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for Drugs and Drug Addiction

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EMCDDA

RISK ASSESSMENTS

Report on the risk assessment of mephedrone in the framework of the Council Decision on new psychoactive substances

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for Drugs and Drug Addiction

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EMCDDA project leaders

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Foreword

It is with great pleasure that I present this comprehensive publication, which contains the data and findings of the risk assessment on mephedrone. The European Union has responded to concerns over the availability and use of this stimulant drug by assessing the health and social risks of the substance and, consequently, subjecting it to control measures across the EU Member States. The decision of the Council to control mephedrone was adopted in the final stage of a three-step mechanism set up by Council Decision 2005/387/JHA — on the information exchange, risk assessment and control of new psychoactive substances — designed to respond to potentially threatening new psychoactive drugs in the EU.

The Risk assessment report on mephedrone, which was submitted to the European Commission and the Council of the European Union on 26 July 2010, examines the health and social risks of the drug, and considers the potential implications for placing the drug under control in the EU. On the basis of this report — and on the initiative of the Commission — on 2 December 2010, the Council decided that mephedrone is to be subject to control measures.

Practice and research show that new forms of drug use are usually adopted by a few individuals, among small groups or in particular regions and social settings, and significant time may elapse before new patterns diffuse to larger user groups, or spread geographically. However, the appearance of a large number of new, unregulated synthetic compounds marketed on the Internet as 'legal highs' or 'not for human consumption' and specifically designed to circumvent drug controls, challenges our understanding and the current approaches to monitoring, responding to and controlling the use of new psychoactive substances.

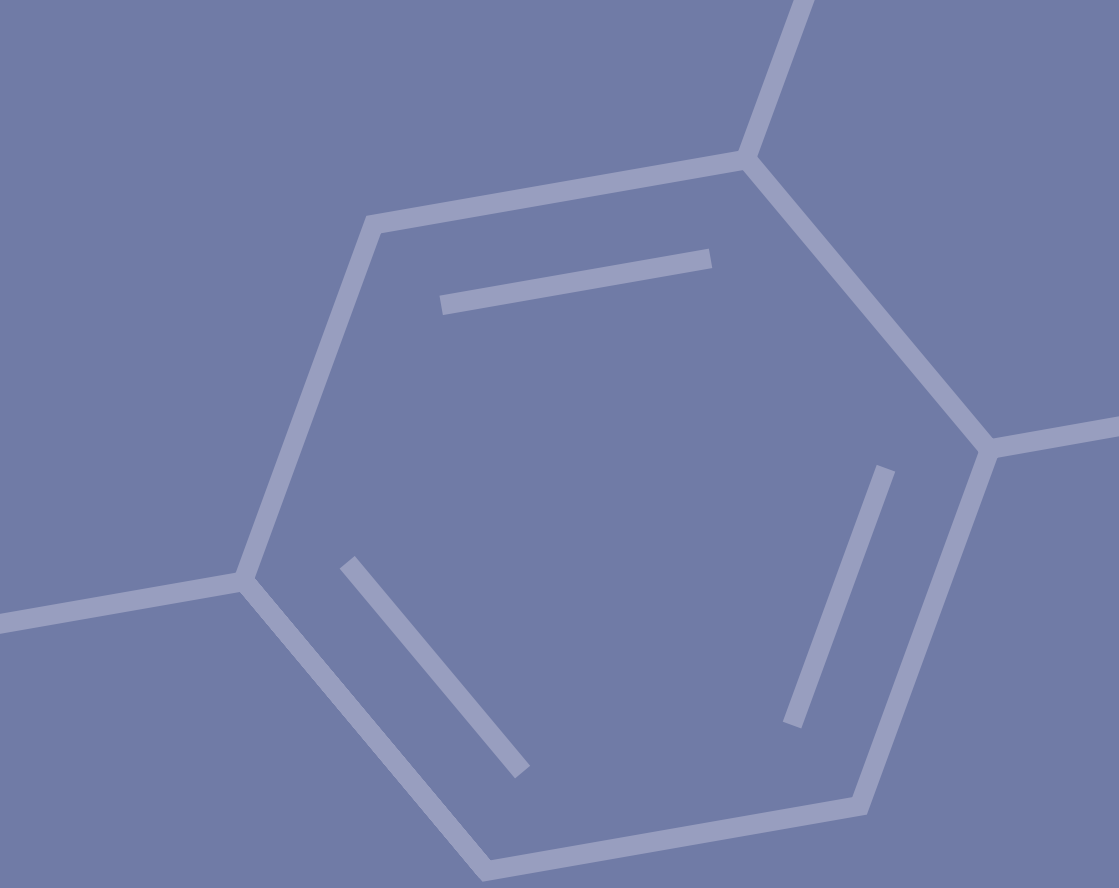
Mephedrone, for example, was widely and legally available from suppliers on the Internet, where it has been openly sold in retail or bulk quantities, providing a higher potential for spread than other new substances previously encountered in Europe. Furthermore, the widespread media coverage on the substance and its potential health consequences may have led to increased awareness of the drug amongst young people in general, and established user groups in particular.

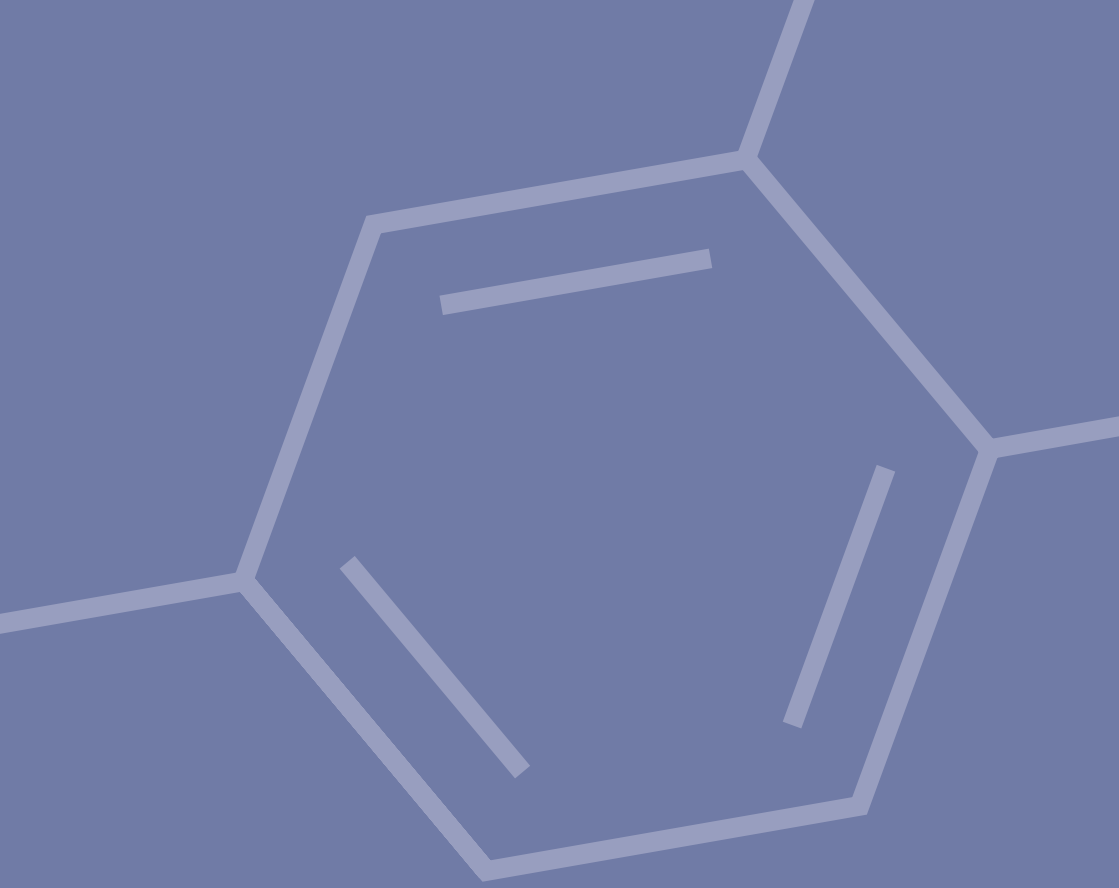
I would like to acknowledge the contribution and thank the members of the EMCDDA extended Scientific Committee, the EU Member States experts, the European Commission, Europol, the European Medicines Agency (EMA) and the EMCDDA, who participated in the formal risk assessment meeting, which took place on 15 July 2010 at the EMCDDA in Lisbon. The resulting report is a valuable contribution at European level, which gives clear support to political decision-making. Furthermore, I would like to recognise the excellent work done in preparing the risk assessment by the networks of the EMCDDA, Europol and the EMA — the Reitox national focal points, Europol national units and the national competent authorities responsible for medicinal products — who once again played an essential role in collecting and providing national data, thus completing this truly multidisciplinary effort.

Mephedrone is the second substance after BZP to be risk-assessed and subsequently controlled under Council Decision 2005/387/JHA. Such concrete results at technical and political level confirm the effectiveness of the rapid-response mechanism and provide the Commission with useful insight and concrete information for the ongoing assessment of the functioning of Council Decision 2005/387/JHA, as foreseen by the EU Drugs Action Plan for 2009–12.

Wolfgang Götz

Director, EMCDDA





Abbreviations

2-FMC	2-fluoromethcathinone
3-FMC	3-fluoromethcathinone
4-FMC	4-fluoromethcathinone
4-MAB	4-methoxymethylaminobutyrone
4-MMC	4-methylmethcathinone (mephedrone)
4-MoxyMC	4-methoxymethcathinone
API	active pharmaceutical ingredient
Bk-MDMA	β-keto-MDMA (methylone, 3,4-methylenedioxymethcathinone)
BMI	body mass index
bpm	beats per minute
BZP	1-benzylpiperazine
CAS	Chemical Abstracts Service registry number
Cath	cathinone
CNS	central nervous system
Coc	cocaine
CT	computed tomography
DIMS	Drugs Information and Monitoring System (Netherlands)
DMC	dimethylcathinone
DSM	Diagnostic and Statistical Manual of Mental Disorders
EC	ethylcathinone
ED	emergency department
ECG	electrocardiograph
EMA	European Medicines Agency

ENU	Europol national units
EWS	early warning system (EMCDDA–Europol)
FMC	fluoromethcathinone
FSS	Forensic Science Service (UK)
GC-MS	gas chromatography-mass spectrometry
GCS	Glasgow Coma Scale
GBL	gamma-butyrolactone
GHB	gamma-hydroxybutyrate
ICD	International Classification of Diseases (WHO)
IUL	International units per litre
IUPAC	International Union of Pure and Applied Chemistry
Ket	ketamine
LC-MS/MS	liquid chromatography-mass spectrometry tandem mass spectrometry
MC	methcathinone
***m*CPP**	1-(3-chlorophenyl)piperazine
MDAI	5,6-methylenedioxy-2-aminoindane
MDMA	3,4-methylenedioxymethamphetamine
MDPV	3,4-methylenedioxypyrovalerone
MeOPP	methoxyphenylpiperazine
mmHg	millimetres of mercury
mmol/L	millimetres per litre
Nor	normephedrone (4-methylcathinone)
NPIS	National Poisons Information Service
np-SAD	national programme on substance abuse deaths (UK)

NFP	national focal point of the Reitox network
NMR	nuclear magnetic resonance spectroscopy
ORs	odds ratios
***p*MPP**	para-methoxyphenylpiperazine
RTA	road traffic accident
SD	standard deviation
SOCA	Serious Organised Crime Agency (UK)
TFMPP	3-trifluoromethylphenylpiperazine
TREND	recent trends and new drugs, from the French *tendances récentes et nouvelles drogues*
WHO	World Health Organization
'XTC'	ecstasy

Introduction

The new drugs phenomenon has undergone dynamic change in the last few years. This is seen in the increased number, and diversity in type, of substances which have appeared on the European market, as well as new developments in the way that these substances are being produced, distributed and marketed. Quite a number of new synthetic cathinones with stimulant properties have appeared on the European drug scene, notably mephedrone, methylone and MDPV. These substances are structurally related to cathinone, the naturally occurring psychoactive principal of khat.

Mephedrone is the first cathinone derivative to be 'risk-assessed' by the extended Scientific Committee of the EMCDDA as part of the process established by Council Decision 2005/387/JHA. This risk assessment builds on the lessons learnt during previous exercises, in particular the risk assessment of BZP (2007), but also introduces a new methodological approach through the implementation, for the first time, of the new EMCDDA *Operating guidelines for risk assessment of new psychoactive substances*. The guidelines provide a useful overall conceptual framework for conducting a scientifically sound risk assessment in a timely fashion, where information sources are limited. Furthermore, the use of a semi-quantitative scoring system introduced by the guidelines has been useful in reaching consensus, although it showed a number of limitations. In my opinion, it would be useful to consider the added value of this kind of systematic approach to the assessment of the risk of new psychoactive substances, when considering the development of national initiatives in this area.

The absence of information and research findings has been a problem for all risk assessment exercises conducted by the Scientific Committee. Therefore, the risk assessment conclusions are inevitably based on partial knowledge and, consequently, are tentative. The risk assessment on mephedrone was particularly difficult, due not only to limited data available on this substance, but also to the fact that there was very little similarity to other compounds which have been previously risk-assessed through the Council Decision mechanism.

I am pleased to note that for this risk assessment, the EMCDDA made it possible to conduct a toxicological screening in the framework of an exploratory study, which examined the patterns of use and adverse effects of mephedrone amongst

a group of self-reported cathinones users. This study presented the Scientific Committee with important additional information, thus greatly facilitating the work and allowing the findings to be better grounded in evidence. In this respect, the Committee is of the opinion that follow-up research is likely to be equally valuable and provide epidemiological, sociological and criminological evidence, in order to identify trends and assess the impact of control measures.

In conclusion, I would like to note that the risk assessment exercise, linked to the early warning system under Council Decision 2005/387/JHA, is a unique element of the European action on drugs and constitutes an important instrument to support decision-making on new drugs at EU level. It can also be viewed as a useful mechanism to provide added value and support to national efforts in this area, and may serve as a good example of an evidence-based approach to sensitive policy issues.

Finally, I would like to thank all our colleagues from the extended Scientific Committee for their hard work. Furthermore, I would like to express my gratitude to the external experts and to EMCDDA staff who worked hard before, during and after the meeting to finalise the reports, in order to provide detailed and precise conclusions and to ensure a speedy completion of the process. I hope that these combined efforts will be appreciated by those to whom this report is addressed.

Prof. Michael Farrell

Chairperson of the EMCDDA's Scientific Committee

Council Decision

Council Decision 2010/759/EU of 2 December 2010 on submitting 4-methylmethcathinone (mephedrone) to control measures

THE COUNCIL OF THE EUROPEAN UNION,

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

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

Having regard to the initiative of the European Commission,

Whereas:

(1) A Risk Assessment Report on 4-methylmethcathinone (mephedrone) was drawn up on the basis of Article 6 of Decision 2005/387/JHA by a special session of the extended Scientific Committee of the European Monitoring Centre for Drugs and Drug Addiction, and was subsequently received by the Commission on 3 August 2010.

(2) Mephedrone is a synthetic cathinone which is legally produced and distributed mainly in Asia, while final packaging seems to occur in Europe. Mephedrone is mostly sold as powder, but also as capsules or tablets. It is commercially available on the Internet, from 'head shops' and from street-level dealers. On the Internet, mephedrone is often marketed as 'plant food', 'bath salt', or 'research chemical'. It is very rarely marketed as a 'legal high' (licit psychoactive substance) and there is usually no reference or concrete information about its potential psychoactive effects.

(3) Mephedrone's specific effects are difficult to assess because it is primarily used in combination with substances like alcohol and other stimulants. Mephedrone is deemed to have similar physical effects to other stimulant drugs, in particular ecstasy (MDMA). However, its relatively short duration of action, leading to repeated dosing, is more analogous to

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

cocaine. Some evidence suggests that it may be used as an alternative to illicit stimulants, that it has a high abuse liability and a potential to cause dependency. More in-depth studies would be required to explore in detail the dependence potential of this drug.

(4) There are two reported fatalities in the European Union in which mephedrone appears to be the sole cause of death. There are at least another 37 deaths in which mephedrone has been detected in post-mortem samples.

(5) Twenty-two Member States have reported seizures of mephedrone in powder or tablets. There is little information that may suggest large-scale processing or distribution of mephedrone and the involvement of organised crime. Some evidence suggests that where mephedrone has been controlled, the drug continues to be available on the illicit market.

(6) Mephedrone has no established or acknowledged medical value or use in the European Union and there is no indication that it may be used for any other legitimate purposes.

(7) Mephedrone is currently not under assessment and has not been under assessment by the United Nations system. Eleven Member States control mephedrone under drug control legislation by virtue of their obligations under the 1971 United Nations Convention on Psychotropic Substances. Two Member States apply control measures to mephedrone under their medicines legislation.

(8) The Risk Assessment reveals limited scientific evidence and points out that further studies are needed on the overall health and social risks of mephedrone. However, because of its stimulant properties, its ability to produce dependence in users, its potential attractiveness, the risk to health, the lack of medical benefits, and therefore the need to apply precaution, mephedrone should be controlled.

(9) Since eleven Member States already control mephedrone, placing it under control across the European Union may help avoid problems in cross-border law enforcement and judicial cooperation,

HAS ADOPTED THIS DECISION:

Article 1

Member States shall take the necessary measures, in accordance with their national law, to submit 4-methylmethcathinone (mephedrone) to control measures and criminal penalties, as provided for under their legislation complying with their obligations under the 1971 United Nations Convention on Psychotropic Substances.

Article 2

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

Done at Brussels, 2 December 2010.

For the Council
The President
M. Wathelet

Chapter 1

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

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 standalone 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' can be found in Chapter 3 of this publication.

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 ([2]) (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 ([3]) 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

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

([3]) 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.

that, if applicable, measures in the Member States for the control of narcotic and psychotropic substances ([4]) 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) ([5]). 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 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, can be found at the end of this publication, under 'Participants in the risk assessment process'.

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

([4]) In compliance with the provisions of the 1961 UN Single Convention on Narcotic Drugs and the 1971 UN Convention on Psychotropic Substances.
([5]) 8145/10 CORDROGUE 36/SAN 68.

(i) Annex 1 to the Risk assessment report on mephedrone (Chapter 3 of this publication); 'Technical report on mephedrone' (July 2010); Appendix 1 to the Technical report (Chapter 4 of this publication) 'Mephedrone: assessment of health risks and harms' (July 2010) (EMCDDA-commissioned cross-sectional survey of UK clubbers); and Appendix 2 to the Technical report (Chapter 5 of this publication) 'Mephedrone: additional studies — Overview of prevalence, use patterns, effects' (July 2010).

(ii) Europol–EMCDDA Joint report on a new psychoactive substance: 4-methylmethcathinone (mephedrone) ([6]);

(iii) Scientific articles, official reports, media articles and grey literature;

(iv) *Operating guidelines for risk assessment of new psychoactive substances*, (EMCDDA, 2010) ([7]);

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

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 $C_{11}H_{15}NO$, 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

([6]) http://www.emcdda.europa.eu/themes/new-drugs/early-warning
([7]) http://www.emcdda.europa.eu/html.cfm/index100978EN.html

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 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.

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 stereo-selective. 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.

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 a 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 sub-populations.

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' ([8]), mephedrone use has been identified in the clubbing and party scene, 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 purchases 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

([8]) 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.

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.

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.

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.

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.

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 (9) — as well as Croatia and Norway control mephedrone under drug control legislation.

(9) In European Union protocol order.

In Belgium, the Royal Decree of 13 June 2010 includes the substance in Article 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 No 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 (Statutory Instrument) No 199 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 as of 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 (Statutory Instrument) 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).

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 (EC) No 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 ([10]).

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.

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

([10]) 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).

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.

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.

Chapter 2

Europol–EMCDDA Joint report on mephedrone

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

At the end of 2009 and January 2010, the EMCDDA and Europol examined the available information on a new psychoactive substance, 4-methylmethcathinone (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 available on mephedrone satisfies the above criteria. The two organisations, therefore, concluded that sufficient information has been accumulated to merit the production of a Joint report on mephedrone as stipulated by Article 5.1 of the Decision. Accordingly, the Reitox NFPs, the ENUs, the EMA and WHO have been formally requested to provide the relevant information within six weeks from the date of the request, i.e. by 3 March 2010 at the latest.

The resulting Joint report on mephedrone was submitted to the Council, the Commission and the European Medicines Agency (EMA) on 29 March 2010. The report concluded that 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.

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

http://www.emcdda.europa.eu/themes/new-drugs/early-warning

Chapter 3

Technical report on mephedrone

Dr Paul Dargan and Dr David Wood

Summary [11]

'Mephedrone' (4-methylmethcathinone) is a synthetic cathinone. It has no known legitimate uses as a research, industrial, cosmetic or medicinal compound. There is evidence of its availability in Europe since 2007, with seizures and detections of mephedrone reported in 28 European and neighbouring countries to date. The size and number of mephedrone seizures has increased year on year. Most of the seizures and detections are from 2009 and 2010, but there were reports from Scandinavia, France and the UK of seizures and detections in 2008 and from Finland of seizures in 2007.

There are a number of other synthetic cathinones that are used recreationally — these include methedrone, methylone and methylenedioxypyrovalerone (MDPV). These, along with other non-cathinone drugs, e.g. methadone, have similar sounding names to mephedrone which can cause confusion amongst users, healthcare professionals and law enforcement agencies. Mephedrone is commonly sold as 'plant food' and there has been confusion amongst users as to whether all plant foods contain mephedrone.

Evidence of the use of mephedrone and toxicity associated with its use has been increasing, particularly in 2009 and 2010. There are currently no coordinated national or European population surveys on mephedrone use. However, recent surveys in students and clubbers in the UK have suggested high use prevalence rates. Over a third of clubbers surveyed reported use of mephedrone within the last month and one in five students surveyed reported previous use of mephedrone (the youngest user was aged 12 years).

[11] This chapter is an annex to the Risk assessment report. This chapter follows the format of the Technical report as set out in 'Risk assessment of new psychoactive substances: operating guidelines', EMCDDA, 2010. The information included reflects the situation as of July 2010.

It is supplied either as powder or tablets/capsules and used predominantly orally and by nasal insufflation; unwanted nasal effects associated with nasal insufflation appear to lead to some users to change to oral ingestion. There are reports of use by rectal insertion and intramuscular/intravenous injection of dissolved powder. Mephedrone is used in single use doses of 5–250 mg, although users report re-dosing due to short-lived effects and total doses used per session are typically 0.5–1 g.

Mephedrone is widely available from Internet suppliers. These are mostly based in Europe and particularly the UK, although there is some suggestion of a decrease in UK-based sites since control of mephedrone in the UK. Most sites do not restrict the countries that they will ship mephedrone to and some sites actively promote that they can ship to countries where mephedrone is controlled. These sites differ from sites selling other 'legal highs', as they are typically mephedrone/cathinone specific. There is generally limited information available to users on the content/dose of mephedrone in products and the potential for unwanted effects associated with its use. Many sites supply mephedrone in bulk (kilogram) quantities in addition to single user doses. The number of Internet sites selling mephedrone increased from December 2009 to March 2010. There is some indication that subsequent to the April 2010 classification of mephedrone in the UK, the number of Internet sites based in the UK that sell mephedrone has decreased. Mephedrone is also available from high street head shops and established street-level drug dealers.

It is likely that mephedrone sold in Europe is largely manufactured in China and bordering countries in South East Asia. Final packaging of mephedrone prior to sale does occur by suppliers in Europe and there have been seizures of tabletting/capsule machines for mephedrone processing in Europe. Analysis of seized and purchased mephedrone has shown that it is generally of high purity (>95 %). However, some samples of mephedrone have been found to contain pharmaceutical agents, other synthetic cathinones and/or classified recreational drugs. There is limited evidence that precursors used in the manufacture of mephedrone are found within the final product.

There are very few reports of crime and anti-social behaviour related to mephedrone use and supply; these have largely been from the UK and in particular Guernsey.

There are no published studies on the pharmacodynamics of mephedrone and no animal or *in vitro* studies reporting on its acute or chronic toxicity. Data on the pharmacokinetics of mephedrone is limited to one study with data on the likely metabolites of mephedrone. Therefore, information on the pharmacodynamics and pharmacokinetics of mephedrone is limited to user reports and clinical data on individuals presenting to hospital with acute mephedrone toxicity. From these, it appears that both the desired and adverse effects of mephedrone are similar to those seen with other stimulant drugs such as MDMA (3,4-methylenedioxymethamphetamine) and cocaine. Some users report a 'longer and better' high with mephedrone than with cocaine. There is detailed information available on the acute health effects associated with mephedrone toxicity from clinical case series from the UK and Sweden; including one series of analytically confirmed acute mephedrone toxicity. 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 minority of cases to date. Since experience on the toxicological profile of mephedrone is currently limited to a few hundred cases, it is difficult to be sure that rare, but clinically significant, severe effects are not associated with mephedrone use.

There are reports on user Internet forums to suggest that some individuals with a particularly high dose and/or frequent use of mephedrone develop significant 'cravings' for it. There is one confirmed report of mephedrone dependence in a patient from Scotland and anecdotal reports of mephedrone dependency in mephedrone user surveys and in reports from drug treatment agencies in the UK and other areas of Europe such as Slovenia.

There has been widespread coverage in the 'popular media' in Europe, particularly the UK, of mephedrone and in particular of potential mephedrone-related deaths. There is some suggestion that media coverage of mephedrone may have increased public knowledge of mephedrone and increased its use.

There are two reported fatalities in which mephedrone was the sole cause of death (one in Sweden and one in the UK). In addition to these cases, there are at least another 37 deaths in the UK 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 coroner/procurator fiscal inquests into death are pending for the majority of these cases and so it is not possible at this time to determine the contribution of mephedrone to death in all of these additional cases.

In conclusion, mephedrone is a synthetic cathinone which is used for is stimulant effects and there is increasing evidence of its use and availability in Europe. Given the scale of use of mephedrone, its potential for significant acute health effects and emerging reports of fatalities associated with its use, there is a significant risk of increasing acute toxicity, chronic morbidity and mortality related to mephedrone use in Europe, with associated health care utilisation and social costs.

Physical, chemical, pharmaceutical and pharmacological information

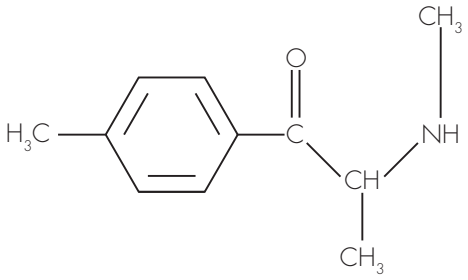
Physical and chemical description

'Mephedrone' is the common name for the synthetic cathinone 4-methylmethcathinone. The systematic (International Union of Pure and Applied Chemistry, IUPAC) name for mephedrone is 2-methylamino-1-(4-methylphenyl)propan-1-one. The Chemical Abstract Service (CAS) Registry Numbers for mephedrone are 1189805-46-6 (base) and 1189726-22-4 (hydrochloride salt). Other names for mephedrone include *N*-methylephedrone; β-keto-(4,*N*-dimethylamphetamine); 4,*N*-dimethylcathinone; *p*-methyl-methcathinone and 2-aminomethyl-1-tolyl-propan-1-one. In the rest of this document we will refer to this compound as mephedrone. There are no official synonyms, non-proprietary names or trademark names for mephedrone.

Mephedrone 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 $C_{11}H_{15}NO$, equating to

a molecular weight of 177.242 g/mol. Mephedrone has a boiling point of 269.51° C and melting point of 66.61° C.

Figure 1 — Chemical structure of mephedrone



Mephedrone was first synthesized in 1929. The main synthetic route involves a-bromination of 4-methylpropiophenone followed by reaction of the resulting compound (4-methyl-2-bromopropiophenone) with methylamine hydrochloride and triethylamine in an acidic scavenger to produce 4-methylmethcathinone hydrochloride. The reaction is then quenched with gaseous or aqueous hydrogen chloride providing the hydrochloride salt that needs to be recrystallised (Camilleri, A., 2010, Gibbons, S., 2010). This is a relatively straightforward process and the equipment and knowledge required are similar to that required for the synthesis of MDMA and amphetamines. There is limited evidence that precursors used in the manufacture of mephedrone are found within the final product. There is the potential for other synthetic routes including oxidation of the substituted ephedrine analogue (4-methylephedrine) with potassium permanganate or potassium dichromate in a solution of diluted sulphuric acid. This method is similar to that used for the synthesis of methcathinone. One of the possible hazards of the permanganate process could be contamination with manganese if the product is not appropriately purified. There is no evidence that this synthetic process is being used.

Common street names for mephedrone include 'miaow miaow', 'meow meow', 'plant feeder', 'plant food', 'bubbles', 'blow', 'Subcoca-1', 'Tornado', 'Real Euphoria', 'top cat', 'Krabba', '4-MMC' and 'MCAT' (Measham, F., 2010, Erowid 1, Psychonaut 2009).

There are a number of other synthetic cathinones that are used recreationally — these include methedrone, methylone and methylenedioxypyrovalerone (MDPV).

These, along with other non-cathinone recreational drugs e.g. methadone, have similar sounding names to mephedrone, which can cause confusion amongst users, healthcare professionals and law enforcement agencies.

Mephedrone and other cathinone derivatives do not give a colour reaction with the Marquis field test. Gas-chromatography mass-spectrometry (GC-MS) and liquid chromatography with mass spectrometry-mass spectrometry (LC-MS/MS) techniques have been developed for the detection of mephedrone and are described in detail by Camilleri et al. and Meyer et al. (Camilleri, A., 2010, Meyer, M.R., 2010, Gibbons, S., 2010). The mass-spectrometry technique does not distinguish between methyl-methcathinone isomers; however, nuclear magnetic resonance spectroscopy (NMR) and other techniques allow the isomers to be differentiated.

Physical/pharmaceutical form

Mephedrone is typically sold in powder form, which is generally described as being a white crystalline powder with a light yellow hue. The free base is a yellowish liquid at ambient temperature (Europol–EMCDDA Joint report). It is reported to have a distinctive unpleasant odour by users (Psychonaut 2009). The powder is readily soluble in water and therefore can be dissolved prior to oral/rectal use or injection. In addition to the powder form being available directly, it is also available as capsules containing the powder or tablets pressed from the powder (Erowid 1, Newcombe, R., 2009). There do not appear to be any distinctive markings specific to mephedrone on the tablets or capsules. However, as summarised in the Prevalence of use section below, a number of mephedrone tablets seizures in European Member States have included tablets with markings.

Mephedrone is sold under a number of brand names including 'plant feeder', 'bath salts', 'Neo Doves' and 'Neo Blues' ([12]). The powder is often sold in small plastic sealed bags labelled 'not for human consumption', 'research chemical' or 'not tested for hazards or toxicity' (Psychonaut 2009, Newcombe, R., 2009).

([12]) Other names include 'Wild Cat', 'The Business', 'Diablo XXX', 'Blow', 'Magic', 'Tornado', 'the Real Euphoria' and 'The Big Sroom Effect'.

Route of administration and dosage

Mephedrone is used by the oral route, nasal insufflation, intramuscular injection, intravenous injection and rectal insertion (Psychonaut 2009, Erowid 2, Drugs-Forum). Because of its physical characteristics, it is unlikely to be suitable for smoking.

Oral use includes swallowing capsules, tablets and/or powder directly. The powder can also be dissolved in water or wrapped in cigarette paper ('bombing') prior to swallowing (Measham, F., 2010, Newcombe, R., 2009). The predominant routes currently appear to be oral ingestion and nasal insufflation; in the recent MixMag survey, 70 % of mephedrone users reported use of mephedrone by nasal insufflation and 30 % oral ingestion (Dick, D., 2010, Winstock, A.R., 2010). There are numerous reports of individuals using mixed routes during a single session (oral and nasal, oral and rectal). As mentioned below in the Health risks section, users report significant nasal irritation associated with nasal insufflation and there is the suggestion that they switch to oral administration after initial experience with nasal insufflation (Erowid 2).

There are increasing reports of intravenous injection of dissolved powder, particularly from Guernsey, Ireland, Romania and Slovenia. There is also one case report from the UK of an individual who developed acute mephedrone toxicity after intramuscular injection of dissolved powder (Wood, D.M., 2010a).

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 (Erowid 3). In one mephedrone user focus group study, users reported starting with low doses of mephedrone (50–75 mg) but rapidly increasing the doses used, to doses in the hundreds of milligrams (Newcombe, R., 2009). Users commonly report re-dosing during a single session with total doses typically being 0.5–2.0 g. As mentioned below, under Health risks, doses used in those presenting to healthcare services with acute toxicity range from 0.3–7.0 g. In the UK MixMag clubbers survey, 14.4 % of those who had used mephedrone reported using at least weekly, whilst 44 % used it every three months (Winstock, A.R., 2010).

Pharmacology, including pharmacodynamics and pharmacokinetics

A recent study by Meyer et al. in Germany has provided data on the likely metabolites of mephedrone (Meyer, M.R., 2010). In this study, rats administered a single 20 mg/kg dose of mephedrone by gastric intubation and urine was collected over a 24-hour period after mephedrone administration. In addition to mephedrone, the following metabolites were detected: nor-mephedrone, nor-dihydro mephedrone, hydroxytolyl mephedrone and nor-hydroxytolyl mephedrone. In a human urine sample submitted by a mephedrone user, a further metabolite, 4-carboxy-dihydro mephedrone was also detected. The authors postulated that the overlapping metabolic pathways that were thought to be responsible for these metabolites were as follows:

- N-demethylation to the primary amine (metabolites nor-mephedrone, nor-dihydro mephedrone and nor-hydroxytolyl mephedrone);
- reduction of the keto moiety to the respective alcohol (metabolites nor-dihydro mephedrone and 4-carboxy-dihydro mephedrone);
- oxidation of the tolyl moiety to the corresponding alcohol (metabolites hydroxytolyl mephedrone and nor-hydroxytolyl mephedrone).

It is thought that the hydroxytolyl mephedrone and nor-hydroxytolyl mephedrone metabolites are partly excreted as glucuronides and sulphates. There is no data available to be able to determine how long either mephedrone or its metabolites are detectable in either blood or urine samples in animals or humans.

Users report on Internet users 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 desired effects within 30 minutes. 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. 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 (Erowid 2, Erowid 4).

There are no formal pharmacodynamic studies looking specifically at mephedrone. From the reported clinical effects seen in patients with mephedrone toxicity and effects reported on user discussion forums, it appears that mephedrone has similar stimulant, sympathomimetic effects to MDMA and cocaine.

Psychological and behavioural effects

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.

Therefore, the psychological and behavioural effects related to mephedrone use are based on users' reports and clinical reports of acute mephedrone toxicity. The latter are summarised under Human data, in this chapter.

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 (Dick, D., 2010, Winstock, A.R., 2010, Erowid 4, Measham, F., 2010, Drugs-Forum). The latter effect of mild sexual stimulation was reported in 60 % of mephedrone users in the recent MixMag survey (Dick, D., 2010). Overall, these effects seem comparable to that reported for other stimulant drugs such as MDMA and cocaine. In the MixMag survey, respondents were asked how mephedrone compared with cocaine (Winstock, A.R., 2010). 65 % said that it gave a longer high and 55 % a better high than cocaine. 55 % of respondents said it was less addictive and 25 % reported that mephedrone has 'more risks' than cocaine.

Undesired psychological and behavioural effects reported by users include 'head rushes', inability to concentrate, inability to visually focus, memory problems, altered conscious level, bizarre behaviour, anxiety, agitation, insomnia, hallucinations and delusions (Drugs-Forum, Dick, D., 2010, Winstock, A.R., 2010, Erowid 4, Psychonaut 2009). 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, gamma-hydroxybutyrate/gamma-butyrolactone (GHB/GBL) or other stimulant drugs such as MDMA, amphetamine or cocaine.

There are reports from intravenous mephedrone users of more severe psychological and behavioural effects. These include paracitosis leading to scratching and gauging of the skin particularly of the face, neck and arms; Parkinsonian-like twitching of limbs; paranoia; suicidal ideation and severe insomnia, particularly after prolonged periods of use (personal communication, Mr Callum McVean, Guernsey).

Legitimate uses of the product

There are no known uses of mephedrone as a research, industrial, agricultural or cosmetic compound, despite it being marketed as 'plant feeder', 'bath salts' or 'research chemical'.

Mephedrone was classified under medicines legislation in Finland in 2008 (Medicines Act (395/87)) and is considered a medicine under Dutch law because of its psychoactive properties. However, mephedrone is not a recognised medicinal product in its own right and it is not used for the synthesis of any other medicinal products or active pharmaceutical ingredients (API). Furthermore, it is not recognised as a metabolite of any medicinal products or APIs. There is the theoretical possibility that mephedrone could be used for the synthesis of ephedrine, pseudo-ephedrine and pyrovalerone (EMA, 2010). However, there are no marketing authorisations, current or suspended, which use mephedrone as the precursor to these products.

Dependence and abuse potential

Animal *in vivo* and *in vitro* data

There are no published animal or *in vitro* studies investigating the dependence/abuse potential of mephedrone.

Human data

There have been no formal studies investigating the dependence/abuse potential of mephedrone in humans.

There is one report from the UK of a young professional male who developed dependence following 18 months' use of oral, nasal and rectal mephedrone (Bajaj, N., 2009). He presented with transient psychosis, hallucinations, hypomania

and mood disturbances. He fulfilled the ICD-10 criteria for dependence syndrome and after inpatient treatment with olanzapine, his symptoms resolved.

Addiction/dependence symptoms were reported by 17.6 % of 205 mephedrone users in a Scottish survey of school and college/university students (Dargan, P.I., 2010).

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. The Belfast (Northern Ireland) drugs organisation Forum for Action on Substance Abuse and Suicide Awareness (FASA) has reported a 300 % rise in drug-related referrals to its service between January 2009 and January 2010 which they feel is related to problem mephedrone use. A media report discussing this suggested that 25 % of clients were aged 18 years and under and that this amounted to approximately 1 000 individuals (CYP Now, BBC News 1). There is a report from the Dublin Youth Drug and Alcohol Service in Ireland that in 11 % of assessments (January to June 2010; n=56) 'head shop' drugs (including mephedrone) were the main drug of abuse and 30 % were using head shop drugs as part of their problematic substance use (personal communication, Dr R. Smyth, Youth and Drug Alcohol Service, Dublin, Ireland).

User reports suggest that some individuals with high/frequent use of mephedrone develop a 'craving' for it (Erowid 2, Drugs-Forum, Measham, F., 2010, Psychonaut 2009); this could be due to the high associated with its use and its relatively short duration of action. A report from the Slovenian organisation DrogArt, based on outreach work at dance events and nightclubs and an Internet drug user forum, suggests that many of the users consider craving to be the main problem associated with mephedrone use (Pas, M., 2010). Users in this survey compared their experience with cocaine, methamphetamine and speed and stated that they had not experienced similar craving with these drugs.

These reports of mephedrone 'dependence' suggest that it is associated with psychological rather than physical dependency similar to other stimulant drugs, such as MDMA and cocaine.

For additional information, please see Chapter 4: Mephedrone — assessment of health risks and harms.

Prevalence of use

Mephedrone was first detected in Europe in November 2007 with formal notification of mephedrone to the EMCDDA in March 2008. There are reports to the EMCDDA of seizures and detection of mephedrone from 28 European and neighbouring countries. Seizures have been reported in 22 Member States and 2 other countries that report to the EMCDDA and detections through formal tablet analysis schemes or ad hoc purchases in at least six Member States. Most of the seizures/detections are from 2009 and 2010; however, there are some reports from Scandinavian countries and the UK of seizures/detections in 2008 and reports from Finland of seizures in 2007 ([13]).

Table 1 — Seizures of mephedrone

Country	Amount and details of the seizure
Austria	2009: 11 samples of powder – 2 beige, 3 yellow, 4 white and 2 brown (2 totalling 23.4 g also containing ethylcathinone, 2 totalling 1 082.4 g also containing butylone, MDPV and methylone and 7 seizures of mephedrone totalling 5 911 g). 3 samples of crystal. 2010: 29 powder samples analysed by ChEckiT! Vienna 12 were sold as MDMA/ecstasy, 10 were sold as mephedrone, 1 was sold as cocaine, 3 were sold as speed, 1 as MMC and 2 were sold as unknown powders. All of these were found to contain mephedrone, 2 also contained amphetamine and 1 also contained MDMA.
Belgium	2009: 3 seizures of 8 tablets, one blue-green tablets with a captagon logo containing mephedrone and caffeine, 6 light green tablets with a captagon logo ® containing mephedrone, caffeine and MDMA and one blue-green tablet with a captagon logo ® containing *m*CPP, MDMA, caffeine and amphetamine in addition to mephedrone. 3 white powders containing mephedrone alone. 2010: 4 seizures of mephedrone powder – 1 white powder containing ketamine and caffeine in addition to mephedrone; 1 beige powder containing caffeine and mephedrone and 2 white/beige powders containing mephedrone alone.
Bulgaria	2010: 3 seizures of white powder totalling 1 001.55 g of mephedrone.
Cyprus	2009: 166 tablets containing mephedrone.

([13]) A summary of this information is available in the Europol–EMCDDA Joint report on mephedrone.

Table 1 (continued)

Country	Amount and details of the seizure
Czech Republic	2010: mephedrone was detected in a single white powder sample.
Denmark	2008: 8 mephedrone seizures, including 474.4 g of beige powder. 2009: 9 reported mephedrone seizures.
Estonia	2009: 6 seizures of powder containing mephedrone totalling 47.85 g. 2010: 6 seizures of mephedrone powder totalling 173.36 g.
Finland	2007: 12 capsules containing mephedrone. 2008: 21 seizures totalling 36 capsules containing mephedrone (some found to contain ethylcathinone) and 109.9 g of mephedrone powder. 2009: 10 customs seizures totalling 264.8 g of mephedrone powder and 5 forensic laboratory seizures totalling 31 g of mephedrone powder. 2010: 32 seizures of powder totalling 213.2 g of mephedrone and 3 seizures of a total of 35 mephedrone tablets.
France	2008: Mephedrone identified in one capsule associated with amphetamine and caffeine. 2009: The French SINTES study identified 7 samples of mephedrone, 1 sold as mephedrone, 3 as MDMA, 2 as amphetamine and 1 as MPK.
Germany	2009: One seizure of 4 400 ecstasy tablets seized with a triangle logo were found to contain mephedrone and 6 seizures of mephedrone powder totalling 320.67 g. In addition, in a mixed drug seizure containing 18 ecstasy pills, 3 were found to contain mephedrone. 2010: 2 seizures of mephedrone powder.
Greece	No reported seizures because mephedrone is not included in toxicological screening, as there is no reference standard available.
Guernsey	2009: 96 seizures of powders totalling 1 186.875 g of mephedrone and 7 capsules.
Hungary	2009: 4 seizures of powders total 1 008 g mephedrone, of which 0.22 g contained mephedrone and cocaine. 2010: 15 seizures of 125.64 g of mephedrone powder (2 samples of powder were contained within capsules). 3 seizures of mephedrone tablets totalling 319 tablets (84 green with a star logo and 235 light pink with a smile logo).
Ireland	2009: 2 seizures of powder found to contain mephedrone both sold as legal highs called 'blow'. One was crystalline in nature and also contained benzocaine.

Table 1 (continued)

Country	Amount and details of the seizure
Italy	2010: A total of 161 mephedrone tablets – 150 white/rosy ecstasy tablets with a dolphin logo and 11 white tablets with a dolphin logo. 2 seizures of powder containing 20 g of mephedrone (1 seizure of 10 g beige powder and 1 of 10 g white powder).
Latvia	2009: 3 seizures totalling 678 mephedrone tablets. 2010: Seizure of 74.96 kg of white powder containing mephedrone.
Lithuania	Suspected seizures were reported (minor quantities, about 1 g total weight) but confirmatory analysis was not performed.
Luxembourg	2010: Seizure of 4.4 g of mephedrone powder.
Malta	2009: 0.56 g mephedrone seized at a drug dance scene. 2010: 2 seizures of white powder totalling 2.19 g.
Netherlands	2009: From DIMS: 54 tablets, 9 powders and 2 mixed samples containing mephedrone. From NFI: 103 seizures totalling 286 493 tablets (including one single seizure of 276 000 tablets mainly bearing the Roche 2 implant logo) and 57.5 kg powder containing mephedrone. The tablets contained a range of different logos such as triangle, music notes, ® and Roche 2. 2010: From DIMS: 20 tablets sold as 'XTC'/MDMA contained mephedrone, an additional 39 samples (19 tablets and 20 powders/capsules) were analysed and found to contain mephedrone, 7 samples also contained 4-methylpriopiophenone.
Poland	2009: Seizure of 0.23 g of white powder containing mephedrone 2010: Seizure of 11.3 g of powder containing mephedrone.
Portugal	No information provided by the Reitox focal point in Portugal as to whether there have been any seizures or not.
Romania	2009: 200 collected samples of powder and crystals totalling 50 g mephedrone (also contained fluoromethcathinone, caffeine and lidocaine). 2010: Samples also found to contain fluoromethcathinone, ethcathinone, methoxymethcathinone, benzocaine, bk-MBDB and butylone. The Romanian focal point reports seizures of 'legal highs' from stores which included mephedrone-based products.

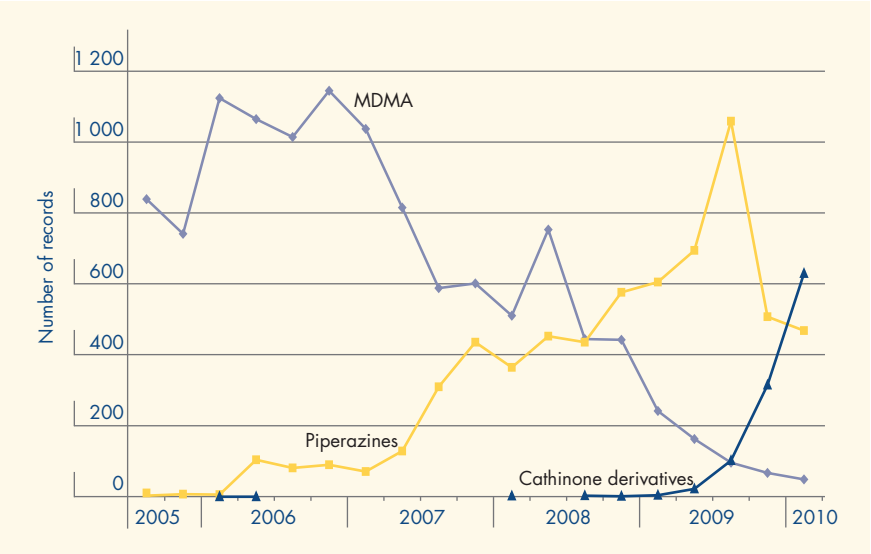
Table 1 (continued)

Country	Amount and details of the seizure
Slovakia	2009: 2 seizures of powder (one white and one blue-green) totalling 3 861 g of mephedrone (also containing caffeine) and 1 seizure of 1 197 light green tablets with a captagon logo containing mephedrone alone.
Spain	No reported seizures.
Sweden	2008: 82 seizures of powder totalling 4 694 g of mephedrone. 2009: 215 seizures of powder totalling 8 703 g of mephedrone, one seizure of 9 capsules of mephedrone and one seizure of a mephedrone tablet. 2010: 8 seizures by customs and 75 'cases' reported by Swedish police.
UK	2008: a capsule containing 62 mg of mephedrone powder and a powder containing 9.7 mg of mephedrone. Four additional Internet purchases tested were found to contain mephedrone and ethcathinone. 2009: 606 seizures of powder containing 39.1 kg of mephedrone, 12 seizures of capsules totalling 164 capsules of mephedrone and 2 seizures of tablets containing 36 mephedrone tablets. One powder was found to contain MeOPP in addition to mephedrone and a further powder was found to contain phenethylamine. 2010: The UK Forensic Science Service report seizures of over 100 powder samples of almost 80 kg of mephedrone. Data from other 2010 UK seizures was not available at the time of writing this report.
Norway	2008: one seizure of 39.8 g of mephedrone. 2009: 9 seizures of powder totalling 765 g of mephedrone and 4 seizures of mephedrone tablets totalling 479.
Croatia	2009: 4 seizures: 17 white tablets without a logo containing mephedrone, 3 mephedrone capsules containing a dirty white crystalline substance, 1 seizure of 28.14 g of white mephedrone powder and one seizure in a post office of a package containing 5 pouches of white mephedrone powder.
Switzerland	2009: Mitsubishi franked tablets seized and on analysis found to contain 68.1 mg MDMA, 12.6 mg caffeine, 6.9 mg mephedrone. 2010: Seized 'XTC' tablets found to contain mephedrone.
Belarus	2010: 1 g of white powder seized which contained mephedrone.

Source: EMCDDA, unpublished.

Data from the UK Forensic Science Service (FSS, see Figure 2) demonstrates a persistent decrease in MDMA seizures analysed by FSS since 2007, with an increase in piperazine seizures from 2007 to the middle of 2009, followed by a decrease since then. There were very few cathinone seizures prior to 2009, but these have increased significantly since early 2009. In March 2010, seizures of cathinones (including mephedrone) were greater than seizures of piperazines and MDMA combined. Data is not currently available on UK seizures analysed by the FSS, following the change in the UK legislation and the classification of mephedrone and other cathinones on 16 April 2010.

Figure 2 — MDMA, piperazine and cathinone derivative seizures: July 2005–March 2010



Source: Forensic Science Service (FSS), UK, 2010.

The price of mephedrone reported to the EMCDDA varies across Europe, some examples of reported prices are: Romania EUR 40–100 per gram, Poland EUR 15 per gram, France EUR 15 per gram, Hungary EUR 30–40 per gram, Latvia EUR 29 per gram, Belgium EUR 50 per gram and Ireland

EUR 30–40 per gram. In addition, information was supplied by Ireland on the prices for pills (EUR 7.5 per pill) and tablets (EUR 6 per tablet).

As noted in Availability and quality of the new psychoactive substance on the market (purity, adulterants, etc.), in the EMCDDA Internet snapshot studies, the price of mephedrone ranged from GBP 9.50–GBP 14.50 per gram; many sites offered discounts for larger purchases with bigger discounts for larger purchases (e.g. 1 kg for GBP 3 100 i.e. GBP 3.10 per gram).

There are currently no coordinated national or European population surveys on mephedrone use. However, it has been reported that the next British Crime Survey will include mephedrone and that the next Irish general population survey will include questions on 'head shop' products.

In a 2009 survey of over 2 000 clubbers in the UK, 33.6 % of those surveyed reported use of mephedrone within the last month (Dick, D. 2010, Winstock, A.R. 2010). This is comparable with other psychoactive substances such as cocaine (47.4 %), ecstasy (48.4 %) and ketamine (32.4 %), but greater than methylone (7.5 %) and amphetamines (speed, 14.7 %). Lifetime use of mephedrone (41.7 %) was lower than other comparable psychoactive substances such as cocaine (86.7 %), ecstasy (91.0 %) and ketamine (67.8 %). This lower lifetime use is likely to be due to the fact that mephedrone has not been available for as long as these other drugs.

In a survey of 1 006 school and college/university students in Scotland in February 2010, 205 (20.3 %) of those surveyed had used mephedrone on at least one occasion (Dargan, P.I., 2010). Of these, 23.4 % reported that they had used mephedrone on one occasion only; however, 4.4 % reported use on a daily basis (particularly in those aged under 21 years of age).

A further survey carried out in Northern Ireland focus groups was conducted with 154 pupils (aged 14–15) in three schools in May 2010 (Meehan, C. 2010). Youth workers and teachers were also interviewed. This study was carried out in Belfast and Derry in areas with high deprivation and in which drug use is prevalent. All of the pupils had heard of mephedrone; approximately 40 % had tried it at least once and 70 % stated that their friends had used mephedrone. Mephedrone use was higher amongst males and cannabis users. Mephedrone

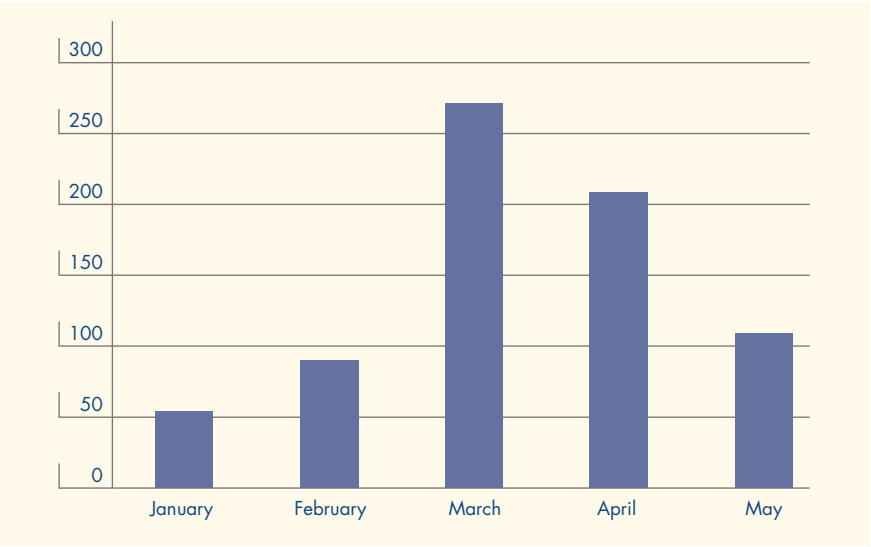
was most commonly used at a party or friend's house, often together with alcohol. Approximately 80 % of respondents reported that they knew where to buy mephedrone — usually from friends or a dealer. Respondents stated that it was easier to obtain mephedrone than cannabis; but there was some concern around the potential for paramilitary violence if they were caught with mephedrone. There was confusion amongst respondents over the difference between methadone and mephedrone and also whether normal plant foods contain mephedrone.

In a study in the Republic of Ireland, 209 urine samples from methadone maintenance patients submitted for 'drugs of abuse screening' were also analysed for the presence of mephedrone and related compounds (McNamara, S. 2010). Overall, 13.9 % of samples were positive for mephedrone and 3.3 % were positive for methylone (all of these were also positive for mephedrone); interestingly only 0.5 % were positive for 1-benzylpiperazine. 46 of these samples were from individuals in a drug treatment clinic (an unspecified proportion self-reported use of 'legal highs'); of these, 37.0 % were positive for mephedrone and 10.9 % were positive for methylone. 163 samples were randomly selected from other samples received for routine drugs of abuse analysis. Of these, 7.4 % were positive for mephedrone and 1.2 % for methylone. Urine samples positive for 'head shop' products were positive for opiates in almost half of the cases, suggesting that 'head shop' products are being used in the problematic opiate using population.

Despite there being no population level surveys looking at the scale of mephedrone use, it is likely based on the seizure data/surveys summarised above and the health risks discussed under Human data, that there is use of mephedrone across Europe and that this has increased from 2008 to 2010.

There has been widespread media interest in mephedrone. The EMCDDA has produced a summary of the number of newspaper articles relating to mephedrone — see Figure 3 (EMCDDA, unpublished).

Figure 3 — Mephedrone-related press articles, 2010



Source: EMCDDA, unpublished, 2010.

The driving force for the increases seen in the first quarter of 2010 appears to have been media interest in what were reported at the time as mephedrone-related deaths in the UK; this is discussed further in Other clinical reports of acute mephedrone toxicity. Additionally, there was a surge in media interest in mephedrone related to statements from school headmasters and the UK Headmasters Association regarding the use and availability of mephedrone in school children in March 2010 (BBC News 2). Media interest in mephedrone has continued since it was controlled on 16 April 2010 and the final driving force appears to have been media interest in law enforcement action concerning the control of mephedrone in a number of countries. These are detailed in Possible effects on society as a whole, together with media interest in whether the control of mephedrone was appropriate.

For additional information, please see Chapter 4: Mephedrone — assessment of health risks and harms and Chapter 5: Mephedrone — additional studies — overview of prevalence, use patterns and effects.

Health risks

For additional information on Health risks, please see Chapter 4: Mephedrone — assessment of health risks and harms and Chapter 5: Mephedrone — additional studies — overview of prevalence, use patterns and effects.

Acute health effects

Animal data

There is no animal data in the scientific literature on the acute health effects of mephedrone.

Human data

User reports

The 2009 MixMag survey of over 2 000 UK clubbers included data reported by users on unwanted effects associated with their 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 %) (Dick, D. 2010).

In a Scottish survey of school and college/university students, 56 % of those who had previously used mephedrone reported at least one adverse effect associated with its use; these are summarised in Table 2 (Dargan, P.I., 2010). In addition to systemic features, a significant number of the adverse effects were local effects that were likely to be related to the irritant effects of mephedrone (sore nasal passages, 24.4 %, sore mouth/throat, 22.9 %, nose bleeds, 22.4 %).

Table 2 — Adverse effects reported among the 205 students who used mephedrone in the Scottish survey

Adverse effect	Number of users	Percentage of users
Bruxism	58	28.3 %
Paranoia	51	24.9 %
Sore nasal passages	50	24.4 %
Hot flushes	48	23.4 %
Sore mouth/throat	47	22.9 %
Nose bleeds	46	22.4 %
Suppressed appetite	44	21.5 %
Blurred vision	43	21.0 %
Palpitations	42	20.5 %
Insomnia	40	19.5 %
Hallucinations	37	18.0 %
Addiction/dependence	36	17.6 %
Nausea/vomiting	35	17.1 %
Burns	35	17.1 %
Blue/cold extremities	30	14.6 %

Source: Dargan, P.I., 2010.

There are numerous symptoms reported by users on user Internet forums (Erowid 2, Erowid 4, Drugs-Forum, Psychonaut 2009), these include:

- numbness and lack of tactile sensitivity with very large amounts
- 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
- 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.

London clinical data

There is data available on two series of acute mephedrone toxicity from the Clinical Toxicology Service at Guy's and St Thomas' NHS Foundation Trust in London (Wood, D.M. 2010a, Wood, D.M. 2010b, updated with unpublished data). The first of these, discussed in Self-reported acute mephedrone toxicity below, is a series of 72 patients who presented with acute toxicity related to self-reported mephedrone use. The second of these, discussed in Analytically confirmed acute mephedrone toxicity below, is a series of nine patients with acute toxicity related to self-reported mephedrone in whom full toxicology screening was undertaken.

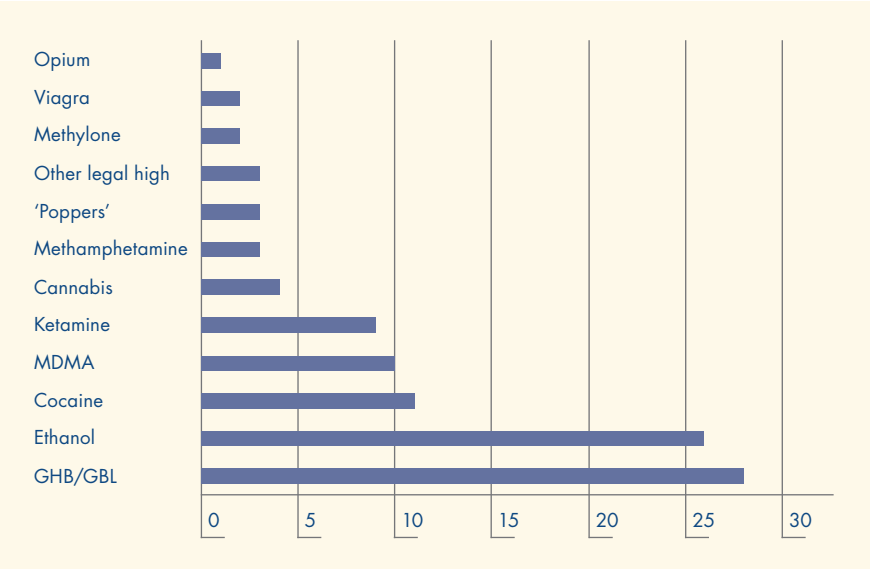
Self-reported acute mephedrone toxicity

Detailed data is available on 72 cases of acute toxicity associated with self-reported mephedrone use in London from 1 January 2009 until 15 June 2010 (Wood, D.M. 2010a, Wood, D.M. 2010b, updated with unpublished data). There were no presentations with mephedrone toxicity to this unit prior to this. Mephedrone was classified in the UK on 16 April 2010 and there was no change in the number of presentations with acute toxicity in the first two months after the change in the legal status of mephedrone.

The mean ± SD (standard deviation) age was 27.8 ± 8.7 years (range 16–54 years), 81.9 % were male. 35 (48.6 %) specified the route of mephedrone use. The most common route was nasal insufflation (19, 54.3 % where route of use was specified); other routes of use included oral ingestion (12, 34.3 %), combined nasal insufflation/oral ingestion (3, 8.6 %) and combined oral ingestion/intramuscular (IM) injection (1, 2.9 %). The dose of mephedrone used was reported in mg/g quantities in 21 (29.2 %) individuals. The mean ± SD (range) dose was 1.9 ± 2.0 (0.3–7.0) g.

Nine patients presented with self-reported mephedrone use, in the remaining 63 patients the mean ± SD number of co-used substances was 1.6 ± 0.9; the substances used and frequency of self-reported use is shown in Figure 4.

Figure 4 — Number of participants reporting co-use



Source: Wood, D. M., 2010a.

The mean heart rate was 93.1 ± 26.1, range 50–158 beats per minute, mean systolic blood pressure was 141.1 ± 23.7, range 99–210 mmHg. 13.9 % had clinically significant hypertension (systolic blood pressure ≥ 160 mmHg), 36.1 % had a tachycardia (heart rate of ≥ 100 bpm) and 8.3 % had a severe tachycardia (≥ 140 bpm). No patients had clinically significant hyperpyrexia; the mean temperature was 36.0 ± 1.0, range 33.0–38.1 °C. GCS wasn't recorded in 2 patients; the majority of patients in which it was recorded (82.9 %) had a GCS of 15 on presentation to the emergency department; of the 12 who had a GCS of ≤ 8, 11 had concomitantly used a CNS depressant (GHB/GBL in 10 presentations and opium in 1 presentation).

The most common clinical symptom/sign on presentation was agitation (38.9 % of patients). There were 18 (25.0 %) who had palpitations, 10 (13.9 %) who had vomiting, 9 (12.5 %) who had chest pain, 5 (6.9 %) who had a self-limiting pre-hospital seizure and 4 (7.2 %) who had a headache. No patients had any skin discoloration or cool/cold peripheries.

Serum urea and electrolytes were taken in 34 patients (47.2 %) and were normal in 33 of them (97.1 % of those measured); one patient had hyponatraemia with a sodium of 125 mmol/L (this case is summarised in Analytically confirmed acute mephedrone toxicity, below. Serum creatinine kinase was measured in 18 (25.0 %) and was raised in 10 of these patients (55.6 % of those in whom it was measured), ranging from 296–4134 IU/L (upper limit of normal 229 IU/L).

Sixty-one (84.7 %) patients were discharged either directly from the ED or the short-stay observation ward. These patients required either a period of observation prior to discharge and/or symptom control (e.g. anti-emetics, intravenous fluids). Ten (13.9 %) patients required the use of benzodiazepines (oral or intravenous) for the management of agitation. Of the 11 (15.3 %) patients who were admitted to hospital, 8 (11.1 %) were admitted for observation/ management on a general internal medicine ward and 3 (4.2 % of all presentations) required admission to the intensive care unit. 71 (98.6 %) survived to discharge from hospital with no long-term sequelae on discharge; the one death is discussed in detail in this section.

The overall mean length of stay following presentation to hospital, after exclusion of one patient who developed aspiration pneumonia secondary to opium toxicity, was 6.7 ± 7.3 (range 0.3–30.0) hours.

Analytically confirmed acute mephedrone toxicity

Toxicology screening of serum samples with GC-MS/LC-MS/MS was carried out in a subset of nine patients presenting during 2009—10 to the Clinical Toxicology Service at Guy's and St Thomas' NHS Foundation Trust, London with acute toxicity associated with self-reported mephedrone use (Wood, D.M., 2010a, personal communication, Dr David Wood, Guy's and St Thomas' NHS Foundation Trust, London). Mephedrone was confirmed to have been used in 7 (77.8 %) of these patients; the remaining two patients presented more than 24 hours after use of mephedrone. Clinical data presented below is for the 7 cases in which mephedrone was detected (the highest mephedrone concentration in this cohort was 0.33mg/L). Mephedrone was the only drug detected on analytical screening in four (57.1 %) of these seven patients; the drugs detected in the other three patients were cocaine (2, 28.6 %), butylone/MDPV (1, 14.3 %).

The mean ± SD age was 24.6 ± 6.5 years (range 16–36 years), all were male. Six (85.7 %) specified the route of mephedrone use. Routes of administration were oral ingestion (2, 33.3 % where route of use was specified), combined nasal insufflation and oral ingestion (2, 33.3 %) nasal insufflation (1, 16.7 %) and combined oral ingestion and intramuscular injection (1, 16.7 %). The dose of mephedrone used was reported in mg/g quantities in 5 (71.5 %) individuals. The mean ± SD (range) dose was 2.1 ± 2.3 (0.3–5.0) g.

The mean heart rate was 109.1 ± 21.8, range 80–140 beats per minute, mean systolic blood pressure was 153.0 ± 39.6, range 110–210 mm Hg. 42.9 % had clinically significant hypertension (systolic blood pressure ≥160 mmHg), 71.4 % had a tachycardia (heart rate of ≥ 100 bpm) and 14.3 % had severe tachycardia (≥ 140 bpm). No patients had clinically significant hyperpyrexia; the mean temperature was 36.6 ± 1.1, range 35.6–38.1 °C. The majority of patients in which GCS was recorded (85.7 %) had a GCS of 15 on presentation to the ED; one patient had a GCS of 11 on presentation.

The most common clinical symptom/sign on presentation was agitation (57.1 % of patients). There were two (28.6 %) patients who had palpitations, two (28.6 %) who had chest pain, one (14.3 %) patient who had a self-limiting pre-hospital seizure and one (14.3 %) who had a headache. No patients had any skin discoloration or cool/cold peripheries and no patients reported vomiting.

Serum urea and electrolytes were taken in all patients, and were normal in six (85.7 %) patients. The one patient who died had hyponatraemia (sodium concentration of 125 mmol/L) on presentation; this case is discussed in more detail below. Serum creatinine kinase was measured in six (85.7 %) patients and was raised in 1 of these patients at a concentration of 3 830 IU/L (upper limit of normal 229 IU/L).

Four (57.1 %) patients were discharged either directly from the emergency department or the short-stay observation ward. These patients required either a period of observation prior to discharge and/or symptom control (e.g. anti-emetics, intravenous fluids). Three (42.9 %) patients required the use of benzodiazepines (oral or intravenous) for the management of agitation. Of the three patients who were admitted to hospital, two were admitted for observation/management on a general internal medicine ward and one (14.3 % of confirmed mephedrone presentations) required admission to the intensive care

unit. Six (85.7 %) patients survived to discharge from hospital with no long-term sequelae on discharge. The overall mean length of stay following presentation to hospital of those who survived was 12.0 ± 10.3 (range 3.4–26.3) hours.

One patient with confirmed mephedrone ingestion died. He was a 29-year old male who was found collapsed and unwell in a nightclub. On arrival in the emergency department, he was noted to have a fluctuating conscious level. A CT head scan showed evidence of significant cerebral oedema and impending tonsillar herniation. He had hyponatraemia with a serum sodium concentration of 125 mmol/L; further biochemical testing suggested water intoxication. Following a seizure he deteriorated further and a repeat CT scan showed tonsillar herniation and so treatment was withdrawn. Ante-mortem toxicological screening confirmed the presence of mephedrone at a concentration of less than 0.01 mg/L in serum; analysis of powder found with the patient also confirmed the presence of mephedrone. No other recreational drugs were detected on an extended screen of both the powder and biological samples from the patient. The patient's formal post-mortem result and the coroner's inquest are still awaited.

UK National Poisons Information Service Data

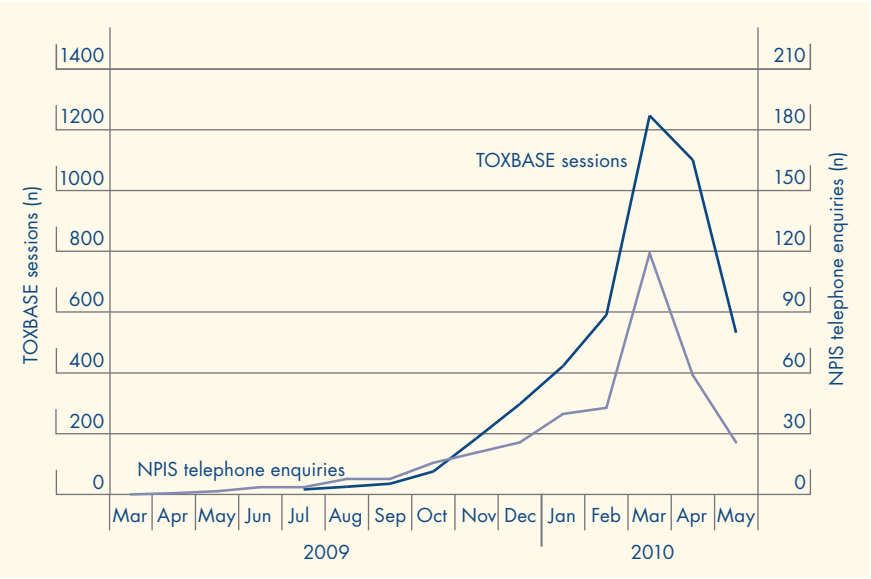
There were no enquiries to the UK National Poisons Information Service (NPIS) concerning mephedrone prior to May 2009. From May 2009 to January 2010, enquiries to both the online TOXBASE service and the telephone service increased month on month. By January 2010 there were over 30 calls to the telephone service and over 450 hits per month on the online TOXBASE service (personal communication, Professor Simon Thomas, National Poisons Information Service, Health Protection Agency). The most common clinical features in the above noted cases discussed with the UK NPIS 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, nausea. Features present in 1–5 % of individuals included abdominal pain, headache, vomiting, stupor, hypertension, increased sweating, abnormal vision, hallucinations, insomnia, renal pain, tremor.

As shown in Figure 5, further data from the UK NPIS shows that the increase in both the online TOXBASE service and the telephone service enquiries continued from January 2010 to a peak in March 2010 (personal communication, Professor Simon Thomas, National Poisons Information Service, Health Protection Agency). Subsequently, there was a significant decline in enquiries to both of these services in both April and May 2010. Data from poisons information services need to be interpreted with caution, as they are not contacted about all cases of toxicity with a particular compound. There are a number of potential explanations for the decline in enquiries to the UK NPIS regarding mephedrone toxicity since April 2010. These include an actual reduction in the number of presentations to hospital with acute mephedrone toxicity; increased awareness amongst clinicians about mephedrone and its associated toxicity/management (and, therefore, a decrease in their use of poisons information services for support in the management of cases of mephedrone toxicity); or a reduction in the use of mephedrone. It is not possible to determine to what extent these and/or other factors have contributed to the decline in NPIS enquiries concerning mephedrone toxicity.

Swedish Poisons Centre Data

The Swedish Poisons Centre received 150 enquiries concerning cathinones in 2008 and 2009 (Hägerkvist, R., 2010). Mephedrone was involved in 100 of these (82 in 2008 and 18 in 2009) (personal communication, Dr Peter Hulten, Swedish Poisons Centre). Tachycardia was present in 54 %, restlessness in 37 %, mydriasis in 25 %, hypertension in 14 % and anxiety in 14 % of these cases (Hägerkvist, R., 2010).

Figure 5 — Online and telephone enquiries at the primary clinical toxicology database of the National Poisons Information Service (TOXBASE)



Source: National Poisons Information Service (NPIS), Health Protection Agency, UK, 2010.

Other clinical reports of acute mephedrone toxicity

There is a report from Ireland of three males with a history of self-reported mephedrone use being admitted to hospital with abnormal ECGs and a clinical diagnosis of myopericarditis; it is important to note that these cases did not have analytical confirmation of mephedrone use or exclusion of cocaine use (personal communication, Professor Joe Barry, Trinity College, Dublin, Ireland).

Mephedrone-related deaths

Reports from European countries to the EMCDDA concerning potential mephedrone-related fatalities are summarised in Table 3.

Table 3 — Mephedrone-related deaths

Deaths reported that are directly related to mephedrone	Sweden, UK
Deaths reported in which mephedrone has been detected analytically and contributed to death	UK
Deaths reported in which mephedrone has been detected analytically but wasn't felt to contribute to death	UK
Deaths reported in which mephedrone has been detected analytically but final conclusions on its contribution to death are awaited	UK, Ireland
No deaths reported either directly or indirectly related to mephedrone	Austria, Belgium, Denmark, Finland, France, Germany, Italy, Latvia, Lithuania, Luxembourg, Netherlands, Poland, Slovakia, Slovenia
Mephedrone not included within analytical libraries and so not possible to determine whether it has been implicated in deaths	Greece, Romania
No information provided to the EMCDDA concerning potential mephedrone-related deaths	Bulgaria, Croatia, Cyprus, Czech Republic, Estonia, Hungary, Portugal, Spain

Source: EMCDDA, unpublished.

The first death solely related to mephedrone was from Sweden. This was an 18-year old female who reported use of mephedrone and cannabis (Gustavsson, D., 2009). She had an out of hospital cardio-respiratory arrest and was resuscitated in the emergency department. She had hyponatraemia (serum sodium 120 mmol/L), a metabolic acidosis and cerebral oedema; no samples were taken to determine the aetiology of the hyponatraemia. She was declared brain-dead in the intensive care unit 36 hours later. 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.

UK National Programme on Substance Abuse Deaths (np-SAD) data

The UK National Programme on Substance Abuse Deaths (np-SAD) collates data and provides regular reports in the UK on suspected substance abuse and/or recreational drug-related deaths. Data has been provided to the np-SAD group concerning suspected deaths involving mephedrone in the UK from the following agencies:

- Forensic Toxicology Service at St George's, University of London;
- UK Forensic Science Service (FSS);
- other UK forensic toxicology laboratories;
- Scottish Crime and Drug Enforcement Agency;
- coroners' offices;
- drug and alcohol action teams.

Overall, up to 31 May 2010, mephedrone has been potentially implicated in 35 deaths in the UK that have been reported to np-SAD from these sources (personal communication, John Corkery, np-SAD). We have provided below an overall summary of the current status of all of the cases, followed by a flowchart which provides a breakdown of all of these cases.

This is the current known status of the 35 deaths in which mephedrone has been *potentially* implicated within the np-SAD dataset; these have been broken down by country/region:

Potential mephedrone-related deaths in England

There have been at least 26 suspected mephedrone-related deaths in England reported to np-SAD.

- Five of these deaths have proved negative for the presence of post-mortem mephedrone, seven are awaiting final post-mortem mephedrone and other toxicological analyses and 14 have tested positive for mephedrone in post-mortem toxicological analyses.
- Of the 14 cases in which mephedrone has been detected in post-mortem toxicological analyses:
  - nine are awaiting further inquiries and/or the coroner's inquest and no further information is available at this time;

- one: the coroner concluded that death was due to natural causes (systemic sepsis, resulting in cardiac arrest; related to bronchopneumonia caused by beta haemolytic streptococcal group A infection);
- one: the coroner concluded that death was due to 'combined effects of alcohol and gamma-butyrolactone (GBL) intoxication'. In addition to mephedrone, its metabolite N-desalkyl methylmethcathinone was detected in this particular case;
- one: the coroner handed down a narrative verdict: 'Died following injecting mephedrone repeatedly causing mephedrone poisoning on the background of coronary artery disease';
- one: the coroner concluded that the cause of death was hanging but that 'her (the deceased) mental state had been impacted upon by her use of mephedrone and drink'. In addition to mephedrone, benzodiazepines were detected on toxicological screening of post-mortem samples in this particular case;
- one: the coroner recorded a verdict of misadventure. The cause of death was given as 'early myocardial ischaemia and patchy bronchopneumonia'. The coroner also stated that the death was contributed to by mephedrone and antidepressant medication (citalopram and diazepam were found on post-mortem analysis).

Potential mephedrone-related deaths in Scotland

There have been eight suspected mephedrone-related deaths in Scotland:

- one was negative for the presence of post-mortem mephedrone and seven tested positive for mephedrone in post-mortem toxicological analyses;
- of the seven cases in which mephedrone has been detected in post-mortem toxicological analyses;
  - five are awaiting further inquiries and procurator fiscal inquests:
    - one: mephedrone was detected in an individual with atherosclerotic coronary artery disease;

  - two: mephedrone was detected in individuals involved in road traffic accidents;
  - two: mephedrone was detected and, in at least one of these, the np-SAD Programme Manager has stated that it is likely from the information available that mephedrone was the cause of death;
- one: the Procurator Fiscal concluded that death was as the result of the 'adverse effects of methadone and mephedrone';
- one: the Procurator Fiscal concluded that death was related to 'mephedrone intoxication'.

Potential mephedrone-related deaths in Guernsey

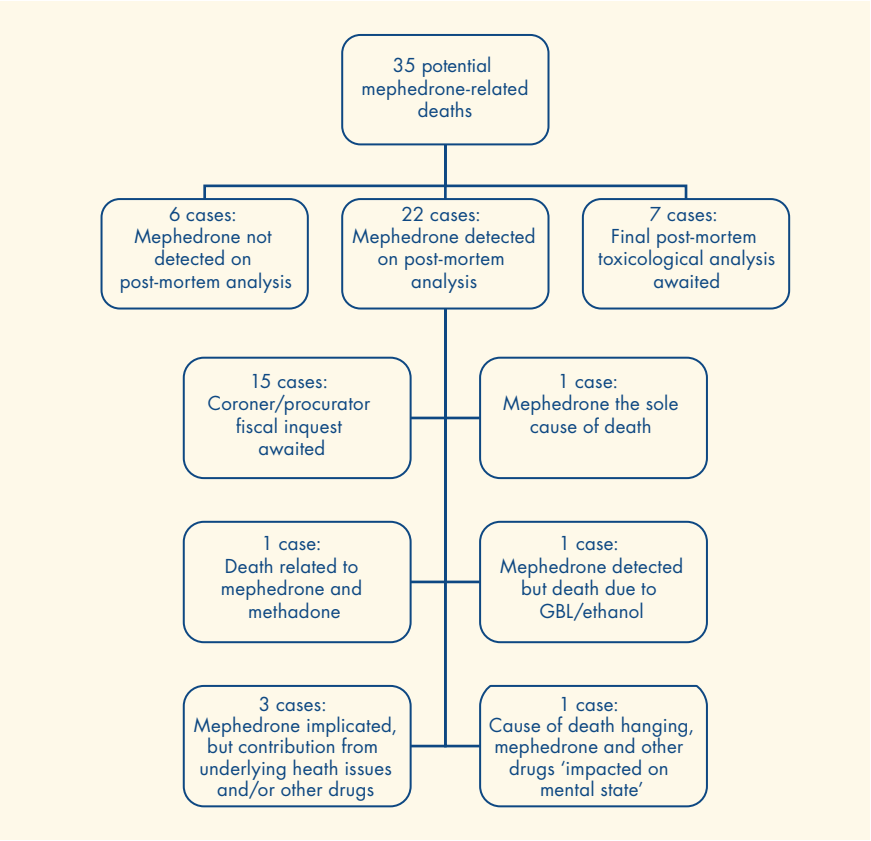
There is one death in Guernsey in which mephedrone has been detected in post-mortem analyses; further inquiries and the inquest are awaited in this case.

Potential mephedrone-related deaths in other areas of the UK

np-SAD are not aware of any suspected cases of mephedrone-related deaths in Wales, Northern Ireland, Jersey, or the Isle of Man.

Figure 6 shows a flowchart summarising the 35 cases in this np-SAD dataset in which mephedrone has been potentially implicated in death.

Figure 6 — Cases of potential mephedrone-related deaths in the UK



Source: np-SAD (National Programme on Substance Abuse Deaths), 2010.

Despite the small number of confirmed mephedrone-related fatalities in the UK from the np-SAD dataset, there has been a large amount of media coverage in relation to deaths that have been attributed within press articles to mephedrone. The involvement of mephedrone in media coverage shortly after the time of a death is generally based on reports of use of mephedrone in the deceased by family and/or friends, and coverage is often 'sensational' rather than factual (Belfast Telegraph, BBC News 3, Daily Mail 1, BBC News 4, The Guardian 1, Daily Mail 2, The Sun).

As noted above in the summary of np-SAD cases from the UK, a number of deaths in which mephedrone has initially been implicated have subsequently been demonstrated not to be related to mephedrone, either on analytical toxicological screening and/or based on the findings of the inquest (held by the coroner in England and Wales or the Procurator Fiscal in Scotland) (The Times, Daily Mirror, The Guardian 2, The Independent). Media coverage stating that a death is not attributable to mephedrone has generally not been as widespread or high profile as the initial coverage attributing death to mephedrone.

ROAR Forensics Limited data

In addition to the np-SAD dataset on UK mephedrone-related deaths, data is also available from ROAR Forensics Limited on the results of post-mortem samples that have been submitted to them for toxicological analysis that were positive for mephedrone (personal communication, Simon Elliot, ROAR Forensics Limited, UK). Their first cases, in which mephedrone was detected, was in March 2010; between March 2010 and early June 2010, urine and/or blood samples were positive for mephedrone in 16 deaths; four of these were from the Republic of Ireland and 12 from the UK. Mephedrone was the only drug detected in three of these cases. Interestingly, six of the cases involved mechanical suicide (hanging in five and gunshot in one); the significance of this is difficult to determine, as comparative data for violent death associated with other recreational drugs is not available. It is not known whether these cases have yet proceeded to coroners' inquests and relatively limited information is available on the circumstances of, and other factors that may have contributed to, death. The data that is available on these cases is summarised in Table 4.

Table 4 — Toxicological analysis of post-mortem samples that have been submitted to ROAR Forensics Limited that were positive for mephedrone

Age/sex	Blood cathinones	Urine cathinones	Other drugs detected	Other cause of death?
UK cases				
24 yrs (F)	Mephedrone 0.15 mg/L	Mephedrone 16 mg/L	Citalopram, diazepam	No
18 yrs (M)	Mephedrone 0.016 mg/L	No urine sample	Ketamine (trace), ethanol	Hanging
29 yrs (M)	Mephedrone <0.08 mg/L, methylone 0.10 mg/L	Mephedrone <0.08 mg/L, methylone 2.79 mg/L	Cocaine, ketamine, levamisole, paracetamol, ethanol	Hanging
20 yrs (F)	No mephedrone	Mephedrone 1.18 mg/L	(Hospital drugs given therapeutically)	No
23 yrs (M)	No mephedrone	Mephedrone, methylone	Cocaine, atropine, ethanol	Gunshot
30 yrs (M)	Mephedrone 0.158 mg/L	Mephedrone 12.15 mg/L	Ethanol	Hanging
19 yrs (M)	Mephedrone 0.24 mg/L	Mephedrone 65.5 mg/L	Diazepam, noscapine, papaverine, cannabis morphine/metabolites	Death likely to be heroin related
25 yrs (M)	Mephedrone 0.53 mg/L	Mephedrone 70.6 mg/L	Cocaine, levamisole, cannabis, ethanol	RTA* passenger
40 yrs (M)	Mephedrone 1.20 mg/L	Mephedrone 8.84 mg/L	Cocaine, citalopram, ethanol	RTA* passenger
19 yrs (M)	Mephedrone 0.67 mg/L	Mephedrone 1.52 mg/L	Ethanol	Hanging
20 yrs (M)	Mephedrone 0.48 mg/L	Mephedrone 2.85 mg/L	Cocaine, levamisole, ethanol	Hanging
?, (M)	Mephedrone, FMC¢, MDPV§	Mephedrone, FMC¢, MDPV§	Amphetamine	Data not available

Table 4 (continued)

Age/sex	Blood cathinones	Urine cathinones	Other drugs detected	Other cause of death?
Republic of Ireland cases				
39 yrs (M)	No mephedrone, methylone 11.0 mg/L, butylone 1.72 mg/L	Mephedrone <0.125 mg/L, methylone 256 mg/L, butylone 3.77 mg/L	Data not available	Data not available
19 yrs (F)	Mephedrone 0.20 mg/L, butylone <0.125 mg/L	Mephedrone 38.6 mg/L, butylone 1.18 mg/L	Morphine and metabolites, quetiapine, venlafaxine, zopiclone, diazepam	Data not available
27 yrs (M)	No mephedrone	Mephedrone <0.125 mg/L	Morphine, zopiclone, methadone	Data not available
24 yrs (M)	Mephedrone <0.125mg/L, MDPV§	Mephedrone 1.34 mg/L, MDPV§	Data not available	Data not available

Source: ROAR Forensics Limited, UK, 2010.
Key: RTA *: road traffic accident
FMC ♦: fluoromethcathinone
MDPV §: methylenedioxypyrovalerone

Other information concerning potential mephedrone deaths

There was a report in the Irish Times, on 22 June 2010 of a death in Ireland of a 19-year old student (Irish Times). Mephedrone was detected in a post-mortem blood sample at a concentration of 0.2 mg/L; in addition, 'heroin', butylone, venlafaxine, zopiclone, diazepam and quetiapine were detected. The coroner's inquest has been held and confirmed that the medical cause of death was found to be 'cardiorespiratory arrest as a consequence of multiple drug toxicity including heroin, mephedrone, butylone, diazepam, nordiazepam, quetiapine, zopiclone and venlafaxine' (personal communication, Professor Desmond Corrigan, Trinity College, Dublin, Ireland).

There have also been reports in the popular press in Romania of deaths potentially related to mephedrone (Bolezatu, O., 2010), however, these have not been confirmed as being related to mephedrone by the Romanian Legal Medicine Institute and as noted in the table above, mephedrone is not included within analytical libraries in Romania.

There is one further report from Maryland, USA of a 22-year old male, found collapsed and unresponsive in his living quarters, who was unsuccessfully resuscitated both at home and in the hospital. Urine screening by GC-MS was positive for 6-acetylmorphine, codeine, morphine, doxylamine and mephedrone (198 mg/L). Mephedrone was also detected in a post-mortem blood sample at a concentration of 0.5 mg/L. The medical examiner reported the cause of death as 'accidental multiple drug toxicity'. It is not possible to determine from the data presented in this case report what role mephedrone played in this death. A urine sample from a room-mate (who confirmed that both he and the deceased had used mephedrone by nasal insufflation, oral ingestion and intravenous injection) was positive for mephedrone at a concentration of 28.1 mg/L (Dickson, A.J., 2010).

The data on potential mephedrone-related fatalities needs, like all data on drug-related deaths, to be interpreted carefully. Detection of a drug in post-mortem samples does not necessarily mean that this drug is responsible for, or has contributed to, death. Furthermore, as noted in the table, there are a number of countries in which mephedrone is not part of the standard analytical library and so it has not been possible to determine whether it has been implicated in any deaths. There is also the potential that mephedrone-related or mephedrone-associated deaths in other countries may not have been detected because mephedrone was not screened for in post-mortem samples or samples were not taken for toxicological analysis. Finally, the stability of mephedrone and its metabolites in post-mortem samples has not been established.

Chronic health effects

Animal data

There is no published data in this area.

Human data

Amongst users with high frequency/high-dose use of mephedrone, there are reports on Internet user forums of post-use depression (Erowid 2, Erowid 4, Drugs-Forum). There are no experimental or clinical data to support the users' hypotheses that this relates to depletion of serotonin or dopamine. As noted in Other clinical reports of acute mephedrone toxicity, above, one death in the UK np-SAD dataset and six deaths in the ROAR forensics dataset in which mephedrone was detected, were violent suicide deaths. It is not possible, given the amount of information available on these cases and the lack of comparative data on the association between short- and long-term recreational drug use and violent suicide death, to be certain of the significance of this.

As noted in the Dependence and abuse potential section of this publication, there are some reports suggesting the potential for a dependence syndrome associated with prolonged mephedrone use.

There are no reported studies suggesting chronic long-term physical health effects relating to mephedrone use. However, there is the potential for long-term physical harm as a direct result of acute mephedrone toxicity (e.g. prolonged seizures resulting in cerebral hypoxia).

Factors affecting public health risks

Availability and quality of the new psychoactive substance on the market (purity, adulterants etc.)

Mephedrone is readily available, either from Internet suppliers, many of which were (prior to the classification of mephedrone under the Misuse of Drugs Act (1971) in the UK on 16 April 2010) based in the UK, in retail outlets (head shops) and from street-level drug dealers (Measham, F., 2010, Drugs-Forum, Erowid 1). Individuals are often able to purchase unlimited amounts and there are reports of individuals purchasing kilogram amounts from Internet sites. The main precursor of mephedrone (4-methylpropiophenone) is also available on the Internet and there is the potential for self-manufacture of mephedrone, although this does not currently appear to be occurring in Europe. Europol reports that several Member States

have identified that mephedrone sold via the Internet originates from China and bordering countries in South East Asia (Europol).

The EMCDDA has been carrying out snapshots of Internet 'legal high' sites since 2006. Two of these exercises have been carried out to assess mephedrone availability over the Internet. A snapshot on 9 December 2009 was followed by a second study from 8–10 March 2010 (EMCDDA, unpublished). These snapshot studies targeted online English language websites, both retail and wholesale, that would be easily accessible to Internet users who were interested in buying mephedrone.

The December 2009 study used the meta-search engine metacrawler.com and google.com. Online mephedrone shops were identified using the search string 'buy mephedrone' (in English). All metacrawler hits (typically 20–70) were examined, followed by an examination of the first 50 Google hits. For the second snapshot in March 2010, the metacrawler methodology was unchanged, but the examination of the Google search was expanded to include the first 100 hits (the search was discontinued after 20 consecutive 'irrelevant' hits). A search in Yahoo was also performed. The following data was collected from each website: country of origin, scale of sales (retailer, wholesale), price, marketing strategy, information on legality and information on warnings.

The table below summarises the number of sites identified in the two snapshot studies. There was a two-fold increase in the number of sites identified as selling mephedrone, using an identical search term on metacrawler between December 2009 and March 2010.

Table 5 — Number of websites identified in the two EMCDDA snapshot studies

	Snapshot (9 December 2009)	Snapshot (8–10 March 2010)
Metacrawler	25	50
Google	6	27
Yahoo	Not applicable	0
Total number of sites identified	31	77

Source: EMCDDA, unpublished, 2010.

Seventy-five (97 %) sites had one or more parameters suggesting that the 'country of origin' was the UK. The majority of sites, 50 (65 %), did not have restrictions on delivery (some posted under the disclaimer that the customer had to check legal status in the country of delivery). 27 (35 %) sites had restrictions on countries that they would ship to, but typically the reason was not given.

All of the sites were English-language based, one also had a Polish language interface. All of the sites accepted UK pounds sterling (GBP) as currency, five also accepted euros and US dollars (USD). The prices of mephedrone ranged from GBP 9.50 to GBP 14.50 per gram; many sites offered discounts for larger purchases with bigger discounts for larger purchases (e.g. 1 kg for GBP 3 100, i.e. GBP 3.10 per gram). All of the sites provided information on the purity of mephedrone and claimed to have a very high level of purity of 99.7–99.9 %.

Unlike many other 'legal high' sites that offer a wide variety of substances, 74 (96 %) of the sites identified sold mephedrone and other synthetic cathinones only. Only three (4 %) sites were generic 'legal high' sites. Another significant difference was that more of the mephedrone sites (37 (48 %)), were both wholesalers and retailers compared to only 10–15 % of general 'legal high' sites.

Mephedrone was most often sold as a 'plant feeder' or 'plant food', although 'research chemical', 'bath salts', 'for botanical research' or 'hoover freshener' were other terms used. 67 (87 %) of the sites provided the warning 'not for human consumption' next to pictures and/or descriptions of mephedrone.

One limitation of these studies was that the searches were performed in English. However, as shown in the Google Insight search for 'buy mephedrone' in 2009, interest has been centred in the UK (an equivalent search in the next five most spoken languages in the EU did not have sufficient search volume to produce a map).

Whilst there are some limitations to these snapshot studies, they give a good insight into the widespread availability of mephedrone over the Internet and they also suggest that online supply of mephedrone increased from December 2009 to March 2010.

These snapshot studies were carried out prior to the classification of mephedrone in the UK on 16 April 2010. On 16 April 2010, only nine (12 %) of the 77 online shops identified in the March study were still openly selling mephedrone,

and seven (9 %) sites were selling alternative 'legal highs' such as MDAI or naphylpyrovalerone (marketed as NRG-1). This is confirmed by the UK Serious Organised Crime Agency (SOCA) who report that since 16 April 2010, the number of UK-based websites openly selling mephedrone has decreased; however, there is concern that there is now covert sale of mephedrone through Internet sites (personal communication, Debbie Maylon, SOCA, UK). Furthermore, a number of websites are now openly advertising that they are based outside the UK and therefore 'the UK legislation does not affect the shipping and processing of orders'. These websites do not provide information to UK purchasers that possession of mephedrone would be illegal in the UK.

EMCDDA focal points have identified instances of mephedrone being supplied across European borders through Internet sales. One such example is of the site www.londonunderground.co.nl selling and delivering mephedrone containing products to Croatia.

It is thought that most mephedrone is manufactured in Asia, particularly China and bordering countries in South-east Asia (Europol), rather than being directly produced within Europe. There is some anecdotal evidence that mephedrone shipped to Europe by air freight is being labelled as other chemicals by suppliers potentially due to their misconception that it is illegal in the country it is being shipped to (personal communication, Mr John Ramsey, TICTAC Communications Ltd, UK). Furthermore, there is some evidence that 'final packaging' of mephedrone prior to sale does occur by suppliers in Europe. There is also increasing anecdotal data, and information from the Scottish school and university/college survey, that mephedrone is being supplied by established street level drug dealers (Newcombe, R., 2009, Measham, F., Dargan, P.I., 2010). A report from the Slovenian organisation DrogArt suggests that most users in Slovenia buy mephedrone from a dealer (Pas, M., 2010). Users stated that although it was more expensive and of lower purity than if ordered over the Internet, they trusted a dealer more than an 'unknown Internet vendor'. Finally, there is the potential for self-manufacture of mephedrone; however, there is no evidence that this is currently widespread in Europe.

As noted above, the EMCDDA Internet snapshot survey demonstrated that most websites claim >99 % purity of mephedrone. Analysis of seized and purchased

products sold as mephedrone appears to show that most mephedrone is of high purity (> 95 %). Analysis of 21 tablets by the National Forensic Institute in the Netherlands revealed a range of mephedrone content from 116–187 mg per tablet. However, importantly, a number of reports from Reitox focal points reported mephedrone seizures containing a wide range of classified drugs, in addition to mephedrone, as shown in the table under Prevalence of use. Additionally, analysis has detected the following pharmaceutical adulterants: benzocaine, lidocaine, caffeine and paracetamol (personal communication, Dr Mark White, UK Forensic Science Service).

There is insufficient data to determine the overall prevalence of adulteration of mephedrone at this time. Reports suggest that users suspect that dealers and suppliers are adulterating mephedrone (Newcombe, R., 2009). However, this is largely based on the unpleasant smell associated with mephedrone and may be a misconception by users.

Availability of information, degree of knowledge and perceptions amongst users concerning the psychoactive substance and its effects

As summarised in the paragraphs above, other than labelling the products 'not for human consumption' or 'research chemical', Internet sites selling mephedrone typically provide minimal information on dosage of mephedrone or the potential for adverse effects. Any information that is provided is in broad terms and often cryptic in nature; for example, mephedrone sold as 'plant food' may contain advice on 'number of doses for an average size plant'. It is likely that users will interpret this information as the number of doses to be taken by an adult.

There is anecdotal evidence that increased media coverage of mephedrone has led to increased general population and user knowledge of mephedrone and, in particular, the fact that it is legally available over the Internet for delivery to Europe (Newcombe, R., 2009, Measham, F., 2010). Some users have stated that they first bought and used mephedrone after reading reports about it in the popular press.

User websites appear to suggest that users are aware that mephedrone is effective in producing the desired high and that some users chose to take mephedrone because of their perception that it has greater purity compared to other stimulant drugs currently available, such as MDMA and cocaine (Erowid 2, Drugs-Forum, Newcombe, R., 2009, Pas, M., 2010).

Characteristics and behaviour of users (including risk factors, vulnerability, etc.)

A recent survey amongst clubbers in the UK has shown high prevalence of use of mephedrone amongst over 2 000 clubbers: 33.6 % had used mephedrone in the last month, 41.7 % had ever tried mephedrone (Dick, D., 2010, Winstock, A.R., 2010). There is currently no comparative general population data currently available.

There has been coverage in the popular press in the UK of mephedrone use amongst schoolchildren; one newspaper article reported that 'children as young as 11' were using mephedrone (Westmorland Gazette) and another that mephedrone was being sold outside school gates (Teesside Evening Gazette). In the Scottish survey of school and university/college students, the youngest individual who reported mephedrone use was 12 years of age (Dargan, P.I., 2010).

It is likely that the characteristics and behaviours of those using mephedrone will be similar to those using 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 are switching to mephedrone.

There are reports from Guernsey, Romania and Slovenia of intravenous heroin users switching to intravenous mephedrone, and it is now reported to be the drug of choice in Guernsey for intravenous drug users. Furthermore, it appears that there has been a change in the population using mephedrone since Guernsey introduced a ban on its importation (personal communication, Mr Callum McVean, Guernsey). Prior to the ban, mephedrone was used in all sections of the community in Guernsey, whereas following the ban it is largely only used by habitual intravenous drug users; there are also anecdotal reports that some users have substituted mephedrone for heroin and/or cocaine.

Nature and extent of health consequences (e.g. acute emergencies, road traffic accidents)

The acute health effects of mephedrone have been discussed under the section Human data. There is no currently available data to suggest that the impact of these acute health effects would be any different to that from other stimulant drugs such as MDMA and cocaine.

As noted in Mephedrone-related deaths, mephedrone has been detected on post-mortem analysis in four road traffic accident related deaths in the UK; however, coroner/procurator fiscal inquests into these deaths are awaited and so it is not possible to determine what role mephedrone has played in these deaths. 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/accidents in other areas of Europe. This may, at least in part, be due to the fact that mephedrone is not widely tested for by forensic laboratories in many areas of Europe at this time.

Long-term consequences of use

As discussed in the Animal data and Human data sections above, there is no animal data and very limited human data on the chronic health effects of mephedrone use. In particular, there have been no long-term follow up studies to determine whether mephedrone users are at greater risk of health deterioration later in life, or of developing chronic or life-threatening medical conditions.

Conditions under which the new psychoactive substance is obtained and used, including context-related effects and risks

As noted under Availability of the information, degree of knowledge and perceptions amongst users concerning the psychoactive substance and its effects, mephedrone is readily available from a variety of Internet suppliers and also high street retail outlets. There is increasing anecdotal data that mephedrone is being supplied by established street-level drug dealers (Newcombe, R., 2009, Measham, F., 2010).

In the Scottish survey of school and college/university students, the most common source of mephedrone, amongst the 205 individuals who reported previous use of mephedrone, was a street-level dealer in 48.8 % (Dargan, P.I., 2010). The survey was conducted prior to the classification of mephedrone in the UK; despite this, only 10.7 % of users reported purchasing mephedrone over the Internet. There was a trend to increasing the sourcing of mephedrone from the Internet with increasing age (8.3 % in those aged 13–15 years compared to 30.8 % in those aged over 24 years). Most users found mephedrone very easy (66.6 %) or easy (31.3 %) to obtain and only 2.1 % reported it was difficult to obtain mephedrone.

The MixMag survey did not contain data on where those that had used mephedrone had sourced it, but 92 % of clubbers had purchased 'legal highs' on the Internet (Dick, D., 2010).

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 such as MDMA, amphetamine and cocaine. This would be within home environments, bars/pubs, discotheques/nightclubs and outdoor music festivals.

As shown in the figure in Self-reported acute mephedrone toxicity, in patients presenting with acute mephedrone toxicity to healthcare services in London, the majority of individuals have used at least one other substance together with mephedrone (Wood, D.M., 2010b, updated with unpublished data). This is similar to individuals presenting with acute toxicity related to other stimulant drugs, such as MDMA and cocaine.

Social risks

For additional information, please see Chapter 4: Mephedrone — assessment of health risks and harms and Chapter 5: Mephedrone — additional studies — Overview of prevalence, use patterns and effects.

Individual social risks

There is no published data to be able to determine the impact of mephedrone in this area.

Possible effects on direct social environment

There are reports from Guernsey of violence amongst intravenous mephedrone users attending needle exchange programmes. However, there is no other available data to suggest that mephedrone is linked with violent crime in other populations.

Possible effects on society as a whole

The only reports of acquisitive crime related to mephedrone use to date are from Guernsey, where there are reports of increased crime amongst intravenous mephedrone users including burglary, theft and weapons related crime. This appears to have occurred after the importation of mephedrone was controlled in Guernsey leading to a significant increase in its street price. There have been media reports of other crimes committed in the UK by individuals using mephedrone; these include a man who was jailed for arson of a house (BBC News 5) and criminal damage and assault (Worcester News), both committed whilst under the influence of mephedrone. Additionally, there are reports from Ireland of an increase in teen-related violence and muggings secondary to the use of 'head-shop drugs', which include mephedrone (Irish Independent).

Economic costs

As noted in Acute health effects — Human data, there are increasing reports of acute health effects relating to mephedrone use, particularly in the UK and Sweden. Most of these involve short assessments within the emergency department. As noted in Characteristics and behaviour of users (including risk factors, vulnerability, etc.), there is anecdotal evidence that individuals are switching from other controlled stimulant drugs to using mephedrone with the potential, therefore, of mephedrone-related toxicity necessitating hospital assessment and management. However, it is not possible at this time to estimate whether mephedrone is associated with greater healthcare costs than other stimulant drugs.

Possible effects related to the cultural context — for example, marginalisation

A number of surveys have demonstrated that mephedrone use is common in school and college/university students. In addition, use appears to be common amongst clubbers, similar to other stimulant drugs such as MDMA and cocaine.

Possible appeal of the new psychoactive substance to specific population groups within the general population

Mephedrone is widely used amongst clubbers and there is the potential that it appeals to this group because it is currently legal and widely available through the Internet, without the same possible consequences for purchase/possession as controlled drugs. Additionally, anecdotal reports suggest that there is appeal for mephedrone due to its perceived greater purity than other controlled drugs which currently appear to be decreasing in purity (in particular, MDMA and cocaine) (Measham, F., 2010).

Involvement of organised crime ([14])

Evidence that criminal groups are systematically involved in production, trafficking and distribution for financial gain

Europol reports that no Member State or neighbouring country, has information that suggests large-scale production of mephedrone within Europe. It is felt that mephedrone available within Europe is manufactured within China and neighbouring countries in South East Asia.

However, Europol reports that information has been provided from Estonia and the Netherlands on the trafficking/sale of mephedrone by organised crime groups (EMCDDA–Europol Joint report). They also report suggestions from Germany, Latvia and Slovakia that organised crime may be involved in the trafficking of mephedrone, as tablets seizures contained logo-imprinted tablets that were being sold in the user environment as 'ecstasy' (EMCDDA–Europol Joint report). There

([14]) Detailed information is available in the *Europol–EMCDDA Joint report on mephedrone*.

are three reports from the Netherlands of tabletting units being seized; two from 2009 and the third in February 2010 (Europol). Professional punches originating from China were found with the logo 'Roche 2' engraved in the February 2010 seizure; however, there was no information provided to Europol on the total amount of mephedrone seized at this location. Finally, the UK Serious Organised Crime Agency (SOCA) report seizure of capsule-making equipment in the UK which has been reported to have been used for encapsulating mephedrone and other cathinones (personal communication, Debbie Maylon, SOCA, UK).

Media reports from Ireland have suggested that 'gangsters' were stocking up on head shop drugs, including mephedrone (Irish Herald). It was postulated that this stockpiling of mephedrone by 'drugs gangs' was occurring prior to its anticipated ban in Ireland in May 2010.

In the UK, mephedrone was controlled on 16 April 2010 under the Misuse of Drugs Act (1971). Following this change in the legal status of mephedrone in the UK, there have been numerous reports in the UK press relating to large seizures of mephedrone (worth GBP 3 000–70 000 each) (BBC News 6, The Northern Echo, Shropshire Star), arrests for possession of and/or intent to supply mephedrone (Bolton News, BBC News 7, BBC News 8, Ulster Herald, Dumfermline Press, Wales Online) and a conviction in Scotland for 'intent to supply' mephedrone (The Scotsman). It is not clear from the media reports whether these arrests/mephedrone seizures are related to criminal gangs or individuals.

Impact on the production, trafficking and distribution of other substances, including existing psychoactive substances as well as new psychoactive substances

In February 2010, the Netherlands reported via Europol the seizure of an additional tabletting unit, as well as professionally made punches originating from China with the logo imprint 'Roche 2' engraved.

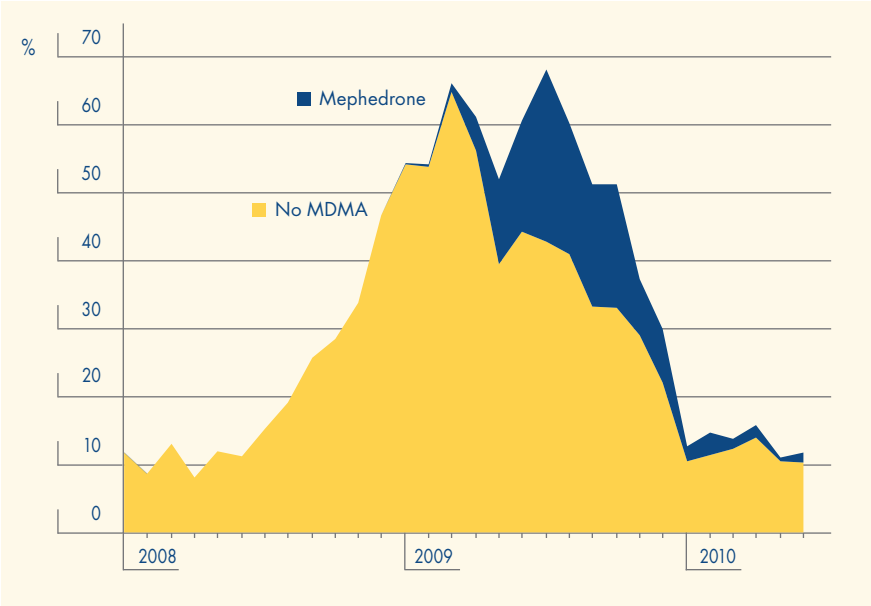
Mephedrone has been encountered together with the cathinones, bk-MBDB and bk-MDMA (Belgium), and 4-methylpropiophenone (the Netherlands); with *m*CPP and MDMA (Finland); and with well established drugs such as heroin (Romania). In addition, mephedrone has been identified as the active ingredient in several 'legal high' products (EMCDDA–Europol JRQ updated).

11.5 % of all 'XTC' (ecstasy) tablets analysed by the Dutch Drugs Information and Monitoring System (DIMS) in 2009 contained mephedrone. However, there has been a decrease in the proportion of 'XTC' tablets containing mephedrone in the first half of 2010 (Brunt, T., 2010).

From January until June 2010, 20 tablets containing mephedrone and bought as XTC/MDMA were analysed by DIMS. In addition, 39 samples (19 tablets and 20 powders/capsules) analysed were found to contain mephedrone and 7 samples also contained 4-methylpropiophenone (a mephedrone precursor).

Data from the UK Forensic Science Service (FSS) shows that there was a significant increase in the number of cathinone seizures (including mephedrone) analysed by the FSS during 2009. By the end of 2009, the number of cathinone seizures exceeded the number of MDMA and piperazine seizures combined.

Figure 7 — Percentage of ecstasy tablets containing mephedrone analysed by the Dutch Drugs Information and Monitoring System (DIMS)



Source: Brunt, 2010.

Evidence of the same groups of people being involved in different types of crime

There is no published data to be able to determine the impact of mephedrone in this area.

Impact of violence from criminal groups on society as a whole or on social groups or local communities (public order and safety)

There are reports from Guernsey of violence amongst intravenous mephedrone users attending needle exchange programmes. However, there is no other available data to suggest that mephedrone is linked with violent crime in other populations. Furthermore, Europol reports that no information was received by them on incidences of violence in connection with the production, wholesale and/or distribution of mephedrone in Europe (EMCDDA–Europol Joint report and Europol).

Press articles published in June 2010 (Belfast Telegraph 2) indicate that an Irish organisation called Republican Action Against Drugs (RAAD) might have shot a mephedrone suspected drug dealer in Derry (Ireland).

Evidence of money-laundering practices, or impact of organised crime on other socioeconomic factors in society

Europol reports that no information was received by them on incidences of money laundering in connection with the production, wholesale and/or distribution of mephedrone (EMCDDA–Europol Joint report and Europol). Processing activities by organised crime are limited to tabletting (Europol).

Economic costs and consequences (evasion of taxes or duties, costs to the judicial system)

There is no published data to be able to determine the impact of mephedrone in this area.

Use of violence between or within criminal groups

Europol reports that no information was received by them on incidences of violence in connection with the production and/or distribution of mephedrone (EMCDDA–Europol Joint report).

Evidence of strategies to prevent prosecution — for example, through corruption or intimidation

There is no published data to be able to determine the impact of mephedrone in this area.

Chapter 4

Mephedrone: assessment of health risks and harms

Prepared by Dr Adam Winstock and Dr John Marsden

Background ([15])

Psychoactive substance use is a shifting phenomenon, in which new and emerging substances take their place in communities across the EU as recreational drugs used by young people. While substances have been produced and marketed with the explicit aim of circumventing legislative restrictions for several decades, their current potency, profile and availability in combination with global web-based marketing and distribution networks poses a new challenge for policymakers (Winstock and Ramsey, 2010). There is wide variability in the use of substances both within and between Member States, but several substances have attracted widespread concern in Europe, none more so than mephedrone (Winstock, Marsden and Mitcheson, 2010). Despite these concerns and recent legislation scheduling cathinones and a number of other synthetic stimulants in the UK and elsewhere, there has been no systematic assessment of the perceived effects of these drugs on users and the associated health and social risks and harms arising from their consumption. The aim of the current study is to shed light on these questions.

Mephedrone appears to be used by several population groups, including young adults involved in the dance and music scene, mainstream young adults, and also younger users in mid-to-late adolescence and young adulthood (15–19 years). Young adult users of psychoactive substances (who are the main population using these substances) are unlikely to be in contact with treatment services. They tend to be a sentinel, but somewhat difficult to access population. Traditional survey and screening methods are problematic and there are very few epidemiological surveys of drug use among the general adult population in Europe. Aside from the substantial cost of staging large-scale surveys using

([15]) The study presented in this chapter is an appendix to the Risk assessment report.

probability sampling methods, the target populations are relatively hidden and may not respond well to direct contact. Although considerable caution must be exercised when using purposive sampling methods, this approach compares well with probability methods.

Moreover, cross-sectional surveys using the sample methodology enable some basic conclusions to be drawn about time trends, where threats to the reliability and validity of data can be shown to be constant (McCambridge, 2005 and 2007). Since 1999, our research group has been staging an annual survey of nightclub drug users, which has been conducted in conjunction with *Mixmag*, a specialist dance music magazine. Mixmag had a history of extended drug-related copy in its pages. It was considered a credible vehicle to use for opportunistic research that provided inexpensive and rapid access to large numbers of the target population (Winstock, 2001). With research-ethical approvals secured, readers were invited to return by freepost a questionnaire printed in the magazine itself. This option was supplemented by online access to the questionnaire in 2003. In 2009, the annual survey was conducted for the first time in five years and, with the support of the editorial staff and research team, we developed an innovative web-based survey platform as part of the website called *Don't Stay In* (DSI). This website is the first accessed by open text search using this phrase in Google (http://www.dontstayin.com/). It attracts young people with an interest in music, dance and events. The annual survey was heavily published on both the 'www.dontstayin' website and the Mixmag homepage. Between November 2009 and May 2010, over 3 500 people completed the online survey.

Method

Sample population

Approximately 600 participants in the online survey gave contact details and expressed a willingness to participate in further research. The current sample was drawn from members of this group, who were identified as ever having used mephedrone and who had provided their mobile telephone numbers (>200 individuals).

Design and research questions

The study was a cross-sectional survey, administered as an abridged structured telephone interview, with biological screening for mephedrone and similar compounds. Naturally, the most desirable approach to assess the profile of a new drug of abuse would have been via a comprehensive data-gathering exercise with a large sample from diverse using populations. The study did not provide this opportunity — so the work inevitably has limitations; but it is expected that the approach may have valuable implications for the design, implementation, analysis and interpretation of substance use risk and harm research. It may also be the case that in studying relatively new users of a substance, there may be little harm experienced — but on the other hand, early assessment of emerging negative effects and experiences is also valuable in its own right.

Study interview instrument

The team already had some early data on mephedrone from the initial online survey as to what the profile of use and associated harms may be. Based on a review of available online discussion fora and a review of mephedrone conducted by the Psychonaut group, the research team developed an abridged structured interview for telephone administration. The questions were aimed at identifying the abuse liability and patterns of use of mephedrone, its risk and positive effect profile and motivation for use. The questionnaire also explored the drug in comparison to cocaine and MDMA in a broad attempt to 'footprint' the drugs, in terms of abuse potential and overall effect profile. Through a pool of candidate items and cognitive testing, the team has developed a 20-minute interview with 61 items (the full questionnaire is provided in Annex I). The structure and variable set is summarised in Table 6.

Table 6 — Interview structure

Section 1: Demographics	1.1 Age 1.2 Sex 1.3 Height 1.4 Weight 1.5 Employment status
Section 2: Stimulant comparisons	2.1 Frequency of cocaine and ecstasy use 2.2 Effects comparison between ecstasy, cocaine and mephedrone 2.3a Influence of mephedrone on ecstasy 2.3b Preference to use mephedrone over ecstasy and cocaine
Section 3: First mephedrone session	3.1 First dose amount and route taken 3.2 Number of doses 3.3 Session duration 3.4 Total amount used in session 3.5 All administration route(s) used 3.6 Other drugs taken during session
Section 4: Summary of mephedrone use	*Estimate of total sessions* 4.1 Month/year first and last occasion 4.2 Days used each month from first to last 4.3 Max number of 2+ consecutive days used *Typical session* 4.4 Use alone or in company 4.5a Amount and admin route for first dose 4.5b Estimated number of lines/bombs from 1 g 4.6 Number of doses 4.7 Time between first and second dose 4.8 Total amount respondent uses in typical session 4.9 Total amount used 4.10 All admin routes used in session 4.11 Alcohol and other substances consumed 4.12 Estimate of total amount of mephedrone used most recent month *Max session* 4.13 Total amount respondent used on max session 4.14 Duration of max session 4.15 Alcohol and other drugs used *Overall summary* 4.16 How ever obtained mephedrone 4.17 Internet sites bought from 4.17a Typical amount from single Internet purchase 4.17b Max amount from single Internet purchase 4.18 Appearance and odour 4.19 All different situations/places used

Table 6 (continued)

	4.20	Mephedrone use motivations
	4.21	Frequency and intensity of effects
	4.22	Most common routes
	4.23	Routes wouldn't use again
	4.24	Hangover/withdrawal effects
	4.25	Mephedrone dependence
	4.26	Had emergency medical treatment
	4.27	Ever fainted, collapsed, fitted (other drugs)
Section 5: Other cathinones use	5.1	Ever used methylone (times used)
	5.2	Ever used butylone (times used)
	5.3	Ever used MDPV (times used)
	5.4	Ever used flephedrone (times used)
	5.5	Mephedrone makes the user more likely to use other stimulant drugs
	5.6	Will use mephedrone again? (if not, reason?)

Source: Assessing the health risks, harms and addiction liability among recreational cathinone (mephedrone) users study, Winstock, A. and Marsden, J., 2010.

Biological analysis

One of the often-cited limitations of self-report studies of emerging drugs of abuse is the uncertainty that the participants are actually taking the substance they think they are consuming. In order to address this concern and provide further information on the toxicological and metabolic profile of mephedrone, we requested all participants who expressed an intention to use mephedrone again to send us a urine sample as soon after use as possible for laboratory analysis. The team at St George's who contributed to this study have developed a protocol for cathinone derivative screening by GC-MS and LC-MS/MS. For GC-MS screening, they have also developed a procedure for 10 methcathinone-related compounds (Cath, MC, EC, 4-MMC, 2-FMC, 3-FMC, 4-FMC, dimethylcathinone (DMC), 4-methoxymethylaminobutyrone (4-MAB) and 4-methoxymethcathinone (4-MoxyMC)). Cath and MC have been purchased from Sigma-Aldrich. 4-MMC was purchased from LGC Promochem. All other derivatives of Cath and MC were synthesized 'in-house' by Kingston University. The contents of capsules or powders were dissolved in methanol and analysed by gas chromatography with mass spectrometric (GC-MS) detection in scan mode. Chromatographic separation was

achieved for all derivatives over a 12 min run. All urine samples will be analysed on a Shimadzu QP2010 gas chromatograph mass spectrometer with an HP5MS column (30 m x 0.25 mm, 0.50 µm).

For the LC-MS/MS screening, a quantitative method has been developed for two of the principle derivatives seen in biological samples (4-MMC and 3-FMC). Liquid chromatography with tandem mass spectrometric detection will be used to confirm and quantitative 4-MMC and 3-FMC in the urine samples. 4-Methylmethcathinone metabolites, 4-methylephedrine and 4-methylcathinine, are currently being added to this method for screening and confirmation.

Statistical note

The Adjust ORs are output from a backwards elimination (using likelihood ratio criterion) logistic regression, blocked with the following personal demographic variables: age, sex, height and weight, followed by alcohol, cocaine, cannabis and ketamine use on a typical mephedrone session covariates and the mephedrone effects, withdrawal symptoms (indicator coded 0,1) and the problem (dependence) items.

Table 7 — Risk co-variates

Demographic	• Age • Gender • body mass index
Other substance use	• Other substances taken during mephedrone session
Mephedrone	• Uses alone • Route (oral vs. smoking/injecting) • Whether bought from the Internet (maximum purchased) • Use of other cathinones • Total number of mephedrone sessions (initiation to survey) • Number of doses on typical session (and maximum session) • Duration of session • Total amount used on session (possibly log transformed) • Using mephedrone for two or more days consecutively • Number of different forms of mephedrone used

Source: Assessing the health risks, harms and addiction liability among recreational cathinone (mephedrone) users study, Winstock, A. and Marsden, J., 2010.

The core measures in the interview relate to mephedrone harms experienced acutely during a session, as well as in the days following a session (withdrawal symptoms).

Table 8 — Symptoms of mephedrone use

Mephedrone	• Negative effects:
	  • restless, agitated, aggressive, panicky
	  • paranoid-type delusions
	  • cardiovascular
	  • circulatory/peripheral
	  • neurological
	• Withdrawal symptoms
	• DSM-IV dependence symptoms
	• Emergency medical treatment presentation
	• Collapsed while using

Source: Assessing the health risks, harms and addiction liability among recreational cathinone (mephedrone) users study, Winstock, A. and Marsden, J., 2010.

Results

This report presents a headline summary of the patterns of use (including dependence), acute positive and negative effects and withdrawal symptoms associated with the use of mephedrone and then profile these, according to sub-groups which we identify. It also includes the analysis results of submitted urine samples. The majority of the findings are given in the form of graphs, with explicit numerical clarification only provided for sentinel findings.

Sample size

A total of 100 participants completed the questionnaire and form the basis of this report. A total of 14 urine samples were received for GCMS and LC-MS/MS analysis.

Table 9 — Sample size

Sample	n
Completed interview and data coded	100
Respondents invited to send urine sample	28
Samples arrived at laboratory	14

Source: Assessing the health risks, harms and addiction liability among recreational cathinone (mephedrone) users study, Winstock, A. and Marsden, J., 2010.

Sample characteristics

The sample was 23 % female, with a mean age of 25.1 years. The average height of the males was 1.80 m, weight 74.5 kg (mean BMI 23), of the females 1.64 m, weight 59.1 kg (mean BMI 21.8). 55 % of the sample were employed, 31 % in education and 5 % unemployed. In keeping with the sample that they had been drawn from, their lifetime use of other stimulants was very high, with 96 % ever having used ecstasy and 92 % cocaine.

First use

Detailed information was obtained regarding the time and pattern of their first ever use as a baseline measure. All participants reported their first use between 2008–10 (88 % in 2009). 83 % reported their first dose was administered as a 'line' of the drug (as opposed to tipped out powder, a pill or an emptied capsule) that estimated as being 96.6 mg. The route of administration of this first dose was most commonly (73.5 %) intranasal (snorting), with 10.8 % reporting bombing (swallowing often in a cigarette paper); 14.5 % in drink and 1.2 % intravenously. A mean of 5.6 doses (totalling an average of 605.5 mg) was administered on this first occasion of use over a session that lasted a mean of 8.6 hours. On this first occasion of use, 89 % reported drinking alcohol, 17 % used cocaine, 23 % used ecstasy, 34 % used cannabis, and 24 % used ketamine.

Typical mephedrone session

Information was then obtained on a typical session of use focusing on dosage, frequency and setting. On average, participants reported having been using for 6.1 months (SD = 3.1). All participants reported using with others (a mean of 10 (SD = 7.9) other users), with no reports of typical use being alone. 83 % administer the first dose of a session as a line of the drug, most commonly through the intranasal route (79.0 %), with 9.9 % reporting bombing; 11.1 % in drink and 0 % intravenously). The first administered dose was estimated to be 124.8 mg (28.2 mg more than first ever use), with the modal time between doses being 30 minutes or 1 hour. Over the course of a mean typical session lasting 13.9 hours (SD = 16.59) an average

of 1.09 g was consumed, though the range was huge (100–9 000 mg). During a typical session, 82 % reported drinking alcohol, 36 % cannabis, 35 % ketamine, 26 % using cocaine, 23 % ecstasy, 2 % GBL and 1 % amphetamine.

Summary of use over the last month of use

Participants were asked to estimate the total amount of mephedrone used over the last month of use. The range was 50 mg–15 g (median = 1.5 g; mode = 1 g).

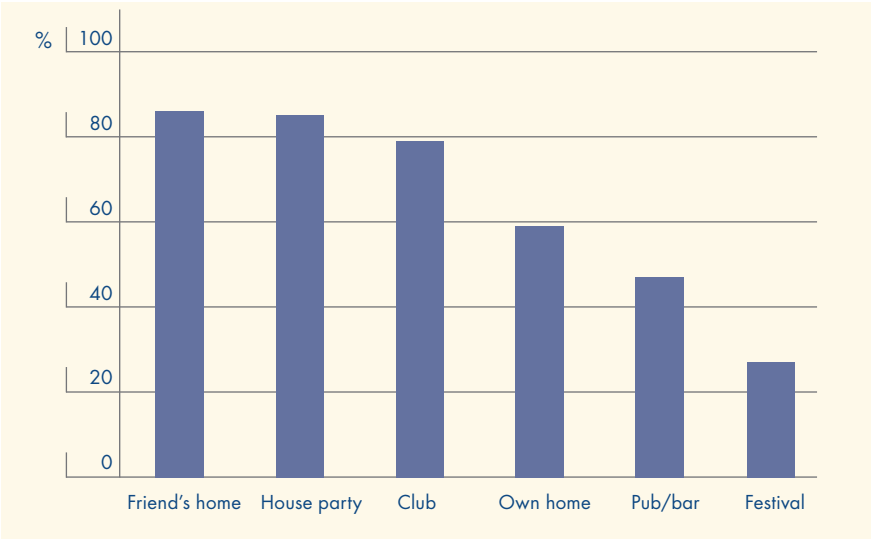
Maximum session since initiation

Participants were asked to describe their heaviest session of use since they started taking mephedrone and what proportion had used the drug on more than two consecutive days. Participants estimated that the total amount used in their heaviest session ranged from 100 mg–16 g (median = 1.5 g; mode = 1 g). The estimated duration of a maximum session varied widely between 1–192 hours with a median/mode of 12 hours. 47 % reported that they had used for more than two days in a row. For these participants, a median of three days consecutive use was reported.

Situations where mephedrone has been used

Participants reported ever having used mephedrone at a friend's home (86 %), a house party (85 %), a club (79 %), at home (59 %), pub/bar (47 %), and a festival (27 %). Most common were a friend's home or house party (see Figure 8).

Figure 8 — Where people use mephedrone

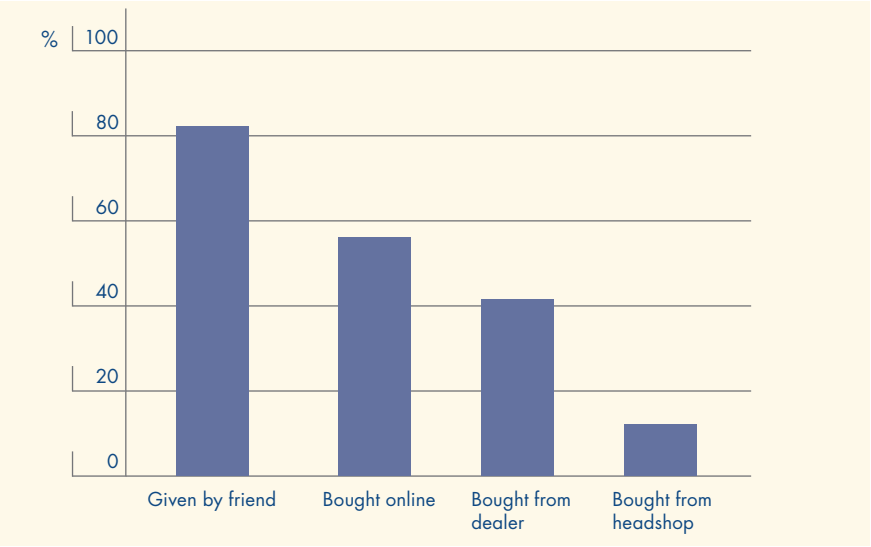


Source: Assessing the health risks, harms and addiction liability among recreational cathinone (mephedrone) users study, Winstock, A. and Marsden, J., 2010.

Ways of obtaining mephedrone

Participants were asked how they had ever obtained mephedrone, the most common places were online and from friends (Figure 9). The median amount purchased was 5 g, with a mode of 2 g (range 1–50 g). Research Chemicals, UK Legals, Mephedrone2U, PlantFoodPalace and Mr Meph were the most commonly reported sites for purchase.

Figure 9 — Ways of obtaining mephedrone

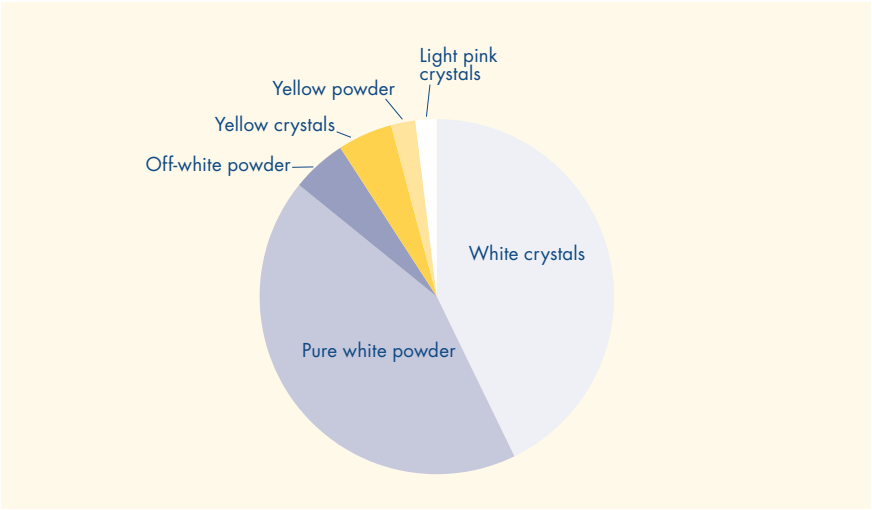


Source: Assessing the health risks, harms and addiction liability among recreational cathinone (mephedrone) users study, Winstock, A. and Marsden, J., 2010.

Physical appearance

Participants were asked to describe physical characteristics (from a selection of provided options) of the purchased product (see Figure 10).

Figure 10 — Physical characteristics of purchased mephedrone

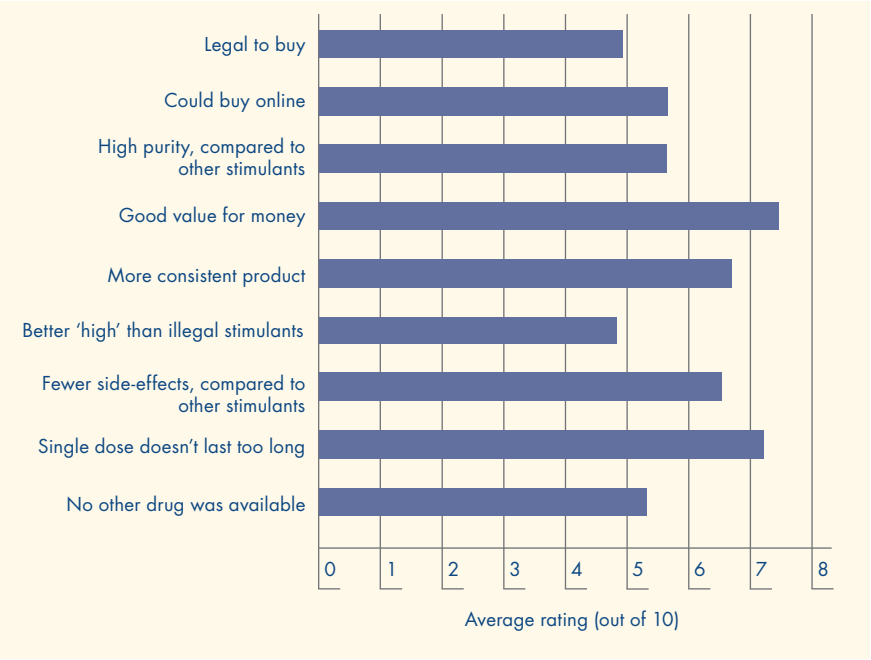


Source: Assessing the health risks, harms and addiction liability among recreational cathinone (mephedrone) users study, Winstock, A. and Marsden, J., 2010.

Motivations for use

Participants were asked what motivated them to use mephedrone and were asked to rate on a scale from 0 to 10 where 0 is 'no influence at all' and 10 would be 'the maximum influence possible', how motivating a range of factors have been to use mephedrone. Value for money, consistency of product, side-effect profile and short duration of effect were reported as being more important than its legal status or availability online.

Figure 11 — Motivation to use mephedrone

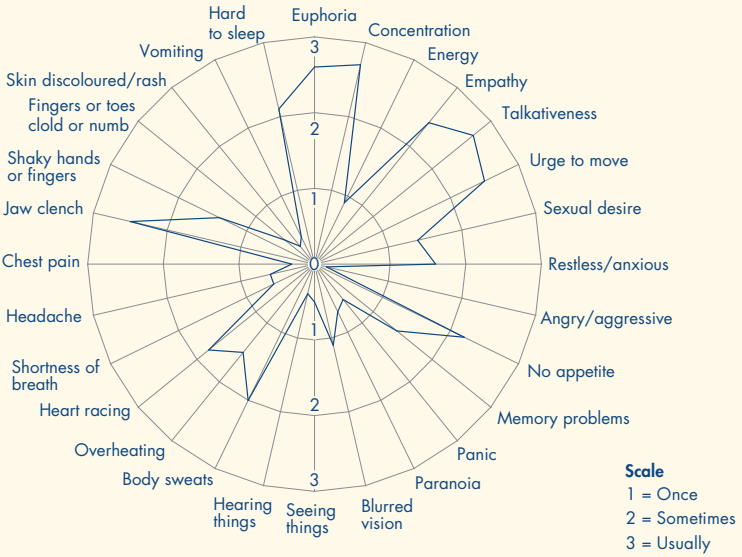


Source: Assessing the health risks, harms and addiction liability among recreational cathinone (mephedrone) users study, Winstock, A. and Marsden, J., 2010.

Effect profile

Participants were asked about the frequency (how often; 'never', 'once', 'sometimes', 'most of the time' *and* intensity (how intense; 'mild', 'moderate', 'intense') of 28 typical stimulant and empathogen drug effects (both positive and negative and physical and psychological). The results are shown in Figure 12. Mephedrone's predominant effect profile is that of a typical stimulant drug with evidence of frequent sympathomimetic physical effects. The drug also appears to have a quite marked pro-social profile with relatively infrequent adverse psychological effects.

Figure 12 — Frequency of intensity of mephedrone effects

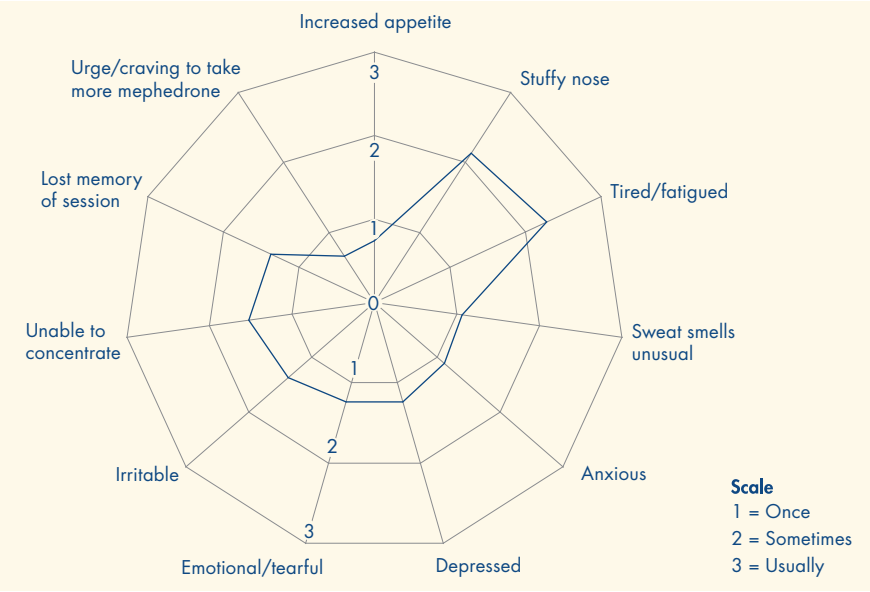


Source: Assessing the health risks, harms and addiction liability among recreational cathinone (mephedrone) users study, Winstock, A. and Marsden, J., 2010.

Withdrawal effects

Participants were asked about how they felt during the next day or two after a session by indicating how frequently each of a number of typical stimulant withdrawal symptoms were experienced and their intensity. The frequency of withdrawal symptoms is shown in Figure 13.

Figure 13 — Frequency of mephedrone withdrawal effects

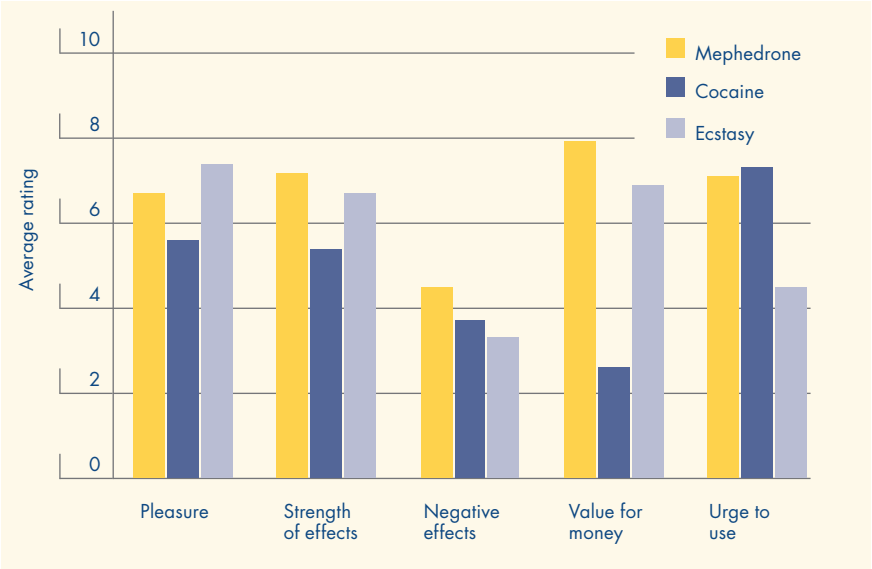


Source: Assessing the health risks, harms and addiction liability among recreational cathinone (mephedrone) users study, Winstock, A. and Marsden, J., 2010.

Subjective effects compared to cocaine and ecstasy

Participants were asked to rate each of the three drugs (as they are available currently) out of 10 (0 = low; 10 = high) across a range of broad descriptors; the 'pleasurable high' of the drug, the 'negative effects of the drug when high', the 'strength of effect', the 'urge to want more of the drug when using' and value for money. As can be seen in Figure 14, mephedrone scored very high in most of the subjective effects. The impression from these questions is that mephedrone is more similar to ecstasy except that its urge profile is comparable to cocaine.

Figure 14 — Subjective comparisons of mephedrone, cocaine and ecstasy (rating 0–10 scale)



Source: Assessing the health risks, harms and addiction liability among recreational cathinone (mephedrone) users study, Winstock, A. and Marsden, J., 2010.

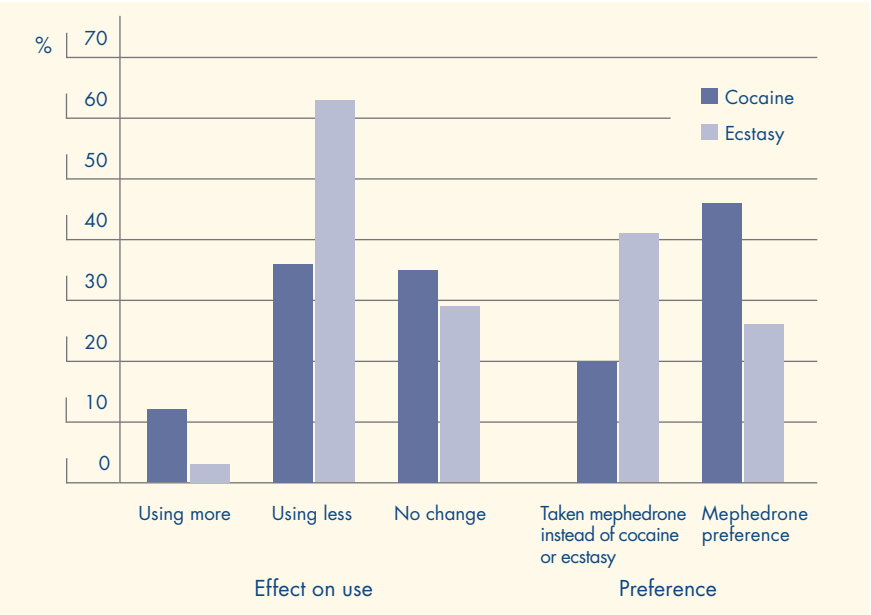
Effects of mephedrone on consumption of cocaine and ecstasy and preferred drug

Participants were asked about the impact of their mephedrone use on their consumption of cocaine and ecstasy.

63 % reported that they now took less MDMA (ecstasy), 36 % reported that they now took less cocaine. 41 % said they had ever taken mephedrone instead of ecstasy with 20 % saying they used it instead of cocaine.

Finally, participants were asked if there was a choice between mephedrone and ecstasy and mephedrone and cocaine, which would they choose. 46 % reported they would choose mephedrone over cocaine with only 26 % saying they would take mephedrone over ecstasy (see Figure 15).

Figure 15 — The effect of mephedrone on cocaine and ecstasy use and preference

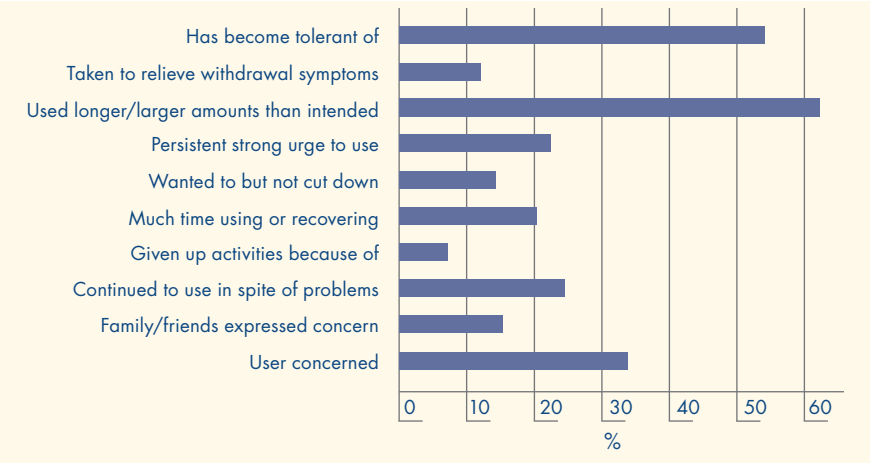


Source: Assessing the health risks, harms and addiction liability among recreational cathinone (mephedrone) users study, Winstock, A. and Marsden, J., 2010.

Assessing for DSM dependence

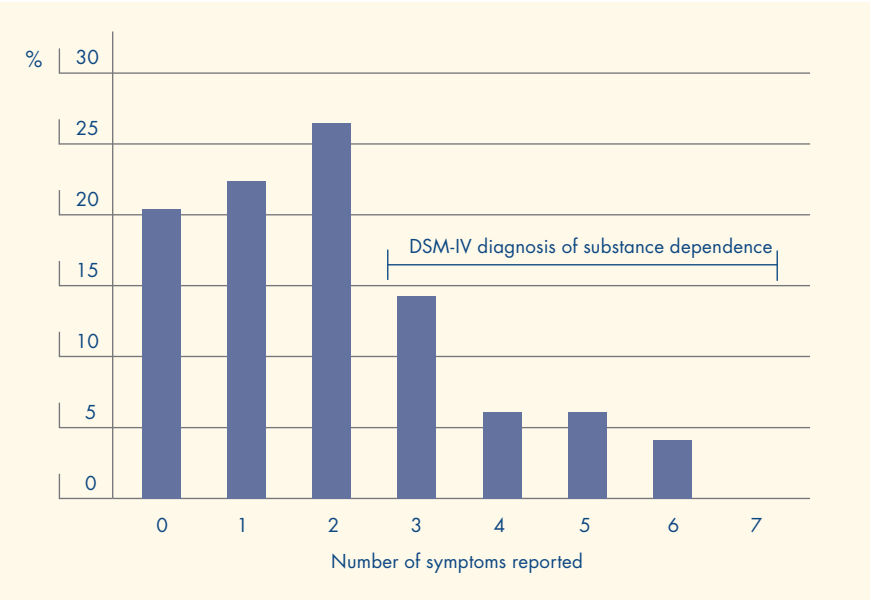
Participants were assessed against DSM-IV dependence criteria (see Figure 16). One third met three or more criteria and may be considered as dependent (see Figure 17).

Figure 16 — Incidence of mephedrone-related problems (%)



Source: Assessing the health risks, harms and addiction liability among recreational cathinone (mephedrone) users study, Winstock, A. and Marsden, J., 2010.

Figure 17 — DSM-IV criteria symptoms



Source: Assessing the health risks, harms and addiction liability among recreational cathinone (mephedrone) users study, Winstock, A. and Marsden, J., 2010.

Intention to use next month

Participants were asked if they intended to use mephedrone again. 37 % said 'no' or 'that it was very unlikely', 47 % said yes in the next month and 16 % yes in the next two months. Of these 47 participants, 26 agreed to send in a urine sample. 14 samples at the laboratory have been received (54 %). Correlates of intention to use next month are shown in Table 10.

Table 10 — Correlates of intention to use next month

Variable	P-value	Adjusted OR
Heavier maximum use	0.02	4.87
Has developed tolerance	0.02	3.37
Felt strong urge to use	0.03	4.12
Using for longer periods	0.02	0.24

Source: Assessing the health risks, harms and addiction liability among recreational cathinone (mephedrone) users study, Winstock, A. and Marsden, J., 2010.

Biological screening ([16])

Toxicological findings (GC-MS and LC-MS/MS) are provided in Tables 11a, 11b and 11c.

Participants who expressed the intention to use mephedrone in the subsequent month were requested to provide a urine specimen for toxicological analysis. In addition to the sample, participants were all asked to record how much mephedrone they had used and what other substances, if any, they had taken in the three days prior to providing the sample. All samples received confirmed the self-reported consumption of mephedrone.

A total of 14 samples were received. All were analysed fully using GC-MS and LC-MS/MS. Stability and metabolite studies were carried out, dependent upon accessing reference samples.

The results available do suggest a limitation of GC-MS in detecting the metabolites. The recorded peaks appear to be of different strengths in different people, and not obviously dependant on the amount of mephedrone taken. For example, some people with a greater peak for mephedrone still do not show a clear metabolite peak, when compared to someone with an enormous metabolite peak and small mephedrone peak. The precise pattern appears to depend on the time the mephedrone was taken and individual variations in metabolism. However, the work does confirm that the use of mephedrone can be adequately detected by the

([16]) See also the detailed research protocol in Annex I.

identification of mephedrone or the desmethyl-metabolite in the urine by GC-MS. Clearly, having only one urine sample from each individual precludes work on the pharmacokinetics of mephedrone.

One interesting finding is the occasional mismatch between declared drugs consumed and those identified at screening. This may represent adulteration at the point of sale, incomplete disclosure or failure to recall accurately all the substances taken over a period of use.

Table 11a — Self-declared substance use

Case No (mephedrone)	Mephedrone declared (yesterday, unless stated)	Other drugs declared (yesterday, unless stated)
1	<2 g	Cigarettes, 6 pints of alcohol, cannabis <1 g,
2	<0.5 g	<0.5 g cocaine
3	<1 g (yesterday) <1 g (2 days)	<1 g methylone
4	<1 g	0.1 g MDMA
5	<2 g	Ecstasy, 5 pills, <0.5 g cocaine
6	<0.5 g	None stated
7	<3 g	None stated
8	<0.5 g	None stated
9	<0.5 g	<0.5 g MDMA
10	<0.5 g	<2 g cocaine
11	Yesterday: <1 g 2 days ago: <1 g 3 days ago: <0.5 g	Yesterday: <0.5 g cocaine cup of coffee 2 days ago: <0.5 g cocaine
12	<2 g	<0.5 g cocaine
13	Yesterday: <0.5 g 2 days ago: <0.5 g	Yesterday: <0.5 g ketamine, <0.5 g cocaine 2 days ago: <0.5 g cocaine
14	<0.5 g	None stated

Source: Assessing the health risks, harms and addiction liability among recreational cathinone (mephedrone) users study, Winstock, A. and Marsden, J., 2010.

Table 11b — GC-MS urine toxicological analysis

Case	4MMC	Nor.	MDMA	Coc.	Ket.	BZP	TFMPP	pMPP	bkMDMA
1	×	×							
2	×	×							
3	×	×							×
4	×	×	×						
5	×	×	×		×	×	×	×	
6	×	×				×	×		
7	×	×							
8	×								
9	×	×	×						
10	×		×	×	×				
11	×	×							
12	×								
13	×	×		×					
14	×								

Key:
K4MMC = 4-Methylmethcathinone (mephedrone)
Nor = Normephedrone (4-methylcathinone)
MDMA = 3,4-Methylenedioxymethamphetamine ('ecstasy')
Coc.= Cocaine
Ket.= Ketamine
BZP = Benzylpiperazine
TFMPP = 3-Trifluoromethylphenylpiperazine
pMPP = para-Methoxyphenylpiperazine
bkMDMA = β-keto-MDMA (methylone)

Source: Assessing the health risks, harms and addiction liability among recreational cathinone (mephedrone) users study, Winstock, A. and Marsden, J., 2010.

Table 11c — LC-MS/MS urine toxicological analysis

	Approximate concentration of target compounds (mg mL-1)			
Case	Mephedrone	4-Methylephedrine	4-Methylcathine	Normephedrone
1	0.50	0.92	Unclear	0.31
2	1.77	2.78	Unclear	0.82
3	0.01	0.48	Unclear	0.00
4	0.02	1.22	Unclear	0.01
5	5.05	0.89	Unclear	0.41
6	0.00	0.01	Unclear	0.00
7	7.35	0.55	Unclear	0.71
8	0.08	0.02	Unclear	0.01
9	1.34	0.18	Unclear	0.23
10	2.30	1.60	Unclear	0.23
11	0.16	0.42	Unclear	0.10
12	2.44	0.26	Unclear	0.26
13	0.07	1.63	Unclear	0.02
14	0.06	0.06	Unclear	0.02

Source: Assessing the health risks, harms and addiction liability among recreational cathinone (mephedrone) users study, Winstock, A. and Marsden, J., 2010.

Limitations

As with any study that explores patterns of drug use and effects that relies upon self-report measures, there is the possibility of recall and response bias. There are inherent limitations of studies that use non-random self-selecting samples. However, such approaches are often required when conducting early research in a new drug. The sample, although representing sentinel groups of harder users may not be typical of users who are not associated with the dance drug scene. The sample is small in size compared to the large number of users and there is no way of determining the representativeness of this sample to the wider population, particularly younger users, those with less drug-using experience and those who

regularly inject drugs. Users may be reluctant to disclose adverse experiences to a researcher and, thus, the findings may represent an overly positive view of the substance. The fact that approximately one third said they did not intend to use again does suggest, however, that this is not the case. Finally, it is possible that the reported effects do not reflect the results of consuming mephedrone in isolation. The concurrent consumption of other psychoactive substances, especially alcohol with mephedrone was common among this group and it is possible that the effect profile described above, represents a combined drug effect in some users. There is also further toxicological work to be conducted.

Discussion

This is one of the first studies that provides a structured assessment of the patterns of use, effect profile and abuse liability associated with the use of mephedrone. It is the first to incorporate toxicological analysis and thus provides important information on the utility of existing screening methods and its metabolism.

The major findings of the study to date are that mephedrone has an effect profile that is more similar to ecstasy than cocaine except for its shorter duration of action and urge to use which are more similar to cocaine. Clinical presentations are likely to share features seen in association with other commonly used illicit substances such as MDMA and cocaine. The reported effect profile suggests a relatively low incidence (compared to cocaine) of adverse psychopathological experiences and aggressive behaviours, perhaps offset by quite marked empathogenic effects and its short duration of action. Its physical effect profile is very typical of stimulants and does suggest that mephedrone may have the potential at higher doses to result in a sympathetic toxidrome with emergency presentations related to agitation, panic, dehydration, overheating and cardiovascular dysregulation and paranoid episodes. These findings are consistent with its chemical structure and a presumed mechanism of action that involves the release and or inhibition of reuptake of monoamine neurotransmitters. The effect profile reported in this study is consistent with previously reported dose-related subjective effects including euphoria, increased energy, increased libido, sweating, tachycardia, headache and teeth grinding (Psychonaut web mapping project, Measham, 2010, Newcombe, 2009, Winstock and Mitcheson, 2009).

The withdrawal symptoms (perhaps more accurately described as a 'comedown') 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, respectively. However the other reported findings, if clustering in a subgroup of heavier users would be consistent with a stimulant withdrawal syndrome.

Of particular interest is the data collected on mephedrone related problems and dependence. The findings suggest that the drug has a high abuse liability with over 30 % of the 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. The findings are consistent with the high abuse liability reported in the Mixmag survey (Winstock, 2010).

The study also adds to the limited literature on patterns of use, dosing schedules and typical amounts used. Intranasal use is by far the most consistent route of administration with doses being administered every 30–60 minutes over the course of a session (typically 8–12 hours in length) which may last several days in the case of some users. Although the average consumption over a session is approximately 1 g, there are sub-groups of heavier users who report consuming far more (maximum reported session in this study was 16 g).

A finding that will warrant further study is the very high level of concurrent consumption of other illicit drugs and alcohol. It is unknown how the consumption of these substances may modify the effect profile of mephedrone or the pattern of risk behaviours or metabolism of the drug. It is likely that combined stimulant consumption will increase the risk of sympathomimetic toxicity. The concurrent consumption of alcohol may increase both disinhibition and memory impairment, increasing the likelihood of a range of high risk behaviours. How combined use will impact upon the potential development of more toxic metabolites is not known. The very high level of combined use with ketamine may be reflective of the population from which the study population was drawn. However, the combination of a dissociative substance with one that is more prosocial may be considered as unexpected. The acute risks of combining ketamine with mephedrone will most probably be related to unintended injury, excess dosing, adverse psychopathological experience or those related to cardiovascular overstimulation.

More importantly, from a policy point of view, are the findings on motivation for use and the impact of mephedrone upon the use of cocaine and ecstasy.

The findings support the complex relationship between factors such as availability, cost, perceived quality and drug effect in determining the choice of which drug to use (Measham, 2010). These factors seem more important than the legal status of a drug and it was interesting to note that over 40 % of the sample reported ever having purchased mephedrone from a dealer. Whether recent legislation will lead to an increase in price and fall in purity remains to be seen. If this is the case then at least some of the motivating factors for use such as value for money and perceived high purity compared to other drugs may be given less weight.

Summary findings from the toxicological investigations to date are that you can adequately detect the use of mephedrone by the detection of mephedrone or the desmethyl-metabolite in the urines by GC-MS. Subsequent data from further analytical work will be provided to the Centre when they are completed.

Finally, the authors consider the approach adopted in the current study to be appropriate to the rapid investigation and risk assessment of new substances of abuse. Benefiting from access to sentinel drug-using participants who are often the first to experiment with novel substances, the research group believe that the approach taken could be used in subsequent risk assessment processes to allow 'footprinting' of drug effect, risk and abuse liability.

Chapter 5

Mephedrone: additional studies — Overview of prevalence, use patterns and effects

Jane Mounteney

Introduction

This chapter is an appendix to the Risk assessment report and includes a summary of additional material collected in the course of the risk assessment on mephedrone that has not been (or has only partially been) incorporated in Chapter 3: Technical report of mephedrone. Summaries of six reports are presented, three from the UK and one each from France, the Netherlands and Slovenia. Two studies came as reports from the Reitox network of national focal points, two are as yet unpublished academic studies, and two are published as research reports. These reports provide additional insight into mephedrone's prevalence, patterns of use and effects. In terms of structure, key findings from individual studies and reports are presented first in this chapter, then results and implications summarised under the main topics of individual, public health and social risks.

Internet survey with clubbers (UK)

During the autumn of 2009, an online cross-sectional survey was undertaken amongst readers of a popular UK dance music publication called Mixmag. The following results are based on an analysis of a subset of 2 295 UK responses.

41.7 % of the survey sample had used mephedrone at some point in their lives. Mephedrone came sixth in the list of any drug used in the previous month. It came in fourth place if alcohol and tobacco are removed, with a third of the sample having used it — see Table 12.

Table 12 — Mixmag Internet survey, 2010

	Ever used (percentage)	Used last year (percentage)	Used in last month
Cannabis (any)	93	70	54.4
Ecstasy (any)	91	80	53.1
Cocaine (powder)	86.7	83.1	47.4
Mephedrone	41.7	37.3	33.6
Amphetamine (speed/base)	72	30.1	14.7

Source: Winstock, A., 2010.

900 users reported consumption of mephedrone in the last 12 months. In terms of route of administration, 70 % commonly snort it, 30 % take it orally. 14.5 % reported using at least weekly, whilst 44 % used once every 3 months. When asked what amount they used in an average session, just over a quarter of respondents (28 %) used ¼ g or less, 50 % used between ½–1 g with 8 % using more than 2 g. The reported experiences of users after taking mephedrone are summarised in Table 13.

Table 13 — Self-reported effects of mephedrone

	Often Always/nearly always	Never
Excessive sweating	22.9	32.9
Increased sex drive	22	40.3
Headache	12	48.8
Palpitations	10.4	57
Nausea	7.2	62.7
Cold blue fingers	3.3	84.6

Source: Winstock, A., 2010.

Respondents were asked how mephedrone compared with cocaine. 65 % said it gave a longer high and 55 % a better high than cocaine. 55 % of respondents said it was less addictive and 25 % reported mephedrone has 'more risks' than cocaine.

Focus groups with schoolchildren (UK)

As part of a larger PhD study on drug education in Northern Ireland, focus groups were conducted with 154 pupils (aged 14–15) selected from three post-primary schools in May 2010. Individual interviews with six teachers and youth workers with the responsibility for the provision of drug education in schools were also undertaken. The sample was drawn from Belfast and Derry, from areas characterised by deprivation, drug use and paramilitary activity.

All of the pupils reported having heard of mephedrone, most commonly known as 'magic' in Belfast and 'monkey madness' in Derry. Roughly 40 % of the young people admitted trying mephedrone at least once and approximately 70 % stated that their friends had tried or used mephedrone. Males reported highest levels of personal use/friends' use and those who smoked cannabis were more likely to have used mephedrone. The most common method of use was snorting. The most common setting was at a party or friend's house and its use was usually coupled with alcohol. Approximately 80 % of pupils reported knowing where to buy mephedrone and the most customary method of purchase was from friends or a dealer. The pupils suggested that mephedrone was more easily accessible than cannabis at present but they purported that they were more afraid of paramilitary violence if caught with mephedrone.

None of the pupils who participated in the study were aware of the contents of mephedrone. The majority of young people received their information concerning mephedrone from their friends and the media. There was some confusion over the difference between mephedrone and methadone and whether 'regular' plant food contains mephedrone (Meehan, C., 2010).

Focus groups with mephedrone users (UK)

A 2009 study from Middlesbrough UK reports on three focus groups with a total of 10 mephedrone users, nine males and one female. All participants were polydrug users, and were mainly users of three recreational drugs: cannabis, alcohol and amphetamine. Most participants also mentioned being users of

cocaine and ecstasy in the past. Eight members were in their late teens to mid-20s, largely unemployed, and generally reported using mephedrone and other recreational drugs while in nightclubs and parties. Two members were in their 40s/50s and were long-term dedicated users of hallucinogens (psychonauts).

Awareness and knowledge

Most participants had become aware of mephedrone during 2009 through coverage in the mass media and on the Internet. However, few knew anything about the chemical nature and origins of mephedrone. Six participants reported obtaining their supplies of mephedrone from drug dealers (who sold other drugs such as amphetamine, cocaine and ecstasy), or from friends. Four participants mainly obtained their supplies from the Internet.

Participants reported that mephedrone was mainly sold in gram-bags, at the price of GBP 10 to GBP 15 per gram/bag — typically GBP 10 when purchased from the Internet, and GBP 15 when bought from drug dealers. Most participants also stated that given that mephedrone was generally high purity and that several doses could be had from one gram-bag, its price was fairly cheap, particularly when compared with the price of standard deals of other popular drugs — notably cocaine (GBP 25–GBP 40 per gram) or skunk-cannabis (GBP 20–GBP 30 for an 'eighth' — typically about 2.5 grams).

Prevalence and use

Asked about how common mephedrone use was in Middlesbrough, the clear consensus was that 'everyone is doing it' — presumably meaning most or all of the local recreational drug users and/or clubbers. Though users appeared to be largely young adults (16–29 year olds), comments by participants suggested that the age range of local mephedrone users stretched from the early teens to the late 50s, with more male than female users.

The reasons given for using mephedrone were similar to those given by users of recreational drugs in other research. In short, the reasons for starting to use mephedrone included curiosity, liking the effects of drugs, and having nothing else to do. The reasons for continuing to use mephedrone included pleasure (wanting to repeat a desirable fun experience), and developing a habit (craving and dependence). The main settings of use were nightclubs, parties and people's homes.

Mephedrone powder was usually sniffed or swallowed. Sniffing mainly took the forms of 'keying it': sticking a key into the bag of powder, piling up some powder on the thin end of the key, and then holding the key under a nostril and sniffing vigorously. Swallowing took one of two forms: 'bombing' (wrapping a dose of powder in a paper wrap) or drinking (mixing the powder into a beverage, and drinking it quickly). Many participants reported switching from sniffing to swallowing mephedrone, mainly because of its painful effects on the nasal membranes.

Many participants stated that when they first tried mephedrone it was effective in fairly small doses — equivalent to about 50 to 75 mg. But with regular use — even within the first session — the amounts used soon escalated. All participants began as experimental occasional users of mephedrone, but most had quickly progressed to regular recreational use, with weekend use being the norm. However, two reported that they had been using on a near daily basis for the past six weeks. In addition, some participants reported having friends and associates who had become daily users. The most common drugs used in the same session as mephedrone were alcohol and skunk-cannabis — with some participants mentioning ecstasy and ketamine.

Effects of mephedrone

The initial physical effects of mephedrone were related to methods of administration. Most participants reported nose burns and nose-bleeds when it was sniffed. As the effects 'came on', physical effects were the most common, along with 'head rushes'. These physical effects often continued into the main stage of effects, and included fully dilated pupils, rapid eye-movements, blurred vision, dry mouth, hot flushes, fast/erratic heartbeats, and muscular tension in the face and limbs — including trismus and bruxism (jaw-clenching and teeth-grinding). These are all common effects of the amphetamine group of drugs, both stimulant and hallucinogenic. One sexual effect was reported by most participants: shrunken penis and testicles.

The mental effects reported by most participants started with the rapid onset of 'head rushes', similar to the onset of the effects of ecstasy (MDMA, etc.). A number of participants mentioned trips or hallucinations. But the main effects of mephedrone were reported to be intense feelings of euphoria and boundless energy, similar to the effects produced by cocaine, speed and ecstasy: over half of the participants also mentioned ecstasy-like feelings of friendliness and enhanced empathy.

Several participants commented that they were surprised at how intense and pleasant the effects of mephedrone were, and that the effects were clearly distinguishable from those of other recreational drugs. There was a general consensus that the effects of mephedrone were similar to the effects of ecstasy and cocaine: 'the effects are in the middle, between E (ecstasy) and coke (cocaine)' and half of participants explicitly stated that mephedrone's effects were superior to those of cocaine and ecstasy.

Consequences of mephedrone use

Though most participants had become regular users of mephedrone, none explicitly indicated that they felt dependent on it or that they had become daily users. Even so, though withdrawal symptoms were not reported, craving and tolerance were clearly evident in the experiences of most participants. In addition, about half of participants stated that they knew several people who had developed a mephedrone 'habit' — as evidenced by consumption factors like daily use and heavy use; by psychological indicators like craving and tolerance; and by behavioural indicators like taking mephedrone to the exclusion of other activities, continuing regular use despite health problems like skin rashes.

The main damage to health reported by most participants included nose-bleeds (when mephedrone was sniffed), though some also mentioned skin rashes. Around half of participants also reported experiencing amnesia about sessions of mephedrone use. Given that all participants had been using mephedrone for between one and three months only, it is perhaps to be expected that more serious health problems associated with regular and long-term drug use were hardly mentioned (Newcombe, R., 2009).

Pill testing and interviews with mephedrone consumers (Netherlands)

The Dutch Drugs Information and Monitoring System (DIMS) analysed 12 331 ecstasy tablets from individual consumers during the period 2008–09. In addition, information was gathered on the acute subjective effects of mephedrone from interviews with 70 regular drug consumers (mainly ecstasy users) between June 2009 until December 2009.

A sharp rise of mephedrone in ecstasy tablets was detected during 2009. DIMS received 995 mephedrone tablets in 2009 (11.5 % of the total).

60 users indicated that they anticipated effects of ecstasy, the rest were already acquainted with mephedrone. The different reported effects are summarised in Table 14. The most frequently reported emotional effects were euphoria, improved mood and craving (often reported as 'redosing' after a short period) and the most frequently described somatic effects were increased energy and accelerated heartbeat. Most users experienced the overall mephedrone effects as enjoyable and were considering using the substance again if the opportunity arose.

Table 14 — Most frequently reported acute subjective effects by 70 drug consumers that have tried mephedrone tablets

Emotional (n)	Somatic (n)
Increased alertness, more focused (28) Euphoria, excitement, improved mood (63) Urge to talk, openness in communication (51) Craving for the drug (61) Depressed, feeling down or sad (11) Anxiety, panicky or nervous (19)	Increased energy, hyperactivity (56) Dizziness (17) Distorted vision, restless eye movements (33) Hyperthermia, warm all over (24) Nausea, feeling sick (20) Accelerated heart/heartbeat, tachycardia (44) Loss of appetite (29) Bruxism, jaw clenching (26) Disturbed sleep-pattern (33) Low energy, exhaustion, lethargy (23)
Overall experience: pleasant, enjoyable *Overall experience: unpleasant, undesirable*	*58* *12*

Source: Brunt, T., 2010.

TREND — report from national early warning system (France)

The French TREND system results are based on toxicological analysis, ethnographic research and interviews with drug users. Mephedrone was first reported by the Metz TREND site at the end of 2008. In the second half of 2009 ethnographic reports of mephedrone came in from the Parisian gay milieu, where it was being used as an alternative to other psychotropics for its ecstasy-like effects. However, up until March 2010, mephedrone was relatively unknown on the French techno scene.

April 2010 saw the first media coverage in France of the UK situation regarding mephedrone. There followed reports of increased curiosity about legal stimulants amongst party goers and members of the Parisian gay scene. This remains a localised and limited phenomenon according to reports so far.

Information was collected from seven users presenting mephedrone powder for testing. Three users presented the powder as MDMA, two as amphetamine, one as 'MPK' and only one as mephedrone. All users were aged between 25 and 30 and all described the drug's effects as ecstasy-like or amphetamine-like. In terms of route of use, four users sniffed the drug and three swallowed. Quantities presented varied between 0.1 g and 0.25 g. The mephedrone was taken in combination with alcohol (7 cases), cannabis (7 cases), cocaine (3 cases) and heroin (1 case).

Only one user described unwanted side-effects — cramps when the mephedrone was taken along with alcohol, cannabis and cocaine (Lahaie, E., 2010).

Outreach and Internet monitoring (Slovenia)

A report from the Slovenian organisation DrogArt summarises findings on mephedrone use and users between 2008 and 2010. Sources used include: outreach work at dance events and nightclubs throughout Slovenia; an Internet forum with more than 6 000 users; and Internet, telephone and personal counselling. August 2008 saw the first reports of mephedrone on the Internet forum. In the following months, the number of reports increased. It appears consumption really started to spread at the end of 2008 and the beginning of 2009 in the population of Slovenian partygoers.

Main reasons for mephedrone use

The primary reason given for mephedrone use was the absence of MDMA and/or bad quality of cocaine and amphetamine. For some users, mephedrone has become a drug of choice, because they like the effect, but many users report that they stopped using mephedrone over the time. The main reasons for ceasing the use of mephedrone are:

— people get bored of it;
— users experience more and more negative side effects;
— tolerance increases;
— user concern about signs of psychological addiction;
— worry at amount of money spent on mephedrone.

Most users use mephedrone orally (wrapped in a cigarette rolling paper) or nasally. More recently, a few anecdotal reports have been received about mephedrone injecting among intravenous heroin users.

Effects of mephedrone, based on user reports

All of the users that gradually increased their use, speak of a 'honeymoon period'. During the first few uses, they report very pleasant effects with practically no unwanted side effects. With increasing the frequency of use and the amounts of the substance, users report less and less pleasant effects and more and more unwanted side effects. A lot of users report this as a main reason to stop using mephedrone. Reported negative acute effects included:

— irritation of nasal and pharingeal mucosa;
— unintended, long binges that can last for days;
— very strong craving;
— tachycardia;
— retrograde amnesia, especially in combination with alcohol;
— unpleasant skin smell after use.

Negative chronic effects

— dry mucosa, infections of genitals;
— skin rash;
— psychical dependency;
— tolerance for the effects of mephedrone and also other substances;
— difficulties with concentration and memory;
— poor vision;
— numbing of the distal parts of the limbs.

Craving and psychological dependence

Many users consider craving to be the main problem with mephedrone. Even the users with a lot of experience with other substances (cocaine, methamphetamine, speed, etc.) emphasised that they have never experienced such craving with any other substances and that craving was the main reason they used more mephedrone than they planned.

Users mostly buy mephedrone from their dealer, even though it is more expensive and of lesser purity than if ordered over the internet. The main reason for that is that they trust their dealer more than some unknown Internet vendors and that they don't want to expose their data over the Internet (Pas, M., 2010).

Summary

Individual health risks

Similarities and differences to other reference substances

Reports suggest mephedrone is, on occasion, being used as an alternative to other illegal stimulants. Poor availability or low quality of other stimulants, particularly cocaine, amphetamine and ecstasy/MDMA are among the reasons given by users for starting and continuing to use mephedrone (Slovenia, UK).

Route of administration

Routes of administration used for mephedrone are reported as snorting/sniffing and swallowing. In addition to health risks, concerns were raised that school children were experimenting with and ritualising snorting the drug, a route of administration otherwise associated with illegal substances such as amphetamine and cocaine. As such, there is a potential role for mephedrone to influence new legal snorting practices amongst young people. Anecdotal reports (Slovenia, UK) mention a small number of heroin users injecting mephedrone.

Effects of mephedrone

Mephedrone users report on their overall positive experience of taking the drug, with effects having much in common with ecstasy and cocaine. Four of the above studies/reports (Slovenia, Netherlands, UK Internet, UK focus group with users) identify negative short-term effects related to consumption — these effects are listed in Table 15, alongside the number of studies mentioning the problem. Palpitations were reported by mephedrone users in all four reports.

Table 15 — Negative effects of mephedrone	
Negative effects of mephedrone	**No of studies**
Palpitations	4
Craving	3
Sweating	3
Blurred vision	3
Nasal irritation	2
Amnesia	2
Nausea	2
Bruxism (jaw clenching)	2
Skin rash	2
Source: Winstock, A., Mimag, 2010, Newcombe, R., 2009, Brunt, T., 2010, Pas, M., 2010.	

Public health risks

Extent, frequency and patterns of use

Mephedrone consumption has been identified in a range of sub-populations. In addition to psychonauts (UK), mephedrone use has been identified in clubbing and party milieu (France, UK, Netherlands, Slovenia), amongst school pupils (UK) and gay men (France). There is some evidence to suggest rapid spread of mephedrone use, particularly in the UK, but also among clubbers in Slovenia. Use reported in France is described as rather localised and limited, whilst in the Netherlands, the study is confined to a group of primary ecstasy users. Whilst much of the evidence is linked to recreational use amongst clubbers, the UK samples also include unemployed users and young people from deprived communities in Northern Ireland.

In terms of frequency of use — the reports suggest recreational weekend/monthly use is a common pattern for those who try and choose to continue to use mephedrone. As such, it is used in a similar way to ecstasy or cocaine in party and nightlife

settings. Around 15 % of the Internet survey respondents reported using mephedrone at least weekly. A small number of users appear to progress to daily use.

Strong cravings for the substance is reported (Netherlands, Slovenia, UK) — stronger than otherwise experienced stimulant users are used to (Slovenia) and this is cited as a main reason for use of more mephedrone than intended — and for longer periods than planned.

Prevalence

In the absence of epidemiological data on prevalence, user self-reports from convenience samples in subgroups place lifetime use of mephedrone at around 40 % amongst UK clubbers responding to the Internet survey (33 % last month use), (20 % amongst Scottish students) and 40 % amongst the Northern Irish schoolchildren attending focus groups. On the other hand, French TREND reports describe use as restricted to a small, primarily Parisian milieu.

Availability and quality of substance

Relatively easy availability, legality and high substance quality are all cited as factors in mephedrone's popularity. A majority of UK clubbers responding to the Internet survey report mephedrone gave a longer and better high than cocaine.

Availability of information

Media reports on mephedrone appear to have played a role in stimulating curiosity and encouraging spread to a wider user population. The media is also cited as a primary source of (often inaccurate) information about the drug. With the exception of psychonauts, there seems to be a low level of awareness of the 'content' or chemical make-up of mephedrone. There are reports of confusion with methadone (UK), and the focus groups with school pupils highlighted some curiosity as to whether regular plant food contained mephedrone. Information from pill/powder testing (Netherlands, France) indicates a majority of these users did not realise the substances they were using were mephedrone — before testing results were provided.

Characteristics of users

Mephedrone users are reported to be primarily male (as with most illicit substances) and aged between their late teens and late-20s, although both younger and older users are identified in UK studies. The majority are recreational polydrug users, with alcohol, cannabis and often cocaine, amphetamine and ecstasy in their drug using repertoire. The evidence suggests mephedrone has some appeal for a range of recreational stimulant users: specifically, UK respondents in the clubbers survey also used cocaine/ecstasy, the Dutch respondents were using ecstasy, and the Middlesbrough users were using cannabis and amphetamine.

Conditions under which substance obtained

Where information on the purchase of mephedrone is available (UK and Slovenia), it appears most common to buy the drug from a dealer or friends. Some users reported purchasing from the Internet — and that this tended to be higher quality mephedrone, but for some users the risk of Internet data security was a deterrent (Slovenia).

Social risks

There are 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 regarding the sale and use of mephedrone. The focus group on schoolchildren suggested that mephedrone was more easily accessible than cannabis at present, but they purported that they were more afraid of paramilitary violence if caught with mephedrone.

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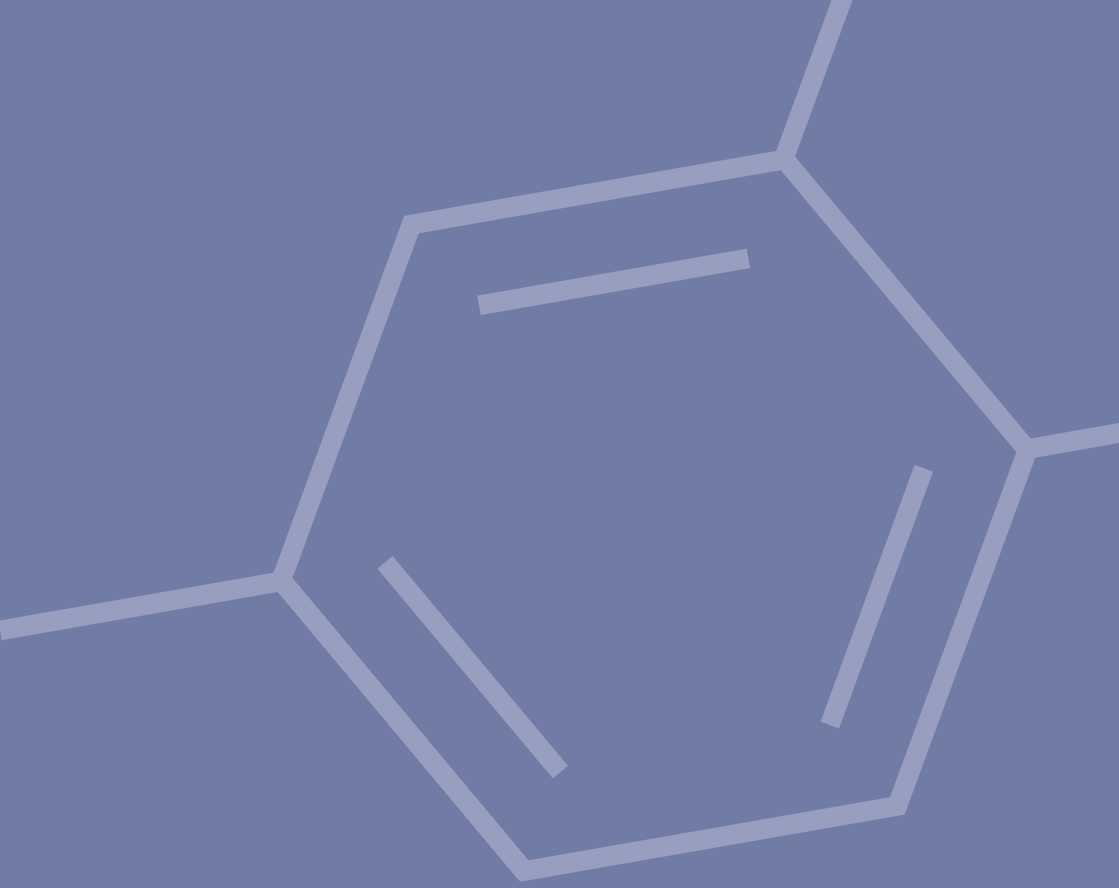

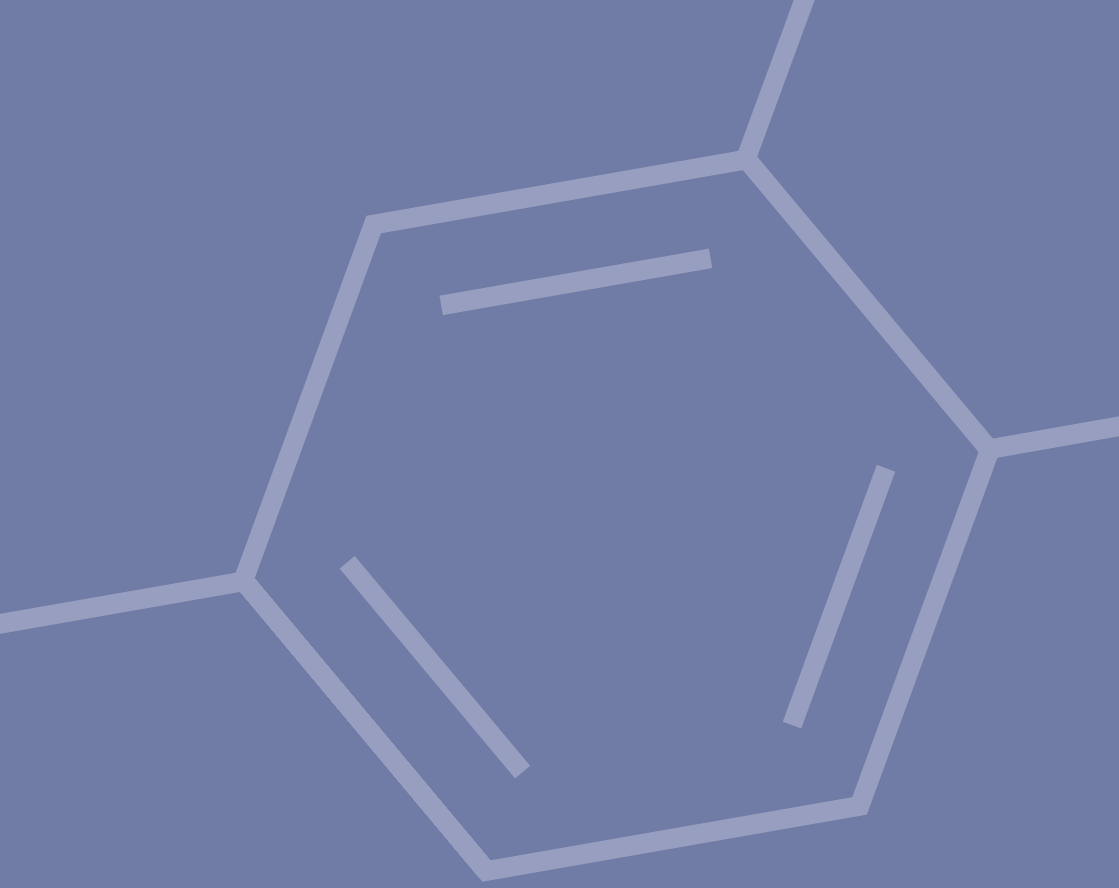

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([17]) This is an annex to the Risk assessment report.

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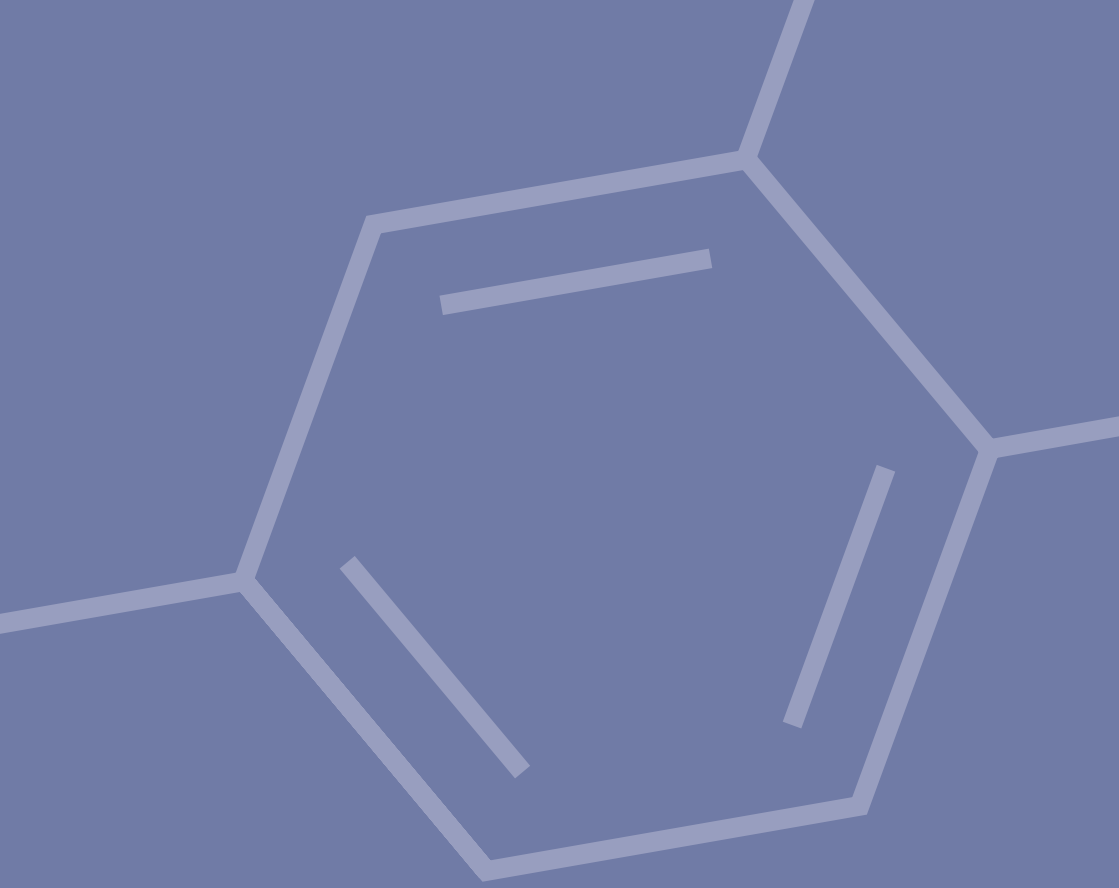

Annex I

Mephedrone survey 2010

Institute of Psychiatry, King's College London

Dr Adam R. Winstock and Dr John Marsden

Study ethical approval number: 141/02 Field version: 3.2

PRN ☐ **Date of contact** ☐ **Date of interview** ☐ **Interview ID** ☐

Read out

Hi [contact name:], My name is _____. I am a researcher at **King's College London**.

Can I just check that you completed the **Mixmag/Don't Stay In** survey and may be/are interested in taking part in further research we do on drug issues? ☐
If No ☐ – thank the individual and terminate.

We're doing some research focusing on **MEPHEDRONE** (pronounced: *mef-e-drone*).
This is sometimes called '**Meow Meow**', **M-Cat** or **4-MMC**). [if asked, chemical name is 4-methylmethcathinone]

We are trying to find out what people think of this drug, what effects they are getting, both good things and also the less good things. There's been almost no research on this drug and we don't know what effects people are getting. Our aim is to develop health information for mephedrone users.

Have you ever taken mephedrone?
Yes ☐ If 'No, never' ☐ – thank the individual and terminate.

Would you be interested in taking part in our survey? It will take about 15 minutes to complete.

If 'No, not convenient right now' ☐
When can I call back? Day _ _ Month _ _ Time _ _:_ _ [24 hr]

[check the date and time and the number to use].

If convenient to complete interview:

Read out

I just need to record your consent to take part.

I'm going to ask about your experiences of using mephedrone and any other stimulants you may have tried.

I'm not going to ask for your full name and the data will only be seen by myself, Adam and our team.

Let me stress that we are asking everyone the same questions, so some of them may not apply to you. If you prefer not to answer a question, just let me know and we'll move on.

Of course, you can decide to stop the interview at any time and withdraw from the study without giving a reason. And if you wish, we will remove your contact details from our database.

So, are you happy to take part in the survey? Yes ☐ No ☐

If No – would you like us to delete your details from our database and not contact you again about our future research?

Yes, withdraw completely ☐ No, happy to be contacted about other research ☐

Time interview started: _ _:_ _ [24 hour format]

Section 1 — Demographics

Let's start by recording some background information about you.

1.1 How old are you? _____ (age last birthday)

1.2 Record Male ☐ Female ☐

1.3 What is your height? (*'about' if uncertain*) _____ Feet **or** _____ Metres

1.4 What is your weight? ('about' if uncertain) _____ Kilos **or** _____ Stones **or** _____ Pounds

1.5 Are you: Working (FT) ☐ Working (PT) ☐ College (FT) ☐ College (PT) ☐ Unemployed ☐

Section 2 — Stimulant comparisons

2.1 Ok, let's set the scene for the interview in the context of other stimulants and your views on how mephedrone compares with these. Have you:

	Ever taken? No	Yes	***If Yes***	Age first used?		*How often taken in most recent month used?* Number sessions or tick>	Once a week (4)	Twice a week (8)	Three times a week (12)	Four times a week (16)	Five sessions a week (20)
Ecstasy	☐	☐	→		→		☐	☐	☐	☐	☐
Cocaine	☐	☐	→		→		☐	☐	☐	☐	☐

2.2 ***Interviewer – complete for ecstasy and cocaine (if ever used either or both) and for mephedrone***

Thinking about the ecstasy and cocaine that is generally around now, using a scale from 0 to 10, how would you rate:

	Ecstasy	**Cocaine**	**Mephedrone**
The pleasurable high: *(where 10 = best ever had)*			
Strength of effect: *(where 10 = extremely strong)*			
Negative effects when high: *(where 10 = best ever had)*			
Value-for-money of: *(where 10 = best experienced)*			
The urge to want more of the drug when taking: *(where 10 = extremely)*			

2.3 Since the time you started taking mephedrone, have you: (tick **one** only)

	Ecstasy	**Cocaine**
Been using more:	☐	☐
Been using less:	☐	☐
Or, has using mephedrone not changed how often you take:	☐	☐
Has there ever been a time when you took mephedrone instead of:	☐	☐
If there was a choice to make between …		
…. mephedrone or ecstasy, would choose to take mephedrone?	Yes ☐	No ☐
… mephedrone or cocaine, would choose to take mephedrone?	Yes ☐	No ☐

Section 3 — First mephedrone session

3.1 Can you now think back to the ***first time*** you ever took ***MEPHEDRONE***:

First time you took:	What amount was this dose? 50 mg	100 mg	125 mg	250 mg		How did you take it? Snort	Bomb	In drink	Inject
Line	☐	☐	☐	☐	→	☐	☐	☐	☐
Tipped out powder	☐	☐	☐	☐	→	☐	☐	☐	☐
Capsule	☐	☐	☐	☐	→	☐	☐	☐	☐
Pill	☐	☐	☐	☐	→	☐	☐	☐	☐

Other ☐ ***record verbatim and*** **amount** and **how taken**: _____

3.2 On that first session, how **many more doses** did you take? _____ Dose(s)

3.3 How **long** would you say that first session **lasted for in total**? _____ Hour(s)

(the time between **first dose** on that session and when you had come down form the **last dose** but were still awake)

3.4 How much would you estimate you took **in total** on that **first session**?

50 mg ☐ 100 mg (1/10 g) ☐ 125 mg (1/8 g) ☐ 250 mg (¼ g) ☐ 500 mg (½ g) ☐

1 gram ☐ 1.5 grams ☐ 2 grams ☐ More than 2 grams ☐ ***Or verbatim:*** _____

3.5 Did you take it any other way, apart from _____ (route for first dose)?
Probe: 'any other way?'

Snort ☐ Bomb ☐ In drink ☐ Rubbed on gums ☐ Smoked ☐ Injected ☐

Other ☐ ***describe:*** _____

3.6 Did you drink **alcohol** during that first session? Yes ☐ No ☐

Did you take **any other drugs** during the session (before you slept)?
Probe 'anything else?'

No ☐ Cocaine ☐ Ecstasy ☐ Cannabis ☐ Ketamine ☐ Amphetamine ☐

Other(s) ☐ ***describe:*** _____

Section 4 — Summary of mephedrone use

ESTIMATE OF TOTAL SESSIONS

4.1	So, when was that **first** session you used?	Year	Month
	And when was the **last** time you used?	Year	Month

So you've been using mephedrone for _____ (months) **[time between first and last month]**

Interviewer – complete session record – starting with FIRST month and ending with LAST month

4.2	Start FIRST	No Sessions or tick →	Once a week (4)	Twice a week (8)	Three times a week (12)	Four times a week (16)	Five sessions a week (20)
	M___ Yr___						
	M___ Yr___						
	M___ Yr___						
	M___ Yr___						
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	M___ Yr___						
	M___ Yr___						

4.3	Have you used mephedrone for **2 or more days in a row**?	Yes ☐	No ☐
	If Yes: what's the **total number of consecutive days** you have used?		

TYPICAL SESSION

I want to ask you about a ***typical*** session in the ***most recent month*** you have used (**clarify month**).

4.4	Generally, do you use: **alone** ☐ ***or*** are **other people** using with you ☐
	If use with others, about **how many** other people use as well? ☐

4.5	In a **typical session**, think about your **first dose**:										
		What amount?						How takes?			
	First dose is:	50 mg	100 mg	125 mg	250 mg	500 mg		Snort	Bomb	In drink	Inject
	Line	☐	☐	☐	☐	☐	→	☐	☐	☐	☐
	Tipped out powder	☐	☐	☐	☐	☐	→	☐	☐	☐	☐
	Capsule	☐	☐	☐	☐	☐	→	☐	☐	☐	☐
	Pill	☐	☐	☐	☐	☐	→	☐	☐	☐	☐
	Other ☐ ***record verbatim and*** **amount** and **how taken**:										
	If taken as a 'line' – ask: **How many lines would you say you would get out of 1 g?** ☐										
	If bombed/oral – ask: **How many bombs/doses would you say you would get out of 1 g?** ☐										

4.6	On average, how **many more doses** do you take? ☐ Dose(s) (if 1 only skip to Q. 4.8)

4.7	**If more than one dose**, about **how much time** is there on average between doses?
	30 minutes ☐ 1 hour ☐ 1.5 hrs ☐ 2 hrs ☐ 2.5 hrs ☐ 3 hrs ☐ Longer ☐
	If > 3hrs record verbatim answer ☐

4.8	How **long** would you say a typical session **lasts for in total**? ☐ Hour(s)
	(the time between **first dose** on that session and when you had come down from the **last dose** but are still awake)

4.9	How much would you estimate you take **in total** during a **typical session**?
	50 mg ☐ 100 mg (1/10 g) ☐ 125 mg (1/8 g) ☐ 250 mg (¼ g) ☐ 500 mg (½ g) ☐ 1 gram ☐
	1.5 g ☐ 2 g ☐ 2.5 g ☐ 3 g ☐ 3.5 g ☐ 4 g ☐ 4.5 g ☐ 5 g ☐ >5 g — ***specify*** ☐

4.10	Do you take it **another way**, apart from _____ (route first dose in Q. 3.5)? ***Probe: any other way?***
	Snort ☐ Bomb ☐ In drink ☐ Rubbed on gums ☐ Smoked ☐ Injected ☐
	Other ☐ ***describe***: _____

4.11	Do you drink **alcohol** during a typical session? Yes ☐ No ☐
	Do you take **any other drugs**? ***Probe 'anything else?'***
	No ☐ Cocaine ☐ Ecstasy ☐ Cannabis ☐ Ketamine ☐ Amphetamine ☐
	Other ☐ *describe*: _____

4.12	Could you estimate how **much mephedrone in total** you use in the most recent month?
	50 mg or less ☐ 100 mg (1/10 g) ☐ 125 mg (1/8 g) ☐ 250 mg (¼ g) ☐ 500 mg (½ g) ☐
	1 gram ☐ 1.5 grams ☐ 2 grams ☐ 3 grams ☐ 4 grams ☐ 5 grams ☐ 6 grams ☐
	Or verbatim: _____

4.13	What the most **mephedrone** you have **ever taken** in one session?
	50 mg or less ☐ 100 mg (1/10 g) ☐ 125 mg (1/8 g) ☐ 250 mg (¼ g) ☐ 500 mg (½ g) ☐
	1 gram ☐ 1.5 grams ☐ 2 grams ☐ 3 grams ☐ 4 grams ☐ 5 grams ☐ 6 grams ☐
	Or verbatim: _____

4.14	How **long** would you say that session **lasted for in total**? _____ Hour(s)
	(the time between **first dose** on that session and when you had come down from the **last dose** but are still awake)

4.15	Do you drink **alcohol** during that big session? Yes ☐ No ☐
	Do you take **any other drugs**? ***Probe 'anything else?'***
	No ☐ Cocaine ☐ Ecstasy ☐ Cannabis ☐ Ketamine ☐ Amphetamine ☐
	Other(s) ☐ *describe*: _____

Overall summary

I'm going to ask you some overall questions about mephedrone.

4.16	Thinking about how you have obtained mephedrone, have you **ever**: **(ask each)**		
	Been given mephedrone by a friend? ☐	Bought from a dealer? ☐	Bought from a head shop? ☐
	Bought from an Internet site? ☐	**Which most commonly obtained from?: underline**	
	(if No Internet, skip to Q. 4.18)		

4.17	*If bought on the Internet*: can you recall the name of the website, or websites, you have most commonly bought mephedrone from: **(don't prompt, just record all mentioned)**		
	AmazingPlantFood ☐	BrandCrazy ☐	Broadening-Horizons ☐
	BuyMephedroneOnline ☐	BuyMephedrone ☐	Charlie-Boy ☐
	DiscoFood ☐	FlowerPowderFeeder ☐	Mephedrone2U ☐
	Mephindustries ☐	MrMeph ☐	NaughtPlantFood ☐
	Plant-food.net ☐	PlantFoodPalace ☐	PolatzoPlantfood ☐
	PureChem ☐	ResearchChemicals ☐	ShopMephedrone ☐
	The-Cats-Meow ☐	TopDogPlantFood ☐	TrancePlants ☐
	4-MMC-shop ☐	UK-Legals ☐	
	Other ☐ name(s) _____ _____		
	If more than one: underline name of site most frequently bought from		
	4.17a What's the **typical amount** you have bought from a **website** in a **single purchase**?		
	0.5 g ☐ 1 g ☐ 2 g ☐ 5 g ☐ 10 g ☐ 20 g ☐ 50 g ☐ 100 g ☐ 200 g ☐		
	Other ☐ specify _____		
	4.17b What's the **maximum amount** you have bought from a **website** in a **single purchase**?		
	0.5 g ☐ 1 g ☐ 2 g ☐ 5 g ☐ 10 g ☐ 20 g ☐ 50 g ☐ 100 g ☐ 200 g ☐		
	Other ☐ specify _____		

4.18 What has the mephedrone you have most commonly taken **looked like when first taken out of the wrap or packet?** Tick most common type, then ask about any smell.

		Before using, did you notice that this had a particular smell?					
	No	Slight sweet	Strong sweet	Slight chemical	Strong chemical	Other — describe	
White crystals ☐ →	☐	☐	☐	☐	☐	☐	_____
Yellow crystals ☐ →	☐	☐	☐	☐	☐	☐	_____
Light pink crystals ☐ →	☐	☐	☐	☐	☐	☐	_____
Pure white power ☐ →	☐	☐	☐	☐	☐	☐	_____
Off-white power ☐ →	☐	☐	☐	☐	☐	☐	_____
Yellow powder ☐ →	☐	☐	☐	☐	☐	☐	_____
Pill ☐ →	☐	☐	☐	☐	☐	☐	_____
Capsule ☐ →	☐	☐	☐	☐	☐	☐	_____
Other ☐ →	☐	☐	☐	☐	☐	☐	_____

4.19 Can you list the different **situations** (places) you've **ever** taken mephedrone? ***Prompt***:

At your home ☐ At a friend's home ☐ At a house party ☐ At a club ☐ A festival ☐

At a pub/bar ☐ Other ☐ *describe*: _____

4.19a Where have you taken mephedrone most often? ***Interviewer***: underline one of the above

4.20 Here's a list of some things that can **motivate** someone to use mephedrone. On a scale from '0' to '10' where '0' is 'no influence at all' and 10 would be 'the maximum influence possible', how motivating have the following been when you've taken mephedrone:

	(***one*** number only)
It was legal to buy it	☐ 0-10
It was easy to buy on the Internet and delivered to my home	☐ 0-10
Mephedrone has a high level of purity, compared to illegal stimulants	☐ 0-10
It was good value for money	☐ 0-10
It is a more consistent product	☐ 0-10
You get a better high from mephedrone, compared to illegal stimulants	☐ 0-10
It has fewer side effects, compared to illegal stimulants	☐ 0-10
A single dose of mephedrone doesn't last too long	☐ 0-10
No other drug was available to me at the time, so I bought mephedrone	☐ 0-10

4.21 I'll read out a list of some effects that mephedrone can have. When taking mephedrone, please tell me **how often** you have experienced each of these effects by replying '**never**', '**once only**', or '**sometimes**', or '**most of the time**'.

	How often					***How intense***		
How often did you feel:	Never (0)	Once (1)	Some-times (2)	Most of the time (3)	***If experienced*** →	Mild (1)	Mod-erate (2)	Intense (3)
Euphoric	☐	☐	☐	☐	→	☐	☐	☐
Increased energy	☐	☐	☐	☐	→	☐	☐	☐
Improved concentration	☐	☐	☐	☐	→	☐	☐	☐
Empathy with others	☐	☐	☐	☐	→	☐	☐	☐
Urge to talk	☐	☐	☐	☐	→	☐	☐	☐
Urge to move, do things	☐	☐	☐	☐	→	☐	☐	☐
Increased sexual desire	☐	☐	☐	☐	→	☐	☐	☐
Restless or anxious	☐	☐	☐	☐	→	☐	☐	☐
Angry or aggressive	☐	☐	☐	☐	→	☐	☐	☐
Agitated	☐	☐	☐	☐	→	☐	☐	☐
No appetite for food	☐	☐	☐	☐	→	☐	☐	☐
You were forgetting things	☐	☐	☐	☐	→	☐	☐	☐
Panicky	☐	☐	☐	☐	→	☐	☐	☐
Paranoid	☐	☐	☐	☐	→	☐	☐	☐
Blurred vision	☐	☐	☐	☐	→	☐	☐	☐
Seeing things not there	☐	☐	☐	☐	→	☐	☐	☐
Hearing things not there	☐	☐	☐	☐	→	☐	☐	☐
Body sweating	☐	☐	☐	☐	→	☐	☐	☐
Overheating	☐	☐	☐	☐	→	☐	☐	☐

	How often					How intense		
How often did you feel:	Never (0)	Once (1)	Some-times (2)	Most of the time (3)	***If experienced*** →	Mild (1)	Mod-erate (2)	Intense (3)
Heart racing or erratic	☐	☐	☐	☐	→	☐	☐	☐
Shortness of breath	☐	☐	☐	☐	→	☐	☐	☐
Headache	☐	☐	☐	☐	→	☐	☐	☐
Chest pain	☐	☐	☐	☐	→	☐	☐	☐
Clenching jaw, grinding teeth	☐	☐	☐	☐	→	☐	☐	☐
Shaky hands, fingers	☐	☐	☐	☐	→	☐	☐	☐
Fingers/toes cold or numb	☐	☐	☐	☐	→	☐	☐	☐
Skin discoloured (blue/red)	☐	☐	☐	☐	→	☐	☐	☐
Skin rash	☐	☐	☐	☐	→	☐	☐	☐
Vomiting	☐	☐	☐	☐	→	☐	☐	☐
Hard to sleep, end of session	☐	☐	☐	☐	→	☐	☐	☐

4.22 Across all the sessions you've had, what's the way you've **most commonly** taken mephedrone?

Snort/sniff ☐ Bomb ☐ Rub on gums ☐ Smoke ☐ Inject ☐

Other ☐ describe: _____

4.23 Are there any **ways** of taking mephedrone you probably **wouldn't** do again? **Prompt and probe**

Snort/sniff ☐ Swallow in paper ☐ Rub on gums ☐ Smoke ☐ Inject ☐

Other ☐ describe: _____

4.24 Can you think now about how you felt during the **next day or two** after a session. I'll read out some feelings that people can experience. Please summarise for me **how often** you have experienced each one and how **intense the effect** has been.

	How often					***How intense***		
How often did you feel:	Never (0)	Once (1)	Some-times (2)	Most of the time (3)	***If experienced*** →	Mild (1)	Mod-erate (2)	Intense (3)
Increased appetite	☐	☐	☐	☐	→	☐	☐	☐
You had a stuffy nose	☐	☐	☐	☐	→	☐	☐	☐
Tired or fatigued	☐	☐	☐	☐	→	☐	☐	☐
Your sweat smelled unusual	☐	☐	☐	☐	→	☐	☐	☐
Anxious	☐	☐	☐	☐	→	☐	☐	☐
Depressed	☐	☐	☐	☐	→	☐	☐	☐
Emotional or tearful	☐	☐	☐	☐	→	☐	☐	☐
Irritable	☐	☐	☐	☐	→	☐	☐	☐
Unable to concentrate	☐	☐	☐	☐	→	☐	☐	☐
You lost memory of session	☐	☐	☐	☐	→	☐	☐	☐
An urge or craving to take more mephedrone	☐	☐	☐	☐	→	☐	☐	☐

4.25 ***Thinking overall across the time since you have been taking mephedrone:***

	Yes	No
1. Have you found that your usual dose hasn't had the same effect as when you first starting taking it?	☐	☐
2. Have you taken mephedrone for longer or in larger amounts than you had intended?	☐	☐
3. Have you had a persistent desire or strong urge to take it?	☐	☐
4. Have you wanted to cut down or take it less often but have not been successful?	☐	☐
5. Would you say you have spent a great deal of time getting mephedrone, taking it or recovering?	☐	☐

	Yes	No
6. Have you given up important social, occupational, or recreational activities because of it?	☐	☐
7. Have you continued to take it even though you've had physical/ psychological problems?	☐	☐
8. Have friends or family expressed concern to you about your use of mephedrone?	☐	☐
9. Have you been concerned about your use of mephedrone?	☐	☐
10. Have you taken mephedrone or another stimulant drug to help relieve mephedrone withdrawals?	☐	☐

4.26 After taking mephedrone, have you ever had **emergency medical treatment** or gone to **hospital**?

No ☐ Yes ☐

If no, skip to Q. 4.27 ***If Yes:***

a. How much mephedrone had you taken? _____ **record**

b. How long had the session been that time? _____ **hours**

c. Had you been drinking alcohol? Yes ☐ No ☐

d. Had you taken any other drugs in that session? ***Record and probe:***

Cocaine ☐ Amphetamine ☐ Cannabis ☐ Ketamine ☐

Other (specify): _____

e. Did you: Have chest pain? ☐ Were you feeling panicky, or agitated? ☐

Had you been seeing or hearing things that weren't there? ☐

Had you fainted, or collapsed ☐

Tick all or leave blank then skip to Section 5

4.27 After taking mephedrone, have you ever fainted or collapsed?

No ☐ Yes ☐

If no, go to Section 5 ***If Yes:***

a. How much mephedrone had you taken? _____ **record**

b. How long had the session been that time? _____ **hours**

c. Had you been drinking alcohol? Yes ☐ No ☐

d. Had you taken any other drugs in that session? ***Record and probe:***

Cocaine ☐ Amphetamine ☐ Cannabis ☐ Ketamine ☐

Other (specify): _____

Section 5 — Other cathinones

There are some other stimulants with similar effects to mephedrone.

5.1 Have you ever heard of **methylone**? (meth-e-lone)
[aka M1 or Bk-MDMA or MDMC; chemical name: 4-methylenedioxy-N-methylcathinone]

No ☐ Yes ☐ If 'Yes', have you used it? No ☐ Yes ☐ If 'Yes', how many times? ____

Or record verbatim: _____

5.2 Have you ever heard of **butylone** (bew-til-one)
[aka B1, or Bk-MDBD or Mitzseezs; chemical name: 3,4-benzodioxolylbutanamine)]

No ☐ Yes ☐ If 'Yes', have you used it? No ☐ Yes ☐ If 'Yes', how many times? ____

Or record verbatim: _____

5.3 Have you ever heard of **M.D.P.V.**?
[aka SuperCoke; chemical name: MethyleneDioxyPyroValerone]

No ☐ Yes ☐ If 'Yes', have you used it? No ☐ Yes ☐ If 'Yes', how many times? ____

Or record verbatim: _____

5.4 Have you ever heard of **flephedrone**?
[aka 4FMC; chemical name: 4-fluoromethcathinone; 4-FMC]

No ☐ Yes ☐ If 'Yes', have you used it? No ☐ Yes ☐ If 'Yes', how many times? ____

Or record verbatim: _____

5.5 Do you think that using **mephedrone** has made it more likely that you will try other stimulant drugs?

No ☐ Yes ☐ Record any verbatim: _____

TURN OVER

5.6	Do you think you will take **mephedrone** again:
	Yes, in the next month ☐ Yes, in the next 2 months ☐ No, very unlikely ☐
	Or record verbatim: _____

Time interview ended: __ : __ [24 hour format]

If answer to Q. 5.6 is 'No, very unlikely'

What is the main reason for this?

Thanks very much for taking part in our survey!

If answer to Q. 5.6 is 'Yes, in the next month or two months'

Interviewer — read out:

Thanks very much for taking part in our survey. **We have one more request.**

Mephedrone is such a new substance that we don't really know anything about how it is metabolised by the body. Also, there are several different types of cathinone stimulants and we don't know which ones are being used.

So, we'd like to send you a kit in the post and ask you to take a small sample of your urine the day after your next mephedrone session and send it back to our lab.

Our laboratory will screen the sample for mephedrone and other cathinones and the sample is then destroyed. This information is only seen by us and the results will then be made anonymous.

If you like, we can send you a personal feedback report on the results and also a GBP 20 HMV voucher as a thank you. This can also be used at a Waterstones Book store.

It would really enhance our understanding of how mephedrone works if you could help us out like this. Would you be able to help?

Yes ☐ ***No*** ☐ ***If yes — interviewer describes the process***

Biological assessment of cathinone use — research protocol

Overview

This protocol describes the biological assessment of cathinone use among recreational drug users who have completed the brief telephone interview about their cathinone and other use and related health risks and harms (REC 141/03). Only those indicating they may use mephedrone in the future will be approached to participate in the next phase of the study. There will be no obligation to participate. These informed, consenting participants will be sent a urine test collection kit and asked to mail a sample back for analysis the following day after taking a cathinone substance. Their postal address will be kept separate from their survey data. The sample will be analysed at the St George's Hospital Toxicology Unit using LC-MS procedures to determine metabolites of the exact compound(s) consumed. If requested by the participant a brief feedback of these results will be provided in addition to a gift voucher in recognition of their time.

Scientific justification

Cathinone stimulants are increasingly available on the Internet and sold as 'research chemicals' or as 'plant food' or 'bath salts' to hide their identity and intended purpose. The cathinones are β-keto analogues of d-amphetamine, but there are several compounds (including methedrone, 3-fluoromethcathinone, and MDPV (methylenedioxypyrovalerone) — some of which are already controlled by the Misuse of Drugs Act, some not. For example, methcathinone is a Class B drug and pyrovalerone (an obsolete anorectic) a Class C drug. Furthermore, some cathinones are in fact β-keto analogues of ecstasy (MDMA), not amphetamine (e.g. methylone and β-keto MDEA). One of the key issues in the present study is to distinguish mephedrone, methylone and methedrone from each other as well as to confirm that cathinones had in fact been used by participating individuals. This is important because of a potential asymmetrical health risk gradient. For example, methedrone is the β-keto analogue of PMMA. This and PMA are much more toxic than other phenethylamines. Methedrone has been associated with one fatal case in Sweden. But there has been almost no research on this in the UK and little is known about the metabolism of these compounds in humans.

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Ethical issues and confidentiality

Only those participants who have completed our telephone interview on mephedrone use and have indicated at the end of the telephone study that they may use mephedrone again will be offered the opportunity to participate in the biological screening study. Unlike the telephone study, we need some means of contacting participants for this study by e-mail and by post. We will use a mixture of participant identification (name or alias), research number and postal address marked for the attention only of the participant nominated name. Feedback results sent my e-mail or by post will also be identified by the participant's choice of name. Urine samples will be destroyed after testing.

Procedure

There will be seven steps:

(1) At the end of the telephone interview, all cathinone users will be asked if they think it possible that they will use this drug again in the next 30 days. If they answer 'No', the process will be terminated.

(2) The interviewer will then describe our additional study to examine the precise nature of cathinone compounds being used by people taking part in our research and invited to take part. The process of contact, identity protection and feedback of results will be described. If the individual is not interested in taking part, they will again be thanked for their participation in the telephone research and the process will be terminated at this point.

(3) The interviewer will assign the individual a Participant Information Number (PIN) and an alias name. The interviewer will then give this information to the participant and ask them to send a confirmation email to the IoP e-mail address of Dr Winstock. This information will also be sent by text. The participant will be asked to contact Dr Winstock by e-mail indicating their interest in taking part, and giving their address to receive materials. We will ask the subject line on the e-mail to read: 'for the attention of Dr Winstock only'.

(4) Dr Winstock will then send out a test kit to the specified address (see below for description of included material in the test kit).

(5) The participant will provide a sample of their urine the following day on which they have used mephedrone and mail the container back to the St George's Hospital Toxicology Unit, indicating if they would like a feedback report and a gift-store voucher.

(6) After analysis, a pro-forma feedback report will then be sent to Dr Winstock by e-mail. This feedback form will only have the PIN identification (and will indicate if the participant would like a copy and has requested a gift-store voucher). Feedback information will specify the cathinone detected (if any), as well as any amphetamine and phenethylamine metabolites with semi-quantitative information for each compound detected.

(7) Dr Winstock will send out the feedback report to the participant's e-mail address and their voucher to the specified mail address. The feedback report information will then be compiled into the main data file for the telephone survey for research analysis and aggregated reporting of results.

Test kit

The test kit sent to each participant will contain the following materials:

- study information sheet
- study consent form and material transfer agreement
- urine collection cup and mail-safe container
- freepost return envelope.

Annex II – Council Decision

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

THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty on European Union, and in particular Articles 29, 31(1)(e) and 34 (2)(c) thereof,

Having regard to the proposal from the Commission,

Having regard to the opinion of the European Parliament ([18]),

Whereas:

(1) The particular dangers inherent in the development of psychoactive substances require rapid action by the Member States.

(2) When new psychoactive substances are not brought within the scope of criminal law in all Member States, problems may arise in cooperation between the judicial authorities and law enforcement agencies of Member States owing to the fact that the offence or offences in question are not punishable under the laws of both the requesting and the requested State.

(3) The European Union Action Plan on Drugs 2000–04 provided for the Commission to organise an appropriate assessment of the Joint Action of 16 June 1997 concerning the information exchange, risk assessment and the control of new synthetic drugs ([19]) (hereinafter 'the Joint Action') taking into account the external evaluation commissioned by the European Monitoring Centre on Drugs and Drug Addiction (hereinafter 'the EMCDDA') of the early warning system. The assessment showed that the Joint Action had fulfilled its expectations. Nevertheless, the outcome of the assessment made it clear that the Joint Action was in need of reinforcement and reorientation.

([19]) Opinion delivered on 13 January 2004 (not yet published in the Official Journal).
([19]) OJ L 167, 25.6.1997, p. 1.

In particular, its main objective, the clarity of its procedures and definitions, the transparency of its operation, and the relevance of its scope had to be redefined. The Communication from the Commission to the European Parliament and the Council on the mid-term evaluation of the EU Action Plan on Drugs (2000–04) indicated that changes to the legislation would be introduced in order to enhance action against synthetic drugs. The mechanism as established by the Joint Action should therefore be adapted.

(4) New psychoactive substances can be harmful to health.

(5) The new psychoactive substances covered by this Decision may include medicinal products as defined in Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community Code relating to veterinary medicinal products ([20]) and in Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community Code relating to medicinal products for human use ([21]).

(6) The information exchange under the early warning system, established under the Joint Action, has proved to be a valuable asset to the Member States.

(7) Nothing in this Decision should prevent Member States from exchanging information, within the European Information Network on Drugs and Drug Addiction (hereinafter 'the Reitox network'), on emerging trends in new uses of existing psychoactive substances which may pose a potential risk to public health, as well as information on possible public health related measures, in accordance with the mandate and procedures of the EMCDDA.

(8) No deterioration of either human or veterinary health care as a result of this Decision will be permitted. Substances of established and acknowledged medical value are therefore excluded from control measures based on this Decision. Suitable regulatory and public health related measures should be taken for substances of established and acknowledged medical value that are being misused.

([20]) OJ L 311, 28.11.2001, p. 1. Directive as last amended by Directive 2004/28/EC (OJ L 136, 30.4.2004, p. 58).
([21]) OJ L 311, 28.11.2001, p. 67. Directive as last amended by Directive 2004/27/EC (OJ L 136, 30.4.2004, p. 34).

(9) In addition to what is provided for under the pharmacovigilance systems as defined in Directive 2001/82/EC and in Directive 2001/83/EC, the exchange of information on abused or misused psychoactive substances needs to be reinforced and appropriate cooperation with the European Medicines Agency (hereinafter 'EMEA') ensured. The United Nations Commission on Narcotic Drugs (hereinafter 'CND') Resolution 46/7 'Measures to promote the exchange of information on new patterns of drug use and on psychoactive substances consumed', provides a useful framework for action by the Member States.

(10) The introduction of deadlines into every phase of the procedure established by this Decision should guarantee that the instrument can react swiftly and enhances its ability to provide a quick-response mechanism.

(11) The Scientific Committee of the EMCDDA has a central role in the assessment of the risks associated with a new psychoactive substance, it will for the purpose of this Decision be extended to include experts from the Commission, Europol and the EMEA, and experts from scientific fields not represented, or not sufficiently represented, in the Scientific Committee of the EMCDDA.

(12) The extended Scientific Committee that assesses the risks associated with new psychoactive substances should remain a concise technical body of experts, capable of assessing effectively all risks associated with a new psychoactive substance. Therefore the extended Scientific Committee should be kept to a manageable size.

(13) Since the objectives of the proposed action, namely to bring about an exchange of information, a risk-assessment by a scientific committee and an EU-level procedure for bringing notified substances under control, cannot be sufficiently achieved by the Member States and can therefore, by reason of the effects of the envisaged action, be better achieved at European Union level, the Union may adopt measures, in accordance with the principle of subsidiarity as set out in Article 5 of the Treaty. In accordance with the principle of proportionality as set out in that Article, this Decision does not go what is beyond what is necessary in order to achieve those objectives.

(14) In conformity with Article 34(2)(c) of the Treaty, measures based upon this Decision can be taken by qualified majority as these measures are necessary to implement this Decision.

(15) This Decision respects fundamental rights and observes the principles recognised by Article 6 of the Treaty and reflected in the Charter of Fundamental Rights of the European Union,

HAS DECIDED AS FOLLOWS:

Article 1

Subject matter

This Decision establishes a mechanism for a rapid exchange of information on new psychoactive substances. It takes note of information on suspected adverse reactions to be reported under the pharmacovigilance system as established by Title IX of Directive 2001/83/EC.

This Decision also provides for an assessment of the risks associated with these new psychoactive substances in order to permit the measures applicable in the Member States for control of narcotic and psychotropic substances to be applied also to new psychoactive substances.

Article 2

Scope

This Decision applies to substances not currently listed in any of the schedules to:

(a) the 1961 United Nations Single Convention on Narcotic Drugs, that may pose a comparable threat to public health as the substances listed in Schedule I or II or IV thereof, and

(b) the 1971 United Nations Convention on Psychotropic Substances, that may pose a comparable threat to public health as the substances listed in Schedule I or II or III or IV thereof.

This Decision relates to end-products, as distinct from precursors in respect of which Council Regulation (EEC) No 3677/90 of 13 December 1990 laying down measures to be taken to discourage the diversion of certain substances to the illicit manufacture of narcotic drugs and psychotropic substances ([22]), and Regulation

([22]) OJ L 357, 20.12.1990, p. 1. Regulation as last amended by Commission Regulation (EC) No 1232/2002 (OJ L 180, 10.7.2002, p. 5).

(EC) No 273/2004 of the European Parliament and of the Council of 11 February 2004 on drug precursors ([23]) provide for a Community regime.

Article 3

Definitions

For the purpose of this Decision the following definitions shall apply:

(a) 'new psychoactive substance' means a new narcotic drug or a new psychotropic drug in pure form or in a preparation;

(b) '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;

(c) '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;

(d) 'marketing authorisation' means a permission to place a medicinal product on the market, granted by the competent authority of a Member State, as required by Title III of Directive 2001/83/EC (in the case of medicinal products for human use) or Title III of Directive 2001/82/EC (in the case of veterinary medicinal products) or a marketing authorisation granted by the European Commission under Article 3 of Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency ([24]);

(e) 'United Nations system' means the World Health Organization (WHO), the Commission on Narcotic Drugs (CND) and/or the Economic and Social Committee acting in accordance with their respective responsibilities as described in Article 3 of the 1961 United Nations Single Convention on

([23]) OJ L 47, 18.2.2004, p. 1.
([24]) OJ L 136, 30.4.2004, p. 1.

Narcotic Drugs or in Article 2 of the 1971 United Nations Convention on Psychotropic Substances;

(f) 'preparation' means a mixture containing a new psychoactive substance;

(g) 'Reporting Form' means a structured form for notification of a new psychoactive substance and/or of a preparation containing a new psychoactive substance agreed between the EMCDDA/Europol and their respective networks in the Member States' Reitox and the Europol national units.

Article 4

Exchange of information

1. Each Member State shall ensure that its Europol National Unit and its representative in the Reitox network provide information on the manufacture, traffic and use, including supplementary information on possible medical use, of new psychoactive substances and of preparations containing new psychoactive substances, to Europol and the EMCDDA, taking into account the respective mandates of these two bodies.

   Europol and the EMCDDA shall collect the information received from Member States through a Reporting Form and communicate this information immediately to each other and to the Europol National Units and the representatives of the Reitox network of the Member States, the Commission, and to the EMEA.

2. Should Europol and the EMCDDA consider that the information provided by a Member State on a new psychoactive substance does not merit the communication of information as described in paragraph 1, they shall inform the notifying Member State immediately thereof. Europol and the EMCDDA shall justify their decision to the Council within six weeks.

Article 5

Joint Report

1. 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 EMEA and the Commission.

2. The Joint Report shall contain:

(a) a chemical and physical description, including the name under which the new psychoactive substance is known, including, if available, the scientific name (International Non-proprietary Name);

(b) 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;

(c) information on the involvement of organised crime in the manufacture or trafficking of the new psychoactive substance;

(d) a first indication of the risks associated with the new psychoactive substance, including the health and social risks, and the characteristics of users;

(e) information on whether or not the new substance is currently under assessment, or has been under assessment, by the UN system;

(f) the date of notification on the Reporting Form of the new psychoactive substance to the EMCDDA or to Europol;

(g) information on whether or not the new psychoactive substance is already subject to control measures at national level in a Member State;

(h) as far as possible, information will be made available on:

(i) the chemical precursors that are known to have been used for the manufacture of the substance,

(ii) the mode and scope of the established or expected use of the new substance,

(iii) any 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.

3. The EMEA shall submit to Europol and the EMCDDA the following information on whether in the European Union or in any Member State:

(a) the new psychoactive substance has obtained a marketing authorisation;

(b) the new psychoactive substance is the subject of an application for a marketing authorisation;

(c) a marketing authorisation that had been granted in respect of the new psychoactive substance has been suspended.

Where this information relates to marketing authorisations granted by Member States, these Member States shall provide the EMEA with this information if so requested by it.

4. Member States shall provide the details referred to under paragraph 2 within six weeks from the date of notification on the Reporting Form as set out in Article 4(1).

5. The Joint Report shall be submitted no more than four weeks after the date of receipt of the information from Member States and the EMEA. The Report shall be submitted by Europol or the EMCDDA, as appropriate, in accordance with Article 5(1) and (2).

Article 6

Risk assessment

1. The Council, taking into account the advice of Europol and the EMCDDA, and acting by a majority of its members, may request that the risks, including the health and social risks, caused by the use of, the manufacture of, and traffic in, a new psychoactive substance, the involvement of organised crime and possible consequences of control measures, be assessed in accordance with the procedure set out in paragraphs 2 to 4, provided that at least a quarter of its members or the Commission have informed the Council in writing that they are in favour of such an assessment. The Member States or the Commission shall inform the Council thereof as soon as possible, but in any case within four weeks of receipt of the Joint Report. The General Secretariat of the Council shall notify this information to the EMCDDA without delay.

2. In order to carry out the assessment, the EMCDDA shall convene a special meeting under the auspices of its Scientific Committee. In addition, for the purpose of this meeting the Scientific Committee may be extended

by a further five experts at most, to be designated by the Director of the EMCDDA, acting on the advice of the Chairperson of the Scientific Committee, chosen from a panel of experts proposed by Member States and approved every three years by the Management Board of the EMCDDA. Such experts will be from scientific fields that are not represented, or not sufficiently represented, in the Scientific Committee, but whose contribution is necessary for the balanced and adequate assessment of the possible risks, including health and social risks. Furthermore, the Commission, Europol and the EMEA shall each be invited to send a maximum of two experts.

3. The risk assessment shall be carried out on the basis of information to be provided to the scientific Committee by the Member States, the EMCDDA, Europol, the EMEA, taking into account all factors which, according to the 1961 United Nations Single Convention on Narcotic Drugs or the 1971 United Nations Convention on Psychotropic Substances, would warrant the placing of a substance under international control.

4. On completion of the risk assessment, a report (hereinafter the 'Risk Assessment Report') shall be drawn up by the Scientific Committee. The Risk Assessment Report shall consist of an analysis of the scientific and law enforcement information available, and shall reflect all opinions held by the members of the Committee. The Risk Assessment Report shall be submitted to the Commission and Council by the chairperson of the Committee, on its behalf, within a period of twelve weeks from the date of the notification by the General Secretariat of the Council to the EMCDDA referred to in paragraph 1.

The Risk Assessment Report shall include:

(a) the physical and chemical description of the new psychoactive substance and its mechanisms of action, including its medical value;

(b) the health risks associated with the new psychoactive substance;

(c) the social risks associated with the new psychoactive substance;

(d) information on the level of involvement of organised crime and information on seizures and/or detections by the authorities, and the manufacture of the new psychoactive substance;

(e) information on any assessment of the new psychoactive substance in the United Nations system;

(f) where appropriate, a description of the control measures that are applicable to the new psychoactive substance in the Member States;

(g) options for control and the possible consequences of the control measures, and

(h) the chemical precursors that are used for the manufacture of the substance.

Article 7

Circumstances where no risk assessment is carried out

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

2. Where the new psychoactive substance has been assessed within the United Nations system, but it has been decided not to schedule the new psychoactive substance under the 1961 Single Convention on Narcotic Drugs or the 1971 Convention on Psychotropic Substances, a risk assessment shall be carried out only if there is significant new information that is relevant in the framework of this Decision.

3. No risk assessment shall be carried out on a new psychoactive substance if:

(a) the new psychoactive substance is used to manufacture a medicinal product which has been granted a marketing authorisation; or,

(b) the new psychoactive substance is used to manufacture a medicinal product for which an application has been made for a marketing authorisation or,

(c) the new psychoactive substance is used to manufacture a medicinal product for which a marketing authorisation has been suspended by a competent authority.

Where the new psychoactive substance falls into one of the categories listed under the first subparagraph, the Commission, on the basis of data collected by EMCDDA and Europol, shall assess with the EMEA the need for further action, in close cooperation with the EMCDDA and in accordance with the mandate and procedures of the EMEA.

The Commission shall report to the Council on the outcome.

Article 8

Procedure for bringing specific new psychoactive substances under control

1. Within six weeks from the date on which it received the Risk Assessment Report, the Commission shall present to the Council an initiative to have the new psychoactive substance subjected to control measures. If the Commission deems it is not necessary to present an initiative on submitting the new psychoactive substance to control measures, within six weeks from the date on which it received the Risk Assessment Report, the Commission shall present a report to the Council explaining its views.

2. Should the Commission deem it not necessary to present an initiative on submitting the new psychoactive substance to control measures, such an initiative may be presented to the Council by one or more Member States, preferably not later than six weeks from the date on which the Commission presented its report to the Council.

3. The Council shall decide, by qualified majority and acting on an initiative presented pursuant to paragraph 1 or 2, on the basis of Article 34(2) (c) of the Treaty, whether to submit the new psychoactive substance to control measures.

Article 9

Control measures taken by Member States

1. If the Council decides to submit a new psychoactive substance to control measures, Member States shall endeavour to take, as soon as possible, but no later than one year from the date of that decision, the necessary measures in accordance with their national law to submit:

(a) the new psychotropic drug to control measures and criminal penalties as provided under their legislation by virtue of their obligations under the 1971 United Nations Convention on Psychotropic Substances;

(b) the new narcotic drug to control measures and criminal penalties as provided under their legislation by virtue of their obligations under the 1961 United Nations Single Convention on Narcotic Drugs.

2. Member States shall report the measures taken to both the Council and the Commission as soon as possible after the relevant decision has been taken. Thereafter this information shall be communicated to the EMCDDA, Europol, the EMEA, and the European Parliament.

3. Nothing in this Decision shall prevent a Member State from maintaining or introducing on its territory any national control measure it deems appropriate once a new psychoactive substance has been identified by a Member State.

Article 10

Annual report

The EMCDDA and Europol shall report annually to the European Parliament, the Council and the Commission on the implementation of this Decision. The report will take into account all aspects required for an assessment of the efficacy and achievements of the system created by this Decision. The Report shall, in particular, include experience relating to coordination between the system set out in this Decision and the pharmacovigilance system.

Article 11

Pharmacovigilance system

Member States and the EMEA shall ensure an appropriate exchange of information between the mechanism set up by means of this Decision and the pharmacovigilance systems as defined and established under Title VII of Directive 2001/82/EC and Title IX of Directive 2001/83/EC.

Article 12

Repeal

The Joint Action on New Synthetic Drugs of 16 June 1997 is hereby repealed. Decisions taken by the Council based on Article 5 of that Joint Action shall continue to be legally valid.

Article 13

Publication and taking effect

This Decision shall take effect on the day following that of its publication in the *Official Journal of the European Union*.

Done at Brussels, 10 May 2005.

For the Council
The President
J. Krecké

European Monitoring Centre for Drugs and Drug Addiction

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About the EMCDDA

The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) is one of the European Union's decentralised agencies. Established in 1993 and based in Lisbon, it is the central source of comprehensive information on drugs and drug addiction in Europe.

The EMCDDA collects, analyses and disseminates factual, objective, reliable and comparable information on drugs and drug addiction. In doing so, it provides its audiences with an evidence-based picture of the drug phenomenon at European level.

The Centre's publications are a prime source of information for a wide range of audiences including policymakers and their advisors, professionals and researchers working in the drugs field and, more broadly, the media and general public.

EMCDDA risk assessments are publications examining the health and social risks of individual synthetic drugs on the basis of research carried out by the agency and its partners.

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