the methodology used to collate this information. Information provided in case reports and case series of non-fatal intoxications associated with MDPV appear to support some of these effects. The section on 'non-fatal intoxications', above, provides an overview of the other adverse effects reported to be associated with MDPV.

Table 2. Examples of self-reported duration of effects of MDPV per route of administration (tentative) as reported by Erowid (2013c). No information on the doses that were used was provided.

Duration of effects for MDPV	Oral	Insufflated
Total Duration	2.0–7.0 hrs	2.0–3.5 hrs
Onset	15–30 mins	5–20 mins
Coming Up	30–60 mins	15–30 mins
Plateau	30–180 mins	30–100 mins
Coming Down	30–120 mins	30–60 mins
After effects	2–48 hours	1–7 days
Hangover / Day After	?	?

Table 3. Examples of subjective effects of MDPV as reported by Erowid (2013a). No information on the doses that were used was provided.

Subjective effects of MDPV	
Positive	Stimulation (mental and physical) Euphoria, mood lift Increased sociability / talkativeness Increased productivity and motivation Increased mental clarity Enhanced creativity Feelings of empathy Sexual arousal
Neutral	Stimulation (mental and physical) Mild elevation in heart rate
Negative	(Likelihood of negative side effects increases with higher doses) Tightened jaw muscles, grinding teeth (trismus and bruxia) Reduced enjoyment of eating / loss of appetite Disturbed sleep patterns Involuntary body movements (twitching, lip-smacking, etc.) Confusion and/or scrambled thoughts Gastrointestinal disturbance Muscle tension Residual depressed mood Nystagmus / eye spasm Anxiousness / nervousness / paranoia Harsh comedown effects Fiending (redosing repeatedly without planning to do so) Excessive excitation / hyperactivity Headache Very elevated heart rate Hallucinations / psychotic behavior (at high doses or with repeated use)

Availability, supply, price

A search of google.com using the search string 'buy 'MDPV'' conducted by the EMCDDA in December 2013 for the Joint Report identified a number of online shops offering MDPV for sale in both retail and wholesale quantities. In the former case, MDPV may be sold as a 'research chemical'.

Data from the National Drug and Alcohol Research Centre's deep web monitoring programme of the Silk Road marketplace ([22,23]) (Van Buskirk et al., 2013) identified seven retailers in early February 2013 offering MDPV for sale. Details of the specific quantities and prices were not provided. The number of such retailers was relatively

([22]) The National Drug and Alcohol Research Centre (NDARC) is based at the University of New South Wales, Sydney, Australia

([23]) Silk Road is an anonymous, international online marketplace that operates as a Tor hidden service. It uses the peer-to-peer payment network and digital currency Bitcoin for monetary transactions. The original Silk Road marketplace was seized and taken offline on 2 October 2013 by the United States Federal Bureau of Investigation. Since then a new version of Silk Road, sometimes described as 'Silk Road 2.0', has become operational. See Christin (2012) for an overview of the original Silk Road.

stable over the preceding four months of monitoring ([24]). It is important to note that the study was conducted before Silk Road was seized and taken offline in October 2013 by the United States Federal Bureau of Investigation. No studies were identified that have examined the sale of MDPV since Silk Road has reopened.

Seizure data as well as information from collected samples reported by the Member States suggests that MDPV is sold as a drug in its own right and directly on the illicit drug market as cocaine, amphetamine, MDMA and mephedrone.

3.5 Information on whether or not the new substance is currently under assessment, or has been under assessment, by the UN system — Article 5.2(e) of the Decision

The World Health Organization is the specialised United Nations agency designated for the evaluation of the medical, scientific and public health aspects of psychoactive substances under the Single Convention on Narcotic Drugs, 1961 and the Convention on Psychotropic Substances, 1971. On 10 October 2013, the World Health Organization informed the EMCDDA that MDPV is currently under assessment and *'the critical review report will be published only early next year (probably April)'*.

Article 7.1 of Council Decision states that '*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 Joint Report has been produced on the understanding that MDPV is not at an advanced stage of assessment within the United Nations system.

3.6 The date of notification on the Reporting Form of the new psychoactive substance to the EMCDDA or to Europol — Article 5.2(f) of the Decision

The first official EMCDDA–Europol notification of MDPV dates from December 2008 from the Finnish National Focal Point. The Reporting Form details a seizure of two quantities of white powder (each of 1 gram) intercepted by customs authorities on 24 November 2008 in incoming mail. The powders were in packages marked '1-(3,4-

([24]) Nine retailers were identified in late October 2012; 10 in mid-November 2012; 10 in late November 2012; 10 in mid-December 2012; 9 in early January 2013; and 9 in mid-January 2013. See Christin (2012) for a discussion of some of the market characteristics and dynamics of the original Silk Road.

methylenedioxyphenyl)-2-pyrrolidinyl-pentan-1-one, purity 99 +%, 1g'. Identification was based on the analytical technique of GC-MS ([25]).

MDPV was added to the list of new psychoactive substances monitored by the EMCDDA and Europol through the European Union early warning system and a profile of the substance was created in the EMCDDA European Database on New Drugs (EDND). Since then analytical details, background information and information relevant to public health have been exchanged between EMCDDA, Europol and the Member States on an ad hoc basis. The Commission and the EMA were kept duly informed.

3.7 Information on whether or not the new psychoactive substance is already subject to control measures at national level in a Member State — Article 5.2(g) of the Decision

Twenty Member States (Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, France, Germany, Hungary, Ireland, Finland, Italy, Latvia, Luxembourg, Poland, Slovakia, Slovenia, Sweden, and the United Kingdom) as well as Turkey and Norway control MDPV under drug control legislation.

In Belgium it was added to the list of substances on 20 March 2013. In Bulgaria it is controlled under the Narcotic Substances Control Law since February 2011. In Croatia it is included in the List of drugs, psychotropic substances, plants used to produce drugs and substances that can be used in the production of drugs. In Cyprus it is controlled under the Narcotic Drugs and Psychotropic Substances Law of 1977 as a class B drug that is covered by the generic definition of cathinones. In the Czech Republic it has been included in the Act 167/1998 Coll. on addictive substances. In Denmark it is covered by the Executive Order on Euphoriant Substances. In Estonia it is listed in the Regulation No.73 of the Minister of Social Affairs since 29 November 2010. In Finland it has been listed in the Narcotics Act 373 of 2008 since 28 June 2010. In France it was added to the controlled narcotic substance list since 2 August 2012. In Germany it is included in the list covered by the Narcotic Substance Law since 26 July 2012. In Hungary it is listed in Schedule A (psychotropic substances) of Act XXV of 1998 on human pharmaceuticals. In Ireland it was covered by the Misuse of Drugs Acts since 11 May 2010. In Italy it is controlled generically as it is a derivative of 2-amino-1-phenyl-1-propanone, under the Decree of the President of the Republic 309/90 since 29 December 2011. In Latvia it is controlled according to Cabinet Regulation 847 'Regulations regarding narcotic substances, psychotropic substances and precursors to be controlled in Latvia'. In Luxembourg it has been controlled by the drug control legislation since 30 July 2012. In Poland it is covered by the Act of 15 April 2011 amending the Act of Counteracting Drug Addiction. In Slovakia it is in the 1st. schedule of psychotropic substances set by the Act. No 139/1998 Coll. as amended by the Act. No 43/2011 Coll., which came into force on 1 March 2011. In Slovenia it was included by the Decree on amending the Decree on

([25]) Gas chromatography-mass spectrometry

classification of illicit drugs, Official Gazette of RS No. 62/2013. In Sweden it comes under the Narcotic drugs control Act (SFS 1992-860) and the Narcotic drugs control Ordinance (SFS 1994:1554). In the United Kingdom, it was included in the generic definition of substituted cathinone derivatives placed under the Misuse of Drugs Act 1971 in April 2010. In Turkey it is listed in the Law on Control of Narcotics no.2313. In Norway it has been included by generic scheduling since 14 February 2013.

Three Member States (Austria, Portugal and Romania) control MDPV under legislation penalising unauthorised supply of defined or qualifying new psychoactive substances. In Austria it is controlled under the generic definition within the New Psychoactive Substances Act. 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).

In the Netherlands, the sale of MDPV in consumer amounts it is treated as being a medicinal product and must comply with medicines legislation (and general product safety legislation).

Greece, Lithuania and Malta have reported that MDPV is not subject to control measures at the national level.

No information was provided regarding the control status of MDPV in Spain.

3.8 Further information — Article 5.2(h) of the Decision

3.8.1 The chemical precursors that are known to have been used for the manufacture of the substance

No information was reported by the Member States, Turkey or Norway about the chemical precursors or manufacturing methods used to make MDPV. Methods for the production of MDPV are documented in the scientific literature.

3.8.2 The mode and scope of the established or expected use of the new substance

MDPV has been marketed and sold through online shops as a branded ‘legal high’ product and as a ‘research chemical’. MDPV was not declared as an ingredient of the products. This has been confirmed by Denmark, Slovakia and the United Kingdom, each of which reported finding MDPV in samples of branded legal high products purchased from the Internet. Furthermore, both Ireland and Poland reported significant numbers of branded ‘legal high’ products collected from bricks and mortar shops (Kelleher et al.,2011). It is also important to note that information from the Member States (such as seizures, collected samples and non-fatal intoxications) and also from user websites suggest that MDPV may be commonly sold as a ‘legal’

replacement for cocaine, amphetamine or MDMA. It is also sold directly on the illicit drug market as these drugs ([26]). The use of MDPV by injecting drug users has also been noted (see below). As a result, the mode and scope of use of MDPV may, in part, overlap and/or reflect the mode and scope of use of other stimulants used in recreational settings and by problematic drug users including those who inject. Additional research is required in order to examine to what extent, if any, the mode and scope of MDPV use overlaps and/or reflects those groups.

Settings of use

One of the deaths reported by Poland noted the use of MDPV in the context of recreational use (at a party). Samples have been collected from dance venues in Austria and the Netherlands where it was reported to have been sold as mephedrone, cocaine, MDPV and speed (Austria), and cocaine, synthetic cocaine, 'moji', 6-APB, 5-APB, MDPV and 'meferon' (the Netherlands). France reported that MDPV was 'generally used at home during sexual context' (not further described). Sweden reported that 'MDPV was popular two years ago among stimulant users, age group 20-30 years; they used MDPV at parties or at home (private parties that lasted from Friday night till Sunday night) and at times not regularly; at the moment MDPV is not present, the users stopped using it because of negative side effects, mostly depression and strong craving.'

Price

Six countries reported the price of MDPV. France reported that MDPV was sold at between 2 and 15 EUR per gram. Hungary reported a price of 13.5 EUR (quantity not specified). Italy reported that prices were from 14.95 EUR for 0.5 grams to 169 EUR for 10 grams (source: http://www.spicestore247.biz/mdpv-1). The Netherlands reported information from a forum discussion which included prices for MDPV of 35 EUR per gram and 160 EUR for 5 grams. Romania reported a price of 25 EUR (quantity not specified). Spain reported that when MDPV was sold as cocaine the price was 50 to 60 EUR per gram and when it was sold as MDPV the price was 20 EUR per gram. In 2011, the EMCDDA conducted a study of Internet sites selling new psychoactive substances (EMCDDA, 2012). MDPV was found to be on sale in January 2011 and July 2011 in 25 and 32 shops respectively and the price was reported to be 115 to 239 EUR for 10 grams.

3.8.3 Other use of the new psychoactive substance and the extent of such use, the risks associated with this use of the new psychoactive substance, including the health and social risks

No information was provided by any Member State, Turkey or Norway that indicated that MDPV had any other use apart from legitimate scientific research and as an analytical reference standard.

([26]) Other NPS and adulterants such as caffeine and lidocaine have been found in samples.

From the available information it does not appear that MDPV is used in the manufacture of a medicinal product in the European Union. However, the collection of information cannot be considered exhaustive in the absence of an European Union database on the synthetic routes of all medicinal products ([27]).

4. Information from the EMA as requested by Article 5.3 of the Decision

4.1 Marketing authorisation

Twenty-five Member States, Norway and Iceland responded to the EMA's information request (see section 2) reported that the new psychoactive substance MDPV has not obtained a marketing authorisation ([28]).The EMA also reported that the new psychoactive substance MDPV has not obtained a marketing authorisation through the central authorisation procedure.

4.2 Application for a marketing authorisation

Twenty-five Member States, Norway and Iceland responded to the EMA's information request (see section 2) reported that the new psychoactive substance MDPV is not the subject of an application for a marketing authorisation ([28]). The EMA also reported that the new psychoactive substance MDPV is not the subject of an application for a marketing authorisation through the central authorisation procedure.

4.3 Suspended marketing authorisation

Twenty-five Member States, Norway and Iceland responded to the EMA's information request (see section 2) reported that there had been no cases of a suspended marketing authorisation that had been granted in respect of the new psychoactive substance MDPV ([28]). The EMA also reported that the new psychoactive substance MDPV is not the subject of a suspended marketing authorisation through the central authorisation procedure.

5. Conclusions

MDPV is a synthetic cathinone derivative, which is closely related to pyrovalerone. MDPV has been present in the EU drug market since at least November 2008 and has been detected in up to 107 non-fatal intoxications and 99 deaths, particularly in

([27]) i.e. products that have been granted a marketing authorisation, or where an application for a marketing authorisation has been made, or where the marketing authorisation has been suspended.

([28]) Austria, Belgium, Croatia, Czech Republic, Denmark, Estonia, Germany, Greece, Hungary, Iceland, Ireland, Netherlands, Norway, Portugal, Slovenia, Spain, Sweden and the United Kingdom provided responses in relation to both human and veterinary medicinal products. Cyprus, Italy, Lithuania, Malta, Romania and Slovakia provided responses in relation to human medicinal products. France, Latvia and Poland provided responses in relation to veterinary medicinal products. In addition the EMA provided information in relation to both human and veterinary medicinal products in respect to the central authorisation procedure.

Finland and the United Kingdom. There are some indications that it has been sold as a ‘legal’ or synthetic version of cocaine and it has also been found in tablets resembling ‘ecstasy’. Large seizures have been made at borders and police operations have targeted its supply. Powder seizures have been reported including multi-kilogram quantities. Most, but not all the Member States have control measures at national level that cover MDPV, however, it continues to be available and this is concerning. We conclude that the health and social risks caused by the manufacture, trafficking and use of MDPV, and in particular the involvement of organised crime and possible consequences of EU-level control measures, could be thoroughly assessed through a risk assessment procedure in accordance with Article 6 of Council Decision 2005/387/JHA.

References

1. Aarde, S.M., Huang, P.K., Creehan, K.M., Dickerson, T.J., Taffe, M.A. (2013), 'The novel recreational drug 3,4-methylenedioxypyrovalerone (MDPV) is a potent psychomotor stimulant: self-administration and locomotor activity in rats', Neuropharmacology, 71 pp. 130–40.

2. Adamowicz, P., Gil, D., Skulska, A. and Tokarczyk, B. (2013), 'Analysis of MDPV in blood – determination and interpretation', Journal of Analytical Toxicology, 37 pp. 308–12.

3. Bäckberg, M., Westerbergh, J., Al-Saffar, Y., Lindeman, E. and Helander, A. (2013), 'Trends in intoxications of novel psychoactive substances in Sweden during 2012', Clinical Toxicology, 51 pp. 256–57.

4. Baumann, M. H., Clark, R. D., Woolverton, W. L., Wee, S., Blough, B. E. and Rothman, R. B. (2011), 'In vivo effects of amphetamine analogs reveal evidence for serotonergic inhibition of mesolimbic dopamine transmission in the rat', Journal of Pharmacology and Experimental Therapeutics, 337 pp. 218–25.

5. Baumann, M.H., Partilla, J.S., Lehner, K.R., Thorndike, E.B., Hoffman, A.F., Holy, M., Rothman, R.B., Goldberg, S.R., Lupica, C.R., Sitte, H.H., Brandt, S.D., Tella, S.R., Cozzi, N.V., Schindler, C.W. (2013a), 'Powerful cocaine-like actions of 3,4-methylenedioxypyrovalerone (MDPV), a principal constituent of psychoactive 'bath salts' products', Neuropsychopharmacology, 38 pp. 552–62.

6. Baumann MH, Partilla JS, Lehner KR. (2013b), 'Psychoactive "bath salts": not so soothing', European Journal of Pharmacology, 698 pp. 1–5.

7. Csák, R., Demetrovics, Z., Rácz, J. (2013), 'Transition to injecting 3,4-methylene-dioxy-pyrovalerone (MDPV) among needle exchange program participants in Hungary', Journal of Psychopharmacology, 27 pp. 559–563.

8. Drugs Forum 2013
   http://www.drugs-forum.com/forum/showthread.php?t=125796

9. Erowid 2013a
   http://www.erowid.org/chemicals/mdpv/mdpv_dose.shtml

10. Erowid 2013b
    http://www.erowid.org/experiences/subs/exp_MDPV_Combinations.shtml

11. Erowid 2013c
    http://www.erowid.org/chemicals/mdpv/mdpv_effects.shtml

12. Fantegrossi, W.E., Gannon, B.M., Zimmerman, S.M., Rice, K.C. (2013), 'In vivo effects of abused 'bath salt' constituent 3,4-methylenedioxypyrovalerone (MDPV) in mice: drug discrimination, thermoregulation, and locomotor activity', Neuropsychopharmacology, 38 pp. 563–73.

13. Gregg, R.A., Rawls, S.M. (2013), 'Behavioral pharmacology of designer cathinones: A review of the preclinical literature', Life Science. doi:10.1016/j.lfs.2013.10.033.

14. Kelleher, C., Christie, R., Lalor, K., Fox, J., Bowden, M., O'Donnell, C. (2011), 'An overview of new psychoactive substances and the outlets supplying them'. Dublin: National Advisory Committee on Drugs.

15. Lindeman, E., Hultén, P., Carlvik, B., Ström, S., Enlund, M., Al-Saffar, Y., Helander, A. (2013), 'The impact of an MDPV-epidemic on a medium sized Swedish city.' Clinical Toxicology, 51 pp. 257.

16. Marinetti, L. J., Antonides, H. M. (2013), 'Analysis of synthetic cathinones commonly found in bath salts in human performance and postmortem toxicology: method development, drug distribution and interpretation of results', Journal of Analytical Toxicology, 37 pp. 135–46.

17. Meyer, M.R., Du, P., Schuster, F., Maurer, H.H. (2010), 'Studies on the metabolism of the α-pyrrolidinophenone designer drug methylenedioxy-pyrovalerone (MDPV) in rat and human urine and human liver microsomes using GC-MS and LC-high-resolution MS and its detectability in urine by GC-MS', Journal of Mass Spectrometry, 45 pp. 1426–42.

18. Persson, H. E., Sjöberg, G. K., Haines, J. A., Pronczuk de Garbino, J. (1998), 'Poisoning severity score. Grading of acute poisoning', Journal of Toxicology-Clinical Toxicology, 36 pp. 205–13.

19. Ross, E.A., Reisfield, G.M., Watson, M.C., Chronister, C.W., Goldberger, B.A., (2012), 'Psychoactive "bath salts" intoxication with methylenedioxypyrovalerone.' American Journal of Medicine, 125 pp 854–58.

20. Simmler, L.D., Buser, T.A., Donzelli, M., Schramm, Y., Dieu, L.H., Huwyler, J., Chaboz, S., Hoener, M.C., Liechti, M.E. (2013) 'Pharmacological characterization of designer cathinones in vitro,' British Journal of Pharmacology, 168 pp. 458–70.

21. Spiller, H.A., Ryan, M.L., Weston, R.G., Jansen, J. (2011), 'Clinical experience with and analytical confirmation of "bath salts" and "legal highs" (synthetic cathinones) in the United States', Clinical Toxicology, 49 pp. 499–505.

22. Strano-Rossi, S., Cadwallader, A.B., de la Torre, X., Botrè, F. (2010), 'Toxicological determination and in vitro metabolism of the designer drug methylenedioxypyrovalerone (MDPV) by gas chromatography/mass spectrometry and liquid chromatography/quadrupole time-of-flight mass spectrometry', Rapid Communications in Mass Spectrometry, 24 pp. 2706–14.

23. Van Buskirk, J., Roxburgh, A., Bruno, R., Burns, L. (2013). Drugs and the Internet, Issue 1, August 2013. Sydney: National Drug and Alcohol Research Centre. http://ndarc.med.unsw.edu.au/sites/default/files/ndarc/resources/DrugsTheInternet_Newsletter%20FINAL%20with%20ISSN.pdf

24. Watterson, L.R., Watterson, E., Olive, M.F. (2013), ‘Abuse liability of novel 'legal high' designer stimulants: evidence from animal models’, Behavioural Pharmacology, 24 pp. 341–55.

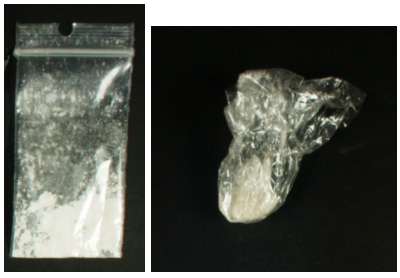
25. Watterson, L.R., Kufahl, P.R., Nemirovsky, N.E., Sewalia, K., Grabenauer, M., Thomas, B.F., Marusich, J.A., Wegner, S., Olive, M.F. (2012), ‘Potent rewarding and reinforcing effects of the synthetic cathinone 3,4-methylenedioxypyrovalerone (MDPV)’, Addiction Biology. doi:10.1111/j.1369-1600.2012.00474.x.

26. Wee, S., Anderson, K. G., Baumann, M. H., Rothman, R. B., Blough, B. E. and Woolverton, W. L. (2005), ‘Relationship between the serotonergic activity and reinforcing effects of a series of amphetamine analogs’, Journal of Pharmacology and Experimental Therapeutics, 313 pp. 848–54.

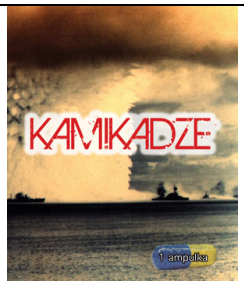
Annex 1

EMCDDA–Europol Joint Report on a new psychoactive substance: MDPV

Images of MDPV from seizures and collected samples

Country	Image	Description
Belgium		**Seizure, November 2010** 40.35 g white powder divided over 74 small bags, seized in Brussels. Seizing authority: police
Germany		**Seizure, September 2010** 1 kilo of a white powder, seized in Feucht. Seizing authority: police
Hungary		**Seizure, July 2009** 300 yellow tablets, seized in Budapest. Seizing authority: police
Hungary		**Seizure, April 2011** 2 white tablets, seized in Pest county. Contents: MDPV and 4-FMC. Seizing authority: police

Ireland		**Collected sample, analysed in March 2010** white/off-white powder (Hurricane Charlie, Dogs Bollix, Doves Red, Doves Ultra, Ivory Wave, Sextasy, Orange Orbits, Stardust), head-shop
Italy		**Seizures, 2011** Numerous seized samples (powders, agglomerated powders, tablets), seized in Treviso. Contents: MDPV, 4-FA, cocaine and lidocaine or procaine. Seizing authority: Police Department, Treviso
Malta		**Seizure, March 2011** 30 packets containing white powder – 15 g in all., seized in Attard. (€ 13.5 per gram) Seizing authority: Police Drug Squad
Slovakia		**Collected sample, analysed in March 2010** 310 mg deep blue powder, colourless capsule Contents: MDPV and mephedrone not quantified Collecting authority: National Drug Service of Bureau of Fight against Organised Crime Police Force Headquarters; analyse was completed by Institute of the Forensic Science of Police Force (IFS).
Slovakia		**Collected sample, analysed in September 2010** 310 mg white powder, colourless capsule Contents: MDPV and Butylone not quantified Collecting authority: National Drug Service of Bureau of Fight against Organised Crime Police Force Headquarters; analyse was completed by Institute of the Forensic Science of Police Force (IFS).

	 KAMIKADZE 1 ampułka	

Annex 2 — Table of non-fatal intoxications and deaths where MDPV has been analytically confirmed in biological samples

Non-fatal intoxications

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. Symptoms included hallucinations and severe psychosis, paranoia, visual and auditory hallucinations, aggressiveness. Hypertension, tachycardia. Treated with antipsychotics. Status normal after 3-4 days
Belgium	Aug 2011 (M, 34)	Urine	+	cocaine (+) amphetamines (+)	First time MDPV use. Drug taken orally. Symptoms included hallucinations and severe psychosis, paranoia, visual and auditory hallucinations, aggressiveness. Hypertension, tachycardia. Treated with antipsychotics. 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 (+)	Symptoms included delirium syndrome, hallucination. Rhabdomyolysis, tachycardia, hypotension, agitation, logorrhea, acute renal failure. Man brought in to the emergency by the police.
France	Date not specified (M, 25)	Blood	+	methylone (4400 ng/ml)	Symptoms included tachycardia, mydriasis, hypertension, agitation, profuse sweating, trembling, scarification, rhabdomyolysis. Paranoid Psychosis, aggressivity. Route of administration: inhaled and oral. 10g. Bought on the internet. In combination with methylone. Forced hospitalization

Country	Date	Sample type	MDPV result	Results for other substances	Notes
France	Date not specified (M, 22)	Hair	+	alcohol (+) cannabis (+)	Intranasal ingestion. Duration of action: 2 days. Symptoms: mydriasis, paranoid psychosis.
Italy	Aug 2011 (M, 20)	Urine	14 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 ([29]) isomers (-) 4-fluoroamphetamine (-) MDAI ([30]) (-)	The patient was admitted to the emergency department and reported having consumed (sniffing) ecstasy and synthetic drugs generally named as “mefre, crystal and energy”. Symptoms included agitation, mild tachycardia (Fc 105 bpm), distress, psychotic symptoms, visual and auditory hallucinations. During the first 24 hours, the patient was treated with fluids, benzodiazepine and haloperidol and transferred to a psychiatric ward.

[29] (Aminopropyl)benzofuran
[30] 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)	At arrival in the emergency department the patient reported having consumed 3,4-methylenedioxypyrovalerone (MDPV) intravenously, for the last 3-4 days together with benzodiazepine, to counteract the excitatory effect of MDPV. Symptoms included psychomotor agitation, confusion and anxiety. Anamnestic information from the patient revealed previous use of pentedrone and 3-methylmethcathinone abandoned for decreased interest on these substances. Three days after admission, the patient had a second urine analyses, and reported having continued his use of MDPV MDPV was purchased via Internet and marketed as "bath salt"
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 symptoms 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]

Deaths

	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*	Sept 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	Sept 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 ([31]) (<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

[31] Δ9-tetrahydrocannabinol, the main psychoactive substance in cannabis

	Country	Date	Biological sample	MDPV result	Results of toxicological analysis for other substances	Notes
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 ([32]) (0.0061 mg/L)	Accidental death, poisoning by drugs or medicaments

[32] Δ9-tetrahydrocannabinol, the main psychoactive substance in cannabis

	Country	Date	Biological sample	MDPV result	Results of toxicological analysis for other substances	Notes
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
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

	Country	Date	Biological sample	MDPV result	Results of toxicological analysis for other substances	Notes
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 ([33]) (+)	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 ([34]) (+) 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

[33] Δ9-tetrahydrocannabinol, the main psychoactive substance in cannabis
[34] (Diphenylmethyl)piperidine.

	Country	Date	Biological sample	MDPV result	Results of toxicological analysis for other substances	Notes
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 ([35]) 71%)
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 ([36]) (0.01 mg/L) amphetamine (1.8 mg/L)	Accidental death, poisoning by narcotics

[35] Carboxyhaemoglobin

	Country	Date	Biological sample	MDPV result	Results of toxicological analysis for other substances	Notes
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 ([37]) (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 ([38]) (0.60 mg/L) amphetamine (1.6 mg/L) Vitreous humor: ketamine (+)	Accidental death, multiple fractures of ribs

[36] 2,3-dimethylmethcathinone
[37] Gammahydroxybutyrate
[38] α-Pyrrolidinovalerophenone

	Country	Date	Biological sample	MDPV result	Results of toxicological analysis for other substances	Notes
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 [39](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

[39] Δ9-tetrahydrocannabinol, the main psychoactive substance in cannabis

	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	Norway	2012	Blood	+	None reported	Cause of death not reported.
44	Poland	Sep 2010	Blood	430 ng/mL	ephedrine (324 ng/mL)	Cause of death: 'metabolic dysfunction' caused by MDPV
45	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]
46	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]
47-49	Sweden	2010	Not specified	+	None reported	3 cases The deaths were intoxications involving several substances (not further described)

	Country	Date	Biological sample	MDPV result	Results of toxicological analysis for other substances	Notes
50-52	Sweden	2011	Not specified	+	None reported	3 cases None of the 3 deaths related only to MDPV
53-61	Sweden	2012	Not specified	+	None reported	9 cases There were several accidents, death by hanging and intoxications with several drugs (not further described)
62-67	Sweden	2013	Not specified	+	None reported	6 cases There was one car accident and intoxications with several drugs (not further described)
68-69	United Kingdom	Jan-Dec 2010	Blood Urine	+	<u>Case 1</u> fluoromethcathinone (+) mirtazapine(+) olanzapine (+) amphetamine (+) <u>Case 2</u> fluoromethcathinone (+) ibuprofen(+)	2 cases Case 1 – hit by train Case 2 – bag over head

	Country	Date	Biological sample	MDPV result	Results of toxicological analysis for other substances	Notes
70-72	United Kingdom	Jan-Dec 2011	Blood Urine	+	Case 1 ketamine (+) Case 2 quetiapine (+) Case 3 fluoromethcathinone (+) MDMA ([40]) (+) methylone (+) MDAI ([41]) (+) 5-IAI ([42]) (+) methoxetamine (+) AMT ([43]) (+)	3 cases Case 1 – hanging Case 2 – no circumstances reported Case 3 – found at home
73-83	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)

[40] Methylenedioxymethylamphetamine (commonly known as 'ecstasy')
[41] 3,4-Methylenedioxyaminoindane
[42] 5-Iodoaminoindane
[43] Alpha-methyltryptamine

	Country	Date	Biological sample	MDPV result	Results of toxicological analysis for other substances	Notes
84	United Kingdom	Jan-Dec 2013	Blood Urine	+	methadone (+) morphine (+) mirtazapine (+) diazepam (+) zopiclone (+) codeine (+)	Methadone intoxication
85	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.
86	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.
87	United Kingdom	Jul 2010 (M, 26)	Blood Gastric	+ (blood) + (gastric)	pyrovalerone (+ in blood) (+ in gastric sample) THC-acid ([44]) (+ 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.
88	United Kingdom	Apr 2010 (F, 45)	Blood	+	mephedrone (+) GBL ([45]) (+) methylone (+)	Mixed drug toxicity. Implicated: methedrone, GBL and methylone. Cause of death non-dependent abuse of drugs. Coroner's verdict: open verdict/unascertained.

[44] Δ9-tetrahydrocannabinolic acid, a breakdown product of Δ9-tetrahydrocannabinol, the main psychoactive substance in cannabis
[45] Gammabutyrolactone

	Country	Date	Biological sample	MDPV result	Results of toxicological analysis for other substances	Notes
89	United Kingdom **	Nov 2010 (F, 29)	Blood Urine	<LOD (blood) + (urine)	alcohol (63 mg/100mL in blood) (118 mg/100mL in urine) mephedrone (<LOD ([46]) 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
90	United Kingdom	Jun 2010 (M, 39)	Blood	0.13 µg/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.
91	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.
92	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

[46] Limit of detection – the lowest amount that can be detected by the method used.

	Country	Date	Biological sample	MDPV result	Results of toxicological analysis for other substances	Notes
93	United Kingdom	Jun 2010 (M, 33)	Unspecified	1.5 mg/L	alcohol (57 mg/100 mL) benzodiazepine (7.4 mg/L) TFMPP ([47]) (1.9 mg/L) lignocaine (+)	Cause of death unascertained. Coroner's verdict: open verdict/unascertained.
94	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.
95	United Kingdom	Apr 2011 (M, 24)	Blood	1.63 mg/L	MDMA ([48]) (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
96	United Kingdom **	May 2011 (M, 53)	Blood Urine	+	MDPBP ([49]) (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

[47] Trifluoromethylphenylpiperazine
[48] Methylenedioxymethylamphetamine (commonly known as 'ecstasy')

	Country	Date	Biological sample	MDPV result	Results of toxicological analysis for other substances	Notes
97	United Kingdom	Dec 2011 (M, 56)	Not specified	+	MDMA ([21]) (+) cocaine (+) cathinone (+)	MDMA, cocaine, MDPV and methylmethcathinone toxicity. Implicated: ecstasy, cocaine and cathinones Coroner's verdict: open verdict/unascertained
98	United Kingdom	Aug 2011 (M, 27)	Unspecified	+	None reported	MDPV and heart attack. Coroner's verdict: open verdict/unascertaine
99	United Kingdom **	Apr 2012 (M, 31)	Blood	<0.1 mg/L	AMT ([50]) (0.89 mg/L)	Cause of death cardiac failure, MDPV and AMT drug toxicity plus left ventricular hypertrophy and obesity. Coroners' verdict: accidental/misadventure

In this table LOD is the limit of detection and LOQ is the limit of quantitation.

* All cases in Finland are from 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 99 is believed to be a duplicate of one of the cases reported in the aggregated data from 2012 and has been counted once only.

[49] 3,4-Methylenedioxy-α-pyrrolidinobutyrophenone
[50] Alpha-methyltryptamine