European Monitoring Centre for Drugs and Drug Addiction

Technical report on 5-(2-aminopropyl)indole

Annex 1 to the Risk Assessment Report of a new psychoactive substance: 5-(2-aminopropyl)indole

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Parts of this technical report contain data which are unpublished or in preparation for publication.

Section A. Physical, chemical, pharmaceutical and pharmacological information

A1. Physical, chemical, and pharmaceutical information

A1.1. Physical and chemical description

Chemical description and names

5-(2-Aminopropyl)indole is a synthetic derivative of indole substituted at the phenyl side of the indole ring system (position 5). It is a positional isomer of alpha-methyltryptamine (AMT) which belongs to the tryptamine family, many of which show hallucinogenic and other psychoactive effects in humans. 5-(2-Aminopropyl)indole also contains the sub-structure of alpha-methylphenethylamine and therefore could be considered to be a substituted phenethylamine, many of which are stimulants. Limited data suggests that 5-(2-aminopropyl)indole has stimulant effects and possible hallucinogenic effects.

The systematic (International Union of Pure and Applied Chemistry, IUPAC) name of 5-(2-aminopropyl)indole is 1-(1*H*-indol-5-yl)propan-2-amine and other names that may be encountered include α-methyl-1*H*-indole-5-ethanamine and 2-(1*H*-indol-5-yl)-1-methyl-ethylamine. A common abbreviation used for 5-(2-aminopropyl)indole is 5-IT ([1]). To a lesser extent the abbreviation 5-API is also used ([2]). Both these abbreviations are used by Internet retailers ([3]) advertising 5-(2-aminopropyl)indole as well as in Internet drug user discussion forums (‘drug discussion forums’). This suggests that '5-IT' and '5-API' are used as 'street names'. The Chemical Abstract Service (CAS) Registry Numbers for 5-(2-aminopropyl)indole are given in Table 1.

Table 1. Chemical Abstract Service (CAS) Registry Numbers for 5-(2-aminopropyl)indole

CAS Registry Numbers	Variant
3784-30-3	Unspecified amine
96875-04-6	Ethanedioate (1:1) / hydrogen oxalate / bioxalate
1336260-35-5	(*R*)-Enantiomer amine
1336564-72-7	(*S*)-Enantiomer amine

Excluding the abstractable proton on the nitrogen atom a total number of six positional isomers exist that can carry the 2-aminopropyl side chain. The synthesis of 5-(2-aminopropyl)indole (Figure 1) and its isomers was first described by Hofmann and Troxler (1963) and Troxler et al., (1968). Another isomer is *N*-methyltryptamine (NMT) which is

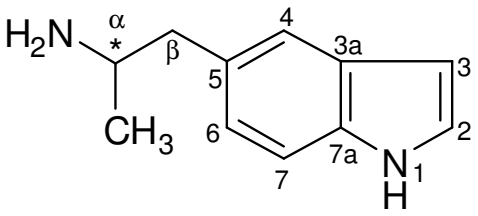
([1]) The origin of the abbreviation ‘5-IT’ is not known at this time.

([2]) The origin of the abbreviation ‘5-API’ is thought to be derived from 5-(2-**a**mino**p**ropyl)**i**ndole.

([3]) The term 'Internet retailers' is used in this report to describe Internet shops that offer new psychoactive substances for sale often advertised as 'legal highs' and 'research chemicals'.

commonly found in nature (Ott, 1996). A more recent example of the preparation of 2-(2-aminopropyl)indole (2-IT) was presented by Alhambra et al., (2001) who employed a solid-phase approach. The synthesis of the 3-(2-aminopropyl)indole (AMT) ([4]) isomer was first published in 1947 (Snyder and Katz, 1947). 5-(2-Aminopropyl)indole contains an asymmetric carbon but data on the availability of its enantiomeric forms on the market (including seized, collected and biological samples referred to in this report) are currently not available.

Figure 1. The numbered molecular structure, formula, weight and monoisotopic mass of 5-(2-aminopropyl)indole ([5]). Asterisk indicates chiral centre.



Molecular formula: $C_{11}H_{12}N_2$

Molecular weights: 174.24 g/mol (base)

Monoisotopic mass: 174.1157 Da

Identification and analytical profile

The free base gives a slightly violet response (Keller test) whereas the van Urk test results in the formation of a red colour (Hofmann and Troxler, 1963). Further information on the presumptive tests for 5-(2-aminopropyl)indole are not available. The reported melting points are: 81–83 °C (free base) (petroleum ether/benzene) (Hofmann and Troxler, 1963 and Troxler et al., 1968); 199–201 °C (bioxalate salt) (methanol/diethyl ether) (Hofmann and Troxler, 1963); 194 °C (dec.) (hemisuccinate) (LGC GmbH, 2012). Analysis by high performance liquid chromatography diode array detection gave λmax values at 218.3 nm and 272.8 nm (Elliott et al., 2013).

Nuclear magnetic resonance spectroscopy (NMR) data of 5-(2-aminopropyl)indole succinate ([6]): ^{1}H NMR (300 MHz, CD_3OD): δ 7.42 (1H, br d, J = 1.1 Hz, H-4), 7.37 (1H, d, J = 8.3 Hz, H-7), 7.23 (1H, d, J = 3.2 Hz, H-3), 6.98 (1H, dd, J = 8.3 Hz, J =1.7 Hz, H-6), 6.41 (1H, dd, J = 3.2 Hz, J = 0.8 Hz, H-2), 3.57-3.45 (1H, m (consistent with predicted dqd), α-CH), 3.02 (1H, dd, J_{gem} = 13.8 Hz, ^3J = 6.5 Hz, CH_AH$_B$), 2.86 (1H, dd, J_{gem} = 13.8 Hz, ^3J = 8.0 Hz, CH$_A$$H_B$), 2.51 (4H, s, succinate), 1.26 (3H, d, ^3J = 6.6 Hz, CH_3). ^{13}C NMR (75 MHz, CD_3OD): δ 179.4 (succinate), 137.0 (C-7a), 129.9 (C-3a), 127.5 (C-5), 126.3 (C-3), 123.5 (C-6), 121.8 (C-4), 112.6 (C-7), 102.2 (C-2), 50.8 (α-CH), 42.2 (CH_2), 32.9 (CH_2, succinate), 18.5 (CH_3) (Elliott et al., 2013).

([4]) Abbreviations and code names for AMT found in the literature include: α-methyltryptamine, AMT, α-MT, 3-IT, IT-290, IT-403, U-14, 162-E, Ro 3-0926, NSC 97069, and Indopan.

([5]) For additional predicted data, see http://www.chemspider.com/Chemical-Structure.25991467.html

([6]) NMR data is provided for 5-(2-aminopropyl)indole succinate as this is the form that was encountered in a collected sample that was analysed.

Mass spectrometry data: 5-(2-aminopropyl)indole (5-IT) and 3-(2-aminopropyl)indole (AMT) have been found to produce virtually identical mass spectra, especially when applying conventional electron ionization mass spectrometry (EI-MS) procedures. Thus, all six potential 2-aminopropyl isomers may be expected to yield very similar mass spectra. However, the implementation of suitable chromatographic techniques would be expected to allow successful separation if the reference materials are available for comparison.

Consistent with mass spectral behaviour reported for isomeric psychoactive tryptamines (Martins et al., 2010), key fragments observed under EI-MS conditions (*m/z*) were: 44 (base peak), 131, 130, 77, 103, 117. The $M^{\bullet+}$ (*m/z* 174) may be detectable at a minor relative abundance but may also be absent. CI-MS (MeOH as liquid CI reagent) gave the $[M+H]^+$ at *m/z* 175 as the base peak and a prominent fragment at *m/z* 158 following the loss of NH_3. Positive electrospray tandem mass spectra (ESI-MS/MS) yielded *m/z* values of 77, 103, 117, 130, 143, 158 (relative abundance values dependent on collision energy) with some in-source fragmentation of the protonated molecule at *m/z* 175. When evaluating the ability to differentiate between 5-IT and AMT under ESI-MS/MS conditions, distinct differences in the relative abundances were observed, allowing for the potential use of ion ratios for multiple reaction monitoring (MRM) transitions. Thus, for AMT: *m/z* 175/158 (100 % abundance), *m/z* 175/143 (78 %), *m/z* 175/130 (30 %) and for 5-IT: *m/z* 175/158 (100 % abundance), *m/z* 175/143 (22 %), *m/z* 175/130 (84 %) (Elliott et al., 2013).

The REACH (Regulation on Registration, Evaluation, Authorisation and Restriction of Chemicals) registered substances database hosted by the European Chemicals Agency (ECHA) was searched using the CAS Registry Numbers listed above and no information was found.

The lack of a rapid qualitative screening method is a limiting factor for the detection of 5-(2-aminopropyl)indole in biological samples. Furthermore, many European forensic/toxicological laboratories may not have procedures in place for analysing 5-(2-aminopropyl)indole in biological samples. In some cases this may be due to the lack of reference standards for the drug or difficulties in distinguishing between 5-(2-aminopropyl)indole and the related compound AMT.

Physical description

The free base form of 5-(2-aminopropyl)indole has been described to form skewed prisms (Troxler et al., 1968) and the bioxalate salt form has also been documented (Hofmann and Troxler, 1963). It has been reported that some Internet retailers have advertised 5-(2-aminopropyl)indole as the succinate salt. NMR data produced as part of the analysis of two collected samples of 5-(2-aminopropyl)indole (reported by the United Kingdom) were found to be consistent with the succinate form (see data above). The structured Internet search conducted by the EMCDDA for the Joint report also noted that 5-(2-aminopropyl)indole hydrochloride was being offered for sale (EMCDDA & Europol, 2012). Analytical reference standards are commercially available ([7]). See section A1.2 for a description of the physical

([7]) For example http://www.logical-standards.com/index.php?mact=Products,cntnt01,details,0&cntnt01productid=1811&cntnt01returnid=57; and,

forms that have been reported.

Methods and chemical precursors used for the manufacture of 5-(2-aminopropyl)indole

There is currently no information regarding manufacturing sites, the chemical precursors or the synthetic routes used for the 5-(2-aminopropyl)indole that has been detected on the drug market.

One classic approach used for the synthesis of 5-(2-aminopropyl)indole includes a condensation reaction using indole-5-carboxaldehyde and nitroethane. These substances are commercially available and are not under international control. The resulting 5-(2-methyl-2-nitrovinyl)indole can then be reduced with lithium aluminium hydride ($LiAlH_4$) (Hofmann and Troxler, 1963; Troxler et al., 1968). Other methods and reagents of reduction, for example those also employed during phenylalkylamine synthesis, may equally be useful (Guy et al., 2008). The reactions are feasible in an amateur laboratory setting and do not require sophisticated equipment. In analogy to the reductive amination procedure used to obtain a range of phenylalkylamines, the use of 1-(1*H*-indol-5-yl)propan-2-one as a potential starting material might also be conceivable. However, an example of this manufacturing procedure is not available in the literature.

Typical impurities encountered in seized samples

There is currently no information available with regards to route-specific by-products produced during the synthesis of 5-(2-aminopropyl)indole. In addition there is no data currently available on the impurities detected in seized and collected samples.

In some samples, 5-(2-aminopropyl)indole has been reported to be the only psychoactive substance detected. Additionally, although not impurities, there have been a small number of reports where 5-(2-aminopropyl)indole has been found in combination with other psychoactive substances. These include: 5,6-methylenedioxy-2-aminoindane (MDAI) in Germany; methylthienylpropamine (1-(thiophen-2-yl)-2-methylaminopropane, MPA) and caffeine in tablets bearing markings resembling the Lexus logo ([8]) in Hungary; diphenyl(pyrrolidin-2-yl)methanol (diphenylprolinol, D2PM) in capsules in Guernsey ([9]); and, ethylphenidate within a beige powder in Sweden. No quantitative data were provided for any seized or collected sample reported to the EMCDDA nor Europol.

A1.2. Physical/pharmaceutical form

Reports of seizures and collected samples have noted that 5-(2-aminopropyl)indole has been detected in: brown, pale/light brown or beige powders; beige tablets bearing markings resembling the Lexus logo; brown glittery tablets; blue/green unmarked tablets; blue unmarked tablets commercially packaged as 'BENZO FURY'; capsules; and, in residues on

https://www.caymanchem.com/app/template/Product.vm/catalog/12042;jsessionid=4E0344937486009FBED6743CFB66E902

([8]) It is common to find markings on tablets sold as 'ecstasy' including those of popular cultural and iconic brands often having an association with quality. Lexus is a luxury Japanese car manufacturer.

([9]) British Crown Dependency of the Bailiwick of Guernsey, report received from the United Kingdom national focal point.

a spoon and in the liquid recovered from a syringe. See section C for further details of the seized and collected samples of 5-(2-aminopropyl)indole.

A1.3. Route of administration and dosage

As noted, 5-(2-aminopropyl)indole has been encountered as powders as well as tablets and capsules. These physical forms suggest that common routes of administration may be oral and by insufflation. Limited information from reports of non-fatal intoxications, deaths and drug discussion forums appear to support this (see below). The succinate salt of 5-(2-aminopropyl)indole, confirmed in the two collected samples reported by the United Kingdom, may be suitable for injection. Significantly, in this respect, Hungary has reported that 5-(2-aminopropyl)indole has been found in residues on a spoon and in the liquid recovered from a syringe. The assessment of the national focal point is that 5-(2-aminopropyl)indole is being injected in some cases.

In two non-fatal intoxications the route of administration was reported as by nasal insufflation. A user report from Shulgin and Shulgin (1997) noted an example of oral administration of 20 mg. Drug discussion forums suggest that routes of administration include: oral ingestion (swallowing, such as 'bombing' ([10])), nasal insufflation (snorting), sublingual, intravenous injection, and rectal insertion ([11]). Reported doses used include: '20mg' [route of administration not specified], '80 mg orally', 'bombed 100 mg', '150Mg swallowed', 'insufflated 65 mg'([12]).

A2. Pharmacology, including pharmacodynamics and pharmacokinetics

Pharmacodynamics

While detailed pharmacological investigations on 5-(2-aminopropyl)indole do not appear to have been published ([13]), one study was identified that investigated the ability of 5-(2-aminopropyl)indole and its five isomers to inhibit monoamine oxidase (MAO). The assay method was based on the ability of guinea pig liver homogenate to absorb oxygen generated from serotonin as the substrate. The activity was expressed as percentage inhibition. The IC_{50} values for 5-(2-aminopropyl)indole, 6-(2-aminopropyl)indole (6-IT) and 3-(2-aminopropyl)indole (AMT), for example, were 22, 4.6 and 58 µM, respectively. These data indicate that 6-IT was the most potent inhibitor amongst those three substances. These substances were also evaluated for their ability to antagonise pentylenetetrazole/reserpine-induced tonic extensor seizures in mice. 5-(2-Aminopropyl)indole appeared to be less active than 6-IT but more active than AMT with regards to anti-reserpine activity (Cerletti et al., 1968). While the AMT isomer has been shown to induce stimulant effects in mice (including body tremor, heightened locomotor activity, mydriasis and hyperthermia) (Lessin et al.,

([10]) 'Bombing' is where a drug is wrapped in cigarette paper (or similar) prior to swallowing.

([11]) http://www.drugs-forum.com/forum/showpost.php?p=1126167&postcount=9

([12]) http://www.drugs-forum.com/forum/showthread.php?t=140331
http://www.drugs-forum.com/forum/showthread.php?t=172223
http://www.bluelight.ru/vb/threads/616728-The-Big-amp-Dandy-5-IT-5-API-Thread

([13]) A literature search on 5-(2-aminopropyl)indole revealed a translated article (USSR, Academy of Sciences) on serotonergic properties of several tryptamines. However, inspection of the English translation did not appear to provide any data on 5-(2-aminopropyl)indole (Buznikov et al., 1965).

1965), the extent to which this extends to the remaining isomers, including 5-(2-aminopropyl)indole, remains to be studied. A short report on the 6-(2-aminopropyl)indole isomer provided some indication that intravenous administration (0.5 mg/kg) resulted in hypertension and related sympathomimetic features in dogs (Maxwell, 1964).

Given the lack of information on the pharmacological and toxicological properties of 5-(2-aminopropyl)indole, and drawing on the study by Cerletti et al., (1968) summarised above, the EMCDDA commissioned a study designed to provide further data on the possible effects of 5-(2-aminopropyl)indole on monoamine oxidase inhibition (Appendix 1). This study used an *in vitro* assay with recombinant human MAO-A and B isoenzymes (using kynuramine as substrate) based on the procedure published by Herraiz and Caparro (2006). The study found that racemic 5-(2-aminopropyl)indole (in the form of the hemisuccinate salt) is a reversible, competitive and highly selective inhibitor of MAO-A (IC_{50} of 1.6 µM and K_i of 0.25 µM) but not MAO-B. In addition, an *in vitro* experimental comparison found 5-(2-aminopropyl)indole to be less potent than the known MAO-A inhibitors clorgyline and harmaline, but more potent than toloxatone and moclobemide (Table 2).

Table 2. Inhibition values determined from recombinant human monoamine oxidase-A assay. Racemic 5-(2-aminopropyl)indole was used in the form of the hemisuccinate salt.

Compound	**IC_{50} (µM)**	**K_i (µM)**	**K_i (µM) from IC_{50}**
Clorgyline	0.016	-	0.016
Harmaline	0.020	-	0.004
5-(2-Aminopropyl)indole	1.6	0.25	0.32
Toloxatone	6.7	-	1.3
Moclobemide	>500	-	-

Shulgin and Shulgin (1997) reported long-lasting stimulant properties of around 12 hours duration following oral administration of 20 mg. Currently, no data are available on the presence and/or properties of single enantiomers. Increased potency was found to reside with the (*S*)-(+)-enantiomer of AMT in both animals and humans (Nichols, 1986). Whether a similar relationship exists with 5-(2-aminopropyl)indole remains to be investigated.

There are appears to be no published data on the biotransformation (metabolism) of 5-(2-aminopropyl)indole in animals or humans. Since this particular isomer carries the side chain at the 5-position it is currently unknown whether similar transformations occur that have been observed with AMT. Early work carried out *in vitro* (in rat liver microsomes) and *in vivo* samples (male albino rat urine following intraperitoneal injection of 5 mg/kg AMT and incubation with bacterial β-glucuronidase) indicated the presence of 6-hydroxy-AMT, 1-(1H-indol-3-yl)propan-2-one and 1-(6-hydroxy-1H-indol-3-yl)propan-2-one, respectively (Szara, 1961). A more recent example of metabolic studies in rats was provided by Kanamori et al. (2008) who observed the formation of 3-(2-aminopropyl)indolin-2-one, 2-amino-1-(1H-indol-3-yl)propan-1-ol, 6-hydroxy-AMT and 7-hydroxy-AMT in urine following enzymatic

hydrolysis. In this study, four male Wistar rats received an oral dose of 10 mg/kg of AMT with urine collected and pooled over a 24 hour period. Overall, AMT was found to be poorly metabolised, as indicated by the relative contribution of signal intensities under GC-MS conditions.

Interactions with other drugs and medicines

Given the limited information that is available on the pharmacology of 5-(2-aminopropyl)indole it is difficult to predict with accuracy any particular potential drug interactions or contraindications. However, as stated above, the ability of 5-(2-aminopropyl)indole to inhibit MAO-A in vitro may result in potential interactions with drugs acting on the monoaminergic system. In particular this may be the case for serotonergic drugs that may present a risk of inducing serotonin syndrome, the symptoms of which can include tachycardia, hyperthermia, muscle rigidity and convulsions (Boyer & Shannon, 2005). In the context of 5-(2-aminopropyl)indole use, there may be a potential risk from the (concomitant) use of medicinal products (e.g. selective serotonin reuptake inhibitors (SSRIs)) as well as stimulant drugs that act on the monoaminergic system. These include amphetamine, MDMA (and other phenethylamines) and cathinone derivatives (e.g. mephedrone, 4-methylethcathinone). In this respect, some of these drugs have been detected in the biological samples from the non-fatal intoxications and deaths detailed in section D. It may be the case that a possible synergistic interaction may have played a role in these cases.

Pharmacokinetics

No animal studies were identified that investigated the pharmacokinetics of 5-(2-aminopropyl)indole. There is limited information available from Internet reports or from drug discussion forums that could be used to determine pharmacokinetic parameters such as time of onset of desired effects, adverse effects, or duration of action of 5-(2-aminopropyl)indole. As noted, Shulgin and Shulgin (1997) provided some limited information noting that 5-(2-aminopropyl)indole has long-lasting stimulant effects in humans of about twelve hours when 20 mg is given orally.

A3. Psychological and behavioural effects

No studies were identified that investigated the psychological and/or behavioural effects of 5-(2-aminopropyl)indole. As mentioned above, Shulgin and Shulgin (1997) provided some limited information noting that 5-(2-aminopropyl)indole may show long-lasting stimulant properties in humans for about twelve hours when 20 mg is given orally. The physical effects reported were increased heart-rate, anorexia, diuresis, and slight hyperthermia. No further relevant details were reported. Section D1.2.1. discusses some of the effects that have been self-reported by users on drug discussion forums.

A4. Legitimate uses of the product

5-(2-Aminopropyl)indole is available as an analytical reference standard and is used in scientific research. 5-(2-Aminopropyl)indole is mentioned in patents that claim derivatives of

this compound and a broad range of other arylethylamines as pro-drugs which may have potential medicinal applications (Jenkins and Sturmer, 2012; Van Wijngaarden et al., 1988). There are currently no other indications that 5-(2-aminopropyl)indole may be used for other legitimate purposes. There are no known uses of 5-(2-aminopropyl)indole as a component in industrial, cosmetic or agricultural products.

There is no information that 5-(2-aminopropyl)indole is currently used in the manufacture of a medicinal product in the European Union. However, in the absence of a European Union database on the synthetic routes of all medicinal products this information cannot be verified. There is no marketing authorisation (existing, ongoing or suspended) for 5-(2-aminopropyl)indole neither in the European Union nor in the Member States that responded to the request for information from the European Medicines Agency (EMCDDA & Europol, 2012).

Section B. Dependence and abuse potential

B1. Animal *in vivo* and *in vitro* data

No published experimental animal studies were identified that examined the dependence and abuse potential of 5-(2-aminopropyl)indole.

As detailed in section A.2, 5-(2-aminopropyl)indole has been shown to act as a relatively potent, selective and reversible inhibitor of monoamine oxidase inhibitor-A (MAO-A) *in vitro*. This suggests that it might either by itself or in combination with other substances potentiate serotonergic effects. Although 5-(2-aminopropyl)indole did not inhibit human recombinant MAO-B *in vitro* up to 500 µM (Annex 1), the possibility of increased levels of other monoamines such as dopamine and noradrenaline may not be fully excluded. However, further studies are needed to investigate the dependence or abuse potential of this substance.

B2. Human data

There are no published cases in the scientific or grey literature nor user reports describing the potential for dependence or abuse potential for 5-(2-aminopropyl)indole. Additionally, there have been no studies investigating the dependence and/or abuse potential of 5-(2-aminopropyl)indole in humans. Information from local, regional or national drug treatment agencies about the dependence and abuse potential of 5-(2-aminopropyl)indole is not available. As noted, Shulgin and Shulgin (1997) provided some limited information that 5-(2-aminopropyl)indole may show long-lasting stimulant properties in humans for about twelve hours when 20 mg is given orally.

Section C. Prevalence of use

Information from seizures, collected and biological samples

The first official notification of 5-(2-aminopropyl)indole to the European Union Early warning system was 1 June 2012 by the Norwegian national focal point. The reporting form details a seizure of one zip-lock bag containing one gram of light brown powder intercepted at Oslo Airport, Gardermoen, on 17 April 2012 by customs authorities. The identification was based on the analytical technique of GC-MS alone.

Seven Member States (Denmark, Germany, Finland, Hungary, the Netherlands, Sweden and the United Kingdom) and Norway have reported seizures of 5-(2-aminopropyl)indole.

At the time of writing the Joint report, several Member States reported that many forensic and/or toxicological laboratories did not have validated procedures for the confirmation of 5-(2-aminopropyl)indole in seized, collected and biological samples (EMCDDA and Europol, 2012). The lack of certified reference material has meant that some laboratories could not distinguish 5-(2-aminopropyl)indole from the related compound AMT which was also present in samples seized on the drug market at the time. Furthermore, in the case of biological

samples there is no rapid qualitative screening method for the detection of 5-(2-aminopropyl)indole. Overall, this may have led to the under-reporting of 5-(2-aminopropyl)indole.

5-(2-Aminopropyl)indole has typically been encountered in seizures and collected samples in the form of powders, as well as in tablets and capsules. Where information has been provided, the quantities of powder ranged from 0.2 grams (Hungary) to 20.5 kilograms (the Netherlands). Hungary reported a seizure of seven beige tablets bearing markings resembling the Lexus logo ([14]). This may suggest that 5-(2-aminopropyl)indole is being sold as 'ecstasy', as Europol have reported that tablets containing MDMA and bearing this logo, as well as a tablet punch (for imprinting logos on tablets as part of the manufacturing process) have been seized in the past. In Sweden, blue/green unmarked tablets and brown glittery tablets were also seized. In the United Kingdom, blue unmarked tablets were seized from a head shop and were found in commercial packages marked 'BENZO FURY' that also displayed an image of the chemical structure of 5-APB (5-(2-aminopropyl)benzofuran) ([15]). There has been one report of residues found on a spoon and one report where 5-(2-aminopropyl)indole was recovered from the liquid in a syringe (Hungary). This may suggest that 5-(2-aminopropyl)indole is being injected by some users. See Annex 1 for details of seizures and collected samples reported to EMCDDA and Europol.

Two collected samples from the United Kingdom that were purchased from Internet retailers were found to be consistent with the succinate form of 5-(2-aminopropyl)indole.

Sweden reported the detection of 5-(2-aminopropyl)indole in ten biological samples (one blood; nine urine) from individuals suspected to have committed minor drug offences or people that are in drug treatment programmes. Further information on these cases are not available.

Availability from Internet retailers

A structured Internet search was conducted in March 2013 using the EMCDDA snapshot methodology to identify Internet retailers offering 5-(2-aminopropyl)indole for sale ([16]). Five Internet retailers were identified that currently offered the substance for sale to consumers in

([14]) It is common to find markings on tablets sold as 'ecstasy' including those of popular cultural and iconic brands often having an association with quality. Lexus is a Japanese car manufacturer.

([15]) Although Internet retailers typically advertise 'Benzo Fury' products (or using synonyms such as 'BENZO FURY', 'BenzoFury', 'Benzo-fury', 'Benzo', and 'Fury') as containing 6-APB or 5-APB, a structured search of the European database on new drugs (EDND) found that seized and collected samples of 'Benzo Fury' products have contained: 6-APB; 5-APB; D2PM; pentylone with caffeine, lidocaine and procaine; AM-2201 (tentative identification); and, 5-(2-aminopropyl)indole. Additionally, published studies involving the analysis of collected and biological samples suggest that 'Benzo Fury' products contain: 6-APB; 5-APB; D2PM; and, 1-benzylpiperazine (BZP) with 3-trifluoromethylphenylpiperazine (3-TFMPP) and caffeine (Ayres and Bond, 2012; Baron et al., 2011; Wood et al., 2011; Wood et al., 2012).

([16]) The Internet search engine 'google.co.uk' was searched (March 2013) for Internet retailers offering 5-(2-aminopropyl)indole for sale. On the advanced search page, Google was configured so that results were not narrowed by language and region. The search string used was: buy '5-IT' OR '5-API' OR '5-(2-aminopropyl)indole'. The first 100 sites were reviewed in full then sampling continued until 20 successive sites unrelated to the sale of 5-(2-aminopropyl)indole were identified. Websites that offered 5-(2-aminopropyl)indole for sale were reviewed and relevant information, such as the amount offered (mass of powder, number of capsules/pellets) and cost of purchase was recorded on a structured reporting form.

the European Union. In addition two further sites were identified that stated that 5-(2-aminopropyl)indole would be available for sale soon. On two of the sites offering the drug for sale all of the 5-(2-aminopropyl)indole products were out of stock and on one of these sites the prices given were promotional prices. Between them, the five retailers offered a total of 21 products for sale that claimed to contain 5-(2-aminopropyl)indole (11 products in powder form, two in capsules and eight for which the physical form was not stated). Three sites quoted prices in GPB, one in EUR and one did not state the price. Three sites offered 5-(2-aminopropyl)indole in powder form. The price per gram ranged from 32 to 40 GBP. The largest quantity offered for sale was 5 grams at 22.95 GBP per gram. One site offered 5-(2-aminopropyl)indole in capsule form although no prices were stated. The quantities of 5-(2-aminopropyl)indole per capsule were 80 mg and 100 mg. The site claimed that the effects of the 80 mg capsules last 3–4 hours and those of the 100 mg capsules last 5–6 hours. Some of the websites suggested that there is a similarity between 5-(2-aminopropyl)indole and 5-APB, 6-APB and MPA. No site offered products that contained both 5-(2-aminopropyl)indole and other new psychoactive substances. In addition a number of suppliers were identified on the trade website tradevv.com that claimed to supply 5-(2-aminopropyl)indole in bulk quantities. However, details of the amounts offered and prices were only available on direct application to these suppliers.

Prevalence of use

No studies were identified that investigated the prevalence of 5-(2-aminopropyl)indole use.

One Member State reported the detection of 5-(2-aminopropyl)indole in biological samples from ten individuals not related to non-fatal intoxications and deaths. The individuals were suspected to have committed minor drug offences or were people in drug treatment programmes. Information on these cases is not available to allow further analysis.

In addition, 5-(2-aminopropyl)indole has been detected in a ‘legal high’ product labelled as ‘Benzo fury’ (see footnote 15). Furthermore, in three non-fatal intoxications ‘Benzo Fury’ was the product reported to have been taken. In several of the fatalities an empty bag labelled 6-APB (6-(2-aminopropyl)benzofuran) was found, but not detected in post-mortem samples. A small number of tablets resembling ecstasy have also been found to contain 5-(2-aminopropyl)indole. It is therefore relevant to discuss the available prevalence data on the use of ‘Benzo Fury’ products, 6-APB and ecstasy.

Information on the use of ‘Benzo fury’ products and 6-APB

Two Internet surveys were identified that examined the use of ‘Benzo Fury’. One of these also examined the use of 6-APB. While these surveys provide some indication of the use of ‘Benzofury’ products, the results are not generalisable to other groups and populations as they are non-probablistic convenience sample surveys. In addition it is important to note both that the surveys predate the detection of 5-(2-aminopropyl)indole on the European drug market and a number of different new psychoactive substances have been detected in products sold as ‘Benzo Fury’ (see footnote 15).

The first survey was conducted among readers of a dance music magazine and the Guardian newspaper. It found that, overall, 2.4 % of respondents (n=7,700) and 3 % of 'regular clubbers' from the United Kingdom reported use of 'Benzo Fury' in the last year. In comparison, the self-reported last year prevalence for 'regular clubbers' of mephedrone was 30 %, MDAI was 3 % and methylone was 2 % (Mixmag, 2012). The second study conducted among self-reported users of new psychoactive substance mainly from Ireland (n=329), found that of the 159 respondents who reported using 'party pills' and 'liquid highs', 1.3 % (2/159) had used a product named 'Benzo Fury'; while none of the respondents reported use of '6-APB' (Kelleher et al., 2011).

Data from National Poisons Information Service (NPIS) in the United Kingdom indicate that there has been a small number of telephone calls and Toxbase access requests in relation to 6-APB. No information was provided on 5-(2-aminopropyl)indole itself (Health Protection Agency, 2012).

5-(2-Aminopropyl)indole in tablets resembling 'ecstasy'

Hungary reported the seizure of seven tablets that contained both 5-(2-aminopropyl)indole and methylthienylpropamine bearing markings resembling the Lexus logo (Annex 2). As noted, Europol have reported MDMA tablets and a tablet punch (for stamping logos on tablets) bearing the Lexus logo have been seized in the past. It may be the case that some ecstasy users are at risk of exposure to 5-(2-aminopropyl)indole. In this respect, drug prevalence estimates suggest that about 2 million Europeans (aged 15–64) have used ecstasy during the last year ([17]) (EMCDDA and Europol, 2013). However, as noted, the total number of such types of tablets containing 5-(2-aminopropyl)indole that have been reported so far is small and limited to one country.

Section D. Health risks

D1. Acute health effects

D1.1. Animal data

No studies were identified that investigated the acute toxicity of 5-(2-aminopropyl)indole in experimental animal models.

While detailed pharmacological investigations on 5-(2-aminopropyl)indole do not appear to have been published ([18]), as noted in section A2., one study was identified that investigated the ability of 5-(2-aminopropyl)indole and its five isomers to inhibit monoamine oxidase (MAO). The assay method was based on the ability of guinea pig liver homogenate to absorb oxygen generated from serotonin as the substrate. The activity was expressed as

([17]) European estimates are computed from national estimates weighted by the population of the relevant age group in each country. They are based on surveys conducted between 2004 and 2010/11 (mainly 2007–2010) and therefore do not refer to a single year. The term ecstasy is used in a broad sense to refer to substances that contain MDMA or other substances that are presented as ecstasy.

([18]) As noted in footnote 13, a literature search on 5-(2-aminopropyl)indole revealed a translated article (USSR, Academy of Sciences) on serotonergic properties of several tryptamines. However, inspection of the English translation did not appear to provide any data on 5-(2-aminopropyl)indole (Buznikov et al., 1965).

percentage inhibition. The IC_{50} values for 5-(2-aminopropyl)indole, 6-(2-aminopropyl)indole (6-IT) and 3-(2-aminopropyl)indole (AMT), for example, were 22, 4.6 and 58 µM, respectively. These data indicate that the 6-IT isomer was the most potent inhibitor amongst those three substances. These substances were also evaluated for their ability to antagonise pentylenetetrazole/reserpine-induced tonic extensor seizures in mice. 5-(2-Aminopropyl)indole appeared to be less active than 6-IT but more active than the AMT isomer with regards to anti-reserpine activity (Cerletti et al., 1968). AMT has been shown to induce stimulant effects in mice (incl. body tremor, heightened locomotor activity, mydriasis and hyperthermia) (Lessin et al., 1965), the extent to which this extends to the remaining isomers, including 5-(2-aminopropyl)indole, remains to be studied. A short report on the 6-(2-aminopropyl)indole isomer provided some indication that intravenous administration (0.5 mg/kg) resulted in hypertension and related sympathomimetic features in dogs (Maxwell, 1964).

D1.2. Human data

D1.2.1. User reports

As noted, Shulgin and Shulgin (1997) reported that 5-(2-aminopropyl)indole may show long-lasting stimulant properties in humans of about twelve hours following oral administration of 20 mg. Effects reported were increased heart-rate, anorexia, diuresis, and slight hyperthermia. No further information was provided.

There are some user reports on drug discussion forums that discuss the use of 5-(2-aminopropyl)indole ([e.g. 19]). These need to be interpreted with caution as there was no analytical confirmation of the substances used. In addition, some of the users describe taking other drugs prior to or with 5-(2-aminopropyl)indole.

Some of the websites suggest that there is a structural similarity between 5-(2-aminopropyl)indole and 5-ABP, MPA and AMT. In addition one websites alludes to 5-(2-aminopropyl)indole having similar effects to 5-APB while another lists the product as '5-IT (similar to 6-APB)'.

Drug Forum:

The first discussion thread on the Drug Forum website for 5-(2-aminopropyl)indole appears to have been started in August 2010; while the first user report relating to this substance appears to be in November 2011. The thread also includes reference to 5-(2-aminopropyl)indole as an isomer of AMT, with citation of various on-line reference sources (e.g. Wikipedia) as well as Shulgin and Shulgin's 'TiKHAL' (1997).

User reports

([19]) http://www.drugs-forum.com/forum/showthread.php?t=140331
http://www.drugs-forum.com/forum/showthread.php?t=172223
http://www.drugs-forum.com/forum/showpost.php?p=1126167&postcount=9
http://www.bluelight.ru/vb/threads/616728-The-Big-amp-Dandy-5-IT-5-API-Thread

One user after an apparent intravenous injection of 5-(2-aminopropyl)indole reported ‘incredible rush, not so strong stimulating properties like speed, feeling is more like.. aMT + weak speed’. Another reported ‘very small psychedelic properties, reminds [me] of aMT’. Following 80 mg ‘bombed’ a user concluded that ‘I would say this somewhere in effects between 6-APB and MDAI with an amphetamine like quality but also quite reminiscent of aMT just nowhere near as psychedelic and with no nausea or body load’. Another user who ‘bombed’ 100 mg of 5-(2-aminopropyl)indole summarised ‘no come down, very stable euphoria and clear thoughts with a little bit of trippiness’. The use of 6-APB was mentioned by a number of users and one indicated a comparison stating that 5-(2-aminopropyl)indole was ‘quite comparable to 6-APB, but not quite as debilitating in its intenseness, not as euphoric, with a slightly shorter duration’.

Bluelight:

Amongst initial user discussions regarding the relative risk of taking ‘new research chemicals’ such as 5-(2-aminopropyl)indole and making predictions of effects, one user who took 20 mg (unknown route) stated that ‘the duration on 5-IT is rather long, with the entire experience lasting about 10 hours, probably slightly more’. Similar duration of effect was also noted by another user who had taken 100 mg: ‘I still felt it after seven hours on a 100mg dose’. However, another user in response to an extended come down experience of 22 hours postulated whether the user had actually taken 5-(2-aminopropyl)indole. Dose discussions also featured and one user surmised that ‘at high doses I have seen reports of dysphoria, delirium, pain, unconsciousness, confusion, hyperthermia, tremors. I experienced only positive effects but I would not recommend a higher starting dose for these reasons’.

D1.2.2. 5-(2-Aminopropyl)indole associated acute toxicity

Two Member States (Sweden and the United Kingdom) reported a total of 20 non-fatal intoxications associated with 5-(2-aminopropyl)indole.

German police reported to Europol a case where a powder was seized from an unconscious person. It is not known if this is a non-fatal intoxication associated with 5-(2-aminopropyl)indole as further details are not available and therefore has not been included in this report.

Non-fatal cases reported by Sweden

Sweden reported 18 non-fatal intoxications where 5-(2-aminopropyl)indole was detected in biological samples. They occurred between January and August 2012.

Of the 18 cases, 16 were male and two were female. Their ages ranged between 17 and 53, however the most common age was 20 to 30 years with 11 of the 18 falling into this bracket. In six cases, the individual stated they had taken ‘5-IT’ (a commonly used abbreviation for 5-(2-aminopropyl)indole), in three cases the stated intake was ‘benzofury’. Other cases mentioned taking ethylphenidate, etizolam, MDPV and/or 6-APB. One person said they had been ‘drinking only coca cola from an unknown source’; another person stated they had taken ‘an unknown substance’. 5-(2-Aminopropyl)indole was analytically confirmed in each

case although the concentration was not determined. Other drugs detected in these cases were: ethylphenidate, 4-,5- or 6-APB, 4-methylethcathinone, buprenorphine, methylphenidate (and metabolites), 4-fluoroamphetamine, oxazepam, temazepam, diazepam metabolites, methylthienylpropamine, methoxetamine, 4-hydroxymidazolam (midazolam metabolite), ketamine, GHB (gamma-hydroxybutyrate), PMMA (*para*-methoxymethamphetamine), amphetamine, *N*-methamphetamine, 4-methylamphetamine, α-PVP, cannabis, thiopental, pentobarbital, benzoylecgonine (cocaine metabolite), ethanol and metabolites. It is not known whether any of these substances (e.g. benzodiazepines and barbiturates) had been administered as part of medical treatment.

The route of administration of 5-(2-aminopropyl)indole was indicated in two cases where the individuals reported having taken it by nasal insufflation. In three cases the individuals reported that they had sourced 5-(2-aminopropyl)indole from the Internet. The sources of 5-(2-aminopropyl)indole for the remaining fifteen cases are not available.

The reported symptoms included dilated pupils, sweating, restlessness, fatigue, disorientation, agitation, mydriasis, anxiety, tachycardia, hypertension and hyperpyrexia. Hallucinations were mentioned in one individual where 5-(2-aminopropyl)indole and benzodiazepines were detected only ([20]).

Non-fatal cases reported by the United Kingdom

The United Kingdom reported two non-fatal intoxications associated with the second death case that is detailed in section D1.2.3. The two individuals had also reportedly ingested 'Benzo Fury' from the same source as the deceased. They were also examined at the hospital but neither appeared to have suffered any significant toxic effects. No further information on drug history or the amounts of 'Benzo Fury' taken is available.

D1.2.3. 5-(2-Aminopropyl)indole associated deaths

Four Member States (Sweden, the United Kingdom, Hungary and Germany) reported a total of 24 deaths associated with 5-(2-aminopropyl)indole (Table 3).

Deaths reported by Sweden

Sweden reported 15 deaths associated with 5-(2-aminopropyl)indole. The deaths occurred between April 2012 and July 2012. In 14 of the cases the cause of death was considered to be related to 5-(2-aminopropyl)indole. In the remaining case the cause was 'disease'. In the large majority of cases the cause of death was considered to be drug related although the ICD10 coding does not include naming 5-(2-aminopropyl)indole specifically. In the remaining cases, the cause was not ICD10 coded as being drug related and were recorded as being due to epilepsy and in another case, sudden cardiac arrest. In 14 cases the 5-(2-

([20]) The example provided in the Joint report of a non-fatal intoxication involving an eighteen year old female who had taken one capsule of 5-(2-aminopropyl)indole of unknown strength actually relates to a self report that was not analytically confirmed. Although in the text of the Joint report it appears that this case was one of the 13 non-fatal intoxications reported by Sweden, further information from the national focal point has confirmed that it was not part of this case series and instead was documented prior to the introduction of biological screening for 5-(2-aminopropyl)indole. See EMCDDA & Europol (2012) for details further details of this case.

aminopropyl)indole concentration in post-mortem femoral blood ranged from between 0.7 and 5.1 µg/g blood. In one case the concentration of 5-(2-aminopropyl)indole was 18.6 µg/g femoral blood. All of the decedents were male. 13 were aged between 20 and 30 years, the remaining two were over 30 years old. In two cases 5-(2-aminopropyl)indole was the only substance reported as detected. In the remaining cases 5-(2-aminopropyl)indole was found in combination with 'pharmaceuticals' or 'other drugs of abuse'. Notably some of these drugs have monoaminergic activity, such as sertraline, venlafaxine and MDMA.

Deaths reported by Hungary

Hungary reported four deaths associated with 5-(2-aminopropyl)indole.Two of these deaths occurred in April 2012 and were originally believed to be related to AMT which was reported as detected in post-mortem biological samples. The decedents, a 40-year-old male and a 35-year-old female were found together in a flat.

The post-mortem concentrations determined as AMT were 34 mg/L and 84 mg/L respectively. These figures are provided only to show them relative to each other. The biological samples were no longer available for re-analysis. However, the reanalysis of powders found at the scene identified the presence of 5-(2-aminopropyl)indole and not AMT. The Hungarian national focal point noted that 'based on the active agent identified in the substance found next to the bodies it is assumed that the cause of the deaths was 5-(2-aminopropyl)indole intoxication rather than AMT intoxication'. As already noted, analytical reference standards were not available at the time and it was difficult to distinguish between 5-(2-aminopropyl)indole and AMT. No other substances were reported as detected.

The pathological cause of death in each case was 'circulatory failure and respiratory failure, where the direct causes of death… were the results of 5-IT intoxication' and in the case of the female 'the respiration of vomited content of stomach might have had a limited impact too'. There were signs of 'prolonged sexual intercourse, extreme hyperthermia and the use of new psychoactive substances'.

The third death occurred in May 2012, an involved a 38 year old male known 'drug abuser' who was found dead in his apartment along with injection paraphernalia. A sachet found next to the body contained 5-(2-aminopropyl)indole. 'The toxicological analysis identified 5-IT in the blood' but no quantitative information was available. No other substances were reported as detected. The cause of death was attributed to drug intoxication and respiratory failure.

The fourth death occurred in June/July 2012, a 24 year old male died having purchased a product called 'Pink' from the Internet. The substance had been dissolved in water and consumed. 'Toxicological analysis identified 5-IT in the blood and stomach'. No other substances were reported as detected. The cause of death was attributed to circulatory and respiratory failure as a result of drug use and overdose.

Deaths reported by the United Kingdom

The United Kingdom reported four deaths associated with 5-(2-aminopropyl)indole. Details are only provided for two of these cases, both of which occurred in June 2012. The decedents were both male; one was 33 years old, the other was 19 years old.

The cause of death in the first case involving the 33 year old was 'fatality following the ingestion of 'Benzo Fury'' and certified as '5-(2- aminopropyl)indole (5-API; 5-IT) and Benzofuran toxicity'. The male was treated in hospital prior to death. Analysis of the blood revealed an approximate 5-(2-aminopropyl)indole concentration of 0.379 mg/L in unpreserved post-mortem blood. Other drugs detected in the blood included 5-APB (0.016 mg/L), 6-APB (0.057 mg/L), diazepam (0.037 mg/L), nordiazepam (0.009 mg/L), temazepam (0.001 mg/L) and AMT (less than 0.01 mg/L). Urine analysis detected amphetamine, 5-(2-aminopropyl)indole, 5-APB, 6-APB, AMT and benzodiazepines. In addition, 5-(2-aminopropyl)indole, 5-APB, 6-APB, AMT and diazepam were detected in the stomach contents.

In the second case involving the 19 year old, the toxicological investigation revealed 5-(2-aminopropyl)indole at a concentration of approximately 0.513 mg/L in ante-mortem blood (the deceased was admitted to hospital prior to death) and approximately 0.30 mg/L in unpreserved post-mortem blood. Other drugs detected included MDMA (0.468 mg/L ante-mortem blood, 0.502 mg/L post-mortem blood), MDA (0.036 mg/L ante-mortem blood, 0.046 mg/L post-mortem blood), 6-APB (0.005 mg/L post-mortem blood only), atropine and lignocaine. These drugs were also detected in the urine and stomach contents. It was noted that there was a high concentration of MDMA, which on its own was considered to be at a fatal level. However, a cumulative/synergistic effect of 5-(2-aminopropyl)indole was not excluded and the cause of death was recorded as 'multidrug toxicity'. This case is linked to the seizure of 116 blue tablets in branded packets labelled as 'BENZO FURY' that were found to contain 5-(2-aminopropyl)indole.

The remaining two deaths were reported in a letter to the British Medical Journal. The letter reports that 5-(2-aminopropyl)indole was detected in the post-mortem blood samples of two young adults. The authors note that 5-(2-aminopropyl)indole was 'found in combination with other drugs in one case'; while in the second case '5-APB/6-APB' was detected (Seetohul et al., 2012). It was ascertained from the national focal point that these cases were distinct from the other two cases reported by the United Kingdom. No further details are available at this time.

Death reported by Germany

Germany reported one death associated with 5-(2-aminopropyl)indole.

The report stated that on 23 May 2012, a 29 year old man who was not known as drug user was found dead in his apartment. A powder was found under his bed which was analysed and found to contain 5-(2-aminopropyl)indole. The initial urine screen indicated a positive result for amphetamine/methamphetamine. The preliminary autopsy report provided 'neither a hint on external assault and battery nor on a pathological-anatomic cause of death'. Further toxicological investigations revealed a high concentration of 5-(2-aminopropyl)indole

in the blood and urine samples (the blood sample contained >1200 ng/ml) (Schäper et al., 2013). No other substances were reported as detected. The final cause of death has not yet been recorded however, the German national focal point reported that intoxication by 5-(2-aminopropyl)indole is plausible.

This case highlights that there may be cross-reactivity issues with some screening tests. Further research is required to investigate this.

Table 3. Summary of deaths associated with 5-(2-aminopropyl)indole (5-IT). For reference against other reported cases µg/g is largely comparable to mg/L.

Date of death	Deceased (age/sex)	5-(2-Aminopropyl) indole toxicological findings (blood)	Other drugs detected (blood unless otherwise indicated)	ICD10 coding or descriptive cause of death
Sweden				
April 2012	23 yr old male	18.6 µg/g	AM2201 4-APB (urine)	Toxic effects of non-medicinal substance
May 2012	31 yr old male	2.3 µg/g	0.05 µg/g hydroxyzine 0.04 µg/g etizolam	Poisoning by hallucinogen
May 2012	24 yr old male	2.4 µg/g	0.03 µg/g zopiclone 0.003 µg/g ethylphenidate 0.03 µg/g ritalinic acid	Un-attended death. No other cause found.
May 2012	28 yr old male	3.8 µg/g	26 µg levitiracetam	Epilepsy
May 2012	20 yr old male	1.1 µg/g	0.02 µg/g benzoylecgonine 0.002 µg/g THC pentedrone [no quantitative data provided]	Sudden cardiac arrest
May 2012	31 yr old male	5.1 µg/g	0.04 µg/g 7-amino-clonazepam 0.01 µg/g perphenazine 0.12 µg /g ethylphenidate 2.6 µg/g ritalinic acid 0.0002 µg/g methylphenidate	Poisoning by drugs
May 2012	33 yr old male	4.2 µg/g		Poisoning by hallucinogen
May 2012	28 yr old male	2.5 µg/g	9.2 µg/g pregabalin	Poisoning by drugs
May 2012	40 yr old male	1.0 µg/g		Poisoning by hallucinogen
June 2012	31 yr old male	1.6 µg/g	0.2 µg/g alimemazine 0.1 µg/g desmethylalimemazine	Un-attended death. No other cause found
June 2012	29 yr old male	0.7 µg/g	0.18 µg/g ethylphenidate 1.9 µg/g ritalinic acid	Accidental poisoning by drugs
June 2012	55 yr old male	2.1 µg/g	0.9 µg/g carisoprodol meprobamate (not quantitated) 0.32 µg/g 7-amino-clonazepam	Poisoning by drugs

June 2012	30 yr old male	2.1 µg/g	0.7 µg/g sertraline 2.5 µg/g desmethylsertraline 1.0 µg/g venlafaxine 0.5 µg/g o-desmethylvenlafaxine	Poisoning by drugs
June 2012	24 yr old male	1.1 µg/g	0.02 µg /g benzoylecgonine 0.53 µg/g MDMA 0.03 µg/g MDA	Poisoning by hallucinogen
July 2012	28 yr old male	1.7 µg/g	0.008 µg/g ethylphenidate	Un-attended death. No other cause found
Hungary				
April 2012	40 yr old male	Not available	None	Circulatory failure and respiratory failure were the direct causes of death that were the results of 5-IT intoxication.
April 2012	35 year old female	Not available	None	Circulatory failure and respiratory failure were the direct causes of death that were the results of 5-IT intoxication, the respiration of vomited content of stomach might had a limited inpact too.
May 2012	38 year old male	Not available	None	Brain oedema, frothy respiratory tract secretion, pulmonal oedema and minor degeneration of cardiac muscle were observed in the body. The report concludes that based on the case history and the diagnostic report drug intoxication and respiratory failure as a consequence of intoxication are the assumed causes of death.
June/July 2012	24 year old male	Not available	None	The cause of death was circulatory and respiratory failure that developed due to metabolic failure, severe brain oedema, pulmonal oedema and cardiac failure. The report concludes that, in all probability, the cause of that was drugs use and overdose.
United Kingdom				
June 2012	33 year old male	0.379 mg/L	0.016 mg/L 5-APB 0.057 mg/L 6-APB 0.037 mg/L diazepam 0.009 mg/L nordiazepam 0.001 mg/L temazepam <0.001 mg/L AMT	The level of 5-IT is an approximate determination in unpreserved post mortem blood. All other analytes were detected in post mortem blood. Urine analysis detected amphetamine, 5-IT, 5-APB, 6-APB, AMT and benzodiazepines. In addition, 5-IT, 5-APB, 6-APB, AMT and diazepam were detected in the stomach contents
June 2012	19 year old male	0.30 mg/L	0.502 mg/L MDMA 0.046 mg/L MDA 0.005 mg/L 6-APB Atropine Lignocaine	The level of 5-IT is an approximate determination in unpreserved post mortem blood. 0.513 mg/L 5-IT was determined in ante mortem blood Cause of death noted to be 'multi-drug toxicity'. All other analytes were detected in post mortem blood.
Prior to 24 August 2012	'young adult'	Not available	'Other drugs'	Reported in letter to the British Medical Journal, no further details available.

Prior to 24 August 2012	'young adult'	Not available	'5/6-APB'	Reported in letter to the British Medical Journal, no further details available.
Germany				
May 2012	29 year old male	>1200 ng/ml	None	The final cause of death has not yet been recorded however, the national focal point reported that intoxication by 5-(2-aminopropyl)indole is plausible.

D2. Chronic health effects

D2.1. Animal data

No studies were identified that investigated the chronic health effects of 5-(2-aminopropyl)indole in animals.

D2.2. Human data

No studies were identified that investigated the chronic health effects of 5-(2-aminopropyl)indole in humans.

D3. Factors affecting public health risks

D3.1. Availability and quality of the new psychoactive substance on the market

5-(2-Aminopropyl)indole is offered for sale by Internet retailers as a substance in its own right. 5-(2-Aminopropyl)indole has also been detected in a 'legal high' type product branded as 'Benzo Fury'. There has also been one report from Hungary where 5-(2-aminopropyl)indole was seized as tablets resembling 'ecstasy'. Some individuals may be exposed to 5-(2-aminopropyl)indole intentionally. Others may be exposed unintentionally and unknowingly after consuming a product with no indication that it contains 5-(2-aminopropyl)indole or following its ingestion as a component of a mixture of other active substances (e.g. MDAI, 5- or 6-APB).

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

There is relatively limited information on drug discussion forums regarding the effects and potential health / adverse effects related to the use of 5-(2-aminopropyl)indole. On some drug discussion forums the use of 5-(2-aminopropyl)indole as a drug in its own right has been discussed. This is supported by the finding that two collected samples from Internet retailers contained 5-(2-aminopropyl)indole (in powders) as well as the fact that Internet retailers offer various dosage forms claiming to contain the substance (section C). Nevertheless, it is likely that the information, degree of knowledge, and perceptions amongst users concerning 5-(2-aminopropyl)indole and its effects are likely to be limited. In addition some users may be exposed to 5-(2-aminopropyl)indole unknowingly given that it has been detected in a 'legal high' type product labelled as 'Benzo Fury' as well as tablets resembling ecstasy.

D3.3. Characteristics and behaviour of users

There are self-reports from users on drug discussion forums who believe that they have specifically taken 5-(2-aminopropyl)indole. In some cases this appears to be in order to determine its relative effects compared to related compounds such as AMT in particular as well as 5- or 6-APB. This suggests a degree of risk-taking behaviour although some of the discussions have included harm reduction measures in relation to use of 'new research chemicals'.

D3.4. Nature and extent of health consequence

The limited documented information on the acute health effects of 5-(2-aminopropyl)indole have been discussed in section D1.2. There is insufficient information in the reported non-fatal intoxications and deaths where 5-(2-aminopropyl)indole has been detected to discuss in detail the circumstances of these cases. However, from the information available, it does not appear that any of these were related to road traffic accidents. The information available indicates that the presence of 5-(2-aminopropyl)indole has been analytically confirmed in a number of acute emergencies associated with the substance.

D3.5. Long-term consequences of use

As noted in sections D2.1. and D2.2. no animal or human data on the chronic health effects of 5-(2-aminopropyl)indole were identified. In particular, there have been no long-term follow up studies to determine whether 5-(2-aminopropyl)indole users are at greater risk of health deterioration later in life, or of developing chronic or life-threatening medical conditions.

D3.6. Conditions under which the new psychoactive substance is obtained and used, including context-related effects and risks

As noted, it appears that the sourcing and use of 5-(2-aminopropyl)indole is generally related to individuals attempting to source the drug itself or when it has been inadvertently taken along with or instead of other stimulants. As noted in section C, the structured Internet search conducted by the EMCDDA identified five English-language Internet retailers that offered 5-(2-aminopropyl)indole for sale to consumers in the European Union. In addition, in one case 5-(2-aminopropyl)indole was detected in a ‘legal high’ type product labelled as ‘Benzo Fury’ that was sold in a bricks and mortar headshop. It is likely that 5-(2-aminopropyl)indole is used in the same environments as other stimulants. This would be typically, but not restricted to, home environments, bars/pubs, discotheques/nightclubs and outdoor music festivals. Limited information from drug discussion forums suggest that 5-(2-aminopropyl)indole is used at home and in nightclubs.

Section E. Social Risks

E1. Individual social risks

There is currently no data to be able to determine the impact of 5-(2-aminopropyl)indole in this area.

E2. Possible effects on direct social environment

There is currently no data to be able to determine the impact of 5-(2-aminopropyl)indole in this area.

E3. Possible effects on society as a whole

Sweden reported the detection of 5-(2-aminopropyl)indole in ten biological samples (one

blood; nine urine) from individuals suspected to have committed minor drug offences or people that are in drug treatment programmes. Further information on these cases are not available to allow further comment.

E4. Economic costs

Given the lack of data available on acute health emergencies and healthcare utilisation related to the use of 5-(2-aminopropyl)indole, it is not possible at this time to estimate whether the substance is associated with greater healthcare costs than other stimulant drugs.

E5. Possible effects related to the cultural context, for example marginalisation

There is currently no data to be able to determine the impact of 5-(2-aminopropyl)indole in this area.

E6. Possible appeal of the new psychoactive substance to specific population groups within the general population

There is currently no data to be able to determine the possible appeal of 5-(2-aminopropyl)indole to specific population groups within the general population.

Section F. Involvement of organised crime

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

No information has been received by Europol of evidence that criminal groups are systematically involved in production, trafficking and distribution of 5-(2-aminopropyl)indole for financial gain.

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

Based on the information available to ECMDDA and Europol it does not appear that the production, trafficking and distribution of 5-(2-aminopropyl)indole impacts on other existing psychoactive substances or new psychoactive substances.

F3. Evidence of the same groups of people being involved in different types of crime

No information has been received by Europol of evidence of the same groups of people being involved in different types of crime in connection with 5-(2-aminopropyl)indole.

F4. Impact of violence from criminal groups on society as a whole or on social groups or local communities (public order and safety)

No information has been received by Europol on incidents of violence in connection with 5-(2-aminopropyl)indole.

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

No information has been received by Europol on incidents of money-laundering or impact of organised crime on other socioeconomic factors in society in connection with 5-(2-aminopropyl)indole.

F6. Economic costs and consequences (evasion of taxes or duties, costs to the judicial system)

There is currently no data to be able to determine the impact of 5-(2-aminopropyl)indole in this area.

F7. Use of violence between or within criminal groups

No information has been received by Europol on incidents of violence in connection with 5-(2-aminopropyl)indole.

F8. Evidence of strategies to prevent prosecution, for example through corruption or intimidation

No information has been received by Europol on strategies to prevent prosecution in connection with 5-(2-aminopropyl)indole.

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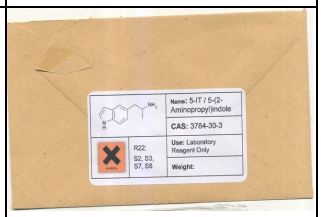
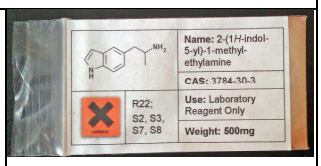
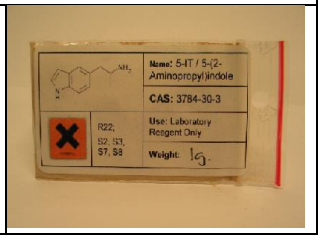
Annex 1

Details of seizures and collected samples of 5-(2-aminopropyl)indole (5-IT) reported to the EMCDDA and Europol

Date of seizure or collection	Amount and physical form	Seizing or collecting authority	Place of seizure or collection	Notes	Images
Denmark					
19/07/2012	One seizure of 5.1 g light brown powder	Customs	Haderslev	Powder was found in a small transparent bag and with a sticker: '5g 5-IT, Research Chemical, Not for human consumption'. The bag was inside a 'normal' brown envelope, and without any sender. The post came from United Kingdom. Identification based on GC-MS, UPLC-TOF, H-NMR.	 
Finland					
01/04/2012	One seizure of 1.1 g of a light brown powder	Customs	Helsinki	Seized in incoming mail. Identification based on NMR.	
Germany					
02/05/2012	1.35 g and a further 0.22 g together with traces of MDAI (together with other new psychoactive substances)	Police	Hannover	The accused stated that he has bought the substances via the internet from an online shop in the United Kingdom.	
12/11/2012	Brown glittery tablets (amount unknown at present	Police	Bavaria	'Further fragmentary information on 5 additional cases of detection of 5-IT in sezizures [sic] of 1-10 tablets per case was reported by the Bavarian Police and one case of 1 gram 5-IT.'	

Hungary*					
04/2012	2.4 g of a beige powder	Police	Tapolca	Confirmed as 5-(2-aminopropyl)indole	
04/2012	Residues on paper, liquid in syringe (0.75 ml)	Police	Debrecen	Confirmed as 5-(2-aminopropyl)indole	
04/2012	2.2 g of a brown powder	Police	Szombathely	Confirmed as 5-(2-aminopropyl)indole	
05/2012	Residues on spoon	Police	Szentes	Confirmed as 5-(2-aminopropyl)indole	
05/2012	10.2 g of a brown powder	Police	Tata	Confirmed as 5-(2-aminopropyl)indole	
06/2012	0.2 g of a light-brown powder	Police	Szigetvár	Confirmed as 5-(2-aminopropyl)indole	
06/2012	7 beige tablets with 'Lexus' logo, also containing, methylthienylpropamine and caffeine	Police	Kiskőrös	Confirmed as 5-(2-aminopropyl)indole. Weight of tablets: 0.285 g, diameter: 8.10 mm, thickness: 5.8 mm. The identification was carried out by TLC and GC/MS based on the laboratory's 'own' reference materials (their structure was confirmed by NMR).	
07/2012	0.2 g of brown powder	Police	Esztergom	Confirmed as 5-(2-aminopropyl)indole	
08/2012	97.3 g of a brown powder, residues on digital scale	Police	Szigetvár	In this case the investigation confirmed the fact of dealing both new psychoactive substances (according to schedule "C" Gov. Decree 66/2012) and illicit drugs (covered by the illicit drugs definition of the Penal Code). Mail delivery and selling from the flat was also confirmed. The business covered the whole country did not concentrate on the area of Szigetvár.	
09/2012	4.1 g of light brown powder	Police	Eger	Confirmed as 5-(2-aminopropyl)indole	
10/2012	0.3 g of light brown powder	Police	Debrecen	Confirmed as 5-(2-aminopropyl)indole	
12/2012	0.1 g of brown powder	Police	Szekszárd	Confirmed as 5-(2-aminopropyl)indole	
Netherlands					
Not available	20.5 kg	Customs		Not available	
Sweden					

	33 seizures incorporating 36.33 g powder and 54 tablets.	Police		The first seizure comprising 13 g beige powder was seized by the police 16/05/2012 in Örnsköldsvik city with identification based on GC-MS, GC-IRD and NMR. Examples of seized tablets: One type of tablet in 6 materials: These are blue, green melange; round and curved with border; diameter 9.0 mm, width 4.0 mm, weight 0.25 g. Another type of tablet that occurred only in one material: brown, glittery tablet; round and flat and scored; diameter 6.0 mm, width 2.9 mm, weight 0.10 g.	
	Four seizures in total, comprising: three seizures of a brown powder weight a total of 11.07 g. One seizure of 5 tablets	Customs	Arlanda Airport, Sweden	The three packages containing powder were from Spain. The package containing tablets were sent from United Kingdom.	 
United Kingdom					
April 2012	500 mg brown powder	State's Analyst Guernsey	Purchased from the Internet	Confirmed as 5-(2-aminopropyl)indole succinate by NMR.	 
May 2012	Pale brown powder	TicTac Ltd.	Purchased from Internet £22.50 for 500 mg	Product label stated '5-IT' '500mg' 'NOT FOR HUMAN CONSUMPTION'. Analysis by GCMS. Molecular formula confirmed by High Res MS. Confirmed as 5-(2-aminopropyl)indole succinate by proton NMR.	

09/06/2012	One seizure of 116 packets. Blue unmarked tablet in packet	Police	Edinburgh, Scotland	During the police investigation of one of the fatal cases from the United Kingdom where the presence of 5-(2-aminopropyl)indole was confirmed, the police were informed that the product consumed by the deceased had been purchased at a 'headshop' in Edinburgh. Police executed a search warrant at the Edinburgh premises and recovered a large quantity of items (160 productions) including bulk quantities of powders, herbal material and packaged products. One of the items submitted to the Forensic Science Laboratory contained 116 yellow packages labelled 'BENZO FURY' with a graphic displaying the structure of 5-APB. Four of these packages, selected at random, were examined and each found to contain a single blue unmarked biconvex tablet which were each analysed and found to contain 5-(2-aminopropyl)indole. Other items of interest recovered from the 'headshop' were: Yellow capsules labelled 'benzofury' found to contain brown powder containing 5/6-APB. 31 g of brown powder found to contain 5/6-APB. 174 packages (98 of one type and 76 of a second type) each containing 1 g of crystalline substance identified as methylthienylpropamine (MPA).	 
08/09/2012	One seizure of seven red and white gelatine capsules with no markings on them. Also contained diphenyl prolinol (D2PM).	Customs	Guernsey	The Guernsey Border Agency seized the capsules along with a number of Class B substances from a person arriving on the Island. Analysis was carried out by the Guernsey States Analyst.	
Norway					
17/04/2012	One seizure of 1 g in a small bag with zip-lock	Customs	Gardermoen, Oslo Airport	Identified with MS only.	

*The Forensic Institute of the National Tax and Customs Administration of Hungary reported no seizures of 5-(2-aminopropyl)indole.

Appendix 1

Study examining the inhibition of human monoamine oxidase (MAO) by the new psychoactive substance 5-(2-aminopropyl)indole, CC.13.SAT.003, February 2013, Herriaz, T., in collaboration with Simon D. Brandt.