

Annex 1 to the Risk assessment report: TECHNICAL REPORT ON MEPHEDRONE

Prepared by Dr Paul Dargan and Dr David Wood

Guy's and St Thomas' NHS Foundation Trust, London, UK

EMCDDA contract CT.10.EPI.057

July 2010

Note: Parts of this report contain data or research which are unpublished or in press.

Table of contents

SUMMARY	4
SECTION A. PHYSICAL, CHEMICAL, PHARMACEUTICAL AND PHARMACOLOGICA	۸L
INFORMATION	
A1. Physical, chemical and pharmaceutical information	
A1.1. Physical and chemical description (including methods of synthesis, precursors,	0
impurities if known – type and level)	9
A1.2. Physical/pharmaceutical form	
A1.3. Route of administration and dosage	
A2. Pharmacology, including pharmacodynamics and pharmacokinetics	
A3. Psychological and behavioural effects	
A4. Legitimate uses of the product	
SECTION B. DEPENDENCE AND ABUSE POTENTIAL	
B1. Animal <i>in vivo</i> and <i>in vitro</i> data	
B2. Human data	
SECTION C. PREVALENCE OF USE	
SECTION D. HEALTH RISKS	
D1. Acute health effects	
D1.1. Animal Data	
D1.2. Human Data	
D2. Chronic Health Effects	
D2.1. Animal Data	
D2.2. Human Data	
D3. Factors Affecting Public Health Risks	
D3.1. Availability and quality of the new psychoactive substance on the market (purity,	54
adulterants etc)	54
D3.2. Availability of the information, degree of knowledge and perceptions amongst users	
concerning the psychoactive substance and its effects	
D3.3. Characteristics and behaviour of users (including risk factors, vulnerability, etc.)	
D3.4. Nature and extent of health consequence (e.g. acute emergencies, road traffic	
accidents)	62
D3.5. Long-term Consequences of Use	
D3.6. Conditions Under Which the New Psychoactive Substance is Obtained and Used,	
Including Context-Related Effects and Risks	63
SECTION E. SOCIAL RISKS	
E1. Individual Social Risks	
E2. Possible Effects on Direct Social Environment	
E3. Possible Effects on Society as a Whole	
E4. Economic Costs	66
E5. Possible Effects Related to the Cultural Context, for example Marginalisation	66
E6. Possible Appeal of the new Psychoactive Substance to Specific Population Groups within	
General PopulationSECTION F. INVOLVEMENT OF ORGANISED CRIME	68
F1. Evidence that criminal groups are systematically involved in production, trafficking and	
distribution for financial gain	68
F2. Impact on the production, trafficking and distribution of other substances, including existing	
psychoactive substances as well as new psychoactive substances	
F3. Evidence of the same groups of people being involved in different types of crime	71
F4. Impact of violence from criminal groups on society as a whole or on social groups or loca	
communities (public order and safety)	
F5. Evidence of money laundering practices, or impact of organised crime on other	
socioeconomic factors in society	72
F6. Economic costs and consequences (evasion of taxes or duties, costs to the judicial syste	
F7. Use of violence between or within criminal groups	
F8. Evidence of strategies to prevent prosecution, for example through corruption or intimidate	tion
REFERENCES	74

SUMMARY

'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 methodrone, 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, health care 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 co-ordinated 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).

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 – 250mg, although users report redosing due to short lived effects and total doses used per session are typically 0.5 – 1g.

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 with those seen other stimulant drugs such as MDMA (3,4methylenedioxymethamphetamine) 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 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.

SECTION A. PHYSICAL, CHEMICAL, PHARMACEUTICAL AND PHARMACOLOGICAL INFORMATION

A1. Physical, chemical and pharmaceutical information

A1.1. Physical and chemical description (including methods of synthesis, precursors, impurities if known – type and level)

'Mephedrone' is the common name for the synthetic cathinone 4methylmethcathinone. The systematic (International Union of Pure and Applied Chemistry, IUPAC) name for mephedrone is 2-methylamino-1-(4methylphenyl)propan-1-one. The Chemical Abstract Service (CAS) Registry mephedrone are 1189805-46-6 (base) and 1189726-22-4 Numbers for (hydrochloride salt). Other names for mephedrone include N-methylephedrone; βketo-(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.

The chemical structure of mephedrone is shown below:

Mephedrone was first synthesized in 1929. The main synthetic route involves α 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 contamination with managanese 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 methodrone, 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, health care 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-MSMS) 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 MR 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.

A1.2. 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 2009l. There do not appear to be any distinctive markings specific to mephedrone on the tablets or capsules. However as summarised in Section C., a number of mephedrone tablets seizures in European member countries have included tablets with markings.

Mephedrone is sold under a number of brand names including 'plant feeder', 'bath salts', 'Neo Doves' and 'Neo Blues' (1). 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].

A1.3. Route of administration and dosage

Mephedrone is used by the oral route, nasal insufflation, intramuscular injection, intravenous injection and rectal insertion [Pyschonaut 2010, 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

 $^(^{1})$ Other names include 'Wild Cat', 'The Business', 'Diablo XXX', 'Blow', 'Magic', 'Tornado', 'the Real Euphoria' and 'The Big Sroom Effect'.

insufflation and 30% oral ingestion [Dick D 2010, Winstock AR 2010]. There are numerous reports of individuals using mixed routes during a single session (oral and nasal, oral and rectal). As mentioned below in Section D., 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 DM 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 (50-75mg) 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 – 2.0g. As mentioned below, in Section D., 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 3 months [Winstock AR 2010]

A2. Pharmacology, including pharmacodynamics and pharmacokinetics

A recent study by Meyer et al in Germany has provided data on the likely metabolites of mephedrone [Meyer MR 2010]. In this study, rats administered a single 20mg/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 detected: nor-mephedrone, were nor-dihydro mephedrone, hydroxytolyl mephedrone and nor-hydroxytolyl mephedrone. In human a urine sample submitted by a mephedrone user a further metabolite, 4carboxy-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, nordihydro 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 it 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.

A3. 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 in Section D1.2..

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 AR 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 AR 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 AR 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].

A4. 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.

SECTION B. DEPENDENCE AND ABUSE POTENTIAL

B1. Animal in vivo and in vitro data

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

B2. Human data (2)

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 [Albert S 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

(2) For additional information please see *Appendix 1 Mephedrone: Assessment of health risks* and harms (A. Winstock and J. Marsden, 2010)

18

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 1000 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 (Jan to Jun 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.

SECTION C. PREVALENCE OF USE (3)(4)

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 6 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 (⁵).

Country	Amount and Details of the Seizure
Austria	2009: 11 samples of powder – 2 beige, 3 yellow, 4 white and
	2 brown (2 totalling 23.4g also containing ethylcathinone, 2
	totalling 1082.4g also containing butylone, MDPV and
	methylone and 7 seizures of mephedrone totalling 5911g). 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

_

For additional information please see *Appendix 1 Mephedrone: Assessment of health risks and harms* (A. Winstock and J. Marsden, 2010)

⁽⁴⁾ For additional information please see Appendix 2 Mephedrone: prevalence, use patterns, effects and related health and social risks (information from surveys, focus groups and interviews with mephedrone users) (J. Mounteney EMCDDA, June 2010)

⁽⁵⁾ Summary of this information is available in the *Europol-EMCDDA Joint report on mephedrone*; for most recent and complete information please check also the European Database on New Drugs (EDND) which is being regularly updated.

	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			
	captalon logo containing mephedrone and caffeine, 6 light			
	green tablets with captalon logo and ® containing			
	mephedrone, caffeine and MDMA and one blue-green tablet			
	with captalon logo and ® containing mCPP, 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 1001.55g of			
	mephedrone.			
Cyprus	2009: 166 tablets containing mephedrone.			
Czech Republic	2010: mephedrone was detected in a single white powder			
	sample.			
Denmark	2008: 8 mephedrone seizures, including 474.4g of beige			
	powder.			
	2009: 9 reported mephedrone seizures.			
Estonia	2009: 6 seizures of powder containing mephedrone totalling			
	47.85g.			

2007: 12 capsules containing mephedrone.			
3: 21 seizures totalling 36 capsules containing			
hedrone (some found to contain ethylcathinone) and			
109.9g of mephedrone powder.			
9: 10 customs seizures totalling 264.8g of mephedrone			
der and 5 forensic laboratory seizures totalling 31g of			
hedrone powder.			
32 seizures of powder totalling 213.2g of mephedrone			
3 seizures of a total of 35 mephedrone tablets.			
3: Mephedrone identified in one capsule associated with			
hetamine and caffeine.			
e: The French SINTES study identified 7 samples of			
hedrone, 1 sold as mephedrone, 3 as MDMA, 2 as			
hetamine and 1 as MPK.			
e: One seizure of 4400 ecstasy tablets seized with			
gle logo were found to contain mephedrone and 6			
ures of mephedrone powder totalling 320.67g. In			
tion, in a mixed drug seizure containing 18 ecstasy pills,			
re found to contain mephedrone.			
2: 2 seizures of mephedrone powder.			
eported seizures because mephedrone is not included			
xicological screening as there is no reference standard			
able.			

Guernsey	2009: 96 seizures of powders totalling 1186.875g of			
	mephedrone and 7 capsules.			
Hungary	2009: 4 seizures of powders total 1008g mephedrone, of			
	which 0.22g contained mephedrone and cocaine.			
	2010: 15 seizures of 125.64g 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.			
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 20g of			
	mephedrone (1 seizure of 10g beige powder and 1 of 10g			
	white powder).			
Latvia	2009: 3 seizures totalling 678 mephedrone tablets.			
	2010: Seizure of 74.96kg of white powder containing			
	mephedrone.			
Lithuania	Suspected seizures were reported (minor quantities, about 1			
	g total weight) but confirmatory analysis were not performed.			
Luxembourg	2010: Seizure of 4.4g of mephedrone powder.			
Malta	2009: 0.56g mephedrone seized at a drug dance scene.			
	2010: 2 seizures of white powder totalling 2.19g.			

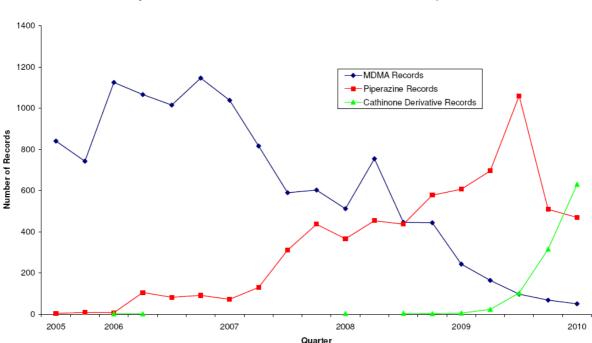
Netherlands	2009:			
	From DMIS: 54 tablet, 9 powder and 2 mixed samples			
	containing mephedrone.			
	From NFI: 103 seizures totalling 286,493 tablets (including			
	one single seizure of 276,000 tablets mainly bearing the			
	Roche 2 implant logo) and 57.5 kg powder containing			
	mephedrone. The 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 0.23g of white powder containing			
	mephedrone			
	2010: Seizure of 11.3g 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			
	50g 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 report			
	seizures of 'legal highs' from stores which included			
	mephedrone based products.			
Slovakia	2009: 2 seizures of powder (one white and one blue-green)			
	totalling 3861g of mephedrone (also containing caffeine)			
	and 1 seizure of 1197 light green tablets with captalon logo			
	containing mephedrone alone.			
Spain	No reported seizures			
Sweden	2008: 82 seizures of powder totalling 4694g of mephedrone.			
	2009: 215 seizures of powder totalling 8703g 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 62mg of mephedrone powder			
	and a powder containing 9.7mg of mephedrone. 4 additional			
	Internet purchases tested were found to contain			
	mephedrone and ethcathinone.			
	2009: 606 seizures of powder containing 39.1kg 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			
	oMEOPP in addition to mephedone and a further powder			
	was found to contain phenethylamine.			

	2010: The UK Forensic Science Service report seizures of		
	over 100 powder samples of almost 80kg of mephedrone.		
	Data from other 2010 UK seizures was not available at the		
	time of writing this report.		
Norway	2008: one seizure of 39.8g of mephedrone		
	2009: 9 seizures of powder totalling 765g 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 28.14g 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 68.1mg MDMA, 12.6mg caffeine, 6.9mg		
	mephedrone.		
	2010: Seized 'XTC' tablets found to contain mephedrone.		
Belarus	2010: 1g of white powder seized which contained		
	mephedrone.		

Data from the UK Forensic Science Service (FSS, see figure below) 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 16th April 2010.



FSS MDMA, Piperazine and Cathinone Derivative Records : Seizure Date July 2005 - March 2010

The price of mephedrone reported to the EMCDDA varies across Europe, some examples of reported prices are: Romania 40-100€ per gram, Poland 15€ per gram, France 15€ per gram, Hungary 30-40€ per gram, Latvia 29€ per gram, Belgium 50€ per gram and Ireland 30-40€ per gram. In addition information was supplied by Ireland on the prices for pills (7.5€ per pill) and tablets (6€ per tablet).

As noted in D3.1., in the EMCDDA Internet Snapshot studies the price of mephedrone ranged from £9.50 - £14.50 per gram; many sites offered discounts for

larger purchases with bigger discounts for larger purchases (e.g. 1kg for £3100 i.e. £3.10 per gram).

There are currently no co-ordinated 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 2000 clubbers in the UK, 33.6% of those surveyed reported use of mephedrone within the last month [Dick D 2010, Winstock AR 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%). Life-time 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 life-time 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 1006 school and college/university students in Scotland in February 2010, 205 (20.3%) of those surveyed had used mephedrone on at least one occasion [Albert S 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 were conducted with 154 pupils (aged 14-15) in three schools in May 2010 [Meehan C 2010]. Youth

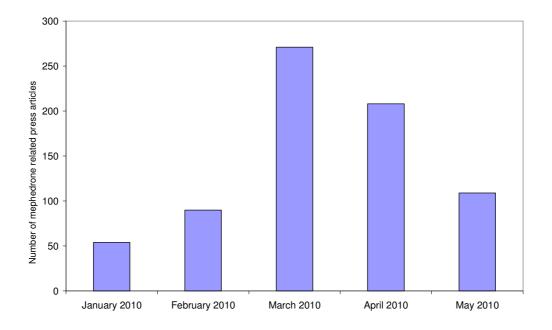
workers and teachers were also interviewed. This study was carried out in Belfast and Derry in areas with high deprivation and in which drug use is prevalent. All of the pupils had heard of mephedrone; approximately 40% had tried it at least once and 70% stated that their friends had used mephedrone. Mephedrone use was higher amongst males and cannabis users. Mephedrone was most commonly used at a party or friends house, often together with alcohol. Approximately 80% of respondents reported that they knew where to buy mephedrone – usually off 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 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 in Section D1.2. 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 below [EMCDDA unpublished].



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 section D1.2.5.. 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 16th April 2010 and the final driver appears to have been media interest in law enforcement action concerning the control of mephedrone in a number of countries. These are detailed in section E3., together with media interest in whether the control of mephedrone was appropriate.

SECTION D. HEALTH RISKS (6)(7)

D1. Acute health effects

D1.1. Animal Data

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

D1.2. Human Data

D1.2.1 User Reports

The 2009 MixMag survey of over 2000 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 the table below [Albert S 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%).

⁽⁶⁾ For additional information please see *Appendix 1 Mephedrone: Assessment of health risks and harms* (A. Winstock and J. Marsden, 2010)

⁽⁷⁾ For additional information please see *Appendix 2 Mephedrone: prevalence, use patterns, effects and related health and social risks (information from surveys, focus groups and interviews with mephedrone users)* (J. Mounteney EMCDDA, June 2010)

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%

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.

D1.2.2. London Clinical Data

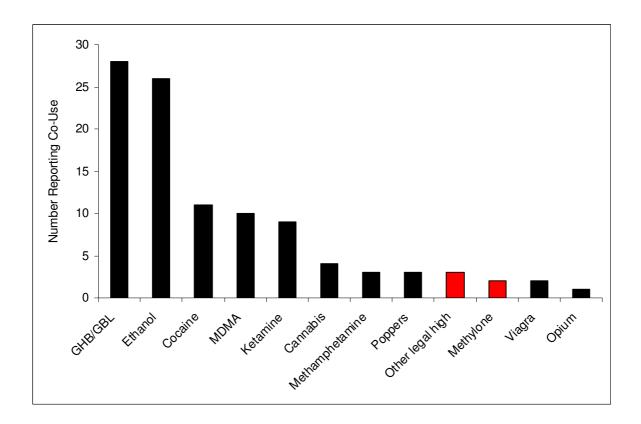
There is data available on two series of acute mephedrone toxicity from the Clinical Toxicology Service at Guy's and St Thomas' NHS Foundation Trust in London [Wood DM 2010a, Wood DM 2010b, updated with unpublished data]. The first of these [D1.2.2.1], is a series of 72 patients who presented with acute toxicity related to self-reported mephedrone use. The second of these [D1.2.2.2], is a series of 9 patients with acute toxicity related to self-reported mephedrone in whom full toxicology screening was undertaken.

D.1.2.2.1 Self-Reported Acute Mephedrone Toxicity

Detailed data is available on 72 cases of acute toxicity associated with self-reported mephedrone use in London from 1st January 2009 until 15th June 2010 [Wood DM 2010a, Wood DM 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 16th April 2010, 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 \pm SD age was 27.8 \pm 8.7 years (range 16-54 years), 81.9% were male. 35 (48.6%) specified the route of mephedrone use. The commonest 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 / IM injection (1, 2.9%). The dose of mephedrone used was reported in mg/g quantities in 21 (29.2%) individuals. The mean \pm SD (range) dose was $1.9 \pm 2.0 \ (0.3 - 7.0)g$.

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



The mean heart rate was 93.1 \pm 26.1, range 50 - 158 beats per minute, mean systolic blood pressure was 141.1 \pm 23.7, range 99 - 210 mmHg. 13.9% had clinically significant hypertension (systolic blood pressure \geq 160mmHg), 36.1% of had a tachycardia (heart rate of \geq 100bpm) and 8.3% had a severe tachycardia (\geq 140bpm). No patients had clinically significant hyperpyrexia; the mean temperature was 36.0 \pm 1.0, range 33.0 - 38.1 $^{\circ}$ 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 ED; 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 prehospital seizure and 4 (7.2%) who had a headache. No patients had any skin discolouration or cool/cold peripheries

Serum urea and electrolytes were taken in 34 (47.2%) and were normal in 33 (97.1% of those measured); one patient had hyponatraemia with a sodium of 125mmol/L [this case is summarised in section D1.2.2.2.]. 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%) of 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 Section

D1.2.2.2.. 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.

D.1.2.2.2. Analytically Confirmed Acute Mephedrone Toxicity

Toxicology screening of serum samples with GC-MS/LC-MSMS was carried out in a subset of 9 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 DM 2010a, personal communication Dr David Wood, Guy's and St Thomas' NHS Foundations 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 4 (57.1%) of these 7 patients; the drugs detected in the other 3 patients were cocaine (2, 28.6%), butylone/MDPV (1, 14.3%).

The mean \pm SD age was 24.6 \pm 6.5 years (range 16-36 years), all were male. 6 (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 \pm SD (range) dose was 2.1 \pm 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 mmHg. 42.9% had clinically significant hypertension (systolic blood pressure ≥ 160 mmHg), 71.4% of had a tachycardia (heart rate of ≥ 100 bpm) and 14.3% had a severe tachycardia (≥ 140 bpm). No patients had clinically significant hyperpyrexia; the mean temperature was 36.6 ± 1.1 , range 35.6 - 38.1 $^{\circ}$ 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 2 (28.6%) who had palpitations, 2 (28.6%) who had chest pain, 1 (14.3%) who had a self-limiting pre-hospital seizure and 1 (14.3%) who had a headache. No patients had any skin discolouration or cool/cold peripheries and no patients reported vomiting.

Serum urea and electrolytes were taken in all patients, and were normal in 6 (85.7%) patients. The one patient who died had hyponatraemia (sodium concentration of 125mmol/L) on presentation; this case is discussed in more detail below. Serum creatinine kinase was measured in 6 (85.7%) and was raised in 1 of these patients at a concentration of 3830IU/L (upper limit of normal 229 IU/L).

4 (57.1%) of 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). 3 (42.9%) patients required the use of benzodiazepines (oral or intravenous) for the management of agitation. Of the 3 patients who were admitted to hospital, 2 were admitted for observation/management on a general internal medicine ward and 1 (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.

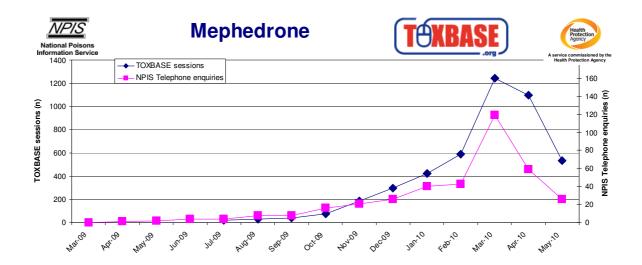
One patient with confirmed mephedrone ingestion died. He was a 29 year old male who was found collapsed and unwell in a nightclub. On arrival in the ED he was noted to have a fluctuating conscious level. A CT head scan showed evidence of significant cerebral oedema and impending tonsillar herniation. 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 0.01mg/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.

D1.2.3. 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 on-line 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 on-line TOXBASE service [Personal communication Prof 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 the figure below, further data from the UK National Poisons Information Service shows that the increase in both the on-line TOXBASE service and the telephone service enquires continued from January 2010 to a peak in March 2010 [Personal communication Prof Simon Thomas, National Poisons Information Service, Health Protection Agency]. Subsequently, there was a significant decline in enquires to both of these services in both April and May 2010. Data from poisons information services needs 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 enquires 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.



D1.2.4. 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].

D1.2.5. Other clinical reports of acute mephedrone toxicity

There is a report from Ireland of 3 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 Prof Joe Barry, Trinity College, Dublin, Ireland].

D1.2.6. Mephedrone related deaths

Reports from European countries to the EMCDDA concerning potential mephedrone related fatalities are summarised in the table below.

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

potential mephedrone related deaths	Republic, Estonia, Hungary, Portugal,	
	Spain	

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 cardiorespiratory 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 on 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.

D1.2.6.1. 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:
- Other UK Forensic Toxicology laboratories;
- Scottish Crime & Drug Enforcement Agency;
- Coroner's offices;

• Drug & Alcohol Action Teams.

Overall, up to 31st 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:

a) Potential Mephedrone-Related Deaths in England

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

- 5 of these deaths have proved negative for the presence of post mortem mephedrone, 7 are awaiting final post-mortem mephedrone and other toxicological analyses and 14 have tested positive for mephedrone in postmortem toxicological analyses.
- Of the 14 cases in which mephedrone has been detected in post-mortem toxicological analyses
 - 9 are awaiting further inquiries and/or the coroner's inquest and no further information is available at this time.

- 1: 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.)
- 1: 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.
- 1: the coroner handed down a narrative verdict: "Died following injecting mephedrone repeatedly causing mephedrone poisoning on the background of coronary artery disease".
- 1: 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.
- 1: 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 postmortem analysis).

b) Potential Mephedrone-Related Deaths in Scotland

There have been 8 suspected mephedrone-related deaths in Scotland.

 1 was negative for the presence of post mortem mephedrone and 7 tested positive for mephedrone in post-mortem toxicological analyses.

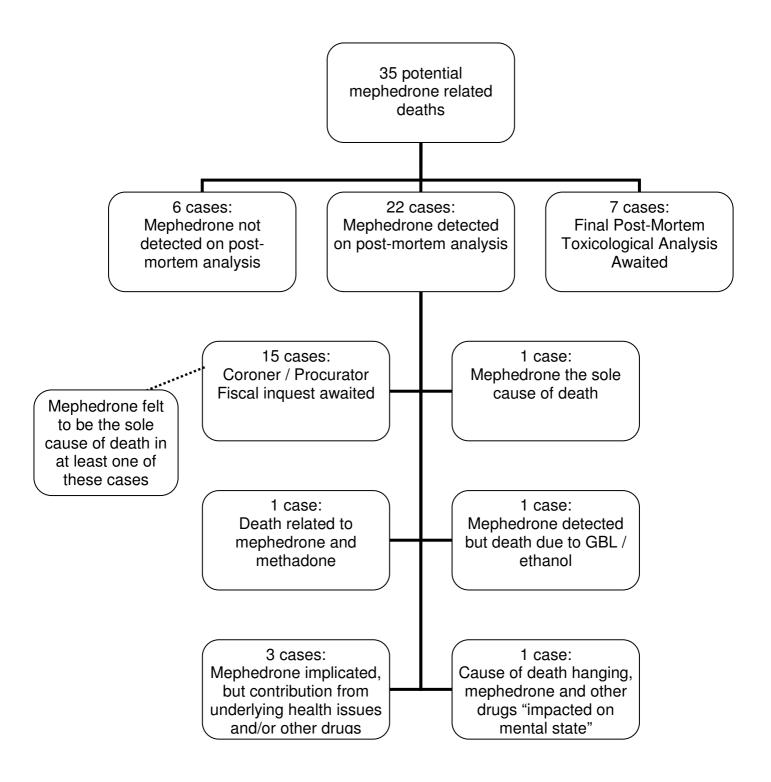
- Of the 7 cases in which mephedrone has been detected in post-mortem toxicological analyses
 - 5 are awaiting further inquiries and procurator fiscal inquests
 - 1: mephedrone was detected in an individual with atherosclerotic coronary artery disease;
 - 2: mephedrone was detected in individuals involved in road traffic accidents;
 - 2: 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.
 - 1: the Procurator Fiscal concluded that death was as the result of the
 "Adverse effects of methadone and mephedrone".
 - 1: the Procurator Fiscal concluded that death was related to "mephedrone intoxication".
- c) Potential Mephedrone-Related Deaths in Guernsey:

There is one death in Guernsey in which mephedrone has been detected in postmortem analyses; further inquiries and the inquest are waited in this case.

d) 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 Isle of Man.

Flowchart summarising the 35 cases in this np-SAD dataset in which mephedrone has been potentially implicated in death:



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.

D1.2.6.2. 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 Forensic 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; 4 of these were from the Republic of Ireland and 12 from the UK. Mephedrone was the only drug detected in 3 of these cases. Interestingly, 6 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 the table below.

Age/Sex	Blood Cathinones	Urine Cathinones	Other Drugs Detected	Other cause of death?
		UK Case:	<u> </u>	deaiii:
	Mephedrone 0.15 Mephedrone 16			
24 yrs F	mg/L	mg/L	Citalopram, diazepam	No
18 yrs M	Mephedrone 0.016 mg/L	No urine sample	Ketamine (trace), ethanol	Hanging
	Mephedrone <0.08	Mephedrone < 0.08	Cocaine, ketamine,	
29 yrs M	mg/L, methylone	mg/L, methylone	levamisole, paracetamol,	Hanging
	0.10 mg/L	2.79 mg/L	ethanol	
20 yrs F NO m	NO monhodrono	Mephedrone 1.18	(Hospital drugs given	No
	NO mephedrone mg/L	mg/L	therapeutically)	INO
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	edrone 0.24 Mephedrone 65.5	Diazepam, noscapine,	Death likely
	mg/L mg/L	papaverine, cannabis	to be heroin	
		morphine/metabolites	related	
25 yrs M	Mephedrone 0.53	Mephedrone 70.6	Cocaine, levamisole,	RTA*
12 7.0 17.	mg/L	mg/L	cannabis, ethanol	passenger
40 yrs M	Mephedrone 1.20	Mephedrone 8.84	Cocaine, citalopram, ethanol	RTA*
.5 ,.5	mg/L	mg/L	, , , , ,	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,	Mephedrone, FMC [⋄] ,	Amphetamine	Data not	
	FMC [¢] , MDPV [§]	MDPV [§]	7 improtermino	available	
Republic of Ireland Cases					
	NO mephedrone,	Mephedrone <0.125			
39 yrs M	methylone 11.0	mg/L, methylone	Data not available	Data not	
	mg/L, butylone	256 mg/L, butylone	Data not available	available	
	1.72 mg/L	3.77 mg/L			
	Mephedrone 0.20	Mephedrone 38.6	Morphine and metabolites,	Data not	
19 yrs F	mg/L, butylone	mg/L, butylone 1.18	quetiapine, venlafaxine,	available	
	<0.125 mg/L	mg/L	zopiclone, diazepam	avallable	
27 yrs M	NO mephedrone	Mephedrone <0.125	Morphine, zopiclone,	Data not	
		mg/L	methadone	available	
24 yrs M	Mephedrone	Mephedrone 1.34		Data not	
	< 0.125mg/L , MDPV [§]	mg/L, MDPV§	Data not available	available	

(*RTA: road traffic accident, *FMC: fluoromethcathinone, *MDPV: methylenedioxypyrovalerone)

D1.2.6.3. Other Information Concerning Potential Mephedrone Deaths

There was a report in the Irish Times, on 22nd 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 0.2mg/L; in addition 'heroin', butylone, venlafaxine, zopiclone, diazepam, 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, Quetapine, Zopiclone

and Venlafaxine" [Personal Communication Prof D Corrigan, Trinity College, Dublin, Ireland].

There have also been reports in the popular press in Romania of deaths potentially related to mephedrone [Bolezatu 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 28.1mg/L [Dickson AJ 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.

D2. Chronic Health Effects

D2.1. Animal Data

There is no published data in this area.

D2.2. 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 D.1.2.5. 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 Section B2. 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).

D3. Factors Affecting Public Health Risks

D3.1. 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 16th 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 report that several member states have identified that mephedrone sold via the Internet originates from China and bordering countries in South East Asia [Europol 2].

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 9th December 2009 was followed by a

second study from $8^{th} - 10^{th}$ 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, information on warnings

The table below summarises the number of sites identified in the two snap shot 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.

	Snapshot	Snapshot
	(9 th December 2009)	(8 th – 10 th March 2010)
Metacrawler	25	50

Google	6	27
Yahoo	Not applicable	0
Total number of sites identified	31	77

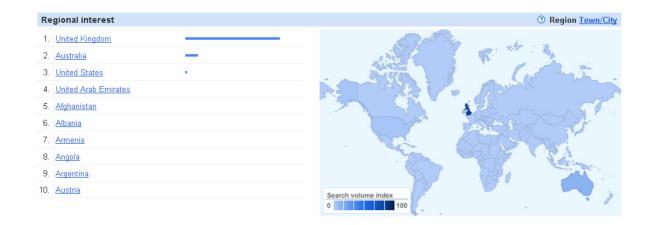
75 (97%) of sites, had one or more parameters suggesting that the 'country of origin' was the UK. The majority of sites, 50 (65%), did not have restrictions on delivery (some posted under the disclaimer that the customer had to check legal status in the country of delivery). 27 (35%) of the sites had 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 (\mathfrak{L}) as currency, 5 also accepted Euros and US dollars. The prices of mephedrone ranged from $\mathfrak{L}9.50$ to $\mathfrak{L}14.50$ per gram; many sites offered discounts for larger purchases with bigger discounts for larger purchases (e.g. 1kg for $\mathfrak{L}3100$ i.e. $\mathfrak{L}3.10$ 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 3 (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 'plantfeeder' or 'plantfood', 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 shows that 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 16th April 2010. On 16th April 2010 only 9 (12%) of the 77 online shops identified in the March study were still openly selling mephedrone, and 7 (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 16th 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 2], 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 2010, Albert S 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 – 187mg 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 in Section C.. 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.

D3.2. Availability of the information, degree of knowledge and perceptions amongst users concerning the psychoactive substance and its effects

As summarised in D3.1, other than labelling the products 'not for human consumption' or 'research chemical', Internet sites selling mephedrone typically provide minimal information on dose 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 taken 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].

D3.3. 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 2000 clubbers: 33.6% had used mephedrone in the last month, 41.7% had ever tried mephedrone [Dick D 2010, Winstock AR 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 school children; 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 [Albert S 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.

D3.4. Nature and extent of health consequence (e.g. acute emergencies, road traffic accidents)

The acute health effects of mephedrone have been discussed in Section D1.2..

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 Section D1.2.6. 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.

D3.5. Long-term Consequences of Use

As discussed in Sections D2.1. and D2.2. 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 lifethreatening medical conditions.

D3.6. Conditions Under Which the New Psychoactive Substance is Obtained and Used, Including Context-Related Effects and Risks

As noted in Section D3.1. 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% [Albert S 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 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 24years). 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 Section D1.2.2.1., 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 DM 2010b, updated with unpublished data]. This is similar to individuals presenting with acute toxicity related to other stimulant drugs such as MDMA and cocaine.

SECTION E. SOCIAL RISKS (8)(9)

E1. Individual Social Risks

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

E2. 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.

E3. 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

⁽⁸⁾ For additional information please see *Appendix 1 Mephedrone: Assessment of health risks* and harms (A. Winstock and J. Marsden, 2010)

⁽⁹⁾ For additional information please see *Appendix 2 Mephedrone: prevalence, use patterns, effects and related health and social risks (information from surveys, focus groups and interviews with mephedrone users)* (J. Mounteney EMCDDA, June 2010)

increase in teen-related violence and muggings secondary to the use of 'head-shop drugs', which include mephedrone [Irish Independent].

E4. Economic Costs

As noted in Section D1.2. 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 Section D3.3., 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.

E5. Possible Effects Related to the Cultural Context, for example Marginalisation

A number of surveys have demonstrated that mephedone 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.

E6. 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].

SECTION F. INVOLVEMENT OF ORGANISED CRIME (10)

F1. Evidence that criminal groups are systematically involved in production, trafficking and distribution for financial gain

Europol report that no member state, or neighbouring country, has information that suggests large-scale production of mephedrone within Europe [Europol 2]. It is felt that mephedrone available within Europe is manufactured within China and neighbouring countries in South East Asia.

However, Europol report 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 are three reports from the Netherlands of tableting units being seized; two from 2009 and the third in February 2010 [Europol 2]. 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 that has been reported to have been used for encapsulating mephedrone and other cathinones [Personal communication Debbie Maylon, SOCA, UK].

^{(&}lt;sup>10</sup>) Detailed information is available in the *Europol-EMCDDA Joint report on mephedrone*; for most recent and complete information please check also the European Database on New Drugs (EDND) which is being regularly updated.

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 the 16th 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 £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, Dumferlinepress, WalesOnline] 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.

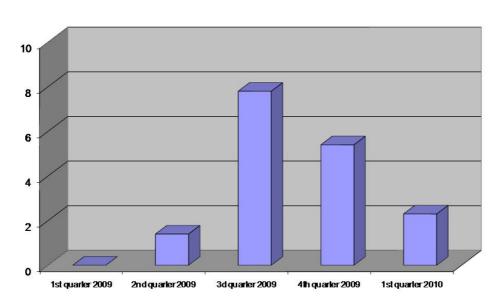
F2. Impact on the production, trafficking and distribution of other substances, including existing psychoactive substances as well as new psychoactive substances

In February 2010 the Netherlands reported via Europol the seizure of an additional tableting unit, as well as professional 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 mCPP 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].

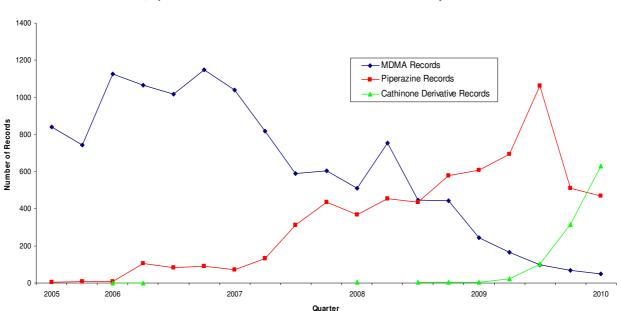
11.9% of all 'XTC' (ecstasy) tablets analysed by the Dutch Drugs Information and Monitoring System (DIMS) in 2009 contained mephedrone. However, there has been a decrease in the proportion of 'XTC' tablets containing mephedrone in the first half of 2010 [Niesink R 2010].



% of XTC tablets containing mephedrone

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 FSS during 2009. By the end of 2009 the number of cathinone seizures exceeded the number of MDMA and piperazine seizures combined (see figure below):



FSS MDMA, Piperazine and Cathinone Derivative Records : Seizure Date July 2005 - March 2010

F3. 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.

F4. 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 report 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 2].

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).

F5. Evidence of money laundering practices, or impact of organised crime on other socioeconomic factors in society

Europol report 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 2]. Processing activities by organised crime are limited to tableting [Europol 2].

F6. 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.

F7. Use of violence between or within criminal groups

Europol report 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].

F8. 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.

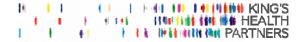
Dr Paul Dargan and Dr David Wood

Guy's and St Thomas' NHS Foundation Trust and King's Health Partners

London, UK

15th July 2010





REFERENCES (11)

Albert S, Dargan PI, Wood DM. Mephedrone use and associated adverse effects in school and college/university students before the UK legislation change. *Q J* Med – In Press.

Bajaj N, Mullen D, Wylie AS. "Legal Highs" Dependence and transient psychosis with 4-methylmethcathinone / mephedrone use. Poster presentation at The Royal College of Psychiatrists Faculty of Addiction Conference in Edinburgh, UK, 2009.

BBC News 1: Anonymous. Group's drug referrals 'up 300%'. [Published: 6th May 2010; Last accessed: 15th July 2010].

http://news.bbc.co.uk/1/hi/northern ireland/8663799.stm

BBC News 2: Anonymous. Schools urge action on legal drug mephedrone. [Published 17th March 2010; Last accessed 15th July 2010].

http://news.bbc.co.uk/1/hi/uk/8571599.stm

BBC News 3: Anonymous. North Yorkshire woman took mephedrone before death. [Published 23rd March 2010; Last accessed 15th July 2010].

http://news.bbc.co.uk/1/hi/england/north_yorkshire/8580975.stm

BBC News 4: Anonymous. N Ireland mother blames mephedrone for son's suicide. [Published 24th March 2010; Last accessed 15th July 2010].

(11) For most recent references please check also the European Database on New Drugs (EDND) which is being regularly updated; all of these references are available on EDND.

http://news.bbc.co.uk/1/hi/northern_ireland/8586309.stm

BBC News 5: Anonymous. Cwmbran man jailed for arson while on mephadrone.

[Published 4th May 2010; Last accessed 15th July 2010].

http://news.bbc.co.uk/1/hi/wales/south east/8659823.stm

BBC News 6: Anonymous. Police in £70,000 mephedrone find. [Published 25th May 2010; Last accessed 15th July 2010].

http://news.bbc.co.uk/1/hi/northern ireland/10158548.stm

BBC News 7: Anonymous. Eight arrested in Gloucester drugs raid. [Published 14th May 2010; Last accessed 15th July 2010].

http://news.bbc.co.uk/1/hi/england/gloucestershire/8704545.stm

BBC News 8: Anonymous. Mephedrone arrest 'thought first since law change'. [Published 16th April 2010; Last accessed 15th July 2010].

http://news.bbc.co.uk/1/hi/england/hereford/worcs/8626314.stm

Belfast Telegraph: Anonymous. Missing mephedrone boy's body found [Published 30th April 2010; Last accessed 15th July 2010].

http://www.belfasttelegraph.co.uk/breaking-news/uk-ireland/missing-mephedrone-boys-body-found-14788923.html?r=RSS

Belfast Telegraph 2: McCann E. Hysteria over drugs gives the green light to killers and thugs [Published 17th June 2010; Last accessed 15th July 2010].

http://www.belfasttelegraph.co.uk/opinion/columnists/eamon-mccann/hysteria-over-drugs-gives-the-green-light-to-killers-and-thugs-14844922.html

Bolezatu O. Romanian newspaper article entitled: "Special Gold" has already killed five residents of Bucharest. [Published 12th January 2010; Last Accessed 15th July 2010]. http://www.evz.ro/articole/detalii-articol/882378/Sarea-de-baie-a-ucis-deja-cinci-bucuresteni

Bolton News: Anonymous. Three arrested for possession of mephedrone. [Published 14th May 2010; Last accessed 15th July 2010].

http://www.theboltonnews.co.uk/news/8165665.Three arrested for possession of mephedrone/

Camilleri A, Johnston MR, Brennan M, Davis S, Caldicott DG. Chemical analysis of four capsules containing the controlled substance analogues 4-methylmethcathinone, 2-fluoromethamphetamine, alpha-phthalimidopropiophenone and N-ethylcathinone. *Forensic Sci Int* 2010; 197: 59-66.

CYP Now: Watson E. Drugs organisation reports huge increase in youth referrals due to mephedrone. [Published 6th May 2010; Last accessed 15th July 2010]. http://www.cypnow.co.uk/news/1001624

Daily Mail 1: James Slack. Is Lois, 24, victim number six of 'legal high' meow meow drug? [Published 24th March 2010; Last accessed 15th July 2010].

http://www.dailymail.co.uk/news/article-1259984/Meow-Meow-Woman-dies-taking-legal-party-drug-mephedrone.html

Daily Mail 2: Chris Brooke. Action pledged on 'Meow, Meow' drug after two teen friends die within hours of taking 'legal high' [Published 17th March 2010; Last accessed 15th July 2010] http://www.dailymail.co.uk/news/article-1258384/Schools-mephedrone-Meow-Meow-ban-teenage-deaths.html

Daily Mirror: Stephen White. Teenagers' deaths not linked to meow meow. [Published 29th May 2010; Last accessed 15th July 2010].

http://www.mirror.co.uk/news/top-stories/2010/05/29/death-teens-not-on-meow-meow-115875-22294052/

Dick D, Torrance C. MixMag Drugs Survey. Mix Mag 2010; 225: 44-53.

Dickson AJ, Vorce SP, Levine B, Past MR. Multiple-drug toxicity caused by coadministration of 4-methylmethcathinon (mephedrone) and heroin. *J Anal Toxicol* 2010;34:162-168.

Drugs Forum: Mephedrone and Beta-Ketones [Last Accessed 15th July 2010]. http://www.drugs-forum.com/forum/forumdisplay.php?f=377

Dunfermlinepress: Anonymous. Two charged as police make first seizure of mephedrone. [Published 11th May 2010; Last accessed 15th July 2010].

http://www.dunfermlinepress.com/news/roundup/articles/2010/05/11/400224-two-charged-as-police-make-first-seizure-of-mephedrone/

EMA 2010: Communications to EMCDDA as part of EMCDDA/Europol Joint Report on Mephedrone [Ref EMA/134303/2010]

EMCDDA-Europol Joint Report: Joint Report on a new psychoactive substance: 4-methylmethcathinone (mephedrone). Reference 8145/10. Cordrogue 36 San 68.

EMCDDA-Europol JRQ updated: Reitox National Focal Point updates to the EMCDDA-Europol Joint report questionnaire on 4-methylmethcathinone (mephedrone), June 2010.

Europol 2: Europol Contribution to the updated Joint Report questionnaire on 4-methylmethcathinone (mephedrone), June 2010.

Erowid 1: 4-Methylmethcathinone basics [Last Accessed 15th July 2010]. http://www.erowid.org/chemicals/4 methylmethcathinone/4 methylmethcathinone basics.shtml

Erowid 2: 4-Methylmethcathinone reports [Last Accessed 15th July 2010]. http://www.erowid.org/experiences/subs/exp_4Methylmethcathinone.shtml

Erowid 3: 4-Methylmethcathinone dose [Last Accessed 15th July 2010].

http://www.erowid.org/chemicals/4 methylmethcathinone/4 methylmethcathinone dose.shtml

Erowid 4: 4-Methylmethcathinone effects [Last Accessed 15th July 2010]. http://www.erowid.org/chemicals/4 methylmethcathinone/4 methylmethcathinone
effects.shtml

Gibbons S, Zloh M. An analysis of the 'legal high' mephedrone. *Bioorg Med Chem Lett* 2010; 20: 4135-4139.

Gustavsson D, Escher C. Mephedrone--Internet drug which seems to have come and stay. Fatal cases in Sweden have drawn attention to previously unknown substance. *Lakartidningen* 2009; 106: 2769-2771.

Hägerkvist R, Hultén P, Personne M. Increasing abuse of new cathinone derivatives in Sweden – a poisons centre study for the years 2008-2009. *Clin Tox* 2010; 48: 291-292.

Irish Herald: Cormac Byrne. Gangsters stock up on head shop drugs before crackdown. [Published 22nd April 2010; Last accessed 15th July 2010]. http://www.herald.ie/national-news/gangsters-stock-up-on-head-shop-drugs-before-crackdown-2147693.html

Irish Independent: Jerome Reilly. Head-shop drugs blamed for huge upsurge in teen violence and muggings. [Published 30th May 2010; Last accessed 15th July

2010]. http://www.independent.ie/national-news/headshop-drugs-blamed-for-huge-upsurge-in-teen-violence-and-muggings-2200540.html

Irish Times: Legal highs contributed to death of a woman (19). [Published 22nd June 2010; Last Accessed 15th July 2010].

http://www.irishtimes.com/newspaper/ireland/2010/0622/1224273030586.html

McNamara S, Stokes S, Coleman N. Head shop compound abuse amongst attendees of the drug treatment centre board. *Irish Med J* 2010; 103 http://www.imj.ie//ViewArticleDetails.aspx?ArticleID=5909 [Last Accessed 15th July 2010]

Meehan C. Doctoral study on adolescent drug taking in Northern Ireland. University of Ulster. Unpublished data supplied to EMCDDA.

Measham F, Moore K, Newcombe R, Welch Z. Tweaking, bombing, dabbing and stockpiling: The emergence of mephedrone and the perversity of prohibition. *Drugs Alcohol Today* 2010; 10: 14-21.

Meyer MR, Wilhelm J, Peters FT, Maurer HH. Beta-keto amphetamines: studies on the metabolism of the designer drug mephedrone and toxicological detection of mephedrone, butylone, and methylone in urine using gas chromatography-mass spectrometry. *Anal Bioanal Chem* 2010; 397: 1225-33.

Newcombe R. Mephedrone. The use of Mephedrone (M-cat, Meow) in Middlesbrough. Lifeline Publications and Research: Manchester, UK.

Niesik R, Brunt T. Pill testing with mephedrone consumers (NL). Report to EMCDDA and submitted for publication 2010.

Pas M. Mephedrone in Slovenia. DrogArt Report (submitted to EMCDDA). May 2010.

Psychonaut WebMapping Research Group (2009). Mephedrone Report. Institute of Psychiatry, King's College London: London, UK

Shropshire Star: Anonymous. Police seize large drug haul. [Published 8th June 2010; Last accessed 15th July 2010].

http://www.shropshirestar.com/news/2010/05/08/police-seize-large-drug-haul/

Teesside Evening Gazette: Naomi Corrigan. Mephedrone 'sold outside Teesside school gates'. [Published: 20th March 2010; Last accessed: 15th July 2010]. http://www.gazettelive.co.uk/news/teesside-news/2010/03/20/mephedrone-sold-outside-teesside-school-gates-84229-26073478/

The Guardian 1: Paul Walker. Three arrested over suspected mephedrone deaths. [Published 17th March 2010; Last accessed 15th July 2010]

http://www.guardian.co.uk/society/2010/mar/17/three-arrested-suspected-mephedrone-deaths

The Guardian 2: Paul Lewis. Banned mephedrone cleared of blame for two deaths. [Published 28th May 2010; Last accessed 15th July 2010]. http://www.guardian.co.uk/society/2010/may/28/mephedrone-cleared-teenage-uk-

The Independent: Jeremy Laurance. Mephedrone did not kill youths, tests reveal. [Published 29th May 2010; Last accessed 15th July 2010].

http://www.independent.co.uk/news/uk/home-news/mephedrone-did-not-kill-youths-tests-reveal-1986193.html

deaths

The Northern Echo: Will Roberts. House in the Manor Grove area of Cockfield raided by police. [Published 14th May 2010; Last accessed 15th July 2010]. http://www.thenorthernecho.co.uk/news/local/bishopauckland/8165567.Mephedron e find largest in county/

The Scotsman: Frank Urquhart. First Scot convicted of mephedrone dealing is sentenced. [Published 10th June 2010; Last accessed 15th July 2010] http://thescotsman.scotsman.com/scotland/First-Scot-convicted-of-mephedrone.6340475.jp

The Sun: Staff Reporter. Two held over 'meow' deaths. [Published 16th March 2010; Last accessed 15th July 2010].

http://www.thesun.co.uk/sol/homepage/news/2894909/Two-held-after-meow-deaths.html

The Times: Sam Lister. Teenagers' deaths were not caused by "legal high" mephedrone. [Published 28th May 2010; Last accessed 15th July 2010]. http://www.timesonline.co.uk/tol/news/uk/article7139387.ece

Ulster Herald: Alan Rodgers. Dramatic raid leads to 'mephedrone' arrest. [Published 22nd April 2010; Last accessed 15th July 2010]. http://www.nwipp-newspapers.com/UH/free/329525953607620.php

WalesOnline: Robin Turner. Man is first arrested over mephedrone. [Published 1st May 2010; Last accessed 15th July 2010].

http://www.walesonline.co.uk/news/wales-news/2010/05/01/man-is-first-arrested-over-mephedrone-91466-26356593/

Westmorland Gazette: Emma Lidiard. 11-year-olds using mephedrone in South Cumbria [Published: 1st April 2010; Last accessed: 15th July 2010]. http://www.thewestmorlandgazette.co.uk/news/5198452.Concerns rising in Cumb ria about Mephedrone/

Winstock AR, Mitcheson LR, Deluca P, Davy Z, Corazza O, Schifano F. Mephedrone, new kid for the chop? *Addiciton* – In Press.

Wood DM, Davies S, Puchnaewicz M, Button J, Archer R, Ovaska H, Ramsey J, Lee T, Holt DW, Dargan PI. Recreational use of Mephedrone (4methylmethcathinone, 4-MMC) with associated sympathomimetic toxicity. *J Med Toxicol* 2010a; Apr 1 Epub ahead of print [DOI: 10.1007/s13181-010-0018-5]

Wood DM, Greene SL, Dargan PI. Clinical pattern of toxicity associated with the novel synthetic cathinone Mephedrone. *Emerg Med J* 2010b; 26 Jun Epub ahead of print [DOI: 10.1136/emj.2010.092288]

Worcester News: Lauren Rogers. Defendant claims: 'mephedrone has wrecked my life'. [Published 10th May 2010; Last accessed 15th July 2010].