



#### Europol–EMCDDA Joint Report on a new psychoactive substance: 4-methylmethcathinone (mephedrone)

In accordance with Article 5 of Council Decision 2005/387/JHA on the information exchange, risk assessment and control of new psychoactive substances

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#### 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) (²) and the Commission.

In January 2010, Europol and the EMCDDA examined the available information on a new psychoactive substance, mephedrone, 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 mephedrone satisfied all criteria (1 to 6). The two organisations therefore concluded that sufficient information had been accumulated to merit the production of a Joint Report on mephedrone as stipulated by Article 5.1 of the Decision.

#### 2. Information collection process

In compliance with the provisions of the Decision, on 20 January 2010 Europol and the EMCDDA launched a procedure for the collection of information on mephedrone, in order to prepare the Joint Report. The information was collected mainly through the respective networks in the Member States — the Europol national units (ENUs) and Reitox national focal points (NFPs). In addition, the EMA collected information through the Member States' national competent authorities (NCAs) responsible for medicinal products. The information collection process was largely concluded by 3 March 2010; however, additional information and clarifications from some Member States were received up to four weeks after this date.

Europol asked the ENUs to provide information on:

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

OJ L 127, 20.5.2005, p. 32

<sup>(2)</sup> Formerly referred to as the EMEA.

Europol received responses from 22 Member States (3).

According to Article 5.3 of the Decision, the EMA asked the Member States' national authorities responsible for human and veterinary medicinal products to provide information on whether:

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

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

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

Twenty-one Member States (4) replied to the EMA's request.

The rest of the information included in the Joint Report was collected by the EMCDDA through a structured questionnaire from the Reitox NFPs. The EMCDDA received replies from all 27 EU Member States as well as Croatia and Norway. A specific information request on whether or not mephedrone is under assessment by the UN system was also made to the World Health Organization (see section 3.5). Furthermore, a literature review and structured Internet searches were carried out by the EMCDDA. To facilitate the reading of the report, the full references of the quoted scientific articles are usually not included in the text; however, a list of the main information sources is annexed (Annex 1).

Thus, information included in sections 3.2.1, 3.3 and 3.6 (partly) 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 (partly), 3.7, 3.8.1 and 3.8.2. The information included in sections 3.8.3, 4.1, 4.2 and 4.3 was provided by the EMA. The summary findings and the conclusion of the Joint Report were prepared and agreed by the two organisations responsible — the EMCDDA and Europol.

#### 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 exactly as they appear in Article 5.2(a) to (h) and Article 5.3(a) to (c) of the Decision. Moreover, all sections are cross-referenced with those set down in the Decision.

Belgium, Bulgaria, Czech Republic, Denmark, Germany, Estonia, Spain, France, Italy, Cyprus, Latvia, Lithuania, Hungary, Netherlands, Poland, Portugal, Romania, Slovenia, Slovakia, Sweden and United Kingdom.

Belgium, Bulgaria, Czech Republic, Denmark and Malta did not provide information.

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

Chemical description and names

Mephedrone is the common name for 4-methylmethcathinone. The systematic IUPAC name is: (RS)-2-methylamino-1-(4-methylphenyl)propan-1-one (5).

Mephedrone is a psychoactive substance which belongs to the group of synthetic cathinone derivatives. All known cathinone derivatives are either N-alkylated or the nitrogen atom is part of a pyrrolidine ring. Like mephedrone, most of the cathinone derivatives marketed are ring-substituted.

Many synthetic cathinones are N-methylated, e.g. mephedrone, methylone, metamfepramone, methedrone, flephedrone (6) — and can be considered as ephedrone (methcathinone (7)) derivatives — i.e. mephedrone can be named as 4methylephedrone. or *p*-methylephedrone. Other names dimethylcathinone and p-methylmethcathinone. Cathinone derivatives are closely related to the phenethylamine family of psychostimulants — thus, mephedrone itself is β-keto-(4, N-dimethylamphetamine). Pyrrolidine derivatives (e.g. PPP, MDPV (8)) can be regarded as a subset of cathinones sharing the same skeleton as pyrovalerone (9).

Mephedrone is also known by some of its codenames – MMC or 4-MMC (which is an abbreviation for 4-methylmethcathinone), M-CAT or MMCAT, subcoca-I, etc. However, as code names could be confusing, they should be used only for initial orientation. Some of the users' and brand names by which mephedrone is known in the European Union Member States are included in subsection 3.8.2 of this report.

The molecular structure, formula and weight of mephedrone are shown below.

Molecular formula: C<sub>11</sub>H<sub>15</sub>NO

Molecular weight: 177.242

Identification and analytical profile

Chemical Abstracts Service (CAS) registry numbers of mephedrone: 1189805-46-6 (base); 1189726-22-4 (hydrochloride salt).

(<sup>5</sup>) Other chemical names include: 2-methylamino-1-p-tolylpropan-1-one, (RS)-\u03c3-methylamino-4-methylpropiophenone, 4'-methyl-2-methylaminopropiophenone and (RS)-4-(2-methylaminopropionyl)toluol.

(<sup>6</sup>) Methylone (3,4-methylenedioxy-N-methylcathinone or βk-MDMA), metamfepramone (N,N-dimethylcathinone), methedrone (4-methoxymethcathinone or βk-PMMA) and flephedrone (4-fluoromethcathinone, 4-FMC).

Methcathinone is listed in Schedule I of the United Nations 1971 Convention on Psychotropic Substances.

α-Pyrrolidinopropiophenone (PPP) and 3,4-methylenedioxypyrovalerone (MDPV)

Pyrovalerone is listed in Schedule IV of the United Nations 1971 Convention on Psychotropic Substances.

Colour screening test results: cathinone derivatives and in particular mephedrone do not give a coloured reaction with the Marquis field test.

Mass spectral data for mephedrone (m/z): 58 (base peak, 100 %). This technique does not distinguish between methylmethcathinone isomers (i.e. 4-methylmethcathinone from 3-methylmethcathinone).

Analysis using gas chromatography coupled with mass spectrometry (GC/MS) and infrared spectroscopy (IR) is straightforward. Nuclear magnetic resonance spectroscopy (NMR) allows the elucidation of the stereochemistry of the molecule. Immunoassay field tests for methamphetamine give false positive reactions with some cathinone derivatives (10).

#### Physical description

Mephedrone hydrochloride salt is a white powder, while its free base is a yellowish liquid at ambient temperature. Mephedrone is sold as its stable, water-soluble, white or lightly coloured hydrochloride salt; most likely as a racemic mixture of the two enantiomers.

Mephedrone is commercially available from chemical suppliers on the Internet where it can be purchased in bulk. The purity of mephedrone offered on the Internet is very high — purportedly over 99 %.

Although some concerns have been raised on the purity of the most probable mephedrone precursor 4-methylpropiophenone (see section 3.8.1), which may contain its isomer 3-methylpropiophenone, NMR analysis of several samples of seized mephedrone in the United Kingdom showed no evidence of the 3-isomer, and IR analysis indicated that most of the seized mephedrone is pure.

A more detailed description of mephedrone dosage unit forms and seizures encountered in the European Union Member States can be found in subsections 3.2.1 and 3.2.2 below. Description of various mephedrone forms sold online can be found in subsections 3.2.2 and 3.8.2. A full account of the available images of seizures and collected samples is annexed (Annex 2).

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

Level of production, distribution and trafficking

As mephedrone is legally available in powder form via the Internet and smart shops, processing activities by organised crime are limited to tableting.

Eleven Member States reported seizures of mephedrone to Europol. Germany, Estonia, Ireland, Italy, Latvia, Romania, Slovenia, Slovakia and Finland reported minor seizures, ranging from 2 grams seized in Italy to approximately 320.36 grams

<sup>(10)</sup> Detailed analytical profiles of mephedrone and other synthetic cathinone derivatives are available at the EMCDDA's European database on new drugs (EDND).

of powder seized in six incidents and one seizure of 4 400 tablets with a 'triangular' logo imprint seized in Germany. The Latvian seizures totalling 678 tablets and 1.26 grams of powder made in three seizures during 2009 had an 'R' logo imprint on all the tablets. Also, Slovakia reported one seizure of 1 197 tablets, all with a 'Captagon' logo imprint on the front and an '®' imprint on the back of the tablets. Furthermore, the United Kingdom reported 48 seizures totalling 14.8 kilograms of powder and eight tablets during 2009. Included in these seizures was 4.95 kilograms of powder marked as 'Glucose', which were intercepted concealed in two cardboard boxes en route from China. In addition, in January 2010, an additional parcel originating from China on its way to the United Kingdom, containing approximately 5.1 kilograms of mephedrone, was intercepted before entry.

Information received from Dutch law enforcement to one of Europol's expert systems revealed the seizure of one tableting site and four related storage locations in October 2009, with preliminary estimated seizures of more than 130 kilograms of mephedrone (equalling approximately 260 000 tablets). Most were in the form of tablets with a 'ROCHE 2' imprint, whilst smaller quantities of both powder and liquid forms of mephedrone were also found at all seized locations. Further, information submitted from this Member State revealed a seizure of an additional tableting unit during 2009 where powders containing mephedrone together with mCPP, 2C-B and MDMA were found. In addition, known legal importations of mephedrone from China took place during 2008 totalling 34.7 kilograms. However, planned further distribution of the imported mephedrone is not known.

One Member State, Austria, reported a case involving an 'Internet online shop' where legal substances, including mephedrone, were sold sourced from China and the Netherlands for EUR 3 000–7 000 per kilogram. Afterwards, these were sold in powder form to buyers for EUR 20–40 per gram. Also, it was found that approximately 600 orders were made on a monthly basis. Additionally, Germany reported that the Austrian case had led to the discovery of several kilograms of mephedrone sold to German customers.

One Member State, Estonia, reported that intelligence suggested that two organised crime groups in that country were involved in the trafficking of mephedrone sourced from Ireland and the United Kingdom.

Two Member States reported on legal importations: in Ireland, mephedrone was sold throughout the country in retail outlets known as 'head shops', whilst the United Kingdom similarly reported this substance to be legally available as a 'legal high' sold via the Internet and in 'smart shops' advertised as 'plant food'.

Apart from the Dutch law enforcement contribution to one of Europol's expert systems, no other Member State provided further information suggesting European Union wide large-scale processing of, and/or trafficking in mephedrone. However, contributions from Germany, Estonia, Austria and the United Kingdom indicated legal production and distribution from Asia and in particular from China, where it was available in bulk via the Internet.

Eight Member States: Greece, France, Cyprus, Lithuania, Luxembourg, Hungary, Poland and Portugal reported to Europol that they made no seizures of mephedrone, whilst three Member States: Ireland, Spain and Sweden did not specify whether seizures had taken place and, if so, the amounts.

#### 3.2.2 Information provided to the EMCDDA

Twenty Member States reported mephedrone detections (11) as follows: Belgium, Czech Republic, Denmark, Germany, Estonia, Ireland, France, Cyprus, Latvia, Hungary, Malta, Netherlands, Austria, Poland, Romania, Slovenia, Slovakia, Finland, Sweden and United Kingdom; as well as Croatia and Norway.

The reported mephedrone detections refer to various physical forms, mostly powders of various colours (white, yellowish, beige and brown) — found in Belgium, Belgium. Denmark, Germany, Estonia, Ireland, France, Latvia, Hungary, Malta, Netherlands. Austria, Poland and Finland; but also tablets of various colours, weight, diameter, thickness, shape, with or without a logo and/or markings — found in Belgium, Germany, Ireland, Cyprus, Latvia, the Netherlands, Romania, Slovakia, Sweden, the United Kingdom, Croatia and Norway; capsules — found in France, Finland, Sweden, the United Kingdom and Croatia; and a liquid — seized in a small quantity from a head shop in Romania (exact composition not specified) (12).

#### Seizures

Most of the Member States reported small to medium-size seizures, which varied from a single seizure in Cyprus (166 tablets (13)), Malta and Slovenia (a small quantity of powder), to few seizures of 1 to 20 dosage units (tablets or capsules) or small quantities of powder (Belgium, Denmark, Estonia, France, Poland, Finland and Croatia).

Latvia, Hungary and Austria reported slightly bigger seizures mainly in powder form (amounting to approximately 1 kg in total for each country). Bigger seizures, mainly tablets (between 1 000 and 5 000 units) were reported by Germany, Slovakia and Norway. Finally, the biggest seizure reported in 2009 was from the Netherlands -276 000 tablets and about 50 kg of powder (see also section 3.2.1 above).

Two countries – Sweden and the United Kingdom – reported analyses for seizures by year and/or by semester. Sweden provided a breakdown for 2008 (82 seizures amounting to approximately 4.7 kg) and for 2009 (346 seizures totalling 8.7 kg).

The United Kingdom reported an increasing trend in seizures: from 2 in 2008 to 20 in the first half of 2009 to 600 in the second half of 2009, which accounted for 88 % of synthetic cathinones seized in this period. Most of the seizures (over 97 %) occurred in powder form and amounted to more than 37 kg (74 % of the total weight of seized cathinones). Data provided by the United Kingdom Forensic Science Service (UK FSS) showed that, at the end of 2009, the number of cathinones seizures were three times higher than the number of MDMA seizures, and were only slightly lower than the number of piperazines seizures. Mephedrone, MDPV and methylone seizures (in this order) collectively represented over 97 % of the seizures and the total weight of synthetic cathinones (14).

<sup>(&</sup>lt;sup>11</sup>) 'Detections' is an all encompassing term, which may include seizures and/or collected and/or biological

The Romanian police undertook an action in about 300 shops and seized big quantities of psychoactive substances in various physical forms (powders, tablets, bags, cigarettes and liquids). The exact composition of the seized material was not identified.

Identification of mephedrone was not confirmed by analysis

<sup>(13)</sup> (14) A Google search (9/2/10) revealed that these top three cathinone derivatives collectively represented 87 %of all hits for the seven synthetic cathinones most commonly encountered in the United Kingdom.

In Ireland, Customs and the Police requested the Forensic Science Laboratory to analyse several 'head shop' products that contained cathinones. In Romania, in the period between August 2009 and January 2010, 100 samples of mephedrone were analysed by the Central Laboratory of Drug Analysis and Profiling of the General Inspectorate of Police. Most of them were seized from 'legal highs' shops and from drug users, including powders and syringes with liquids. The samples of mephedrone found in syringes also contained heroin (see section 3.8.2).

In general, it was not uncommon to find mephedrone in combination with other synthetic cathinones — i.e. methylone, butylone and ethylcathinone (Austria), fluoromethcathinone, ethylcathinone, and methoxymethcathinone (Romania), etc.

Furthermore, other substances were also encountered in combination with mephedrone: MDMA and mCPP (<sup>15</sup>) (Belgium), caffeine (Belgium, France, Austria, Romania and Slovakia), lactose (Slovakia), and so on.

Indications of international trafficking were reported by two Member States. In Germany, more than 4 000 tablets were found in a car registered in the Netherlands, and some objects which could be used for mixing, cutting and distribution were seized in an apartment. In the Netherlands a large quantity of tablets and powder were seized at Schiphol airport (see also 3.2.1).

#### Biological samples

The unavailability of a rapid qualitative screening method is a limiting factor for the detection of mephedrone. Furthermore, many European forensic/toxicological laboratories might not have a procedure in place for analysing cathinone compounds in biological samples, often due to the lack of reference standards for the drug or, especially, for its metabolites (<sup>16</sup>). The most complete data sets on mephedrone detections in biological samples (<sup>17</sup>) are available from Ireland, Sweden and the United Kingdom.

The Irish Drug Treatment Centre Board Laboratory analysed 209 urine samples of methadone maintenance patients from a treatment centre in Dublin. Of the total 209 samples, 29 (13.9 %) were positive for mephedrone, 7 (3.3 %) for methylone and 0.5 % for 1-benzylpiperazine (BZP). Seven samples (3.3 %) showed the presence of both mephedrone and methylone. Out of the total number of samples, 163 were from randomly tested maintenance methadone patients — of which 12 (7.4 %) were positive for mephedrone and 2 (1.2 %) for methylone; and 46 were from suspected users of 'head shop' products — of which 17 (36.9 %) were positive for mephedrone and 5 (10.8 %) for methylone.

In Sweden, mephedrone was identified in 133 biological samples in 2008 (35 blood and 98 urine) and in 157 samples in 2009 (32 blood and 125 urine). In December 2008, a toxicologically confirmed fatal case was directly linked to mephedrone use; no other drug or alcohol was found (see *Mephedrone related deaths* in section 3.4.1).

In the United Kingdom, since January 2009 there were 31 presentations to the Emergency Department of Guy's and St. Thomas' Hospital in London, with acute toxicity related to self-reported mephedrone use (for details see *London Clinical Data* 

<sup>(15)</sup> MDMA (3,4-methylenedioxymethamphetamine) and mCPP (1-(3-chlorophenyl)piperazine)
(16) An example of a supplier of pure mephedrone for use as a reference standard is LGC Standards,
http://www.lgc.co.uk/divisions/lgc\_standards.aspx (the cost of 25 mg of the hydrochloride salt is GBP146 +

<sup>(17)</sup> Biological (human) samples, e.g. body fluids (urine, blood), tissues, hair, etc.

in section 3.4.1). Furthermore, about a dozen deaths, where mephedrone was suspected to have been present in post mortem samples and/or implicated in death, are being investigated by different United Kingdom authorities.

Other suspected deaths associated with mephedrone have been reported by the media and a harm reduction NGO in Romania (2009) (18), where a working group on 'mephedrone related issues' was established in February 2010 to investigate non-confirmed mephedrone related deaths. Six rapid urine test analyses of self-reported mephedrone consumers gave false positive results for amphetamine or metamphetamine.

Collected samples, availability and content of mephedrone products

In addition to the seizures and the identifications in biological samples, six Member States (Belgium, Czech Republic, France, Netherlands, Austria and the United Kingdom) also reported collected samples (<sup>19</sup>). In October 2009, in Vienna three samples of white powder containing mephedrone were analysed in the framework of the pilot pill-testing project 'ChEckiT!'. In Belgium, two samples with similar characteristics (white powder) were reported in Gent in August 2009.

Mephedrone was identified in the Czech Republic in a white powder sample bought in a London club for personal use by a young male. In France, five samples of powder containing mephedrone and sold as ecstasy, speed, MDMA or 'MPK' were collected by SINTES (Système national d'identification des toxiques et substances) in different regions between 2008 and 2009.

In the Netherlands, a number of samples were delivered to the Dutch Drugs Information and Monitoring System (DIMS) — 995 tablets containing mephedrone were collected, mostly during June and July of 2009. In almost all cases these tablets were sold to people as ecstasy or MDMA.

A formal report on a collected sample of mephedrone was submitted by the United Kingdom national focal point in October 2008. This consisted of four capsules analysed by TICTAC Communications, Toxicology Unit, St. George's Hospital Medical School; all of them contained mephedrone and ethylcathinone, some also contained caffeine.

#### Availability on the Internet

Despite some seizures on the illicit drugs market described above, it seems that the main source of mephedrone-containing products for recreational users is the Internet where it is widely sold and aggressively marketed by a number of online shops. Mephedrone has been identified in 'ecstasy'-like tablets, but it is also sold as a 'legal high' — a legal alternative to amphetamine and cocaine — and there appears to be indications of an 'end user' market, i.e. specific demand for this designer drug, for which there is an increased awareness among some drug users, at least in the United Kingdom.

On the Internet, mephedrone is advertised as a 'research chemical', 'bath salts', 'for botanical research', 'plant food', 'plant feeder' and even 'hoover freshener', often with a note indicating that it is 'not for human consumption' in order to circumvent potential control mechanisms. There is often no indication of the presence of psychoactive

<sup>(18)</sup> In particular, one death was suspected to be related to the combined use of heroin and mephedrone, however the Institute of Legal Medicine was unable to detect mephedrone.

<sup>(19)</sup> Samples collected and analysed for monitoring, research or prevention/harm reduction purposes.

substances in the list of ingredients of the marketed products. There are, however, online shops which are more explicit about the actual usage of mephedrone (<sup>20</sup>).

Internet sites targeting recreational drug users offer mephedrone powder in retail quantities — 1 g, 5 g, 10 g up to for example 200 g. Furthermore, it can also be bought in bulk from Asian-based chemical laboratories (China) and from high street 'head shops' in Ireland and in the United Kingdom for personal use.

A targeted Internet search for online mephedrone shops conducted in December 2009 in English showed that at least 31 websites were selling the substance, the majority of them being dedicated mephedrone sites based in the United Kingdom (<sup>21</sup>). In March 2010, an Internet audit following the same methodology identified 78 online shops (see Annex 3), of which 39 sold mephedrone in only retail quantities (less than 200 grams), while 38 sold it both in retail and bulk quantities. The vast majority of sites (90–95 %) specialised in synthetic cathinones and only a few (5–10 %) were 'legal highs' shops that also offered mephedrone. In March 2010 the average retail price for the purchase of one gram of mephedrone was GBP 11.90, i.e. slightly lower than in December 2009, with the majority of prices oscillating between GBP 9.50 and GBP 14 per gram.

## 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

The Estonian information provided to Europol indicated the involvement of organised crime in the trafficking of mephedrone, whilst the Dutch information identified one tableting site where mephedrone was manufactured with a logo imprint. Also, an additional tableting site was reported seized in the Netherlands, however not indicating the possible logo punches used. In both cases, the involvement of organised crime was confirmed. Further, the seizures in Germany, Latvia and Slovakia included tablets with logo imprints indicating that they are sold in the user environment as ecstasy. Apart, from the Dutch information, none of the other data received, provides the tablets' origin. The German, Estonian, Dutch, Austrian and United Kingdom information suggest that the production of mephedrone in powder form is taking place in Asia and especially China, where it can be acquired in bulk.

#### Money laundering aspects

No information was received on money laundering in relation to the production and/or trafficking of mephedrone.

Violence in connection with production, wholesale and distribution

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

<sup>(20)</sup> http://www.head-candy.com, http://naughtyplantfood.com, http://www.flowerpowerfeeder.co.uk and http://www.tranceplantfood.co.uk

<sup>(21)</sup> Polish online shops have also been reported as accepting euros or US dollars but not pounds sterling.

## 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 indications of health risks

As with phenethylamines, in the absence of ring-substitution, cathinones behave predominantly as central nervous system (CNS) stimulants, although generally with a lower potency than the corresponding phenethylamine analogue. The lower potency is caused by the  $\beta$ -keto group creating a more polar molecule with lower ability to cross the blood-brain barrier. In the presence of ring substitution, however, the properties are modified towards MDMA-like effects.

There are no formal pharmacokinetic and pharmacodynamic studies on mephedrone. There are no published formal studies assessing the psychological or behavioural effects of mephedrone in humans. In addition, there are no animal studies on which to base an extrapolation of potential effects. Therefore psychological and behavioural effects related to mephedrone use are based on users' reports and clinical reports of acute mephedrone toxicity. From the reported clinical effects seen in patients with mephedrone toxicity and effects reported on user discussion forums, it appears that mephedrone has similar sympathomimetic effects to amphetamine derivatives.

An online cross-sectional survey through a website  $(^{22})$  associated with the specialist dance music magazine Mixmag was carried out in late 2009  $(^{23})$ . The survey collected data from over 2 000 respondents on dance drug use of 29 substances, including a number of 'legal highs', among them mephedrone and methylone. Some results of the survey can be found in the relevant sections below.

#### User reports

The desired psychological and behavioural effects reported by users include euphoria, general stimulation, enhanced music appreciation, elevated mood, decreased hostility, improved mental function and mild sexual stimulation. The latter effect was reported in 60 % of mephedrone users in the Mixmag survey. Overall, these effects seem comparable to that reported for other stimulant drugs such as MDMA, amphetamines and cocaine.

Users report on Internet forums that desired effects are typically seen within 15–45 minutes of oral ingestion. There are some reports of slower onset of action when mephedrone is taken orally on a full stomach. Following nasal insufflation, onset is reported by users to be within a few minutes and with peak effects within 30 minutes. Users report that the effects last approximately 2–3 hours and therefore that they may consume multiple doses during a session to prolong the duration of the desired effects. Reports from intravenous mephedrone users suggest that the high lasts approximately 10–15 minutes with an overall duration of desired effects of approximately 30 minutes.

The Mixmag survey reported on unwanted effects associated with mephedrone use. Commonly reported unwanted effects included: sweating (67 % of those who had used mephedrone), headaches (51 %), palpitations (43 %), nausea (27 %), cold or blue fingers (15 %).

Mixmag Feb 2010, pp. 44–53 and personal communication from contacts in the National Addiction Centre (NAC), Department of Addictions, King's College London.

<sup>(&</sup>lt;sup>22</sup>) www.dontstayin.com (<sup>23</sup>) Mixmag Feb 2010. pp

Undesired psychological and behavioural effects reported by users include 'head rushes', inability to concentrate, inability to visually focus, memory problems, altered level of consciousness, erratic behaviour, hallucinations and delusions. The more severe unwanted effects appear anecdotally to be associated with high dose or prolonged mephedrone use. It is also possible that these may, in part, be related to concomitant use of alcohol, ketamine, heroin, GHB/GBL or other stimulant drugs such as MDMA, amphetamine or cocaine.

Furthermore, numerous symptoms are reported by users on Internet forums, these include: numbness and lack of tactile sensitivity, loss of appetite, insomnia, increased mean body temperature ('mephedrone sweat'), decrease in mean body temperature, bruxism, elevated heart rate and blood pressure, chest pain, nausea and vomiting, painful joints, discoloration of extremities/joints, abdominal pain, painful nasal drip with presence of blood, light headedness and dizziness, tremors and convulsions, headaches, cravings, nightmares, loss of concentration and memory loss, anxiety, dysphoria, depression, hallucinations, paranoia, fatigue and respiratory difficulties. It is not possible to determine the true use-dependence of these symptoms based on the user reports available and it is important to note that these are unconfirmed anecdotal reports from users.

There are reports, particularly after intravenous use of mephedrone of more severe psychological and behavioural effects. These include: (delusional) paracitosis leading to scratching and gauging of the skin particularly of the face, neck and arms; Parkinson-like twitching of limbs; paranoia; suicidal ideation and severe insomnia particularly after prolonged periods of use.

#### Dependence

There are no published animal or *in vitro* studies investigating the 'dependence/abuse potential' of mephedrone. There is one report from the United Kingdom of a young professional male who developed dependence (<sup>24</sup>) following 18 months use of oral, nasal and rectal mephedrone. The clinical presentation included transient psychosis, hallucinations, hypomania and mood disturbances.

There are also anecdotal reports of mephedrone dependence being reported to the UK National Drug Treatment Monitoring system. The reports suggest that there is no reported physical withdrawal syndrome although psychological dependency is possible. User reports suggest that some individuals with high/frequent use of mephedrone develop 'craving' for it; this could be due to the high associated with its use and its relatively short duration of action.

#### London clinical data

Detailed data are available on 31 cases of acute toxicity associated with self-reported mephedrone use in London since January 2009. The most common clinical symptom/sign on presentation was agitation (51.6 % of patients). There were eight (25.8 %) patients presented with palpitations, six (19.4 %) with vomiting, three (9.7 %) with a self-limiting pre-hospital seizure, one (3.4 %) with bruxism and one (3.4 %) with a headache. No patients had any skin discolouration or cool/cold peripheries.

Twenty-five (80.6 %) patients were discharged either directly from the emergency department or the short-stay observation ward. These patients required either a

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<sup>(24)</sup> The ICD-10 criteria were fulfilled

period of observation prior to discharge and/or symptom control medications. Four (12.9 %) patients required the use of benzodiazepines for the management of agitation on presentation to the hospital. Of the six patients who were admitted to hospital, four were admitted for observation/management on a general internal medicine ward and two (6.4% of all presentations) required admission to the intensive care unit. All patients survived to leave hospital with no long-term sequelae on discharge.

#### UK National Poisons Information Service Data

There were no enquiries to the UK National Poisons Information Service (NPIS) concerning mephedrone prior to May 2009. Since this, enquiries to both the on-line TOXBASE service and the telephone service have increased month on month. By January 2010 there were over 30 calls to the telephone service and over 450 hits per month on the online TOXBASE service.

The most common clinical features were tachycardia and agitation; these were present in 10–20 % of individuals. The following clinical features were present in 5–10 % of individuals: anxiety, palpitations, chest pain, dizziness, dyspnoea, mydriasis and nausea. Features present in 1–5 % of individuals included abdominal pain, headache, vomiting, stupor, hypertension, increased sweating, abnormal vision, hallucinations, insomnia, renal pain and tremor.

#### Swedish Poisons Centre Data

The Swedish Poisons Centre received 150 enquiries concerning cathinones in 2008 and 2009. Mephedrone was involved in 100 of these (82 in 2008 and 18 and 2009). Tachycardia was present in 54 % of cases, restlessness in 37 %, mydriasis in 25 %, hypertension in 14 % and anxiety in 14 %.

#### Mephedrone related deaths

There has been only one confirmed death related solely to mephedrone. This case was in Sweden and was an 18 year old female who reported use of mephedrone and cannabis. Toxicological screening of blood and urine revealed the presence of mephedrone only (the mephedrone concentration was not reported), with no other drugs or alcohol detected.

The UK National Programme on Substance Abuse Deaths is aware of 14 cases in which mephedrone has either been detected in post-mortem samples or otherwise potentially implicated in death. Many of these cases are either awaiting full toxicological analysis or the outcome of an inquest into death. To date there are no deaths in the United Kingdom that have been confirmed to be related to mephedrone.

There have also been reports in the popular press in Romania of deaths potentially related to mephedrone; however, these have not been confirmed as being related to mephedrone (see section 3.2.2).

#### 3.4.2 Characteristics of users

Mephedrone has been sold as a 'legal' alternative to 'ecstasy', amphetamines and cocaine. However, the appearance of some of the seizures and information from the Dutch DIMS suggest that mephedrone-containing tablets are also sold on the illicit

market as 'ecstasy'. Therefore, it can be generally assumed that mephedrone users are similar to the populations using the latter. In summary, this is predominantly a youth phenomenon, in particular of 15- to 24-year-olds, with rates of drug use higher in males than in females, predominantly from urban areas, who frequent clubs, discos and dance events.

There are, however, clear indications of the development of an 'end user' market, i.e. specific demand for the drug, particularly from users who purchase it online or from specialised shops. User websites appear to suggest that users are aware that mephedrone is effective in producing the desired high and that it has greater purity compared to other stimulant drugs such as MDMA and cocaine. There are anecdotal reports that due to the decreasing purity of MDMA and cocaine, some individuals previously using these drugs are switching to mephedrone.

A research project in Middlesbrough, the United Kingdom, which included focus groups with 10 mephedrone users — nine men and one woman — provides a useful insight into the main groups of recreational drug users (the main exception being the lack of women). All 10 users were over 18 years of age and polydrug users (mainly cannabis, alcohol and amphetamine). Most participants also mentioned being users of cocaine and ecstasy in the past, but generally indicated that they had ceased or reduced their use of these two drugs because of their low purity (which partly explains their increased interest in 'legal highs'). Some mentioned use of ketamine, and some mentioned use of other hallucinogens (e.g. LSD, magic mushrooms), but none indicated any use of heroin or crack. Six of the participants were males mostly in their late teens and early twenties, unemployed and generally reported using mephedrone and other recreational drugs while in nightclubs and parties. Two participants — a white man in his 50s and a white woman in her 40s — could be described as 'psychonauts' or long-term dedicated users of hallucinogens and other drugs. The remaining two, both white males in their early to mid-20s were moderate weekend users of recreational drugs.

#### Future plans

The EMCDDA has access through UK-based researchers to a unique pool of young recreational mephedrone users. Telephone interviews are planned, carried-out using a structured questionnaire. The structured interview will address the following assessment domains: demographics (gender, age, employment status, sexual orientation); mephedrone use history (initiation, context, supply, route); mephedrone use (quantity, frequency, dose, use with other substances); effects (positive effects, contrasts with other substances); risks and harms (adverse and withdrawal effects, urges to use, control problems, tolerance); and purchasing patterns (suppliers, compounds bought). In addition, all participants will be invited to send a urine sample for toxicological analysis to determine the precise cathinone compounds(s) present after a recent use episode. Quantitative toxicological assessments will be correlated with the self-reported dataset.

# 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 (WHO) is the specialised United Nations (UN) Agency designated for the evaluation of the medical, scientific and public health aspects of psychoactive substances under the 1961 and 1971 UN Conventions.

On 25 January 2010, WHO informed the EMCDDA that mephedrone (4-MMC) is currently not under assessment and has not been under assessment by the UN 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 mephedrone, reported as subcoca, dates from 7 March 2008 from the Finnish NFP. The reporting form details two seizures of incoming post by the Finnish customs: 12 capsules with white powder, in a package marked 'neorganics/supplement to life' seized on 22 February 2008; and 24 capsules with white powder, in a package marked 'Extreme/S.C./Plant Food'/www.feedmybushes.com' seized on 22 November 2007.

Samples of the seized materials were sent by the Finnish Customs Laboratory to the Swedish National Laboratory of Forensic Science (SKL) for confirmation and were found to contain two different substances: subcoca I and subcoca II. On 18 April 2008, the Finish NFP reported the exact chemical structures of both substances: subcoca I — mephedrone and subcoca II — ethylcathinone. The capsules found in Finland contained either only mephedrone or both compounds — mephedrone and ethylcathinone.

Mephedrone was added to the list of new psychoactive substances monitored by the EMCDDA and Europol via the early warning system and a profile of the substance was created in the European database on new drugs (EDND). Analytical details and background information have been exchanged on various occasions between EMCDDA, Europol and the Member States. 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

In 22 Member States, mephedrone is not controlled under the terms of the 1961 or 1971 UN Conventions. Of these, one has initiated such a control that will come into effect in June 2010, and two have controlled the substance by other means.

Five Member States — Denmark, Germany, Estonia, Romania and Sweden — as well as Norway control mephedrone under drug control or equivalent legislation. In Denmark, effective from 21 December 2008, the Ministry of Health and Prevention added mephedrone and other synthetic cathinone derivatives (e.g. ethylcathinone and flephedrone) to list B of controlled substances — mephedrone may only be used for medical or scientific purposes. In Estonia, mephedrone is controlled as of 27 November 2009 by Regulation N. 87 of the Ministry of Social Affairs, which added the substance to the first list of narcotic and psychotropic substances. In Germany, as of 22 January 2010, mephedrone is controlled by the 24th Amending Regulation on Narcotic Drugs. Within this regulation mephedrone falls under schedule I of the Narcotics Act (BtMG) ('narcotics not eligible for trade and medical prescription'). In Romania, as of 10 February 2010 mephedrone has been added by Government decision to Table 1 of law 13/2000 in the category of 'drugs of highest risk'. Accordingly, production, trafficking and possession of mephedrone-based products are illegal. In Sweden, mephedrone is controlled as a narcotic drug since 25 May 2009. In Norway, mephedrone is controlled by virtue of an 'analogue' approach. It is considered to fall within Regulation of 30 June 1978 no. 08 relating to narcotics as a 'derivative' of a listed substance; it is however not included as such in the specific National Narcotic Drug List of the Regulation.

Ireland has recently started a procedure to control mephedrone under drugs legislation together with five other synthetic cathinone derivatives (including methylone) that were found in 'head shop' products. The sale and possession of these substances will be made illegal and subject to criminal sanctions under the Misuse of Drugs Act. The legislation will come into effect in June 2010.

Two Member States — the Netherlands and Finland — apply control measures to mephedrone under their medicines legislation. In the Netherlands, mephedrone is classified as a medicinal product and is, therefore, controlled under medicinal products legislation. In Finland, mephedrone is classified as medicine since September 2008 under the Medicines act (395/87).

In Croatia, mephedrone is controlled under precursors control legislation since 4 January 2010 (OG 02/10).

#### 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

As for other ring-substituted *N*-methylcathinone derivatives, the most likely and straightforward route of synthesis for mephedrone is by reacting the suitably substituted bromopropiophenone with methylamine; the resulting product is always racemic. Therefore, mephedrone is most likely synthesised by bromination of 4-methylpropiophenone (1-(4-methylphenyl)-1-propanone) followed by reaction of the resulting 4-methylbromopropiophenone (1-(4-methylphenyl)-2-bromo-1-propanone) with an excess of methylamine or methylamine hydrochloride and an acid scavenger. The reaction is then quenched with gaseous or aqueous hydrochloride providing the hydrochloride salt that should be recrystallised. This is one of the simplest choices because the starting materials are often commercially available or easily synthesised. This requires similar equipment and chemical knowledge to that needed for the synthesis of e.g. amphetamine or MDMA.

If the substituted ephedrine analogue (4-methylephedrine) is available, then its oxidation with, for example, potassium permanganate is also a feasible method that does not require a professional laboratory. This method, similar to the one used for the clandestine synthesis of methcathinone, requires reacting the precursor with a solution of potassium permanganate in diluted sulphuric acid. The precursor can be obtained in a specific enantiomeric form thereby ensuring that the synthesis is stereoselective. One of the hazards of the permanganate process could be that users can suffer manganese poisoning if the product is not purified.

The synthesis of mephedrone, mentioned as 'toluyl-alpha-monomethyl-aminoethylcetone', was first described in 1929 by Saem de Burnaga Sanchez. Alternative synthetic methods, though more cumbersome, have been described in the literature such as the Hartung-Munch procedure involving isonitrosopropiophenone, as well as the preparation of related compounds. More synthetic routes for mephedrone may exist.

However, as previously noted, mephedrone is readily available on the Internet where it may be purchased in bulk quantities. The main precursor of mephedrone, 4-methylpropiophenone is also available on the Internet.

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

Amongst the Mixmag respondents, mephedrone was the fourth most commonly used drug (after cannabis, ecstasy and cocaine) and the most widely experienced 'legal high', with 33.6 % of the respondents having tried it in the last month, 37.3 % in the last year and 41.7 % in their lifetime. The figures for the second most common synthetic cathinone included in the survey — methylone — were 7.5 %, 10 % and 10.8 % respectively.

Mephedrone is usually available as a powder or tablets so it can be used orally, by nasal insufflation, intramuscular/intravenous injection and rectal insertion. Because of its physical characteristics (lability), it is unlikely that mephedrone is suitable for smoking. Oral use includes swallowing powder, capsules or tablets directly. The powder can also be dissolved in water or wrapped in cigarette paper ('bombing') prior to swallowing. The predominant routes currently appear to be oral ingestion and nasal insufflation. In the Mixmag survey, 70 % of mephedrone users reported nasal insufflation and 30 % oral ingestion. There are reports of individuals using mixed routes during a single session (oral and nasal, oral and rectal). Users report significant nasal irritation and there is the suggestion that they switch to oral administration after initial experience with nasal insufflation.

There are reports of intravenous injection of dissolved powder, particularly from Romania, where mephedrone as well as other synthetic cathinone derivatives have been identified in syringes mixed with heroin. In Ireland, mephedrone-containing products have been reported to be used in combination with or instead of heroin. There is also one case report from the United Kingdom of an individual who developed mephedrone toxicity after intramuscular injection of dissolved powder (<sup>25</sup>). Combined use of mephedrone with alcohol, cocaine and heroine has been reported.

Single use doses reported on Internet user forums vary from 15 to 250 mg for oral ingestion and 5 to 125 mg for nasal insufflation. Users commonly report re-dosing during a single session with total doses typically being 0.5–1 g. Doses used in those presenting to healthcare services with acute toxicity range from 0.1–7.0 g.

There is anecdotal evidence that increased media coverage of mephedrone may have let to an increased general population and user awareness about the substance. EMCDDA has collected more than 200 media articles from January 2010 to the time of drafting this report (March 2010), 161 of them from the United Kingdom and 25 from the Irish popular press.

Reflecting the increased user interest in mephedrone a number of more common user names have emerged, for example: meph, drone, meow or meow meow, miaow or miaow miaow, bubble or bubbles (<sup>26</sup>), bounce and subcoca.

Media reports suggest that injecting mephedrone might have become popular in Guernsey among heroin injecting drug users.

<sup>(26)</sup> In Germany, this is reported to be as a mixture of mephedrone and methylone. In Scotland, five non-fatal overdoses due to consumption of 'Bubbles' (containing mephedrone) were reported at the beginning of 2010.

More local names for mephedrone marketed products are: 'Rush' (Belgium); 'Miaou Miaou' (France); 'MMC Hammer' and 'Magic' (Germany); 'kapszula', 'kata', 'kati', 'mefi', 'mefó', 'mephisto', 'moonshine', 'piercing', 'zsuzsi' (Hungary); 'ronzio' (Italy); 'aka'(Malta); 'Mef', 'Mefko' (Slovenia); and 'Mef', 'Meffe', 'Räka', 'Krabba', 'Kräfta', 'Fisk', 'Torsk', 'Lax' and 'Fiskrens' (Sweden).

Irish head shop products sold as 'legal highs' that appear to contain mephedrone are 'Blow', 'Snow blow xxx'; 'bath salts', 'Hurricane Charlie', 'White Gold', 'White Aroma Crystals', 'Recharge', 'Volt', 'Star Dust', 'Flake', 'Wild Cat Oceanic Charge +', etc; and 'Ketones', 'Am Hi Co Doves', 'Doves', 'Rocket fuel', 'Xtacy', 'Speed Freak', 'Dynamite'and 'Diablos XXX'.

In Romania, samples containing powder and crystals were identified in products sold as 'bath salts' under different names: 'Flower Magic Powder', 'Flower Magic Powder+', 'Charge+' (<sup>27</sup>), 'Flower Power', 'Crush', 'Cristal bath', 'Dark+', 'Special Diamond', 'Special Gold', and 'Special Original'.

# 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

There are no indications that mephedrone may be used for other purposes. Furthermore, there is no evidence of mephedrone use as 'plant growth regulator', 'plant feeder', 'herbal bath salt' or 'hoover freshener', as widely advertised on the Internet.

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

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

A preliminary search by the EMA revealed that mephedrone could theoretically be used in the synthesis of at least three active substances — pyrovalerone, pseudoephedrine or ephedrine. Therefore, in order to confirm the situation in reality, the EMA requested information on whether or not mephedrone is used in the manufacture of medicinal products containing these active substances. In the event of a positive response for any of the four substances, information was requested on:

- the active substance:
- the manufacturer of the active substance;
- the invented name of the medicinal product;
- the marketing authorisation holder (MAH) for the medicinal product.

The above questions were addressed to both human and veterinary competent authorities.

Of the 21 Member States that replied to EMA, 12 (Bulgaria, the Czech Republic, Germany, Estonia, Spain, Cyprus, Latvia, Lithuania, Poland, Romania, Slovakia and

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<sup>(27)</sup> In 2009, mephedrone and fluoromethcathinone were identified in 'Charge+' products, sometimes mixed with caffeine and lidocaine

the United Kingdom) gave a 'negative response'. Two Member States (Italy and Sweden) replied with an 'unknown'. Four Member States (Denmark, Hungary, the Netherlands and Portugal) did not answer these questions, while Belgium, France and Slovenia did not answer the questions but provided specific comments. Specific comments were also provided by Sweden.

Belgium reported that, theoretically, mephedrone could be used for the synthesis of ephedrine and pseudoephedrine, but it is 'unlikely that this is applied in practice' since the yield of such synthesis would not be economically viable. Furthermore, synthesis of pyrovalerone from mephedrone 'is even more unlikely.'

France reported that veterinary medicinal products containing ephedrine as active substance are authorised. The relevant dossiers do not contain any information about the use of mephedrone in the synthesis of this active substance. However, it was noted that some older reported cases do not include information about the manufacture of the active substance. In relation to two recently authorised veterinary medicinal products, there is no information about the manufacturing process of the active substance.

Slovenia reported that according to the data available to the NCA there are no pseudoephedrine and ephedrine-containing medicinal products for the production of which mephedrone is used.

Sweden reported that there are five nationally approved products which contain ephedrine or pseudoephedrine. It cannot be excluded that mephedrone is used in the synthesis of their active pharmaceutical ingredients, due to the fact that there is a lack of detailed information about the synthesis of the starting material. However, it can be noted that mephedrone is not mentioned in any dossier as a degradation product or impurity, which should be controlled by a test, either in the active pharmaceutical ingredients or in the product specifications.

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

#### 4.1 Marketing authorisation

The 21 Member States which responded to the EMA's information request (see section 2) reported that the new psychoactive substance mephedrone has not obtained a marketing authorisation.

#### 4.2 Application for a marketing authorisation

The 21 Member States which responded to the EMA's information request (see section 2) reported that the new psychoactive substance mephedrone is not the subject of an application for a marketing authorisation.

#### 4.3 Suspended marketing authorisation

The 21 Member States which 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 mephedrone.

#### 5. Summary of findings

- 5.1 Mephedrone is a synthetic cathinone, and is the common name for 4-methylmethcathinone. It was first detected in November 2007 and notified via the EMCDDA's Early Warning System in March 2008.
- 5.2 Mephedrone is legally available over the Internet where it can be bought in retail quantities or in bulk. In the last two years, mephedrone and mephedrone-containing products are aggressively marketed by various online mephedrone-specific suppliers as a 'legal-high' a legal alternative to ecstasy or cocaine. In some Member States users may source mephedrone from specialised shops (head/smart shops) or street level drug dealers.
- 5.3 Twenty Member States as well as Croatia and Norway reported to Europol and the EMCDDA seizures of mephedrone in powder form or tablets, ranging from 2 grams up to more than 130 kilograms of mephedrone seized, the latter equalling approximately 260 000 tablets.
- 5.4 There is currently limited information to underpin large-scale processing and distribution of mephedrone and the role of organised crime. However, with one Member State reporting the involvement of organised crime in trafficking and another confirming organised crime involvement with two seizures of large scale tableting sites as well as several seizures of tablets with different logo imprints suggests a possible increasing involvement of organised crime in the trafficking and wholesale distribution of mephedrone.
- 5.5 Five Member States indicate that legal production and distribution takes place from Asia and in particular China with one Member State confirming such importation during 2008.
- 5.6 There are no published studies on the pharmacokinetics or pharmacodynamics of mephedrone in animals or human volunteers. Information on the effects of mephedrone is limited to unconfirmed user reports. From these it appears that the desired effects and common adverse effects are similar to those seen with other stimulant drugs such as MDMA, amphetamines and cocaine. There is detailed information available on the acute health effects associated with mephedrone toxicity from clinical case series. The acute health effects seen in mephedrone toxicity are broadly similar to those seen with other stimulant drugs. Users report 'craving' in relation to mephedrone use which has the potential to lead to mephedrone dependency, and there are confirmed reports of mephedrone-dependence occurring. There has been one confirmed fatality attributed directly to mephedrone use.
- 5.7 Evidence of mephedrone use and associated toxicity has been increasing, in 2009 and 2010, particularly in the United Kingdom.
- 5.8 There are limited reports of crime and anti-social behaviour related to mephedrone use and supply.

- 5.9 Five Member States control mephedrone under drug control or equivalent legislation and two Member States regulate mephedrone under their medicines-related legislation.
- 5.10 Mephedrone is currently not under assessment and has not been under assessment by the UN system.
- 5.11 Mephedrone has no known medical use (human or veterinary) in the European Union. There is no marketing authorisation (existing, ongoing or suspended) for mephedrone in the EU or in the Member States which responded to the EMA.
- 5.12 The main precursor of mephedrone, 4-methylpropiophenone is available on the Internet. There are no indications that mephedrone may be used for other purposes. There is no information that mephedrone is used for the manufacture of a medicinal product in Europe. However, in the absence of an EU database on the synthetic routes of all registered medicinal products, the collection of information cannot be considered exhaustive.

#### 6. Conclusion

The health and social risks caused by the use of, the manufacture of, and traffic in, mephedrone, as well as the involvement of organised crime and possible consequences of control measures, could be thoroughly assessed through a risk assessment procedure as foreseen by Article 6 of Council Decision 2005/387/JHA.

#### **Annexes**

Annex 1 - Main information sources

Annex 2 – Images of mephedrone seizures and collected samples

Annex 3 – List of online mephedrone shops





#### Annex 1

## Europol–EMCDDA Joint Report on a new psychoactive substance: 4-methylmethcathinone (mephedrone)

#### Main information sources

- 1. Europol and its network of Europol National Units (ENUs) standard reporting and replies to Joint Report questionnaire.
- 2. EMCDDA and it network of National Focal Points (NFPs) standard reporting and replies to Joint Report questionnaire.
- 3. EMA and its network of Member States' National competent authorities (NCAs) responsible for human and veterinary medicinal products replies to Joint Report questionnaire.
- 4. Scientific articles published in peer reviewed journals:

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#### Annex 2

## Europol–EMCDDA Joint Report on a new psychoactive substance: 4-Methylmethcathinone (mephedrone)

### Images of mephedrone seizures and collected samples

Country	Image	Description
Belgium		Seizure in November 2009 — 1 tablet, 402 mg, 5 % caffeine and mephedrone. Reported by the NFP.
		Seizure in November 2009 — 6 tablets, 405 mg, 4 % (16 mg) caffeine, 1 % (4 mg) MDMA-HCl and mephedrone. Reported by the NFP.
Croatia		Seizure on 15.072009 in Buje — 17 tablets containing also ketamine, 4.97g. Reported by the NFP. Seizing authority: Croatia Police.
Netherlands		Collected samples analyzed in June/July 2009 Reported by the NFP. Seizing authority: Netherlands Forensic Institute.
Slovakia	PPZ-3016/2009, stopa č. 6	Seizure on 14.06.2009 in Žiar nad Hronom — 3.75 g blue-green powder containing also caffeine Reported by the NFP. Seizing authority: Police.

United Kingdom



Collected samples obtained as a test purchase in September 2008 — 4 capsules containing ethylcathinone, 3 of them also containing caffeine. Reported by the NFP.
Seizing authority: TICTAC Communications, Toxicology Unit, St. George's Hospital Medical School.

#### Images of mephedrone from Internet

Image	Website	Date
	4-mmcshop.co.uk	10/03/2010
Mephedrone PLANT FOOD  WARNING Not by Names consumption Analogous per crops	research-chemicals.co.uk	10/03/2010
	mephedrone-zone.com	10/03/2010





#### Annex 3

## Europol-EMCDDA Joint Report on a new psychoactive substance: 4-methylmethcathinone (mephedrone)

#### List of online mephedrone shops

Online shop information			Substances/highs, prices and deliveries				Additional user-info on site		
URL/ Name of shop	Specialised in synthetic cathinones? S = Specialised G = Generic	Retail, bulk, or both?	Product example  M = Mephedrone	Price in UK pounds	Quantity	Restriction on deliveries?	Do they provide warnings? Info on side effects?  NFHC = ' Not for human consumption'	Info on legality?	
http://www.flowerpowerfeeder.co.uk/	S	Retail	Flower power M	12.5	1 gram	No	NFHC	No	
http://research-chemicals.co.uk	S	Retail	0,5 gram of M powder		½ gram	No	NFHC	No	
http://www.4-mmcshop.co.uk/	S	Both	M / 4-mmc plantfood		1 gram	No	NFHC	No	
http://www.brandcrazy.co.uk/	S	Both	Research chemicals	-	1 gram	No	NFHC	No	
http://www.discountseedcompany.co.uk	G	Retail	M / Research chemicals	-	1 gram	No	NFHC	No	
http://www.cactus-candy.co.uk	S	Both	M - research chemical		1 gram	No	NFHC	Yes	
http://www.chem-world.co.uk	S	Retail	4-mmc research chemical		1 gram	No	NFHC	No	
http://www.mrscat.co.uk/	S	Retail	M		1 gram	No	NFHC	No	
http://rcdrugs.com/	S	Bulk	IVI	5,55	i giaiii	140	WITIO	110	
			M - for the independent						
http://buythemg.com	G	Retail	researcher	19	1 gram	No	No	No	
http://mephedronesales.com	S	Both	M - plant food	50	5 grams	No	NFHC	No	
http://www.plantfood2u.com	S	Both	M - plant food	24	2 grams	No	NFHC	No	
http://www.plantfeeders.co.uk/	S	Both	M - plantfeeder	22	2 grams	No	NFHC	No	
http://polatzoplantfeed.co.uk/	S	Retail	Miaow plantfeed	50	5 grams	Yes	NFHC	No	
http://naughtyplantfood.com	S	Retail	Naughty plant food'		1 gram	No	NFHC	No	
http://www.mrmeph.com/	S	Both	M	8,99	1 gram	No	NFHC	No	
http://www.topdogplantfood.co.uk/	S	Both	M plant food	10,99	1 gram	No	NFHC	No	
http://www.ravegardener.org/	S	Both	Encapsulated plant feeder	10,99	1 gram	No	NFHC	No	
http://www.partygarden.co.uk	S	Retail	M plantfood/research chemical		1 gram	No	NFHC	No	
http://www.tranceplantfood.co.uk	S	Both	M plant food	10,75	1 gram	No	NFHC	No	
http://www.mephman.com	S	Both	M bath salts	165	25 grams	No	No	No	
http://broadeninghorizons.com	S	Both	NRG-1/naphyrone	22	1 gram	No	NFHC	No	
http://www.purelychemical.co.uk	S	Retail	M for research use	15,95	1 gram	Yes	No	No	
http://plantsnacks.co.uk	S	Retail	M plant feeder	10	1 gram	No	No	No	
http://www.mephedrone-zone.com/	S	Both	M	10	1 gram	No	No	No	
http://rc4lab.com	S	Retail	M powder	18,75	1 gram	No	No	No	
http://www.plant-food.net/	S	Both	M - plantfeeder	12,95	1 gram	No	NFHC	No	
http://chem-shop.co.uk/	S	Both	M - plantfeeder		1 gram	No	NFHC	No	
http://charlie-boy.com/	G	Both	M - plantfeeder	11,5	1 gram	No	NFHC	No	
discofood.co.uk/	S	Retail	Bubble (also has M)	15	1 gram	No	NFHC	No	
http://www.mephedrone2u.com/	S	Retail	M - plantfeeder		3 grams	No	NFHC	No	
http://www.plantfoodpalace.co.uk/	S	Retail	M - plantfood	9,7	1 gram	No	NFHC	No	
http://www.mephedrone.net/	S	Retail	M - plantfeeder	10	1 gram	Yes	NFHC	Yes	
http://www.buymeow.co.uk/	S	Retail	M - plantfeeder	9,7	1 gram	No	NFHC	No	
http://www.shopmephedrone.co.uk/	S	Both	M - plantfeeder	10	1 gram	No	NFHC	Yes	
http://www.mkat4u.co.uk	S	Both	M - plantfeeder	65	10 grams	No	NFHC	No	
http://www.slyplants.com/	S	Both	M - plantfeeder	12	1 gram	No	NFHC	No	
http://www.4-mmc.com/	S	Retail	M - plantfeeder	11	1 gram	Yes	NFHC	Yes	
http://meowrightnow.com/	S	Both	M - plantfeeder		1 gram	Yes	NFHC	Yes	
http://www.funkonline.co.uk/	S	Retail	M - plantfeeder	12	1 gram	No	NFHC	No	
http://www.buyplantfeeder.co.uk/	S	Both	M - plantfeeder		1 gram	No	NFHC	No	
http://www.themephshop.com/	S	Both	M - plantfood	13	1 gram	No	NFHC	No	
http://www.fastmephedrone.co.uk/	S	Retail	M - research compound		1 gram	No	NFHC	No	
http://flowerproducts.co.uk/	S	Retail	M - plantfeeder		1 gram	No	NFHC	No	
http://highersales.net/	S	Retail	M - plantfeeder		2 grams	No	NFHC	No	
http://buy-mephedrone.org/	S	Retail	M - plantfeeder		1 gram	Yes	NFHC	No	
http://www.the-cats-meow.co.uk/	S	Retail	M - research chemical	12	1 gram	Yes	NFHC	No	

Online shop information			Substances/highs, prices and deliveries				Additional user-info on site	
URL/ Name of shop	Specialised in synthetic cathinones? S = Specialised G = Generic	Retail, bulk, or both?	Product example  M = Mephedrone	Price in UK pounds	Quantity	Restriction on deliveries?	Do they provide warnings? Info on side effects?  NFHC = ' Not for human consumption'	Info on legality?
http://www.superplantfeed.com/	S	Both	M - plantfeeder	9	1 gram	No	NFHC	No
http://www.plantchemicals.co.uk/	S	Retail	M - plantfeeder		1 gram	Yes	NFHC	No
http://www.buymcat.com/	S	Retail	M - plantfood		1 gram	Yes	NFHC	No
http://www.buymephedroneonline.co.uk	S	Both	M - plantfood	13,95	1 gram	No	NFHC	No
http://www.buycheapmephedrone.co.uk	S	Retail	M - plantfood	9,5	1 gram	No	NFHC	No
http://www.miraclefeeds.co.uk/	S	Both	M - plantfood	9,7	1 gram	No	NFHC	No
http://purechemicals.co.uk/	G	Retail	M - plantfood	10	1 gram	No	NFHC	No
http://mephedrone-buy.com/	S	Both	M - plant fertilizer	50	5 gram	No	NFHC	No
http://www.mephedronebuy.info/	S	Both	M - 'botanical use'	13	1 gram	No	No	No
http://www.mephedrone-storMco.uk/	S	Retail	M Plant Fertiliser	10	1 gram	No	NFHC	No
http://www.buy-mephedrone-online.com/	S	Retail	M Plant feed	12	1 gram	No	NFHC	No
http://www.plantfoodkingdoMco.uk/	S	Retail	M for research use	12	1 gram	Yes	NFHC	No
http://www.mephedrone.me/	S	Retail	M for research use	24	2 grams	No	NFHC	No
http://amazingplantfood.co.uk/	G	Retail	M for research use	10	1 gram	Yes	NFHC	No
http://tranceplants.co.uk/	S	Both	Bubble luv (also has M)	14	1 gram	Yes	NFHC	No
http://www.head-candy.com	S	Both	Energy-1 "Designer" research chemical.	25	1 gram	No	NFHC	No
http://www.plantfeed2u.co.uk/	S	Both	M plant feed	9,5	1 gram	Yes	NFHC	No
http://www.buy-mephedrone-online.net/	S	Both	M (no more no less!)	10	1 gram	No	No	No
http://www.easyplantfood.com/	S	Both	M plant food	9,5	1 gram	No	No	No
http://www.mephedroneforsale.co.uk	S	Retail	M plant feeder	11	1 gram	Yes	No	No
http://www.ordermephedrone.co.uk/	S	Retail	M plant feeder	9,6	1 gram	Yes	NFHC	No
http://www.4mmcplantfeeder.co.uk	S	Both	M plant feeder	11	1 gram	Yes	NFHC	No
http://www.nextdaymephedrone.co.uk	S	Retail	M plant feeder		2 grams	No	NFHC	No
http://gblegals.co.uk/shop/	S	Retail	M plant feeder	25	2 grams	Yes	NFHC	Yes
http://methodrone.co.uk/	S	Both	M plant feeder		2 grams	No	NFHC	No
http://www.mentalmeph.com	S	Both	M plant feeder	10	1 gram	Yes	NFHC	No
http://www.buymeowmeow.co.uk/	S	Both	M plant feeder	11	1 gram	Yes	NFHC	No
http://www.mephdirect.co.uk	S	Both	M plant feeder	12,5	1 gram	Yes	NFHC	No
http://spacegardener.co.uk/	S	Retail	M plant feeder		1 gram	Yes	NFHC	No
http://www.buymephedroneusa.com/	S	Retail	Bubble (also has M)	15	1 gram	No	NFHC	No