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25I-NBOMe

EMCDDA–Europol Joint Report on a new psychoactive substance: 25I-NBOMe (4-iodo-2,5-dimethoxy-*N*-(2-methoxybenzyl)phenethylamine)

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

About this series

EMCDDA–Europol Joint Report publications examine the detailed information provided by the EU Member States on individual new psychoactive substances. Information is collected from the Reitox network, the Europol national units and the national competent authorities of the European Medicines Agency.

Each Joint Report serves as the basis upon which the decision to conduct a risk assessment of the new psychoactive substance is taken. It is part of the three-step procedure involving information exchange, risk assessment and decision-making in the framework of the Council Decision 2005/387/JHA.

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1. Introduction

Article 5.1 of Council Decision 2005/387/JHA ⁽¹⁾ (hereinafter referred to as the 'Decision') stipulates that '*Where Europol and the EMCDDA, or the Council, acting by a majority of its members, consider that the information provided by the Member State on a new psychoactive substance merits the collection of further information, this information shall be collated and presented by Europol and the EMCDDA in the form of a Joint Report (hereinafter the "Joint Report").*' The Joint Report shall be submitted to the Council, the European Medicines Agency (EMA) and the European Commission.

At the end of September 2013, the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) and Europol examined the available information on a new psychoactive substance 4-iodo-2,5-dimethoxy-N-(2-methoxybenzyl)phenethylamine, commonly known by the abbreviation '25I-NBOMe', through a joint assessment based upon the following criteria:

1. the amount of the material seized;
2. evidence of organised crime involvement;
3. evidence of international trafficking;
4. analogy with better-studied compounds;
5. evidence of the potential for further (rapid) spread; and,
6. evidence of cases of serious intoxication or fatalities.

The EMCDDA and Europol agreed that the information collected on 25I-NBOMe satisfied criteria 1, 3, 5 and 6. The two organisations therefore concluded that sufficient information had been accumulated to merit the production of a Joint Report on 25I-NBOMe as stipulated by Article 5.1 of the Decision.

2. Information collection process

In compliance with the provisions of the Decision, on 7 October 2013 the EMCDDA and Europol launched a procedure for the collection of information on 25I-NBOMe, in order to prepare the Joint Report. The information was collected mainly through the Reitox National Focal Points in the Member States, Turkey and Norway as well as the Europol National Units. In addition, the EMA collected information through the national competent authorities responsible for human and veterinary medicinal products in the Member States as well as in Norway and Iceland. The information collection process was largely concluded by 18 November

2013; additional information and clarifications from some countries were received up to four weeks after this date.

Europol asked the Europol National Units to provide information on:

- the level of production of 25I-NBOMe in their country;
- the level of distribution of 25I-NBOMe in their country;
- the level of trafficking of 25I-NBOMe in their country, for internal, transit or export purposes;
- the number of seizures of 25I-NBOMe in their country, the total amount of the seizures, country of origin, details on the physical forms (including photos);
- the role of organised crime, or criminal groups, in the production, distribution and trafficking of 25I-NBOMe in their country; and,
- any known aspect of violence and/or money laundering relating to the production and trafficking of 25I-NBOMe.

Europol received responses from 15 Member States.

According to Article 5.3 of the Decision, the EMA requested the national competent authorities responsible for human and veterinary medicinal products in the Member States as well as in Norway and Iceland to provide information on whether:

- the new psychoactive substance 25I-NBOMe has obtained a marketing authorisation;
- the new psychoactive substance 25I-NBOMe is the subject of an application for a marketing authorisation; and,
- a marketing authorisation that had been granted in respect of the new psychoactive substance 25I-NBOMe has been suspended.

Twenty-four Member States ⁽²⁾, Norway and Iceland responded to the EMA's request. The EMA also provided information as relevant to the central authorisation procedure.

Furthermore, in anticipation of Article 7.3 of the Decision in relation to the manufacturing of medicinal products in the European Union, the EMA also requested whether the new psychoactive substance 25I-NBOMe is used to manufacture a medicinal product:

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

⁽²⁾ Austria, Belgium, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Malta, the Netherlands, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.

⁽¹⁾ OJ L 127, 20.5.2005, p. 32.

Twenty-three Member States ⁽³⁾, Norway and Iceland replied to the EMA's request. The EMA also provided information as relevant to the central authorisation procedure.

The EMCDDA collected data through:

1. a structured questionnaire from the Reitox national focal points. The EMCDDA received replies from 28 Member States as well as from Turkey and Norway;
2. data previously provided to the EU early-warning system via EMCDDA–Europol Reporting Forms, EWS Progress and Final Reports;
3. a specific information request to the World Health Organization on whether or not 25I-NBOMe is under assessment by the United Nations system (see section 3.5), and;
4. a structured search of the scientific literature and of relevant Internet sites.

Thus, information included in sections 3.2.1 and 3.3 of the Joint Report was provided by Europol, while the EMCDDA provided information included in sections 3.1, 3.2.2, 3.4, 3.5, 3.6, 3.7, 3.8.1, 3.8.2 and 3.8.3 (in part). The information included in sections 3.8.3 (in part), 4.1, 4.2 and 4.3 was provided by the EMA. The conclusion of the Joint Report was prepared and agreed by the two organisations responsible — the EMCDDA and Europol. Further details of the seizures and collected samples (including images where available) reported to the EMCDDA are provided in Annex 1. The details of non-fatal intoxications and a death associated with 25I-NBOMe that have been reported to the EMCDDA are provided in Annex 2.

3. Information required by Article 5.2 of the Decision

The order and titles of subsections 3.1 to 3.8 and section 4 below are as they appear in Article 5.2(a) to (h) and Article 5.3(a) to (c) of the Decision; all sections are cross-referenced with those set down in the Decision.

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

Chemical description and names

25I-NBOMe is a derivative of 2C-I (4-iodo-2,5-dimethoxyphenethylamine), a known synthetic derivative of phenethylamine with stimulant and hallucinogenic properties. 2C-I was the subject of a risk assessment at European level in 2003 (EMCDDA, 2004). 25I-NBOMe contains the 2C-I substructure, substituted with a bulky '*N*-(2-methoxy)benzyl' group. The 'I' in 2C-I and 25I-NBOMe denotes the presence of an iodine atom in the structure (Figure 1).

Several similar versions of 25I-NBOMe exist where the iodine atom is exchanged for another halide element, hydrogen atom or organic functional group, i.e. bromine (25B-NBOMe), chlorine (25C-NBOMe), hydrogen atom (25H-NBOMe), -methyl (25D-NBOMe), -ethyl (25E-NBOMe), -nitro (25N-NBOMe) or -isopropyl (25iP-NBOMe). These compounds are informally called the 'NBOMes'. This name comes from the '**N**-benzylmethoxy' substituent (-methoxy being written in chemical shorthand as '**OMe**'). As of 12 December 2013, ten 'NBOMe' compounds have been notified to the EU early warning system and it is important to note that -NBOMe compounds can be derived from all '2C' phenethylamines. Furthermore, two simple variants of 25I-NBOMe are possible by moving the methoxy group, found in position -2 on the benzyl moiety, to position -3 or -4. Furthermore, many other chemical variants are possible by changing the substitution pattern on the benzyl moiety to produce substances, the effects of which may or may not be similar to 25I-NBOMe.

The IUPAC name for 25I-NBOMe is: 2-(4-iodo-2,5-dimethoxyphenyl)-*N*-[(2-methoxyphenyl)methyl]ethanamine.

Additional chemical synonyms have been reported:

2-(4-iodo-2,5-dimethoxyphenyl)-*N*-(2-methoxybenzyl)ethanamine;

2-(4-iodo-2,5-dimethoxyphenyl)-*N*-(2-methoxybenzyl)ethan-1-amine;

4-iodo-2,5-dimethoxy-*N*-(2-methoxybenzyl)phenethylamine;

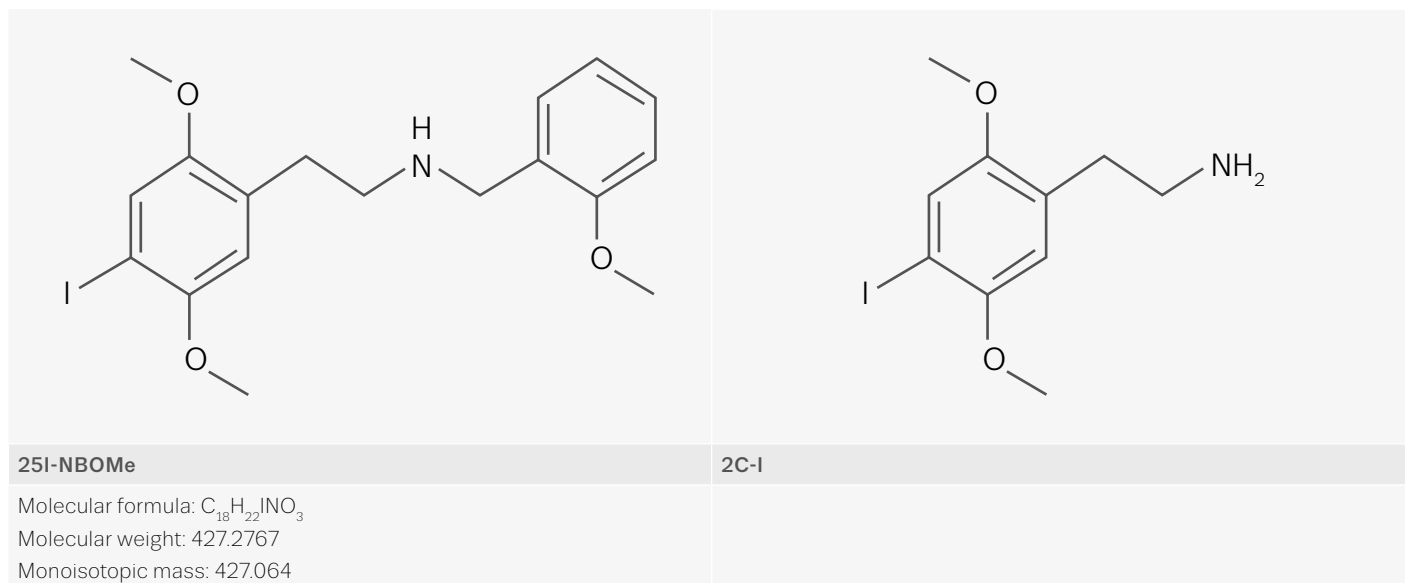
4-iodo-2,5-dimethoxy-*N*-(*o*-methoxybenzyl)phenethylamine;

4-jodo-2,5-dimetoksi-*N*-(2-metoksibentsyyli)fenetyyliamiini (Finnish);

⁽³⁾ Austria, Belgium, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Malta, the Netherlands, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.

FIGURE 1

The numbered molecular structure, formula, weight and monoisotopic mass of 25I-NBOMe. The molecular structure for 2C-I is provided for comparison.



4-iodo-2,5-dimethoxy-N-[(2-methoxyphenyl)methyl]-benzeneethanamine;

N-(2-methoxybenzyl)-2,5-dimethoxy-4-iodophenethylamine;
and,

N-(2-methoxybenzyl)-4-iodo-2,5-dimethoxyphenethylamine.

Furthermore, common names or code names have also been reported: 25I, 2CI-NBOMe or 2C-I-NBOMe, NBOMe-2C-I or NBOMe-2CI, BOM-Cl, Cimbi-5, Solaris and INBMeO.

Finally, the following street names have been reported: '25I', 'dots', 'legal acid', 'N-Bomb', 'NE-BOME', 'smiles', 'INBMeO', 'BOM-Cl', 'Hoffman' and 'N-boom'.

Chemical Abstract Service registry numbers (CAS RN)

919797-19-6 free base

1043868-97-8hydrochloride salt

1248338-50-2 ¹¹C radiolabelled base – ¹¹C on the benzyl methoxy carbon

1404305-56-1 ¹¹C radiolabelled base – ¹¹C on the phenyl 2-methoxy carbon

1043869-41-5 ³H radiolabelled base

The REACH registered substances database hosted by the European Chemicals Agency (ECHA) was searched using the CAS registry numbers listed above. The search returned no results.

Physical description

The hydrochloride salt form of 25I-NBOMe is a crystalline solid at room temperature. It has been reported that some Internet retailers (4) have advertised 25I-NBOMe as the free base and also as a hydroxypropyl-β-cyclodextrin (HPBCD) complex. In both cases no reports have been received by the EMCDDA that have analytically confirmed the base/salt form or the presence of 25I-NBOMe in complex with HPBCD, although it is uncertain whether this would necessarily be detected with routine analytical techniques.

Information provided from seizures and collected samples have noted the presence of 25I-NBOMe in blotters (small paper doses for sublingual/buccal administration), powders, powder-filled capsules and liquids.

A more detailed description of 25I-NBOMe seizures and collected samples encountered can be found in subsections 3.2.1 and 3.2.2 below.

(4) 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'.

3.2. Information on the frequency, circumstances and/or quantities in which a new psychoactive substance is encountered, and information on the means and methods of manufacture of the new psychoactive substance — Article 5.2(b) of the Decision

3.2.1. Information provided to Europol

Europol received replies from 15 Member States (Belgium, Bulgaria, Croatia, Cyprus, Estonia, Finland, Germany, Hungary, Italy, Latvia, Lithuania, Luxembourg, Poland, Slovakia and Slovenia). Of these, nine countries had no data relating to 25I-NBOMe (Bulgaria, Croatia, Cyprus, Estonia, Italy, Latvia, Lithuania, Luxembourg and Slovenia). The remaining six countries (Belgium, Finland, Germany, Hungary, Poland and Slovakia) reported the following information.

The level of production, distribution and trafficking

Belgium reported two cases of 25I-NBOMe that were seized while in transit from China to the Netherlands. In the first case the substance was labelled as 'ETHYLENE VAE' (107 g) and in the second case as 'EGTAZIC ACID' (51 g).

Finland reported that 71 seizures of 25I-NBOMe were made in the first half of 2013. In 68 cases the substance was seized as blotters (10 004 units in total) and in three cases as liquid (20 ml in total).

Germany reported that 11 seizures of 25I-NBOMe were made between November 2012 and August 2013. The substance was seized in powder form in two cases, as a liquid in three cases and as blotters in six cases. In one seizure involving 10.7 g of 25I-NBOMe powder that was made in April 2013, it was labelled as '1,2-Di(2-aminoethoxy)-ethaneN,N,N,N-tetraacetic acid'. All three seizures of 25I-NBOMe in liquid form were made in June 2013 and ranged from 0.61 g to 41.4 g. In the majority of cases, the substance was seized in the form of blotters. 25I-NBOMe was also detected in mixtures with other substances, including: 25H-NBOMe, 25C-NBOMe, JWH-122 N-(4-pentenyl) analogue, 2C-H-NBOMe and 2C-C-NBOMe.

Hungary reported 'a few' seizures of 25I-NBOMe in powder form and blotter form made since 2012.

Poland reported that 25I-NBOMe had been seized on three occasions, with a total of 48 blotters and 'one piece of paper laced with substance' seized.

Slovakia reported one seizure of 25I-NBOMe in the form of a colourless liquid (1 ml).

No reports were received that indicated licit or illicit production of 25I-NBOMe in any of these countries.

3.2.2. Information provided to the EMCDDA

Twenty-three Member States (Austria, Belgium, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, the Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom) and Norway reported detections of 25I-NBOMe ⁽⁵⁾.

Seizures

Twenty-two Member States (Belgium, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, the Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom) and Norway reported seizures of 25I-NBOMe.

25I-NBOMe has typically been seized as 'blotters' or paper 'trips'. These are sheets of absorbent paper designed for sublingual or buccal administration. They are often printed with distinctive designs and perforated so they can be torn into small, single-dose units (typically approximately 7 x 7 mm square). There are also reports of seizures in powder form (including two seizures of capsules containing powder) and in liquid form (5 % of cases).

In most cases, 25I-NBOMe was reported as the only active substance. However, in about 10 % of detections it was found in combination with other substances, including other '-NBOMe' compounds (25B-NBOMe, 25C-NBOMe, 25H-NBOMe, 25N-NBOMe, 2C-C-NBOMe, 2C-I-NBOMe, 2C-H-NBOMe), 2C-B, 2C-C, 2C-I, 2C-T-4, mescaline ⁽⁶⁾, LSD, MDPBP (a synthetic cathinone) and an unknown substance. No quantitative analyses were available.

There is some evidence that 25I-NBOMe has been sold as a replacement for the internationally controlled hallucinogenic substance LSD (lysergic acid diethylamide), which is also commonly taken sublingually in the form of blotters. Seized 25I-NBOMe blotters varied in size (from 5 mm to 10 mm square), colour and design (e.g. Smiley, Felix the cat, Mickey Mouse, Rolling Stones tongue logo, Hoffman Bicycle, etc.). Many

⁽⁵⁾ 'Detections' is an all-encompassing term and may include seizures and/or collected and/or biological samples. Seizure means a substance available (seized) through law enforcement activities (police, customs, border guards, etc.). Collected samples are those that are actively collected by drug monitoring systems (such as test purchases) for monitoring and research purposes. Biological samples are those collected from human body fluids (urine, blood, etc.) and/or specimens (tissues, hair, etc.).

⁽⁶⁾ A naturally occurring hallucinogenic phenethylamine.

of these designs have been associated with LSD in the past. Quantities of seized blotters ranged from one single unit (Denmark, Germany, Estonia, Finland, Poland, Slovakia and Norway) to 5 154 units (Ireland); Finnish customs reported ten single seizures greater than 500 units. In a smaller number of cases, powders (from 0.025 g to 107 g, Belgium), liquids (from 0.2 ml, Slovenia, to 75.2 g, Poland) and capsules containing powder (10 units in Finland and 48 units in Norway) were seized.

Finland reported more than half of the total number of seizures between June 2012 and October 2013: a total of 107 seizures from Helsinki Airport postal customs and 14 seizures from the police. 25I-NBOMe was seized as blotters in most cases (111 seizures); the quantities seized ranged from a single blotter to 1 200 units, with a total of 15 796 units. Small quantities were seized in other physical forms: powder (five seizures, ranging from 0.1 g to 4.5 g), liquid (four seizures, from 4 ml to 12 ml) and capsules containing powder (one seizure of 10 capsules).

Denmark reported 10 seizures of blotters (up to 263 units, from April to July 2013) and a seizure of powder (1.5 g, January 2012).

Germany reported ten seizures made in 2013. These included six seizures of blotters, three seizures of liquids (from 0.61 g to 41.4 g) and one powder (10.7 g, labelled '1,2Di(2-aminoethoxy)-ethaneN,N,N,Ntetraacetic acid').

In Poland, the first seizure of 25I-NBOMe (reported in 2011) was in liquid form; it has mostly been seized as blotters (up to 391 units) but also in powder form on two occasions (0.4 g and 5.5 g).

Sweden detected 25I-NBOMe for the first time in May 2012 when seven green blotters were seized. It reported a similar number of seizures of blotters and powders (5 to 583 units and 1.49 g to 13.82 g, respectively).

Norway reported nine seizures of blotters ranging from 1 to 250 units and one seizure of 48 capsules containing powder.

France, Hungary, Italy and the United Kingdom reported more than five seizures. France reported mostly blotters (in some cases, blotters came in a plastic bag labelled '2 extra stamps') but also one seizure of liquid and two of powders; most of the seizures were made by customs authorities at Roissy Airport (Paris). In Hungary, small quantities of blotters (from 2 to 17 units) and powders (10.66 g and 12.73 g) were seized by the police. Italy (from 4 to 52 units) and the United Kingdom (from 3 to 2 561 units) reported only seizing 25I-NBOMe in the form of blotters.

Belgium, Estonia, Greece, Ireland, Portugal and Spain reported fewer than five seizures. Belgian police seized 10

blotters and customs authorities at Bierset Airport (Liège) reported three seizures of powder, two of 75 g and one of 107 g, which had arrived from China. Two seizures of blotters were reported by Estonia (1 and 299 units) and Greece (2 and 103 units). Ireland reported the biggest single seizure of blotters, totalling 5 154 units; Portugal reported four seizures of blotters (from 2 to 50 units) from June to September 2013; and Spain reported three detections of powder with no further details provided.

Seven countries reported one seizure of 25I-NBOMe: blotters in the Czech Republic (120 units), Latvia (124 units) and Romania (3 units); powder in Lithuania (0.025 g) and the Netherlands (0.5 g); and liquids in Slovakia (1 ml) and Slovenia (0.2 ml).

Biological samples

Three Member States (Belgium, Sweden and the United Kingdom) reported detections of 25I-NBOMe in biological samples. These included 15 non-fatal intoxications (Belgium, three cases; Sweden, five; and the United Kingdom, seven) and one death in the United Kingdom. The United Kingdom also reported the detection of 25I-NBOMe in three further cases: two criminal suspects in a drug-related death and an intoxicated driver. Further details are provided in section 3.4.1 and Annex 2.

Collected samples

Five Member States (Austria, Belgium, Italy, the Netherlands and Spain) reported the detection of 25I-NBOMe in collected samples.

Austria reported six samples (all blotters), collected and analysed between February and October 2013 as part of the 'pill'-testing project run by 'ChEckiT!' In five cases, the samples were sold as LSD and in the remaining case the sample was sold as mescaline. An unknown substance was also detected in one of the samples.

Belgium reported a sample of five blotters collected in August 2013 as part of the investigations into one of the three non-fatal intoxications reported below. The blotters were collected from the patient and were found to contain 25I-NBOMe and traces of 25C-NBOMe.

Italy reported a red blotter with a weight of 20 mg with a logo of a yellow/orange 'smile', collected in the Veneto region. No substances other than 25I-NBOMe were detected.

The Netherlands reported 25I-NBOMe in six collected samples. Four cases involved blotters (amounting to a total of 16 blotters) and two involved samples of powder collected in

2012 and 2013. The samples were sold at consumer level either as 25I-NBOMe (three cases), LSD (two cases) or 2C-E (one case).

Spain reported three samples of blotters containing 25I-NBOMe, which were collected at different venues in January 2013.

Further details of these collected samples, including information on the product labels, are provided in Annex 1.

3.3. Information on the involvement of organised crime in the manufacture or trafficking of the new psychoactive substance — Article 5.2(c) of the Decision

Germany reported that no links have been identified between organised crime groups and the production, trafficking and/or distribution of 25I-NBOMe. They also noted that it should be borne in mind that given the easy access to substances (which can be in large amounts) via Internet retailers it cannot be excluded that a certain level of organisation may exist. In addition, organised crime groups' interest and presence in the phenomenon of new psychoactive substances can be easily concluded from the substantial profits that can be obtained from this type of activity.

Money laundering aspects

No information was received on money laundering connected to the production and/or trafficking of 25I-NBOMe.

Violence in connection with production, wholesale and distribution

No information was received on incidents of violence in connection with the production, wholesale and/or trafficking of 25I-NBOMe.

3.4. A first indication of the risks associated with the new psychoactive substance, including the health and social risks, and of the characteristics of users — Article 5.2(d) of the Decision

3.4.1. First indication of health risks

A total of 32 non-fatal intoxications and three deaths associated with 25I-NBOMe were reported by four Member States: Belgium, Poland, Sweden and the United Kingdom. Not all of these cases have been analytically confirmed. See Annex 2 for further details on toxicologically confirmed cases.

Non-fatal intoxications

Belgium

Belgium reported three non-fatal intoxications, which occurred in August 2013. The cases were linked, as the subjects had all been at the same party. All cases had analytical confirmation with 25I-NBOMe detected in urine and negative results for other drugs. 25I-NBOMe was not quantified but a pharmacokinetic study is being performed on the collected blood samples. The patients were admitted to hospital and registered as having consumed 'synthetic LSD'; their symptoms included lowered consciousness, insufficient breathing, mydriasis, tachycardia, hypertension and 'lessened strength in four extremities' (see the details for all patients in Annex 2). The treatment was reported in two cases and included sedation, intubation and ventilation. The outcome is known for one patient, whose symptoms disappeared after being under observation for a couple of hours. The patient reported having used 25I-NBOMe in the past.

Poland

Poland reported four linked non-fatal intoxication cases, which occurred in August 2013. None of these cases were confirmed analytically. One of the patients reported they all had used 25I-NBOMe.

Sweden

Sweden reported 18 non-fatal intoxications, which occurred between June 2012 and July 2013. Five of these cases have been analytically confirmed. Symptoms reported included mydriasis, anxiety, agitation, hallucinations, psychotic symptoms, tachycardia and hyperthermia. The noted routes of administration were oral, nasal and by injection.

United Kingdom

The United Kingdom reported seven non-fatal intoxications where 25I-NBOMe was detected and which occurred over the course of one week (Hill et al., 2013).

The first case described by Hill et al. (2013) involved a 29-year-old male who had purchased the drug from a 'dealer' in liquid form, labelled '25I-NBOMe'. This person injected 3 ml of the liquid of unknown concentration intravenously. This case had the most severe symptoms reported by the United Kingdom, including agitation, aggression, seizures and self-harming behaviour associated with tachycardia, hypertension, tachypnea, oxygen desaturation, pyrexia and rhabdomyolysis. The patient also developed anuria with a subsequent acute kidney injury. A computed tomography (CT) scan revealed mild cerebral oedema but no other intracranial pathology.

Treatment consisted of initial resuscitation with intubation, ventilation, intravenous sedation, antibiotics and fluids. Ongoing jerking seizure-like movements were noted and managed with atracurium infusion. Large doses of multi-modal sedation were administered during stabilisation. On day 18 of treatment a percutaneous tracheostomy was performed. The patient was discharged from intensive care on day 38, and discharged from hospital on day 43.

In the other six cases, 25I-NBOMe had been taken at a house party after it had been purchased from the Internet. The 25I-NBOMe was in the form of powder contained in purple capsules, labelled as '2C-B'. The six cases were analytically confirmed either in plasma alone or in urine and plasma. Amphetamine and methamphetamine were detected together with 25I-NBOMe in all six patients. 2C-I⁽⁷⁾ was also detected in all available urine samples (four of the seven cases); this may suggest that 2C-I is a metabolite of 25I-NBOMe. In three cases the capsules were swallowed, and in the other three cases the powder from the capsule was nasally insufflated. The quantities consumed are inexact, but were reported to range from one capsule (three cases) to 'small amount' or '~0.1 g' of powder. The patients typically presented with agitation, aggressive behaviour, palpitations, visual and auditory hallucinations, mydriasis and pyrexia, but the symptomatology varied slightly between patients. One of these patients suffered severe toxicity, which required hospitalisation for five days (see the details of symptoms for all patients in Annex 2). He was treated with intravenous diazepam for agitation, was intubated and received pressure-controlled ventilation, anaesthesia with infusions of propofol, midazolam, and atracurium. The remaining five patients were discharged from hospital on the same day as admission or within 15 hours and were treated with benzodiazepines (information available for three cases). Regular use of other illicit drugs was reported for three of the cases: one was a regular user of cocaine, cannabis and ecstasy and had previously used LSD; another had a history of regular amphetamine and ecstasy use; and, the third was a regular user of cannabis. One patient suffered from asthma and one patient was being treated with fluoxetine for depression.

Deaths

Belgium

Belgium reported one death, which occurred in October 2013. The cause of death has not been reported. The person died after consuming a blotter that was believed to contain LSD at a party; no LSD was detected in the toxicological analyses.

Further details are not available at present. The results of the analytical confirmation on biological samples are awaited.

Poland

Poland reported a death, which occurred in August 2013. The death was linked with the four non-fatal intoxications reported above. As noted, one of the four patients who received treatment reported they all had used 25I-NBOMe. The cause of death has not been reported and no analytical confirmation is expected.

United Kingdom

The United Kingdom reported a death by drowning, which occurred in May 2013. 25I-NBOMe was found on analysis of the post mortem blood of the deceased as well as amphetamine, ketamine, lignocaine, 5-MeO-DiPT⁽⁸⁾, DOI⁽⁹⁾, 25C-NBOMe⁽¹⁰⁾ and 2C-I (see footnote 7). No further information is available.

Pharmacology and mode of action

Data from *in vitro* studies has shown that 25I-NBOMe has nanomolar affinity for the serotonin 5-HT_{2A} receptor and is a full agonist (Braden et al., 2006; Ettrup et al., 2010, 2011; Nichols et al., 2008). The addition of the 2-methoxybenzyl group significantly enhances the affinity and potency of 25I-NBOMe (Braden et al., 2006) compared to 2C-I (Blaazer et al., 2008).

Stimulation of the 5-HT_{2A} receptors appears to be essential for the hallucinogenic effects of drugs such as LSD (Egan et al. 1998; Marek and Aghajanian, 1996; González-Maeso et al., 2007; Hanks and González-Maeso, 2013; Nelson et al., 1999). Given the fact that 25I-NBOMe is a potent full agonist for the 5-HT_{2A} receptor and there have been reports of its hallucinogenic effects when used as a recreational drug, Halberstadt and Geyer (2013) studied the effect of 25I-NBOMe on the head-twitch behavioural response (HTR) in mice, which is used as a surrogate marker of the hallucinogenic effect of 5-HT_{2A} receptor activation in humans (Hanks and González-Maeso, 2013). The study found that 25I-NBOMe induces HTR in mice in a dose-dependent manner, with a dose of 0.01 mg/kg s.c. inducing significant HTR compared to controls. HTR was dose-dependently antagonised by pre-treatment of the mice with the 5-HT_{2A} receptor antagonist M100,907 suggesting that the HTR induced by 25I-NBOMe is mediated through 5-HT_{2A} receptor activation.

⁽⁸⁾ 5-Methoxy-di-isopropyl-tryptamine.

⁽⁹⁾ 2,5-Dimethoxy-4-iodoamphetamine.

⁽¹⁰⁾ 2-(4-Chloro-2,5-dimethoxyphenyl)-N-[(2-methoxyphenyl)methyl] ethanamine.

⁽⁷⁾ 2,5-Dimethoxy-4-iodophenethylamine.

Toxicology

No studies were identified that have examined the toxicity of 25I-NBOMe *in vitro*, in animals, or in humans.

The clinical features of acute toxicity associated with 25I-NBOMe use, as reported by the Member States, are provided in section 3.4.1 ‘non-fatal intoxications’ and Annex 2. These include a number of analytically confirmed cases (including those reported by Hill et al., 2013), and, in a subset, 25I-NBOMe was the only substance detected in the toxicology screen. Additional case reports/series from the United States were identified in the scientific literature (Kelly et al., 2012; Poklis et al., 2013; Rose et al., 2012; Rose et al., 2013; Stellpflug et al., 2013).

Dependence and abuse potential

No studies were identified that have examined the dependence and abuse potential of 25I-NBOMe *in vitro*, in animals or in humans.

Some self-reported experiences on user websites suggest re-dosing of 25I-NBOMe (e.g. Erowid, 2013a, 2013b) although the available information does not allow for further comment.

3.4.2. Characteristics of users

No studies were identified that examined the characteristics of users of 25I-NBOMe. The section below includes a discussion of the characteristics of users, which includes information from self-reported use from Internet drug discussion forums and related websites (hereafter ‘user websites’). As such, it is important to note that it is not possible to confirm the specific substance(s) used, nor the purity, dose, etc. Analysis of products containing new psychoactive substances that are sold on the drug market has shown that the composition can differ between that claimed by the retailer, and also over different geographical areas and time. Similar caveats apply to these types of information that have been provided in case reports/series unless biological and collected samples were taken and subjected to toxicological and forensic analysis. In addition, the information provided by patients in case reports/series, and that provided on user websites, should be regarded as illustrative only and not taken as representative of users of 25I-NBOMe in general. Finally, information from seizures, collected samples and user websites suggests that 25I-NBOMe has been commonly sold as a ‘legal’ replacement for LSD ⁽¹¹⁾ or sold directly as LSD on the illicit drug market. In the latter case users may be unaware that they are using 25I-NBOMe. Additional research is

required in order to examine to what extent the characteristics of 25I-NBOMe users overlap and/or reflect those who use LSD.

Route of administration, dose and drug regimens

Information provided by the Member States, and from case reports/series and user websites, suggests that the routes of administration for 25I-NBOMe include sublingual, buccal, nasal (insufflation and absorption of liquid solutions), oral, injection (intravenous and intramuscular), rectal and smoking.

Information from case reports/series and user websites suggests that a range of doses are used, and dosage may depend on the route of administration. Example doses reported on the Erowid user website include: ‘750 ug, sublingual’; ‘3 750 ug, sublingual’; ‘1 000 ug, sublingual’; ‘1 mg, buccal’; ‘1 blotter hit, sublingual/buccal’; ‘1 000 ug, insufflated’; ‘500–1 000 ug, smoked’ (Erowid, 2013a). Further examples are provided in the section on ‘non-fatal intoxications’ (above) (see also: Drug Enforcement Administration, 2013a, 2013b, 2013c; Erowid, 2013a, 2013b; Google, 2013a, 2013b; Hill et al., 2013 ⁽¹²⁾; Stellpflug et al., 2013).

Information from user websites suggests that 25I-NBOMe may be used on its own as well as in combination with other new psychoactive substances and/or controlled drugs (Erowid, 2013b; Google, 2013a, 2013b). In some of the non-fatal intoxications and deaths reported by the Member States and in case reports/series, other new psychoactive substances and/or controlled drugs were detected in biological samples (section 3.4.1 and Annex 2).

Subjective effects

No clinical trials were identified that have examined the subjective effects of 25I-NBOMe in humans; information is largely limited to that provided in case reports/series (see ‘non-fatal intoxications’, above) and self-reported experiences from user websites. Table 1 provides an overview of the duration of effects when 25I-NBOMe is taken by the sublingual/buccal routes and when insufflated, as reported by Erowid (2013a). Table 2 provides an overview of subjective effects of 25I-NBOMe, as reported by Erowid (2013a). In both cases the information was collated from users, research and other resources. No further details were provided on the methodology used to collate this information. Information

⁽¹²⁾ In six of the seven cases reported by Hill et al. (2013), it is not clear if the patients intended to purchase and use 25I-NBOMe. The paper reports that ‘Cases 2–7 had used the 25I-NBOMe together at a house party after it had been purchased via the Internet. The drug had arrived by mail as a powder enclosed in purple capsules and was labeled as “2C-B”. The ‘2C-B’ presumably refers to 2-(4-bromo-2,5-dimethoxyphenyl)ethylamine, a ring-substituted phenethylamine that is subject to international control.

⁽¹¹⁾ For example use of the street names ‘legal acid’ and ‘Hoffman’.

provided in case reports and case series of non-fatal intoxications associated with 25I-NBOMe appears to support some of these reports.

TABLE 1
Examples of self-reported duration of effects of 25I-NBOMe per route of administration (tentative), as reported by Erowid (2013a). No information on the doses that were used was provided

Duration of effects for 25I-NBOMe	Sublingual/buccal	Insufflated
Total duration	6–10 hrs	4–6 hrs
Onset	15–120 mins	5–10 mins
Coming up	30–120 mins	10–30 mins
Plateau	120–240 mins	60–120 mins
Coming down	60–240 mins	120–180 mins
After effects	1–7 days	1–7 days
Hangover/day after	?	?

TABLE 2
Examples of subjective effects of 25I-NBOMe, as reported by Erowid (2013a). No information on the doses that were used was provided.

Subjective effects of 25I-NBOMe	
Positive	Strong open and closed eye visuals, including trails, colour shifts, brightening, etc. Mood lift Euphoria Mental and physical stimulation Increase in associative and creative thinking Increased awareness and appreciation of music Life-changing spiritual experiences Erotic, sexual thoughts and sensations Feelings of love and empathy
Neutral	General change in consciousness Pupil dilation Difficulty focusing Unusual body sensations (facial flushing, chills, goose pimples, body energy) Change in perception of time, time dilation Slight increase in heart rate Yawning, especially when coming up Does not suppress appetite
Negative	Confusion Looping Scrambled communication Nausea Insomnia Looping, recursive, out of control thinking Paranoia, fear and panic Unwanted and overwhelming feelings Unwanted life-changing spiritual experiences Vasoconstriction, peripheral numbness, swelling of feet, hands, face

Availability and supply

A search of google.com using the search string ‘buy “25I-NBOMe”’ conducted by the EMCDDA in December 2013 for the Joint Report identified a number of online shops offering 25I-NBOMe for sale in both retail and wholesale quantities. In the former case, 25I-NBOMe appears to be sold as a ‘research chemical’.

Data from the National Drug and Alcohol Research Centre’s deep web monitoring programme of the Silk Road marketplace^(13,14) (Van Buskirk et al., 2013) identified 29 retailers in early February 2013 offering compounds from the ‘NBOMe family’ for sale. Details of the specific compounds offered, quantities, dosage forms and prices were not provided. The number of such retailers was relatively stable over the preceding four months of monitoring⁽¹⁵⁾. It is important to note that the study was conducted before Silk Road was seized and taken offline in October 2013 by the United States Federal Bureau of Investigation. No studies were identified that have examined the sale of ‘NBOMe’ compounds, including 25I-NBOMe, since Silk Road has reopened.

Seizure data and information from collected samples reported by the Member States suggest that 25I-NBOMe is sold as a drug in its own right and directly on the illicit drug market as lysergic acid diethylamide (LSD). No information was reported on the price of 25I-NBOMe when sold as LSD.

Prevalence of use

Data from prevalence surveys

No prevalence surveys were identified that have examined the use of 25I-NBOMe in the general population or in targeted populations.

The recent report on the ‘NBOMe’ compounds by the Advisory Council on the Misuse of Drugs in the United Kingdom noted that ‘there was no evidence of significant use in recent self-report user surveys [it is unclear in the report if it refers to 25I-NBOMe or “NBOMe” compounds] (Global Drug Survey,

⁽¹³⁾ The National Drug and Alcohol Research Centre (NDARC) is based at the University of New South Wales, Sydney, Australia.

⁽¹⁴⁾ Silk Road is an anonymous, international online marketplace that operates as a Tor hidden service. It uses the peer-to-peer payment network and digital currency Bitcoin for monetary transactions. The original Silk Road marketplace was seized and taken offline on 2 October 2013 by the United States Federal Bureau of Investigation. Since then a new version of Silk Road, sometimes described as ‘Silk Road 2.0’, has become operational. See Christin (2012) for an overview of the original Silk Road.

⁽¹⁵⁾ 29 retailers were identified in late October 2012; 33 in mid-November 2012; 27 in late November 2012; 29 in mid-December 2012; 24 in early January 2013; 24 in mid-January 2013. See Christin (2012) for a discussion of some of the market characteristics and dynamics of the original Silk Road.

2013), although there is evidence from club outreach services that “NBOMe” is a popular club drug and that it is mostly bought from the Internet’. The report also notes that the ‘prevalence of NBOMe compounds is very low in surveys with young adults conducted in nightclubs and festivals (personal correspondence with Professor Fiona Measham). They do not seem to be a drug of choice; they are not particularly prevalent and there is no evidence that they are associated with criminal behaviour, either through violent or acquisitive crime’ (Advisory Council on the Misuse of Drugs, 2013).

Information from seizures and collected samples suggests that 25I-NBOMe is being sold directly as LSD on the illicit drug market. It may therefore be relevant to consider the prevalence of LSD use. Among young adults (15- to 34-year-olds), lifetime prevalence of LSD use in Europe varies between countries, from 0.1 % to 5.4 % ⁽¹⁶⁾. Last year use of LSD in this age group ranges from 0 % to 1.7 % ⁽¹⁷⁾. Last 30 days prevalence of LSD use in this age group ranges from 0 % to 0.6 % ⁽¹⁸⁾. Lifetime prevalence of LSD (or other hallucinogen use, excluding hallucinogenic mushrooms) among 15- to 16-year-old school students ranged from 1 % to 5 % in 25 Member States and Norway with ESPAD ⁽¹⁹⁾ surveys in 2011, with only the Czech Republic reporting a prevalence level of 5 %.

3.5. Information on whether or not the new substance is currently under assessment, or has been under assessment, by the UN system — Article 5.2(e) of the Decision

The World Health Organization is the specialised United Nations agency designated for the evaluation of the medical, scientific and public health aspects of psychoactive substances under the Single Convention on Narcotic Drugs, 1961 and the Convention on Psychotropic Substances, 1971. On 10 October 2013 the World Health Organization informed the EMCDDA that 25I-NBOMe is currently under assessment and ‘the critical review report will be published only early next year (probably April)’.

Article 7.1 of Council Decision states that ‘no risk assessment shall be carried out in the absence of a Europol/EMCDDA Joint Report. Nor shall a risk assessment be carried out where the new psychoactive substance concerned is at an advanced stage of assessment within the United Nations system, namely once the WHO expert committee on drug dependence has published its critical review together with a written

⁽¹⁶⁾ For further details, including the countries reporting data, see: <http://www.emcdda.europa.eu/stats13#display:/stats13/gpstab1c>

⁽¹⁷⁾ For further details, including the countries reporting data, see: <http://www.emcdda.europa.eu/stats13#display:/stats13/gpstab2b>

⁽¹⁸⁾ For further details, including the countries reporting data, see: <http://www.emcdda.europa.eu/stats13#display:/stats13/gpstab3b>

⁽¹⁹⁾ European School Survey Project on Alcohol and other Drugs.

recommendation, except where there is significant new information that is relevant in the framework of this Decision’.

The Joint Report has been produced on the understanding that 25I-NBOMe is not at an advanced stage of assessment within the United Nations system.

3.6. The date of notification on the Reporting Form of the new psychoactive substance to the EMCDDA or to Europol — Article 5.2(f) of the Decision

The first official EMCDDA–Europol notification of 25I-NBOMe dates from 21 June 2012 from the Swedish National Focal Point. The Reporting Form details a seizure of seven green blotters (paper doses) seized by police in Borlänge on 31 May 2012. The identification was based on the analytical technique of GC-MS ⁽²⁰⁾ (library match).

25I-NBOMe was added to the list of new psychoactive substances monitored by the EMCDDA and Europol through the European Union early-warning system and a profile of the substance was created in the EMCDDA European Database on New Drugs (EDND). Since then, analytical details, background information and public health alerts have been exchanged between EMCDDA, Europol and the Member States on an ad hoc basis. The Commission and the EMA were kept duly informed.

3.7. Information on whether or not the new psychoactive substance is already subject to control measures at national level in a Member State — Article 5.2(g) of the Decision

Five Member States (Denmark, Latvia, Slovenia, Sweden and the United Kingdom) and Norway reported that 25I-NBOMe is subject to control measures under drug control legislation. In Denmark it is controlled by the generic classification of phenethylamines in the Executive Order on Euphoriant Substances. In Latvia it is controlled according to Cabinet Regulation 847 ‘Regulations regarding narcotic substances, psychotropic substances and precursors to be controlled in Latvia’. In Slovenia it was included in a Decree amending the Decree on classification of illicit drugs, Official Gazette of RS No. 62/2013. In Sweden it is controlled under the Narcotic Drugs Control Act (SFS 1992-860) and the Narcotic Drugs Control Ordinance (SFS 1994-1554). In the United Kingdom it was placed under a temporary class drug order in June 2013. In Norway it is controlled by the generic scheduling of phenethylamines introduced on 14 February 2013.

⁽²⁰⁾ Gas chromatography-mass spectrometry.

Four Member States (Austria, Hungary, Poland and Romania) reported that 25I-NBOMe is subject to control measures under legislation covering unauthorised supply of defined or qualifying new psychoactive substances. In Austria it is controlled under the New Psychoactive Substances Act. In Hungary it falls within the generic definition of phenethylamines in Schedule C of Government Decree 66/2012. In Poland, 25I-NBOMe falls under the definition of a ‘substitution drug’ under the Act amending the Act on Counteracting Drug Addiction and the Act on State Sanitary Inspection, 2010 and as such its marketing and production is penalised with a fine (administrative sanctions). In Romania it is controlled under Law 194 2011, which stipulates that all substances with psychoactive potential are subject to control until proven harmless by a special designated commission.

Two Member States (Finland and the Netherlands) reported that 25I-NBOMe is subject to control measures under medicines legislation. In Finland it has been controlled since 15 March 2013 under the Medicines Act (395/87). In the Netherlands, 25I-NBOMe sold in consumer amounts is treated as being a medicinal product and must comply with medicinal product legislation and general product safety legislation.

Sixteen Member States (Belgium, Bulgaria, Croatia, Cyprus, the Czech Republic, Estonia, France, Germany, Greece, Ireland, Italy, Lithuania, Luxembourg, Malta, Portugal and Slovakia) and Turkey have reported that 25I-NBOMe is not subject to control measures at the national level ⁽²¹⁾.

No information was provided regarding the control status of 25I-NBOMe in Spain.

3.8. Further information — Article 5.2(h) of the Decision

3.8.1. The chemical precursors that are known to have been used for the manufacture of the substance

No information was reported by the Member States, Turkey or Norway about the chemical precursors or manufacturing methods used to make 25I-NBOMe. Methods for the production of 25I-NBOMe are documented in the scientific literature.

⁽²¹⁾ Germany and Turkey reported that they intend to introduce control measures for 25I-NBOMe.

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

No studies were identified that have examined the mode and scope of established or expected use of 25I-NBOMe. Given the limited information currently available, much of the relevant information reported by the Member States as well as that from case reports/series published in the scientific literature and from user websites has been included in the previous sections. It is important to note in this respect that information from the Member States (such as seizures, collected samples, non-fatal intoxications) and user websites suggest that it is possible that 25I-NBOMe is commonly sold as a ‘legal’ replacement for LSD or sold as LSD directly on the illicit drug market. As a result, the mode and scope of use of 25I-NBOMe may, in part, overlap and/or reflect the mode and scope of use of LSD. Additional research is required to examine to what extent the mode and scope of 25I-NBOMe use overlap with and/or reflect those of LSD.

Settings of use

Information from the Member States and from case reports/series suggests that 25I-NBOMe may be used in a range of settings, including the home environment (where an individual is on their own or in the company of others) and recreational settings. In the latter case this includes informal settings (such as ‘house parties’) and organised events (such as ‘techno’ music events).

The recent report on the ‘NBOMe’ compounds by the Advisory Council on the Misuse of Drugs in the United Kingdom noted that ‘evidence from club outreach services [indicates] that “NBOMe” is a popular club drug and that it is mostly bought from the Internet’ (Advisory Council on the Misuse of Drugs, 2013).

3.8.3. Other use of the new psychoactive substance and the extent of such use, the risks associated with this use of the new psychoactive substance, including the health and social risks

No information was provided by the Member States, Turkey or Norway that indicated that 25I-NBOMe had any other use apart from legitimate scientific research and as an analytical reference standard.

Researchers have used radiolabelled ⁽²²⁾ 25I-NBOMe as a tool to study the serotonergic system in the brain (Ettrup et al.,

⁽²²⁾ Information on radiolabelled new psychoactive substances may be held by competent authorities at the national level. Such authorities may be able to provide essential information on the uses of such compounds, which may be important in assessing their use.

2010, 2011) as part of work that ultimately aims to further the understanding of the pathogenesis of human disease in which the serotonergic system may play a role. This includes research into its potential use as a tracer in Positron Emission Tomography imaging studies (Ettrup et al., 2010, 2011). Information on the management of health and safety hazards and risks that are associated with the use of such radiolabelled compounds was not provided by the Member States. However, it is possible that these are addressed under relevant national regulatory systems governing the use of radioactive materials.

From the available information it does not appear that 25I-NBOMe is used in the manufacture of a medicinal product in the European Union. However, the collection of information cannot be considered exhaustive in the absence of a European Union database on the synthetic routes of all medicinal products ⁽²³⁾.

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

4.1. Marketing authorisation

Twenty-four Member States, Iceland and Norway responded to the EMA's information request (see section 2). They reported that the new psychoactive substance 25I-NBOMe has not obtained a marketing authorisation ⁽²⁴⁾. The EMA also reported that the new psychoactive substance 25I-NBOMe has not obtained a marketing authorisation through the central authorisation procedure.

4.2. Application for a marketing authorisation

Twenty-four Member States, Iceland and Norway responded to the EMA's information request (see section 2). They reported that the new psychoactive substance 25I-NBOMe is

not the subject of an application for a marketing authorisation ⁽²⁴⁾. The EMA also reported that the new psychoactive substance 25I-NBOMe is not the subject of an application for a marketing authorisation through the central authorisation procedure.

4.3. Suspended marketing authorisation

Twenty-four Member States, Iceland and Norway responded to the EMA's information request (see section 2). They reported that there had been no cases of a suspended marketing authorisation that had been granted in respect of the new psychoactive substance 25I-NBOMe ⁽²⁴⁾. The EMA also reported that the new psychoactive substance 25I-NBOMe is not the subject of a suspended marketing authorisation through the central authorisation procedure.

5. Conclusions

25I-NBOMe is a substituted phenethylamine. It is a potent full agonist of the serotonin 5-HT_{2A} receptor and appears to have hallucinogenic effects. It has been available on the European Union drug market since at least May 2012 and has been detected in 23 Member States and Norway. Severe toxicity associated with its use has been reported in four Member States and one death associated with 25I-NBOMe has been analytically confirmed. Seven countries have reported that it has been sold as LSD or as a 'legal' alternative to LSD. On this basis the potential impact from the further spread of 25I-NBOMe (and related 'NBOMe' compounds) on public health is a key concern. We conclude that the health and social risks caused by the manufacture, trafficking and use of 25I-NBOMe, and the involvement of organised crime and possible consequences of control measures, could be thoroughly assessed through a risk assessment procedure in accordance with Article 6 of Council Decision 2005/387/JHA.

⁽²³⁾ I.e. products that have been granted a marketing authorisation, or where an application for a marketing authorisation has been made, or where the marketing authorisation has been suspended.

⁽²⁴⁾ Austria, Belgium, Croatia, the Czech Republic, Denmark, Estonia, Germany, Greece, Hungary, Iceland, Ireland, the Netherlands, Norway, Portugal, Slovenia, Spain, Sweden and the United Kingdom provided responses in relation to both human and veterinary medicinal products. Cyprus, Italy, Lithuania, Malta and Slovakia provided responses in relation to human medicinal products. France, Latvia and Poland provided responses in relation to veterinary medicinal products. In addition, the EMA provided information in relation to both human and veterinary medicinal products in respect of the central authorisation procedure.


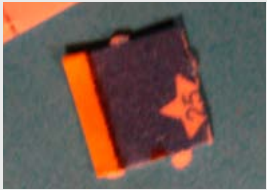

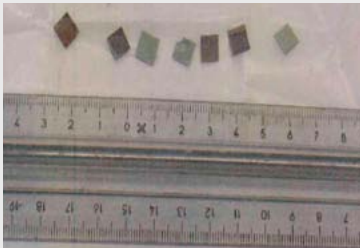


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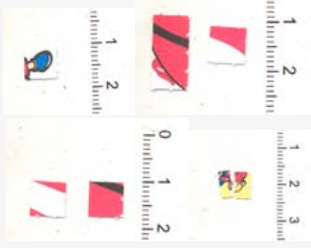


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Annex 1

Images of 25I-NBOMe from seizures and collected samples

Country	Image	Description
Austria		Collected sample, analysed in February 2013 1 blotter, sold as LSD (street name 'DOC'). Contents: 25I-NBOMe and an unknown substance. Collecting authority: ChEckIT!
Austria		Collected sample, analysed in February 2013 1 blotter, sold as LSD (street name 'Hoffmann'). Collecting authority: ChEckIT!
Austria		Collected sample, analysed in March 2013 3 blotters, sold as LSD (EUR 4–10). Contents: amphetamine (95 mg/g), caffeine (65 mg/g). Collecting authority: ChEckIT!
Italy		Seizure: January 2013 8 blotters, seized in Bologna. Seizing authority: State Police of Bologna
Latvia		Seizure: October 2013 124 impregnated paper fragments, seized in Daugavpils. Seizing authority: Forensic Service Department by State Police
Norway		Seizure: March 2012 250 squares of paper, seized in Stavanger. Seizing authority: police

Country	Image	Description
Norway		<p>Seizure: February 2013</p> <p>1 piece of blotter paper, consisting of 59 squares with size: 1 x 1 cm, seized in Ålesund. Seizing authority: customs</p>
Poland		<p>Seizures: May 2012</p> <p>5.4 g of powder (package declared as containing 1-Bromoindoline), seized in Kraków. Seizing authority: customs services Warsaw</p>
Poland		<p>Seizures: March and April 2013</p> <p>Stamps, seized in Łódź, Kraków and Katowice.</p>
Romania		<p>Seizure: October 2013</p> <p>Blotter paper, seized in Alba Iulia. Seizing authority: police</p>
United Kingdom		<p>Seizure: May 2013</p> <p>19 apparent LSD tabs, seized in north-east of Scotland.</p>

Annex 2

Non-fatal and fatal intoxications associated with 25I-NBOMe

Country	Date (gender, age)	Sample type	25I-NBOMe result ⁽²⁵⁾	Results for other substances ⁽²⁶⁾	Notes
Belgium	Aug 2013	Urine	+	None reported	Lowered consciousness, insufficient breathing, mydriasis, tachycardia (100/min).
Belgium	Aug 2013	Urine	+	None reported	Lowered consciousness, insufficient breathing, mydriasis, tachycardia (100/min).
Belgium	Aug 2013	Urine	+	None reported	Headache, lessened strength in 4 extremities, mydriasis, tachycardia (90/min), hypertension (150/85). Symptoms disappeared after being under observation for a couple of hours.
Sweden	2012–13	Not reported	+	None reported	25I-NBOMe detected in five non-fatal intoxications (no further details provided).
United Kingdom	Jan 2013 (M, 29)	Urine and plasma	+	2C-I, traces of amphetamine and methamphetamine	Severe clinical toxicity. Agitation, aggression, seizures, self-harming behaviour, tachycardia (160/min), hypertension (187/171), tachypnea, oxygen desaturation, pyrexia, rhabdomyolysis. Respiratory and metabolic acidosis, elevation of creatine kinase, impaired renal function. Anuria with a subsequent acute kidney injury. Acute respiratory distress syndrome. Discharged from intensive care unit on day 38, released from hospital on day 43.
United Kingdom	Jan 2013 (M, 20)	Urine and plasma	+	2C-I, traces of amphetamine and methamphetamine	Severe clinical toxicity. Convulsions (predominantly affecting face), high agitation, poor respiratory effort and clenched jaw. Tachycardia, hypertension, tachypnea, urinary retention, pupillary dilatation, pyrexia, elevated creatine kinase. Visual hallucinations. Released from hospital on day 5.
United Kingdom	Jan 2013 (M, 20)	Urine and plasma	+	2C-I, traces of amphetamine and methamphetamine	Palpitations, visual hallucinations. Pupillary dilatation, 3 inducible beats of ankle clonus, sinus tachycardia. Discharged on the day of admission.
United Kingdom	Jan 2013 (M, 20)	Urine and plasma	+	2C-I, traces of amphetamine and methamphetamine	Palpitations, visual and auditory hallucinations. Tachycardia, pupillary dilatation. Discharged on the day of admission.
United Kingdom	Jan 2013 (M, 19)	Plasma	+	Traces of amphetamine and methamphetamine	Euphoria with visual and auditory hallucinations, violent and agitated behaviour. Discharged after 15 hours.
United Kingdom	Jan 2013 (M, 22)	Plasma	+	Traces of amphetamine and methamphetamine	Nausea and visual hallucinations. Tonic-clonic seizure. Agitated and aggressive behaviour. Creatine kinase elevated. Discharged on the day of admission.
United Kingdom	Jan 2013 (M, 21)	Plasma	+	Traces of amphetamine and methamphetamine	Initial chaotic feeling followed by agitation, hallucinations and violent behaviour. Tachycardia and pyrexia. Discharged after 15 hours.
United Kingdom	May 2013 (M, 22)	Blood (post-mortem)	+	Amphetamine, ketamine, lignocaine, 5-MeO-DiPT, DOI, 25C-NBOMe and 2C-I	Fatal intoxication. Cause of death: drowning.

⁽²⁵⁾ A '+' in this column indicates 25I-NBOMe was detected but no quantification was provided.

⁽²⁶⁾ 2C-I is 2,5-dimethoxy-4-iodophenethylamine.

5-MeO-DiPT is 5-methoxy-diisopropyl-tryptamine.

DOI is 2,5-dimethoxy-4-iodoamphetamine.

25C-NBOMe is 2-(4-chloro-2,5-dimethoxyphenyl)-N-[(2-methoxyphenyl)methyl]ethanamine.

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