

# ACMD

## Advisory Council on the Misuse of Drugs

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Home Secretary  
Rt Hon. Theresa May MP  
Home Office  
2 Marsham Street  
London  
SW1P 4DF

29 May 2013

Dear Home Secretary,

I am writing to formally request that you consider laying a temporary class drug order (TCDO) pursuant to section 2A of the Misuse of Drugs Act 1971 on the following two groups of novel psychoactive substances (NPS). We consider the laying of TCDOs is appropriate as a pre-emptive measure in advance of the summer music festival season. Both classes of drugs have been associated with serious harm and drug-related deaths.

### **‘Benzofury’ compounds**

5- and 6-APB and related substances are phenethylamine-type materials, related to ecstasy (MDMA). There have been several deaths and hospitalisations in the UK associated with these NPS, although poly-substance use often complicates the case. Research indicates that there is a potential risk of cardiac toxicity associated with the long-term use of 5- and 6-APB. Anecdotal user reports suggest that the consumption of these substances can cause insomnia, increased heart rate and anxiety, with some users reporting MDMA like symptoms. The related compound 5-IT has been subject to an EMCDDA-Europol joint report and an EMCDDA risk assessment exercise. [[www.emcdda.europa.eu/publications/joint-reports/5-IT](http://www.emcdda.europa.eu/publications/joint-reports/5-IT)]

The substances recommended for control are:

- 5- and 6-APB: (1-(benzofuran-5-yl)-propan-2-amine and 1-(benzofuran-6-yl)-propan-2-amine) and their N-methyl derivatives.
- 5- and 6-APDB: (1-(2,3-dihydro-1-benzofuran-5-yl)-propan-2-amine and 1-(2,3-dihydro-1-benzofuran-6-yl)-propan-2-amine), and their N-methyl derivatives
- 5- and 6-IT: (2-(1*H*-indol-5-yl)-1-methylethylamine and 2-(1*H*-indol-6-yl)-1-methylethylamine).

#### **‘NBOMe’ compounds**

The NBOMe substances are highly potent hallucinogens (doses are in micrograms). At these levels of potency, attempting to use powder or liquid dosage forms is dangerous, as there is a great risk of overdose related to errors in user dose measurement. The materials, like LSD, act via the 5-HT<sub>2A</sub> receptors and are probably regarded as alternatives to LSD. The ACMD recommends urgent action because of the high risk of overdose with these potent drugs, and the report from SOCA of large quantities entering the UK.

The substances recommended for control are:

- 2-(2,5-Dimethoxy-4-methylphenyl)-N-[(2-methoxyphenyl)methyl]ethanamine
- 2-(4-Bromo-2,5-dimethoxyphenyl)-N-[(2-methoxyphenyl)methyl]ethanamine
- 2-(4-Iodo-2,5-dimethoxyphenyl)-N-[(2-methoxyphenyl)methyl]ethanamine
- 2-(4-Chloro-2,5-dimethoxyphenyl)-N-[(2-methoxyphenyl)methyl]ethanamine

I have pleasure in providing the ACMD’s consideration of the evidence concerning these two groups of novel psychoactive substances in the attached reports.

In providing this advice I would like to convey my thanks to the Home Office for its provision of information obtained via the Drugs Early Warning System (DEWS) and the Forensic Early Warning System (FEWS), and to the Serious Organised Crime Agency (SOCA) for providing information by means of their ENDORSE report on these compounds.

Yours sincerely,



Professor Les Iversen  
ACMD Chair

Cc Jeremy Browne, Minister of State for Crime Prevention

# ACMD

Advisory Council on the Misuse of Drugs

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**Title: 6-APB and 5-APB: A review of the evidence of use and harm**

## Introduction

### The Issue

1. In early June 2012 the ACMD became aware of a suspected 6-APB (“Benzofury”)-related death at the Scottish RockNess Music Festival, although this turned out not to be related to 6-APB, ACMD was prompted to review this series of chemicals. This paper reviews the evidence of misuse and harm in relation to the benzofuran-type substances. The evidence concerning these substances, and closely related analogues was considered by the ACMD at meetings of the Novel Psychoactive Substances Working Group and by the full Council in 2012 and 2013. The ACMD also requested information from the Home Office Drugs Early Warning System (DEWS). At an ACMD Council meeting on May 16, 2013 it was agreed that recommendation be made for a TCDO for these substances and some closely related analogues.

### Background

2. Two materials, 5- and 6-APB: (1-(benzofuran-5-yl)-propan-2-amine and 1-(benzofuran-6-yl)-propan-2-amine) and their N-methyl derivatives are being sold as “Benzofury” (the colloquial name presumably refers to the materials being benzofurans) (<http://www.officialbenzofury.com/>). They are phenethylamine-type materials, related to methylenedioxyphenethylamines such as the Class A drugs ecstasy (MDMA) and 3,4-methylenedioxyamphetamine (MDA). 5- and 6-APB are very similar to each other in structure (structural isomers). Benzofuran analogues of MDA were originally synthesised in the 1990s by David Nichols at Purdue University who was examining structure-activity relationships of ecstasy-type materials (Monte, et al., 1993).
3. Chemically, 5- and 6-APB molecules are two steps away from MDA (in the methylenedioxy ring, one oxygen is replaced by a carbon and a double bond is present). As a result of these differences, they fall outside the generic controls on phenethylamine derivatives within the Misuse of Drugs Act 1971.
4. The materials are being marketed as a legal form of Ecstasy (<http://rclondon.co.uk/benzofury>). They are on sale as powder or as tablets, although the latter are always referred to as “pellets”, to avoid any overt suggestion that they are for human use. Packaging usually includes statements that the materials are research chemicals and not for human consumption. “Pellets” claimed to contain a 120 mg dose are being sold at about £10 per pellet, with reductions for multi-unit purchases. Powder is being sold for about £35 per gram.
5. Reports from police seizures from head shops around the country, and from the Serious Organised Crime Agency (SOCA) in 2011 and 2012 indicate that many products which claimed to contain “benzofury” in fact contained other substances, these included piperazines (Class C), cathinone derivatives (Class B), benzocaine (anaesthetic active pharmaceutical ingredient), diphenylprolinol (2DPM), and caffeine rather than 5- or 6-APB. Samples which did contain 5- and 6-APB were found in many different formats, sometimes in combination with other substances, including methiopropamine and caffeine.

6. In 2011, the UK's Forensic Early Warning System (FEWS) identified these two materials as likely to be of interest and funded the development of certified reference standards to support forensic laboratories in their work. When these standards were received by forensic laboratories, it was found that standard analytical techniques cannot distinguish between the two materials, so laboratory reports normally refer to materials being identified as "5- or 6-APB". Vendors are therefore unlikely to be confident about which form they are selling.
7. There is analytical evidence of use of these compounds in the UK. For example, 5-APB was found in analyses of pooled urine from urinals in both London and the North West of England in July 2012 (Wood et al., 2013 and Archer et al., 2013).
8. A positional analysis of the side chain of both compounds purchased from internet sites has recently been published by Stanczuk et al., (2013).
9. 1-(Benzofuran-5-yl)propan-2-amine (5-APB) was patented by Briner et al., (2000), and has been sold as a designer drug since 2010. Anecdotal user reports suggest that it has emphathogenic and stimulant effects and that 5-APB is stronger than 6-APB.

### **Pharmacology**

10. Iversen, L. et al. (2013), reported that 5- and 6-APB are potent triple monoamine transport inhibitors for dopamine (DAT), norepinephrine (NET) and serotonin (SERT) in vitro, with highest potencies for DAT and NET. Their potencies on the monoamine transporters are similar to those of 3,4-methylenedioxy-methamphetamine ("Ecstasy"). 5- and 6-APB also have high affinities for 5-HT<sub>2B</sub> and  $\alpha$ <sub>2C</sub> receptors. Furthermore, functional assays revealed that both compounds were potent full agonists at the 5-HT<sub>2B</sub> receptor, suggesting that there is a potential risk of cardiac toxicity associated with their long-term use, as has been reported for other 5-HT<sub>2B</sub> receptor agonists, such as fenfluramine (Rothman et al, 2000).

### **Toxicology**

11. A toxicology report from Preston Coroners described a death where a young man consumed 6-APB, which was later confirmed in his urine together with the anti-depressant mirtazapine. The paramedics unsuccessfully attempted resuscitation and were surprised at the elevated body temperature of the deceased 20 min after the resuscitation had finished. Such stimulants are known to cause elevated temperature (hyper-pyrexia).
12. There is a case report of toxicity associated with the use of 6-(2-aminopropyl)-benzofuran (6-APB) [Chan WL 2013; In press]. This case report describes a 21-year old man who presented to an Emergency Department with acute agitation and paranoia following the self-reported use of 6-APB purchased from the Internet and cannabis. Subsequent screening of his urine confirmed the use of 6-APB (urine concentration 2000 ng/mL); also detected were metabolites of the synthetic cannabinoid receptor agonist JWH-122, the tetrahydrocannabinol metabolite 11-nor-9-carboxy-delta-9-tetrahydrocannabinol, 6-(2-methylaminopropane)benzofuran (6-

MAPB) (30 ng/mL), amphetamine (90 ng/mL), chloroquine (5 ng/mL), ketamine metabolites (3 ng/mL), and ephedrine (800 ng/mL). Since there were a number of other substances detected, it is possible that some or all of these other substances may have contributed to the clinical features seen in this individual.

13. The National Poisons Information Service TOXBASE reported 65 telephone enquiries from health professional relating to 5- or 6-APB in the period from March 2009 to March 2013. In the same period there were 741 accesses to TOXBASE online for information on these compounds.
14. The Scottish Borders Alcohol and Drugs Partnership reported a death in 2012 where a young male had consumed “Benzofury”. 2-APB (a structural isomer), methiopropamine and cocaine were listed in the pathology report as the cause of death (2-APB is normally only seen as an impurity in samples of 5- and 6-APB). From the same party 7 other individuals were admitted to hospital but later discharged. Symptoms were tachycardia, increased blood pressure and hyperpyrexia.
15. Scottish Fatalities Unit (North) reported 2 deaths in 2012, one involving 6-APB, 5-IT and ecstasy, the other involving 6-APB and 5-IT only.
16. Seetohul, et al., (2012) reported two deaths involving 5-IT in the UK. In July 2012, the Swedish authorities also reported that 5-IT had been associated with a series of deaths in Sweden.
17. Anecdotal user reports suggest that the consumption of these substances can cause insomnia, increased heart rate and anxiety. Some users report MDMA like symptoms.
18. Detectable levels of 6-APB/5-APB were found in one patient who had allegedly consumed the controlled substance methoxetamine and reported with toxic reactions to an A&E department (Wood et al., 2012).

### **Related Compounds**

19. 5- and 6-APB are closely related to 3,4-methylenedioxyamphetamine (MDA) – see structures in Annex A. Paragraphs 14-17 below describe substances related to 5- and 6-APB which ACMD recommends including in a TCDO, all are currently available for sale in the UK, and carry the potential harms associated with 5- and 6-APB and ecstasy (MDMA).
20. Closely-related are 1-(2,3-dihydro-1-benzofuran-5-yl)propan-2-amine (5-APDB) and 1-(2,3-dihydro-1-benzofuran-6-yl)propan-2-amine (6-APDB) which are the dihydro-derivatives of 5- and 6-APB, synthesised by Monte et al (2003), in which the double bond in the five membered ring is saturated. They have been offered for sale as ecstasy-like “legal highs”.
21. Indanylamino propane (IAP) or 5-(2-aminopropyl-2,3-dihydro-1H-indene (5-APDI) is a further material in this sequence, where both oxygen atoms of MDA have been replaced by methylene groups. This compound has also been offered as a “legal high” and, although reported to have much weaker effects than MDA when used on its own,

is claimed to mimic the effects of Ecstasy when used in combination with a stimulant such as amphetamine.

22. Related materials of interest include 5- and 6-(2-aminopropyl)indole (5- and 6-API), which have structures similar to 5- and 6-APB except that the oxygen atom in the heterocyclic ring is replaced by a nitrogen atom. 5-API is also known as 5-IT and is being sold as a “legal high” [<http://www.purechemicals.net/buy-5-it-87-c.asp>]. It is a positional isomer of alpha-methyltryptamine. Shulgin (1997) reported that an oral dose of 20 milligrams of 5-IT “is a long-lived stimulant producing increased heart-rate, anorexia, diuresis, and slight hyperthermia for about twelve hours”. Concern about this material at European level has resulted in the preparation of an EMCDDA-Europol joint report :[[www.emcdda.eu/publications/joint-reports/5-IT](http://www.emcdda.eu/publications/joint-reports/5-IT)]
23. The N-methyl analogue of 5-APB is offered for sale as “5-MAPB” [[www.buyresearchchemicals.net](http://www.buyresearchchemicals.net); [www. buckledbonzi](http://www.buckledbonzi.com)]. Structurally this material is closer to Ecstasy than the APB’s. The price is the same as for APB’s.

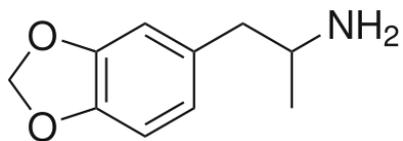
### **Recommendation**

24. Pursuant to Section 2B(6) of the Misuse of Drugs Act 1971, the ACMD consider that, in the case of the compounds listed below, they are drugs that are being, or are likely to be, misused, and that misuse is having, or is capable of having, harmful effects. The ACMD recommends that the following group of novel psychoactive substances are placed under a TCDO.
  - 5- and 6-APB: (1-(benzofuran-5-yl)-propan-2-amine and 1-(benzofuran-6-yl)-propan-2-amine) and their N-methyl derivatives.
  - 5- and 6-APDB: (1-(2,3-dihydro-1-benzofuran-5-yl)-propan-2-amine and 1-(2,3-dihydro-1-benzofuran-6-yl)-propan-2-amine), and their N-methyl derivatives
  - 5- and 6-IT: (2-(1H-indol-5-yl)-1-methylethylamine and 2-(1H-indol-6-yl)-1-methylethylamine).

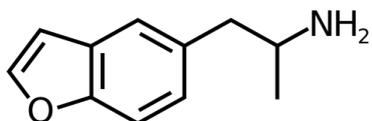
## References

- Archer JRH, Dargan PI, Chan WL, Hudson S, Wood DM (2013). Variability in recreational drugs and novel psychoactive substances detected in anonymous pooled urine samples from street pissoirs (street urinals) over time: A technique to monitor trends in drugs use. *Clin Toxicol (Phila)* 2013; 51:343-344.
- Baron, M.; Elie, M.; Elie, L. (2011). An analysis of legal highs-do they contain what it says on the tin? *Drug Testing and Analysis* 3: 576-581.
- Briner, K.; Burkhart, J. P.; Burkholder, T. P.; et al., (2000). Preparation of aminoalkylbenzofurans as 5-HT<sub>2C</sub> agonists *PCT Int. Appl. WO* 2000044737 A1 20000803.
- Iversen, L. et al., (2013). Neurochemical profiles of some novel psychoactive substances. *Eur. J. Pharmacol.* 700: 147-151
- Monte AP, Marona-Lewicka D, Cozzi NV, Nichols DE. (1993). Synthesis and pharmacological examination of benzofuran, indan, and tetralin analogues of 3,4(methylenedioxy)amphetamine. *J Med Chem.* 36:3700-6.
- Rothman,R.B., Baumann M.H., Savage,J.E. et al. 2000. Evidence for possible involvement of 5-HT(2B) receptors in the cardiac vulvulopathy associated with fenfluramine and other serotonergic medications. *Circulation* 102, 2836-41.
- Seetohul, L.N., Maskell, P.D., De Paoli, G., Pounder, D.J. (2012).Deaths associated with new designer drug 5-IT. *BMJ.* 345:e5625
- Shulgin, A. (1997) "TiHKAL: Tryptamines I have known and loved", Berkeley, Transform Press.
- Stanczuk A, Morris N, Gardner EA, Kavanagh P. (2013) Identification of (2-aminopropyl)benzofuran (APB) phenyl ring positional isomers in Internet purchased products. *Drug Test Anal.* 5: 270-6.
- Wood, D.M., Davies, S., Puchnarewicz, M., Johnston, A., Dargan P.I. (2012). Acute toxicity associated with the recreational use of the ketamine derivative methoxetamine. *Eur J Clin Pharmacol.* 68: 853-6.
- Wood DM, Archer JRH, Measham F, Hudson S, Dargan PI. Detection of use of novel psychoactive substances by attendees at a music festival in the North West of England. *Clin Toxicol (Phila)* 2013;51:340-341

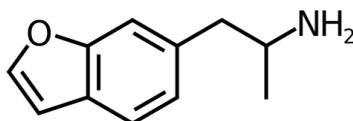
**Annex A - Structures of MDA, 5- and 6-APB and related materials, including '5-IT'**



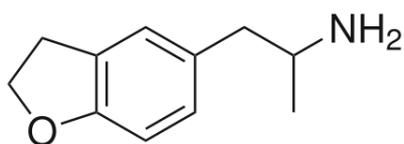
3,4-Methylenedioxyamphetamine (MDA); Class A, Schedule 1



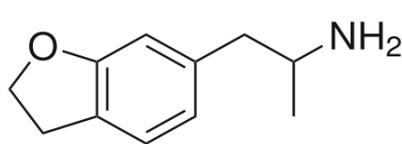
5-(2-Aminopropyl)benzofuran (5-APB)



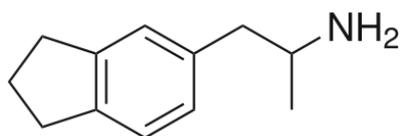
6-(2-Aminopropyl)benzofuran (6-APB)



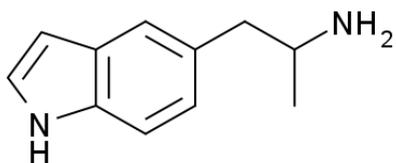
5-(2-Aminopropyl)-2,3-dihydrobenzofuran (5-APDB)



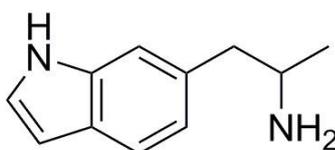
6-(2-Aminopropyl)-2,3-dihydrobenzofuran (6-APDB)



5-(2-Aminopropyl)-2,3-dihydro-1H-indene (5-APDI) or Indanylamino propane (IAP)



5-(2-Aminopropyl)indole (5-API or '5-IT')



6-(2-Aminopropyl)indole (6-API)

# ACMD

Advisory Council on the Misuse of Drugs

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**Title: 'NBOMe' compounds: A review of the evidence of use and harm**

## Introduction

1. In early 2013 the ACMD became aware of a group of novel psychoactive substances (NPS) in the UK, the 'NBOMe' compounds. This paper reviews the evidence of misuse and harm in relation to the 'NBOMe' compounds. The evidence concerning these substances, and closely related analogues was considered by ACMD at meetings of the Novel Psychoactive Substances Working Group in April 2013 and by the full Council in May. The ACMD also requested information from the Home Office Drugs Early Warning System (DEWS). At an ACMD Council meeting on May 16, 2013 it was agreed that recommendation be made for a TCDO for these substances and some analogues related to these compounds.

## Chemistry and Pharmacology

2. The NBOMe materials are variants of the 2C-X series of psychoactive phenethylamines described by Shulgin (2000) in his book 'PIHKAL'. The 2C-X materials are 2,5-dimethoxyphenethylamines with a variety of substituents at the 4-position. The 2C-X materials are controlled under the Misuse of Drugs Act 1971 as Class A drugs. The NBOMe materials were first reported in 2003 by Ralph Heim at the Free University of Berlin (Heim, 2003). David Nichols of Purdue University further developed the 2C-X materials formed by adding a 2-methoxybenzyl (MeOB) onto the nitrogen (N) of the phenethylamine (hence presumably 'NBOMe') (Nichols et al., (2008); Braden et al., (2006)). The full chemical name of 25I-NBOMe, for example, is 4-iodo-2,5-dimethoxy-N-(2-methoxybenzyl)phenethylamine.

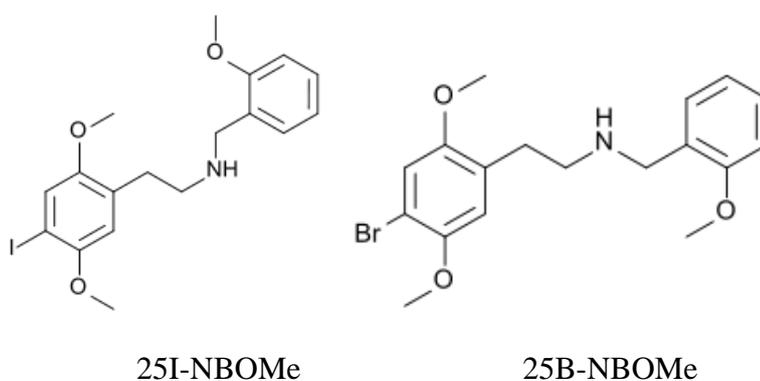


Figure 1. The structure of 25I-NBOMe and 25B-NBOMe

3. This modification significantly enhances the potency of the phenethylamines so, for example, whilst a dose of 2C-I is around 20 milligrams, a dose of the NBOMe form ('25I-NBOMe') is less than one milligram (Blaazer et al., 2008). The common dose is typically 50-100 µg. At these levels of potency, attempting to use powder or liquid dosage forms is dangerous, as there is a greater risk of overdose related to errors in user dose measurement. Some suppliers have therefore opted for selling it in the form of pre-loaded paper doses (blotters), similar to LSD 'tabs', so that users can take prepared dosage units, or as a spray (<http://www.lizardlabs.co.uk/>). The materials are

potent hallucinogens, which act via the 5-HT<sub>2A</sub> receptors (Juncosa et al., 2013; Nichols et al., 2008), and so are probably regarded as alternatives to LSD. The – NBOMe compounds are reported to be inactivated if taken orally and so are usually taken by holding in the mouth (sub-lingual or buccal) or via the nasal membranes. Some Internet suppliers claim to offer the materials as a complex with hydroxypropyl-beta-cyclodextrin to improve their bioavailability.

4. The common and street names include: Bom-25; 2C-I-NBOMe; 25I-NBOMe; 25I; N-Bomb; and Smiley Paper.



Figure 2 . A powder sample of 25I-NBOMe and pre-loaded paper doses on ‘tabs’

### Legislation

5. The Misuse of Drugs Act, Schedule 2 Part 1 (c) controls the following substances of the phenethylamine family as class A substances:

*“any compound (not being methoxyphenamine or a compound for the time being specified in sub-paragraph (a) above) structurally derived from phenethylamine an N-alkylphenethylamine,  $\alpha$ -methylphenethylamine, an N-alkyl- $\alpha$ -methylphenethylamine,  $\alpha$ -ethylphenethylamine, or an N-alkyl- $\alpha$ -ethylphenethylamine by substitution in the ring to any extent with alkyl, alkoxy, alkylendioxy or halide substituents, whether or not further substituted in the ring by one or more other univalent substituents.”*

6. The NBOMe modification has the effect of making the materials outside the scope of the current UK generic controls on phenethylamines.

### Use and prevalence

7. Data on the use of 25I-NBOMe is not included in the Crime Survey for England and Wales or other subpopulation surveys such as MixMag or in-situ club/festival surveys.
8. The ACMD secretariat emailed members of the Novel Psychoactive Substances Working Group for information on the substances and in response received the following information:
  - None of these compound have been identified and included in the npSAD mortality database (14/03/13)

- The substances seem to have been promoted more recently, e.g. [:http://www.lizardlabs.co.uk/category/54-25i-nbome.aspx](http://www.lizardlabs.co.uk/category/54-25i-nbome.aspx) (14/03/13)
9. According to a SOCA report to the ACMD on May 16th, 2013 there is evidence that sizeable amounts of 25I-NBOMe have already arrived in the UK for distribution in blotter format. This appeared to have arrived via a well-established link to producers of the drug in China, from where significant quantities of this and other NPS continue to be acquired in the UK. 25I-NBOMe is potentially a highly profitable drug, since a relatively small amount of powder can generate many doses at prices between £2-£4 (up to 20 million from 1kg). The substance may commonly be mistaken for LSD by sellers and users.

### **Toxicology**

10. Users report that 25I-NBOMe produces effects that can last between 6 and 10 hours if taken sublingually. These self-reported, anecdotal, user reports included the following effects: euphoria, mental/physical stimulation, feelings of love/empathy, a change in consciousness and unusual body sensations. Highly negative effects included confusion, shaking, nausea, insomnia, paranoia and unwanted feelings .
11. On February 28, 2013 the UK Focal Point reported the detection of the new psychoactive substance 25I-NBOMe linked to a series of 7 non-fatal intoxication cases in January 2013. The patients, all young adult males, presented to hospitals in the north east of England with toxicity after recreational drug use. Clinically observed features included tachycardia (n=7), hypertension (n=4), agitation and aggression (n=6), visual and auditory hallucinations (n=6), seizures (n=2), hyperpyrexia (n=3), clonus (n=2), elevated white blood cell count (n=2) and metabolic acidosis (n=3). Two patients required admission to intensive care. 1 patient had severe rhabdomyolysis leading to renal failure, and all of the cases had elevated creatine kinase to varying degrees. Routes of administration were insufflation (4), oral (1) and intravenous (1). LC-MS-MS analysis was performed at the Medical Toxicology Centre, Newcastle University, with 25I-NBOMe identified as the main active substance in the plasma and urine in all 7 cases. One patient had intravenously injected a liquid form of the drug was purchased from a dealer. The six other patients bought the drug from the internet and as a powder inside capsules. Some users swallowed the capsules, whilst others broke them open and insufflated the powder.
12. Northumbria Police reported a hospital case in December 2012 who had binged on alcohol and other substances including 25I-NBOMe (significant amount was found in blood). The patient had impaired kidney function, needed sedation and had to be placed on a ventilator.
13. Surrey Police reported the death of an 18 year old man in February 2013, thought to be related to 25CI-NBOMe – awaiting confirmation.

### **International**

14. In 2012, there was a cluster of hospitalisations associated with 25I-NBOMe in Virginia (USA) (Rose et al., 2013)<sup>1</sup>. There have also been fatalities alleged to be linked to this material<sup>2</sup>. There are internet forum reports of an American ‘chemist’ who imported 2C-I from Europe and then converted it into the more potent NBOMe form before transferring it onto paper doses (apparently with fatal results)<sup>3</sup>. The drug is believed to have been responsible for several deaths. In June 2012, two teenagers in Grand Forks, North Dakota and East Grand Forks, Minnesota fatally overdosed on a substance that was allegedly 25I-NBOMe.<sup>4</sup> A 21-year-old man from Little Rock, Arkansas also died of an apparent overdose in October 2012 after taking a liquid drop of the drug nasally at a music festival.<sup>5</sup>
15. An 18 year old in Scottsdale, AZ died on January 25, 2013 after ingesting 25I-NBOMe sold as LSD. After a toxicology screen the Maricopa County Medical Examiner's Office ruled the cause of death to be acute 25I-NBOMe poisoning. No alcohol, prescription drugs or other illicit drugs were found by the post-mortem toxicology. It is the suspected cause of death in another case in Scottsdale on April 29, 2013, also involving an 18 year old <sup>2</sup>.
16. A similar material (25C-NBOMe) was recently encountered in New Zealand as a ‘legal high’, and was rapidly made illegal there.  
[\[http://www.sciencemediacentre.co.nz/2012/03/13/legal-high-dime-not-so-legal/\]](http://www.sciencemediacentre.co.nz/2012/03/13/legal-high-dime-not-so-legal/) include some useful expert comment about these types of material:
17. 25I-NBOMe has been implicated in a number of deaths in South Australia, one man died in March 2012 after beating himself to death against objects including trees and poles, after consumption of 25I-NBOMe and related substances <sup>2</sup>.

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<sup>1</sup>[http://www.erowid.org/chemicals/2ci\\_nbome/2ci\\_nbome\\_death.shtml](http://www.erowid.org/chemicals/2ci_nbome/2ci_nbome_death.shtml)

<sup>2</sup><http://www.news.com.au/national-news/south-australia/new-hallucinogenic-drug-25b-nbome-and-25i-nbome-led-to-south-australian-mans-bizarre-death/story-fndo4dzn-1226472672220>

<sup>3</sup>[http://www.inforum.com/event/article/id/365948/publisher\\_ID/1/](http://www.inforum.com/event/article/id/365948/publisher_ID/1/)

<sup>4</sup> [Breaking Bad: Digital Drug Sales, Analog Drug Deaths. Craig Malisow, Houston Press, March 13, 2013](#)". houstonpress.com. 2013-0

<sup>5</sup>[21-year-old dies after one drop of 5. new synthetic drug at Voodoo Fest. Naomi Martin, NOLA, November 1, 2012](#)". NOLA.com. 2012-11-01. Retrieved 2012-11-02.

## Recommendation

18. Pursuant to Section 2B(6) of the Misuse of Drugs Act 1971, the ACMD consider that, in the case of the compounds listed below, they are drugs that are being, or are likely to be, misused, and that misuse is having, or is capable of having, harmful effects. The ACMD recommends that the following group of novel psychoactive substances are placed under a TCDO:

- 2-(2,5-Dimethoxy-4-methylphenyl)-N-[(2-methoxyphenyl)methyl]ethanamine
- 2-(4-Bromo-2,5-dimethoxyphenyl)-N-[(2-methoxyphenyl)methyl]ethanamine
- 2-(4-Iodo-2,5-dimethoxyphenyl)-N-[(2-methoxyphenyl)methyl]ethanamine
- 2-(4-Chloro-2,5-dimethoxyphenyl)-N-[(2-methoxyphenyl)methyl]ethanamine

## References

- Blaazer, Antoni R.; Smid, Pieter; Kruse, Chris G. (2008) Structure-activity relationships of phenylalkylamines as agonist ligands for 5-HT<sub>2A</sub> receptors. *ChemMedChem* (2008), 3(9), 1299-1309.
- Braden, M. R.; Parrish, J. C.; Naylor, J. C.; Nichols, D. E. (2006). Molecular interaction of serotonin 5-HT<sub>2A</sub> receptor residues Phe339(6.51) and Phe340(6.52) with superpotent N-benzyl phenethylamine agonists. *Molecular Pharmacology* 70: 1956-1964.
- Heim, R (2003). "Synthese und Pharmakologie potenter 5-HT<sub>2A</sub>-Rezeptoragonisten mit N-2-Methoxybenzyl-Partialstruktur. Entwicklung eines neuen Struktur-Wirkungskonzepts." (in German). [diss.fu-berlin.de.]
- Nichols, David E.; Frescas, Stewart P.; Chemel, Benjamin R.; Rehder, Kenneth S.; Zhong, Desong; Lewin, Anita H. (2008). High specific activity tritium-labeled N-(2-methoxybenzyl)-2,5-dimethoxy-4-iodophenethylamine (INBMeO): A high-affinity 5-HT<sub>2A</sub> receptor-selective agonist radioligand. *Bioorganic & Medicinal Chemistry* (2008), 16(11), 6116-6123.
- Juncosa, J. I.; Hansen, M.; Bonner, L. A.; Cueva, J. P.; Maglathlin, R.; McCorvy, J. D.; Marona-Lewicka, D.; Lill, M. A.; Nichols, D. E. (2013) Extensive Rigid Analogue Design Maps the Binding Conformation of Potent N-Benzylphenethylamine 5-HT<sub>2A</sub> Serotonin Receptor Agonist Ligands. *Chemical Neuroscience* 4: 96-109.
- Rose SR, Poklis JL, Poklis A. (2013). A case of 25I-NBOMe (25-I) intoxication: a new potent 5-HT<sub>2A</sub> agonist designer drug. *Clin Toxicol (Phila)*. 51:174-7.
- Shulgin, A. (2000) "PiHKAL – Phenylethylamines I have known and loved", Berkeley, Transform Press