



European Monitoring Centre  
for Drugs and Drug Addiction

**Risk assessment report  
of a new psychoactive substance: 4-methylmethcathinone (mephedrone)**

In accordance with Article 6 of Council Decision 2005/387/JHA on information exchange, risk assessment and control of new psychoactive substances

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## 1. Introduction

This Risk Assessment Report presents the summary findings and the conclusions of the risk assessment carried out by the EMCDDA's extended Scientific Committee of the new psychoactive substance 4-methylmethcathinone (hereinafter 'mephedrone'). The report has been prepared and drafted in accordance with the conceptual framework and the procedure set out in the *Operating guidelines for risk assessment of new psychoactive substances* (EMCDDA, 2010). It is written as a stand-alone document which presents detailed information on and analysis of the scientific and law enforcement data available at this time. The conclusion section of the report summarises the main issues addressed and reflects all opinions held by the members of the Committee. A more detailed 'Technical report on mephedrone' is annexed to this report (Annex 1).

The risk assessment has been undertaken in compliance with Article 6 of Council Decision 2005/387/JHA of 10 May 2005 on information exchange, risk assessment and control of new psychoactive substances<sup>(1)</sup> (hereinafter the 'Decision'). The Decision establishes a mechanism for the rapid exchange of information on new psychoactive substances that may pose public-health and social threats, including the involvement of organised crime, thus allowing European Union institutions and Member States to act on all new narcotic and psychotropic substances<sup>(2)</sup> that appear on the European Union drug scene. The Decision also provides for an assessment of the risks associated with these new psychoactive substances so that, if applicable, measures in the Member States for the control of narcotic and psychotropic substances<sup>(3)</sup> can be applied to these new substances.

There is emerging evidence that the new psychoactive substance mephedrone is being used as a recreational drug in Europe. In response to this, in compliance with the provisions of Article 5 of the Decision, on 25 March 2010, the EMCDDA and Europol submitted to the Council, the Commission and the European Medicines Agency (EMA) a Joint Report on the new psychoactive substance 4-methylmethcathinone (mephedrone)<sup>(4)</sup>. Taking into account the Joint Report's conclusion, and in accordance with Article 6 of the Decision, on 26 May 2010, the Council formally requested that 'the risk assessment should be carried out by the extended Scientific Committee of the EMCDDA and be submitted to the Commission and the Council within twelve weeks of this notification'.

In accordance with Article 6.2, the meeting to assess the risks of mephedrone was convened under the auspices of the EMCDDA's Scientific Committee with the participation of five additional experts designated by the Director of the EMCDDA, acting on the advice of the Chairperson of the Scientific Committee, chosen from a panel proposed by Member States and approved by the Management Board of the EMCDDA. The additional experts are from scientific fields that are not represented, or not sufficiently represented, on the Scientific Committee, and whose contribution is necessary for a balanced and adequate assessment of the possible risks

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<sup>(1)</sup> OJ L 127, 20.5.2005, p. 32.

<sup>(2)</sup> According to the definition provided by the Council Decision, a 'new psychoactive substance' means a new narcotic drug or a new psychotropic drug in pure form or in a preparation; 'new narcotic drug' means a substance in pure form or in a preparation that has not been scheduled under the 1961 United Nations Single Convention on Narcotic Drugs, and that may pose a threat to public health comparable to the substances listed in Schedule I, II or IV; 'new psychotropic drug' means a substance in pure form or in a preparation that has not been scheduled under the 1971 United Nations Convention on Psychotropic Substances, and that may pose a threat to public health comparable to the substances listed in Schedule I, II, III or IV.

<sup>(3)</sup> In compliance with the provisions of the 1961 UN Single Convention on Narcotic Drugs and the 1971 UN Convention on Psychotropic Substances.

<sup>(4)</sup> 8145/10 CORDROGUE 36/SAN 68.

of mephedrone, including, health and social risks. Furthermore, one expert from the Commission, one expert from Europol and two experts from the European Medicines Agency (EMA) participated in the risk assessment. The meeting took place on 15 July 2010 at the EMCDDA in Lisbon. The risk assessment was carried out on the basis of information provided to the Scientific Committee by the Member States, the EMCDDA, Europol and the EMA. A full list of the extended Scientific Committee, as well as the list of participants, attending the risk assessment meeting, is annexed to this report (Annex 2).

For the risk assessment, the Scientific Committee considered the following:

- (i) Technical report on mephedrone (July 2010) — Annex 1 to the Risk Assessment Report; Appendix 1 to the Technical report, 'Mephedrone: assessment of health risks and harms' (July 2010) (EMCDDA-commissioned cross-sectional survey of UK clubbers); and Appendix 2 to the Technical report, 'Mephedrone: additional studies. Overview of prevalence, use patterns, effects' (July 2010).
- (ii) Europol-EMCDDA Joint Report on a new psychoactive substance: 4-methylmethcathinone (mephedrone)<sup>(5)</sup>;
- (iii) Scientific articles, official reports, media articles and grey literature;
- (iv) *Operating guidelines for risk assessment of new psychoactive substances*, (EMCDDA, 2010)<sup>(6)</sup>;
- (v) Council Decision 2005/387/JHA of 10 May 2005 on the information exchange, risk assessment and control of new psychoactive substances.

## **2. Physical and chemical description of mephedrone and its mechanisms of action, including its medical value**

Mephedrone is the common name for 4-methylmethcathinone. The systematic IUPAC name is: (*RS*)-2-methylamino-1-(4-methylphenyl)propan-1-one. It is a synthetic ring-substituted cathinone closely related to the phenethylamine family, differing only by a keto functional group at the beta carbon. The molecular formula for mephedrone is C<sub>11</sub>H<sub>15</sub>NO, equating to a molecular weight of 177.242 g/mol. Chemical Abstracts Service (CAS) registry numbers of mephedrone are 1189805-46-6 (base) and 1189726-22-4 (hydrochloride salt). In addition to mephedrone, positional isomers of methylmethcathinone include 2-methylmethcathinone and 3-methylmethcathinone.

Mephedrone hydrochloride salt is a white powder, while its free base is a yellowish liquid at ambient temperature. Mephedrone is typically sold as crystalline powder — stable, water-soluble, white or lightly coloured hydrochloride salt; most probably as a racemic mixture of the *R* and *S* enantiomers. The powder is readily soluble in water and can be dissolved for oral/rectal use or for injection. Mephedrone has also been found as capsules containing powder and as tablets pressed from powder.

Mephedrone is metabolised by a number of pathways to the following metabolites: nor-mephedrone, nor-dihydro mephedrone, nor-hydroxytolyl mephedrone, 4-carboxy-dihydro mephedrone, hydroxytolyl mephedrone. It is thought that the hydroxytolyl mephedrone and nor-hydroxytolyl mephedrone metabolites are partly excreted as glucuronide and sulphate conjugates. There is no data available to be able to determine how long either mephedrone or its metabolites remain detectable, nor on their stability in biological specimens.

Gas chromatography coupled with mass spectrometry (GC-MS) and liquid chromatography tandem mass spectrometry (LC-MS/MS) techniques have been developed for the analysis of

<sup>(5)</sup> <http://www.emcdda.europa.eu/drug-situation/new-drugs#102490>

<sup>(6)</sup> <http://www.emcdda.europa.eu/html.cfm/index100978EN.html>

mephedrone and some of its metabolites/precursors. The mass-spectrometry technique does not distinguish between methylmethcathinone isomers; however nuclear magnetic resonance spectroscopy (NMR) and other techniques allow the isomers to be differentiated. Immunoassay field tests for methamphetamine give false positive reactions with some cathinone derivatives.

Mephedrone has no established or acknowledged medical value or use (human or veterinary) in the European Union. There is no marketing authorisation (existing, ongoing or suspended) for mephedrone in the European Union or in the Member States. There is no information that mephedrone is used for the manufacture of a medicinal product or an active pharmaceutical ingredient (API) of a medicinal product in the European Union. There remains a theoretical possibility that mephedrone could be used for the synthesis of some API of veterinary or human medicinal products (e.g. ephedrine, pseudo-ephedrine and pyrovalerone). No data exists to suggest that this is currently the case but it should be noted that there is no European Union database on the synthetic routes of all registered medicinal products.

Mephedrone is commercially available from suppliers on the Internet where it can be purchased in bulk. There are no indications that mephedrone may be used for any other legitimate purposes. There are no known uses of mephedrone as a component in industrial, cosmetic or agricultural products.

Mephedrone is reported to be used in single doses of between 5–250 mg, although due to short-lived effects the total doses used per session may be greater, possibly between 0.5–2 g. Onset of desired effects is typically seen within 15–45 minutes of oral ingestion and a few minutes after nasal insufflation. Users report that the desired 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.

There are no formal pharmacodynamic studies looking specifically at mephedrone. Based on its chemical structure, it is likely that it has a similar mechanism of action to other stimulant drugs (blocks reuptake of, and stimulates the release of stimulant neurotransmitters such as serotonin, dopamine and norepinephrine). This is further supported by the sympathomimetic effects (dilated pupils, tachycardia, hypertension, agitation) seen with mephedrone use that are similar to other stimulant drugs such as MDMA and cocaine.

There are no published formal studies assessing the psychological and/or behavioural effects of mephedrone in humans. In addition, there are no animal studies on which to base an extrapolation of potential effects. However, users report that the desired psychological and behavioural effects of mephedrone include euphoria, general stimulation, enhanced music appreciation, elevated mood, decreased hostility, improved mental function and mild sexual stimulation. These effects are broadly comparable to those reported for better-studied stimulant drugs.

### **3. Chemical precursors that are used for the manufacture of mephedrone**

The synthesis of mephedrone, mentioned as 'toluyl-alpha-monomethyl-aminoethylcetone', was first described in 1929 by Saem de Burnaga Sanchez. The most 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 needs to be recrystallised. This is a relatively straightforward option 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, for example, amphetamine or MDMA. The main precursor of mephedrone, 4-methylpropiophenone, is commercially available on the Internet.

There is the potential that if the substituted ephedrine analogue (4-methylephedrine) is available, then its oxidation with, for example, potassium permanganate or potassium dichromate is also a feasible method that does not require a professional laboratory. There is no evidence that this is currently occurring in Europe. 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, ensuring that the synthesis is stereoselective. One of the possible hazards of the permanganate process could be that users can suffer manganese poisoning if the product is not purified.

However, analysis of seized and purchased mephedrone has shown that it is generally of high purity (>95 %). There is limited evidence that precursors used in the manufacture of mephedrone are found in the final product.

Alternative synthetic methods, though more cumbersome, have been described in the literature such as the Hartung-Munch procedure. More synthetic routes for mephedrone may exist.

Reports from at least four Member States indicated legal production and distribution from Asia and in particular from China and bordering countries in South-East Asia. Final packaging of mephedrone, prior to sale, seems to be carried out by European suppliers. There have also been seizures of tabletting machines used for mephedrone processing in Europe, indicating that the drug has also been prepared for sale on the illicit market.

#### **4. Health risks associated with mephedrone**

Other than clinical data on acute mephedrone toxicity, and limited reports on fatalities, the studies available on mephedrone are few, largely preliminary and focused on user self-reports. To date no epidemiological data on prevalence has been published. The majority of studies originate from the United Kingdom and evidence from other Member States is scarce. The most detailed studies have been undertaken through surveys of UK clubbers, although some information can be found on mephedrone use and potential risks regarding other sub-populations.

##### ***Individual health risks***

The assessment of individual health risks includes consideration of mephedrone's acute and chronic toxicity, its dependence potential, and similarities and differences to other reference stimulants.

Systematic data are not routinely collected in Europe on **acute toxicity** related to mephedrone or closely comparable recreational drugs. Therefore, information on these effects of mephedrone is limited to user reports and clinical data on individuals presenting with acute mephedrone toxicity to specialist hospitals with a focus on recreational drug toxicity. The reported short-term effects of mephedrone use have much in common with those of other stimulants. Some self-reports from users favourably compare mephedrone's effects, saying the high can be both better and longer lasting than cocaine.

The **main routes of administration** for mephedrone are reported as snorting (nasal insufflation) and swallowing (oral ingestion), sometimes after dissolving with water. As

mephedrone is primarily available in powder form, injecting use is reported but appears to be rare.

**Adverse effects** reported by users include sweating, headaches, tachycardia, palpitations, nausea, chest pain, bruxism (teeth grinding), agitation/aggression and paranoia. In addition, nasal insufflation of mephedrone is reported to be associated with significant nasal irritation and pain which has led to some users switching to oral use of mephedrone. Users report increased sexual arousal but there is insufficient information to detect whether this is associated with high-risk sexual behaviour.

Some detailed information on the patterns of acute mephedrone toxicity is available from clinical case series from poisons information services and specialist hospitals in the United Kingdom and Sweden, including one series of analytically confirmed acute mephedrone toxicity from the United Kingdom. In this data, patients typically present with sympathomimetic features (dilated pupils, agitation, tachycardia, hypertension); severe clinical features such as chest pain, significant hypertension, arrhythmias and seizures have been reported in a small number of cases to date. Similar to other stimulant drugs, it is likely that the risk of toxicity is related to the dose of mephedrone used; however there is insufficient information available from toxicity reports to determine a 'dose threshold' and/or whether particular routes of use are more likely to be associated with toxicity. It is possible that certain rare, but clinically significant, severe effects are associated with mephedrone use. However, as experience of the toxicological profile of the drug is currently limited to a few hundred cases it is difficult to be sure.

Data from individuals presenting with acute mephedrone toxicity suggest that the majority of individuals have used at least one other substance together with mephedrone. However there are analytically confirmed cases of lone mephedrone toxicity. This is similar to individuals presenting with acute toxicity related to other stimulant drugs.

There are two reported **fatalities** in which mephedrone appears to be the sole cause of death (one in Sweden and one in the United Kingdom). In addition to these cases, there are at least another 37 deaths in the United Kingdom and Ireland in which mephedrone has been detected in post-mortem blood and/or urine toxicology screening. In some of these cases it is likely that other drugs and/or other medical conditions or trauma may have contributed to or been responsible for death. The inquests into the deaths are pending for the majority of these cases therefore it is not possible at this time to determine the contribution of mephedrone.

Strong craving for the substance is reported by some users' self-reports, sometimes rated higher than that experienced with other stimulant drugs. This is cited as a main reason for using more mephedrone than intended, and for using for longer periods than planned. Withdrawal symptoms do not appear to be significant for most users with the primary symptoms of nasal congestion and fatigue most probably related to route of use and lack of sleep secondary to staying up late. However the other reported findings, in heavier users, would be consistent with a stimulant withdrawal syndrome. There is some evidence that the drug has a high **abuse liability** with over 30 % of the UK telephone survey sample reporting three or more DSM criteria of **dependence** and being classified as dependent. Tolerance, loss of control, a strong urge to use and using despite problems predominate. In addition, there are reports from the United Kingdom of mephedrone dependence being reported to drug treatment services that suggest psychological rather than physical dependency similar to other stimulant drugs.

No studies have been published investigating the potential for **chronic mephedrone toxicity** associated with mephedrone use, including reproductive toxicity, genotoxicity and carcinogenic potential.

Reports suggest mephedrone may be used as an **alternative to illicit stimulants**. The reasons given for using mephedrone include: value for money, product purity and consistency as well as

the poor availability or low quality of other stimulants (cocaine, ecstasy/MDMA). Some users noted a preference for mephedrone over other stimulant drugs with data from the UK clubbers rating mephedrone above ecstasy and cocaine for strength and pleasurable high. Mephedrone users in the UK telephone survey reported on the considerable impact mephedrone had on their consumption of cocaine and ecstasy, with approximately two thirds of the sample reporting that they now took less MDMA, and a third reporting that they now consumed less cocaine. Just under half of the group reported they would choose mephedrone over cocaine and only a quarter said that they would take mephedrone over ecstasy.

The physical effects reported by mephedrone users are typical of other stimulants and may be particularly similar to MDMA. However, mephedrone's relatively short duration of action, leading to repeat dosing, is more analogous to cocaine.

In summary, from the data sources available, it appears that the effect profile and clinical presentations of mephedrone intoxications share some features seen with MDMA and some features seen with cocaine. Additionally, there are very limited reports of fatalities directly related to mephedrone. Some users have reported negative effects and in some cases these have required medical attention. Similar to other stimulant drugs, the extent to which users experience problems requires further investigation. Data also suggest that mephedrone has a potential to cause dependency. However, more in-depth studies would be required to explore in detail the dependence potential of this drug.

### **Public health risks**

The public health risks associated with mephedrone may be categorised in terms of the extent, frequency and patterns of use; availability and quality of the drug; information availability and levels of knowledge amongst users; and negative health consequences.

Evidence of use of mephedrone and toxicity associated with its use has been increasing, particularly in 2009 and 2010. In the absence of representative studies, **prevalence** rates are difficult to estimate. Non-representative studies provide self-reports that place lifetime use of mephedrone at around 40 % amongst UK clubbers responding to an Internet survey (33 % last month use), 20 % amongst Scottish students and 40 % amongst Northern Irish school children attending focus groups. In other countries, levels of use are largely undocumented. Data from the French TREND system describe its use as restricted to a small, primarily Parisian milieu. Qualitative reports note the use of the drug in other countries but give no indication of prevalence even within high-risk subpopulations.

Mephedrone users are reported to be predominantly male and aged between their late teens and late twenties, although both younger and older users are identified in UK studies. Some surveys suggest individuals use mephedrone alone while other surveys suggest that users combine mephedrone with other drugs including alcohol, cannabis and often cocaine, and ecstasy. The evidence suggests mephedrone has some appeal for a range of recreational stimulant users — with respondents from UK studies also using cocaine/ecstasy/amphetamine, and the Dutch respondents also using ecstasy. There is limited data available on where mephedrone is used, although it is likely that it is used in the same environments as other stimulant drugs, typically clubs/discos, bars/pubs, outdoor music festivals and home environments.

Mephedrone consumption has been identified in a range of sub-populations. In addition to 'psychonauts'<sup>(7)</sup>, mephedrone use has been identified in the clubbing and party scene,

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<sup>(7)</sup> There is no agreed definition of the term 'psychonaut' but here it is used to broadly describe individuals who seek to explore their mind by intentionally inducing altered states of consciousness, in particular, by experimenting with psychoactive substances.

amongst school and university students (United Kingdom) and gay men (France). There is some evidence to suggest rapid spread of mephedrone use, particularly in the United Kingdom and in Ireland, but also among clubbers in Slovenia. Use reported in France is described as rather localised and limited, whilst in the Netherlands, the available data are confined to a group of primary ecstasy users. Although much of the evidence is linked to use amongst clubbers, the UK studies also include unemployed users and students from Scotland and Northern Ireland. In addition, there are reports of spread of mephedrone use amongst opiate users in Ireland.

In terms of **frequency of use**, reports suggest recreational, weekend/monthly use is a common pattern for those who try, and choose to continue to use, mephedrone. As such mephedrone is used in a similar way to ecstasy or cocaine in party and nightlife settings. Around 15 % of UK Internet survey respondents reported using mephedrone at least weekly. A small number of users appear to progress to daily use. Mephedrone is reported as being used primarily in combination with alcohol, cannabis and other stimulants. These **combinations of substances** makes it more difficult to identify mephedrone-specific effects. Relatively high concurrent consumption of ketamine was reported by UK clubbers. There are anecdotal reports of opiates injecting users switching to mephedrone when opiates are not available.

Some concerns have been raised about young people experimenting with the practice of snorting the drug, a **route of administration** commonly associated to cocaine. However, a significant proportion of those using mephedrone by nasal insufflation report nasal irritation and pain, leading to a change to the oral route.

Mephedrone is **available for purchase** on the Internet, from head shops and from established street-level dealers. Where information on purchase of mephedrone is available, it appears most common to buy the drug from a dealer or from friends. Some users reported buying from the Internet, and this tended to be higher quality mephedrone, but for some users the risk of Internet data security was a deterrent. Internet suppliers will ship mephedrone to EU countries often marketed as 'plant food', 'bath salt' or 'research chemical', presumably to circumvent control measures. Very rarely mephedrone is sold explicitly as a 'legal high'. EMCDDA Internet monitoring shows that the number of websites selling mephedrone increased from December 2009 to March 2010. But subsequent to the April 2010 classification of mephedrone in the United Kingdom, there was a rapid and considerable decrease in the number of sites found to be operating. Prior to UK control, many suppliers appeared to be based in the United Kingdom, or targeting the UK market.

Most sites do not have restrictions on the countries that they will ship mephedrone to, but advise buyers to check the legal status in their countries. Internet sites selling mephedrone typically differ from those selling other 'legal highs' as they are mephedrone/cathinone specific. There is generally information available on the supposed purity of the product supplied but rarely information on the potential for unwanted effects associated with its use, although most sites state that it is not for human consumption. Many sites supply mephedrone in bulk (kilogram) quantities in addition to single user doses. However, they typically provide minimal information on the dose of mephedrone. Any information that is provided is very general and often cryptic in nature; for example mephedrone sold as 'plant food' may contain advice on 'number of doses for an average-sized plant'. It is likely that users will interpret this information as the number of doses to be taken by an adult. The UK control seems to have prompted the appearance of at least two new substances and products marketed on the Internet as 'legal highs'. There is also some evidence to suggest that where mephedrone has been controlled, the drug continues to be available on the illicit market.

In general, the **quality and purity** of mephedrone available to users is reported as high, and the analysis of seized and purchased mephedrone confirms this. However, some samples of mephedrone have been found to contain pharmaceutical agents (e.g. benzocaine, lidocaine, caffeine and paracetamol), other synthetic cathinones (e.g. butylone, methylone, ethylcathinone,

fluoromethcathinone, methylenedioxypyrovalerone/MDPV) and/or other recreational drugs (e.g. MDMA, *m*CPP, ketamine).

There is anecdotal evidence that extensive **media coverage** of mephedrone has led to increased general population and user awareness of the drug and, in particular, to the fact that it is legally available over the Internet for delivery to Europe. Some users have stated that they first bought and used mephedrone after reading reports about it in the popular press. The media is also cited as a primary source of (often inaccurate) information about the drug. Typically, there appears to be a low level of knowledge amongst some groups of users of the chemical content of products and chemical make-up of mephedrone. However, the Internet has also been a source of information for those interested in drugs. Specialist websites/user forums indicate that users are aware that mephedrone is effective in producing the desired effects and may compare favourably to other stimulants.

**Misunderstanding and misinformation** about mephedrone may also be an important issue both with respect to the use and to the supply of the drug. It should be noted that there are a number of other synthetic cathinones that are used recreationally — these include methedrone, methylone and MDPV. Some of these, along with other non-cathinone drugs such as methadone, have similar sounding names to mephedrone which may cause confusion amongst users, healthcare professionals, law enforcement agencies and the media. As cathinone derivatives are also sold under generic brand names, with no labelling of the active constituent chemicals, both users and sellers may be unaware of what particular substance is being consumed. This problem may be amplified by the fact that products can contain mixtures of cathinones and other drugs. It is likely that this is more of an issue with products purchased mostly from street dealers rather than from the Internet. Feedback from pill/powder-testing (Netherlands, France) report that some users were unaware that the substance they had purchased was mephedrone before test results were provided. This suggests that mephedrone has also been used unknowingly by those buying ecstasy tablets on the illicit market. Finally, the marketing of mephedrone may itself cause further confusion, as illustrated by a report of school pupils being uncertain as to whether all regular plant food also contained the drug.

Mephedrone has been detected on post-mortem analysis in four **road traffic accident** related deaths in the United Kingdom; however inquests into these deaths are awaited and so it is not possible to determine the role that mephedrone played. There is no data available from other European countries or from law enforcement agencies to suggest that mephedrone use has been implicated in road traffic accidents or other trauma. This may, at least in part, be due to the fact that, at this time, mephedrone is not widely tested for by forensic laboratories.

## 5. Social risks associated with mephedrone

The information pertaining to social risks associated with mephedrone is very limited. Whilst there is some limited evidence to suggest greater use of mephedrone compared to other stimulant drugs amongst students of school and college/university age, there have been no studies to determine the impact of mephedrone use on educational outcomes such as attendance, concentration and exam performance. Similarly, there is no data on the effect of mephedrone use on performance/attendance at work, career progression, effects on personal relationships or neglect of family.

There are some healthcare costs associated with cases of acute mephedrone toxicity presenting to hospitals. Most of these involve short assessments within the emergency department; however there are a minority that require critical care admission with greater associated costs. There is also evidence that users are switching from other controlled stimulant drugs to mephedrone. However, it is not possible at this time to estimate whether mephedrone is associated with greater healthcare costs than other stimulant drugs.

There is no evidence related to levels of acquisitive crime resulting from mephedrone use. There have been media and anecdotal reports of some crime and violence reportedly related to mephedrone; however the veracity of these reports is unclear.

There are both media and anecdotal reports of links between mephedrone and violence in Northern Ireland where sellers of the drug appear to have become caught up with the paramilitary activism and informal social control of the drug market. Reports suggest punishment beatings/shootings have been on the increase recently regarding the sale and use of mephedrone. A study with school children reported that mephedrone was more easily accessible than cannabis.

## **6. Information on the level of involvement of organised crime and information on seizures and/or detections by the authorities, and the manufacture of mephedrone**

Since March 2008, mephedrone **seizures** have been reported in 22 Member States and two other countries that report to the EMCDDA. The largest single seizure of mephedrone in Europe occurred in the Netherlands in October 2009 when more than 130 kilograms of mephedrone (equalling approximately 260 000 tablets) were seized from a tabletting site and four related storage locations. However, most of the Member States reported small- to medium-sized seizures. 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. Over 97 % of the seizures in the United Kingdom occurred in powder form and amounted to more than 37 kg.

In addition to seizures, mephedrone was detected either through formal drug analysis schemes or ad-hoc test purchases in at least six Member States. In one Member State, initial growth in **detections** of mephedrone in ecstasy tablets appears to have been followed by a decline. The reported mephedrone detections refer to various physical forms, mostly powder but also tablets, capsules and liquids. In general, it is not uncommon to find mephedrone in combination with other synthetic cathinones. Furthermore, other substances were also encountered in combination with mephedrone e.g. MDMA, *m*CPP and caffeine.

Several Member States reported seizures of mephedrone in tablet form with logo imprints indicating that they are sold in the user environment as ecstasy. As mephedrone is available in powder form on the Internet, **processing** activities by **organised crime** seem to be limited to tabletting. Altogether, three tabletting units were reported from the Netherlands but no other Member State reported processing activities. In one of these cases, other psychoactive substances such as MDMA and *m*CPP were also found on the tabletting site.

There is no information on money-laundering activities in connection with the production, wholesale and/or distribution of mephedrone. Furthermore, there is no data suggesting the involvement of the same groups of people in different types of crime.

Indications of **international trafficking** were reported by two Member States — Germany and the Netherlands. 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 in large-scale tabletting sites, there may be possible involvement of organised crime in the trafficking and wholesale distribution of mephedrone. There is no information on incidences of violence in connection with the production, wholesale and/or distribution of mephedrone.

## **7. Information on any assessment of mephedrone in the United Nations system**

The World Health Organization (WHO) is the specialised UN agency designated for the evaluation of medical, scientific and public-health aspects of psychoactive substances under the 1961 and 1971 UN Conventions. The WHO informed the EMCDDA that 4-methylmethcathinone (mephedrone) is currently not under assessment and has not been under assessment by the UN system.

## **8. Description of the control measures that are applicable to mephedrone in the Member States**

Mephedrone is not listed for control in the UN Drugs Conventions of 1961 or 1971. In 16 Member States, mephedrone is not controlled under the terms of the 1961 or 1971 UN Conventions.

Eleven Member States — Belgium, Denmark, Germany, Estonia, Ireland, France, Italy, Lithuania, Romania, Sweden and the United Kingdom <sup>(8)</sup> — as well as Croatia and Norway control mephedrone under drug control legislation.

In **Belgium**, the Royal Decree of 13 June 2010 includes the substance in Art 2, §2 of the Royal Decree of 22 January 1998, which contains the Belgian list of controlled psychotropics. 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 **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 **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 **Ireland**, since 11 May 2010, mephedrone and related cathinones are designated by name as controlled under the Misuse of Drugs Act, by SI No199 of 2010. In **France**, mephedrone and its salts are classed as narcotics by the decree of 7 June 2010 of the Ministry of Health and Sports, effective 11 June 2010. In **Italy**, on 16 June 2010 a Ministry of Health Decree added mephedrone to Table I of the drug control law. In **Lithuania**, mephedrone was included in the first list in the list of 'Narcotic drugs and psychotropic substances prohibited for medical use' on 20 June 2010 by the order of the Minister of Health No. V-540. 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'. In **Sweden**, mephedrone has been controlled as a narcotic drug since 25 May 2009. In the **United Kingdom**, mephedrone and other cathinone derivatives (using a generic definition) have been added to the list of controlled drugs in Class B by the SI no. 1207 of 2010 as of 16 April 2010. In **Croatia**, mephedrone is controlled under drug control legislation as a psychotropic since 4 January 2010 (OG 02/10). In **Norway**, mephedrone was earlier controlled by virtue of an 'analogue' approach, considered as a 'derivative' of a listed substance. Nevertheless, it was specifically added to the Norwegian National Drug List with effect from 24 March 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 medicine and is therefore controlled under medicinal products legislation. In Finland, mephedrone is classified as a medicine since September 2008 under the Medicines act (395/87).

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<sup>(8)</sup> In European Union protocol order.

## **9. Options for control and the possible consequences of the control measures**

Under Article 9.1 of Council Decision 2005/387/JHA, the option for control that is available at European Union level is for the Member States to submit the new psychoactive substance mephedrone to control measures and criminal penalties, as provided for under their legislation, by virtue of their obligations under the 1971 United Nations Convention on Psychotropic Substances.

There are no specific European studies on possible consequences of such control measures, though the Committee has noted reports from individual countries that have already put mephedrone under national control. If this option of control is pursued, the Committee considers that the following consequences are possible. It should be noted that all of these possible consequences apply to any new psychoactive substance and they are not specific only to mephedrone.

- This control could facilitate the detection and monitoring of trafficking and illegal manufacture of mephedrone. In so doing, it could facilitate subsequent international law enforcement and judicial cooperation. On the other hand, control measures could create an illegal market in mephedrone with the increased risk of associated criminal activity, including organised crime.
- This control could be expected to limit the availability of mephedrone and further expansion of a legal market in this drug by restricting its commercial availability from both Internet and specialised shops.
- The risk exists that post-control there may be covert sales of mephedrone on the Internet, or continuing sales through newly branded products.
- This control could impact on both the quality/purity and price of any mephedrone supply still available on the illicit market. The extent to which this will impact on public health, criminality or levels of use is difficult to predict.
- A health consequence that can be foreseen as a result of control measures are benefits brought about by the presumed reduction in use.
- However, if a significant number of young users continue to use the drug, costs may be incurred by bringing them into contact with the criminal justice system.
- New control measures would imply additional costs related to law enforcement, criminal justice, forensic analysis, testing, etc.
- This control could lead to replacement with other (established or new) psychoactive substances which may in themselves have public health consequences.
- It is not possible to predict whether there will be health or social consequences from any substance that might come to be used as an alternative.
- At present, there is no reason to expect that this control would impact on current or future research by the pharmaceutical or chemical industries. However, the possibility that this drug may become of interest in the future, although unlikely, cannot be ruled out.

Similar to the impact of control of other psychoactive substances such as BZP (1-benzylpiperazine), the Committee further notes from the countries that have already introduced a ban on mephedrone that:

- Other non-controlled drugs have been reported to be marketed as replacement substances for mephedrone. However, it is not clear if these substances would have appeared independently of any action taken on mephedrone.

- There is some evidence to suggest that a ban in some Member States has not resulted in the disappearance of mephedrone from the illicit market. It will be important to monitor whether the mephedrone availability at street level is from stockpiles or has been imported or produced post-ban.

Aside from the option for control under legal parameters of Article 9.1 of the Council Decision, there are various other options for control open to Member States individually. They may choose to control distribution of it under consumer protection or food safety legislation; to control it under medicinal products legislation; and/or to control the importation of the substance.

The EU Regulation 178/2002, and Directives 2001/95/EC and 2001/83/EC, standardise the national definitions of food, safe products intended for consumers, and medicinal products for human use, respectively. Therefore, it may well be that control options under such laws could be applied by all European Union Member States. However, few Member States have reported utilising such control measures, and the details of national enforcement mechanisms and possible penalties for breach are not known <sup>(9)</sup>.

It is possible to consider restrictions that would limit mephedrone use by introducing specific measures related to age limits, or interventions in the production chain. However this option has not been pursued by any Member State.

It should be noted that the three positional isomers of methylmethcathinone are not easily distinguishable by commonly available analytical techniques. Consequently control of only 4-methylmethcathinone (mephedrone) could be difficult to enforce.

## **10. Conclusion**

Mephedrone (4-methylmethcathinone) is a synthetic cathinone found mostly as a powder but also as tablets. It has no established or acknowledged medical value or use (human or veterinary) in the European Union. There are no indications that mephedrone may be used for any other purposes. It is commercially available from suppliers on the Internet where it can be purchased in bulk. The main precursor of mephedrone, 4-methylpropiophenone, is also commercially available.

The physical effects reported by mephedrone users are typical of other stimulants and may be particularly similar to MDMA. There are no published formal studies assessing the psychological and/or behavioural effects of mephedrone in humans and in animals. Furthermore, in the absence of representative studies, prevalence rates are difficult to estimate. The available studies are limited in number, largely preliminary and geographically restricted, and reliant on user accounts. Taken as a whole, the scientific evidence base available for drawing conclusions is limited and this proviso should be borne in mind when interpreting the findings of the risk assessment exercise.

Many of the questions posed by the lack of evidence on the health and social risks of mephedrone, as for any new psychoactive substance, could be answered through timely research. Further studies are needed, especially with respect to potential toxicity, potential to produce dependence and the social consequences related to mephedrone use.

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<sup>(9)</sup> One illustrative example of using import legislation is provided by the United Kingdom. Before entry into force of control under drugs legislation in the United Kingdom, the Home Secretary wrote to local authorities urging them to use powers under the Consumer Protection from Unfair Trading Regulations 2008 and consider enforcement steps to be taken to ensure mephedrone is not advertised as a fertiliser or bath salts, following ACMD confirmation that mephedrone has no such use. They could also use medicines legislation to seize samples labelled for 'human consumption'. Following advice from the ACMD on harms, mephedrone and related compounds were banned from import by removing these substances from the Open General Import Licence (OGIL).

There is sufficient evidence that mephedrone can be an attractive drug for those seeking stimulant psychoactive effects for recreational purposes. In the short time that it has been available, mephedrone has established itself in some countries as a sought-after substance in its own right, for which some users express preference over other established stimulant drugs. Overall, the psychoactive properties of this drug would suggest it has a potential for diffusion to other populations and countries, which may constitute a health and social threat. Future diffusion is likely to be influenced by many factors including the availability and quality of other stimulant drugs.

It appears that the effect profile and clinical presentations of mephedrone intoxications share some features seen with MDMA and some features seen with cocaine. The current evidence base does not allow an accurate assessment to be made of the extent to which mephedrone users are likely to experience health problems. However, sufficient data are available to allow the Committee to conclude that some users of the drug do experience acute health problems. In general, these are similar to the acute problems reported with use of illicit stimulants. Moreover, both user reports and the psychoactive properties of mephedrone would suggest that the drug is able to produce dependence in users. Current data are not sufficient to determine the relative dependence-producing potential of mephedrone. However, a number of factors would suggest that this is a concern that merits further investigation. There have been a very limited number of deaths reported to be related directly to the use of mephedrone.

The chronic health effects related to the consumption of mephedrone remain virtually unknown. No studies have been published investigating the potential for chronic mephedrone toxicity associated with mephedrone use, including reproductive toxicity, genotoxicity and carcinogenic potential.

The social consequences associated with the use of any drug are likely to be influenced by a number of factors. To date, different patterns of use have been observed. Mephedrone has established itself very quickly within the recreational drug market within at least two Member States. However, in another Member State initial growth in use/availability appears to have been followed by a decline. Limited use of mephedrone among problem drug users has also been reported, including mephedrone being injected. Based on the available evidence, it is difficult to draw any firm conclusions on the likely social risks associated with mephedrone, but given the speed at which the drug has become established and its potential attractiveness to different groups of drug users, there is a need for ongoing vigilance.

This drug has been marketed over the Internet and through specialist suppliers; it is also being sold by established street dealers. Organised crime has noted the potential for legally purchased stimulants to be sold in the illicit drugs market, but international trafficking and the involvement of organised crime with mephedrone is relatively limited at present.

The Committee notes that a decision to control this drug has the potential to bring with it both positive and negative consequences. Potential positive consequences may include reduced availability and use of the drug. It is important, however, to anticipate and minimise any potential negative consequences of control. Control measures could create an illegal market in mephedrone with the associated risk of criminal activity. Furthermore, control should not inhibit the gathering and dissemination of accurate information on mephedrone to users and to relevant professionals.

## **11. List of annexes**

**Annex 1:** Technical report on mephedrone, July 2010

- **Appendix 1:** Mephedrone: additional studies. Overview of prevalence, use patterns, effects, July 2010
- **Appendix 2:** Mephedrone: assessment of health risks and harms, July 2010

**Annex 2:** List of participants at the Risk Assessment meeting, 15 July 2010