

ACMD

Advisory Council on the Misuse of Drugs

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Karen Bradley MP
Minister for Preventing Abuse, Exploitation and Crime
Home Office
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16 March 2016

Dear Minister,

RE: ACMD review of alkyl nitrites (“poppers”)

On 23 February 2016 you commissioned the Advisory Council on the Misuse of Drugs (ACMD) to provide its assessment on the harms and psychoactivity of alkyl nitrites.

The ACMD is grateful for this opportunity to look more deeply into the issues surrounding alkyl nitrites. I am pleased to attach the ACMD's first bespoke piece of advice on alkyl nitrites, which is also the first opportunity the ACMD have had to assess the psychoactivity and mode of action of alkyl nitrites in the context of the Psychoactive Substances Act 2016, as enacted.

The ACMD previously considered the harms of “poppers” in our 2011 report on Novel Psychoactive Substances and this report provides an updated assessment of harms.

Yours sincerely,



**Professor Les Iversen
(Chair of ACMD)**

cc Rt. Hon. Theresa May, MP, Home Secretary
Rt. Hon. Jeremy Hunt, MP, Secretary of State for Health
Jane Ellison, MP, Parliamentary Under Secretary of State for Public Health

1. INTRODUCTION

- 1.1. The organic nitrite, amyl of nitrite, was initially used as a therapeutic agent in the treatment of angina pectoris in 1867 (Brunton 1867), but was replaced over a decade later by the organic nitrate, nitroglycerin (NTG), due to the ease of administration and longer duration of action.¹ Alkyl nitrites, “poppers”, have been widely used as recreational drugs since the 1970’s. “Poppers” are sold as liquids that produce a vapour that can be inhaled. The main examples include: isopropyl nitrite, isobutyl nitrite and butyl nitrite.²
- 1.2. The legally available form is isopropyl nitrite, sold in small sealed bottles, often with colourful labels as air freshener, video head cleaner, or finger nail polish remover.³ Other pretences for the sale of alkyl nitrites include labelling the product as boot cleaner, or leather cleaner.²
- 1.3. “Poppers” are widely used for their muscle relaxing effects, to facilitate anal and vaginal sex. Users claim that “poppers” help prolong erections and increase libido.³

2. ARE “POPPERS” PSYCHOACTIVE IN THE CONTEXT OF THE PSYCHOACTIVE SUBSTANCES ACT 2016?

- 2.1. “Poppers” open (dilate) blood vessels, increasing blood flow. It is generally believed that their effects involve the release of nitric oxide from nitrite, and this causes relaxation of smooth muscle in blood vessels, resulting in vasodilation.⁴
- 2.2. Smooth muscle is also found in other parts of the body that need to have an elastic quality, such as the bladder, digestive tract, vagina, and anal sphincter; and alkyl nitrites relax these smooth muscles too.⁵
- 2.3. Inhaled nitrites are rapidly absorbed into the bloodstream, with the onset of effects being seen in seconds. The vasodilatory effects promote an increased blood flow, which often results in temporary reductions in blood pressure accompanied by increased heart rate and lightheadedness. Vasodilation of cerebral blood vessels along with warm sensations and facial flushing are common and contribute to the users’ perceptions of a “rush” or “high”.^{2, 3}

The subjective experience of inhaling “poppers”

“The effects start soon after inhalation but only last for a few minutes. People experience a dizzying ‘rush’ as heartbeat quickens and blood rushes to the head. A pounding headache, dizziness, nausea, a slowed down sense of

time, a flushed face and neck and a feeling of light-headedness are commonly reported effects” (Drugwise, 2016).⁶

2.4. The brain perceives a transient “rush” or “high” as an indirect effect caused by increased blood flow caused by the dilation of blood vessels in brain and periphery. The effects of “poppers” on blood vessels in the brain should be considered to be “peripheral” as these lie outside the “blood-brain barrier”.

2.5. The definition of a “psychoactive substance” in the Psychoactive Substances Act 2016 is not explicit with respect to direct or indirect effects on the central nervous system:

“2.(1) In this Act “psychoactive substance” means any substance which—

(a) is capable of producing a psychoactive effect in a person who consumes it, and

(b) is not an exempted substance (see section 3).

2.(2) For the purposes of this Act a substance produces a psychoactive effect in a person if, by stimulating or depressing the person’s central nervous system, it affects the person’s mental functioning or emotional state; and references to a substance’s psychoactive effects are to be read accordingly.

2.(3) For the purposes of this Act a person consumes a substance if the person causes or allows the substance, or fumes given off by the substance, to enter the person’s body in any way.”

2.6. The ACMD considered three possible options when discussing the question of whether alkyl nitrites fell within the scope of this definition:

- a. That “poppers” are caught under the definition of a “psychoactive substance” and should be controlled under the Psychoactive Substances Act 2016;
- b. That “poppers” are psychoactive, but should be on the list of exemptions from the Psychoactive Substances Act 2016;
- c. Or “poppers” are not caught by the definition of a “psychoactive substance”, and the Psychoactive Substances Act 2016 therefore does not apply.

2.7. The ACMD’s consensus view is that a psychoactive substance has a direct action on the brain and that substances having peripheral effects, such as those caused by alkyl nitrites, do not directly stimulate or depress the central nervous system.

Conclusion on psychoactivity

- 2.8. In the ACMD's view, alkyl nitrites ("poppers") do not fall within the scope of the current definition of a "psychoactive substance" in the Psychoactive Substances Act 2016.
- 2.9. Consequently, the ACMD does not see a need for an exemption under the Psychoactive Substances Act 2016.

3. ACMD'S ASSESSMENT OF HARMS ASSOCIATED WITH POPPERS

Deaths

- 3.1. The ACMD notes that there have been a small number of deaths from their use. The use of "poppers" could lead to methaemoglobinaemia in users, if the product is inhaled or ingested, as they act as oxidising agents, transforming haemoglobin into methaemoglobin, which reduces the ability of red blood cells to transport oxygen to the tissues. Methaemoglobinaemia may cause significant tissue hypoxia, leading to severe, potentially life-threatening clinical features and/or death.⁷ Hunter et al reported three published fatalities occurring in patients with methaemoglobinaemia caused by isobutyl nitrite.
- 3.2. From 1971-2009, of 2488 deaths reported to the Volatile Substance Abuse (VSA) mortality project, 23 involved alkyl nitrites (including isobutyl nitrite and others), of which 10 deaths occurred between 2006-2009.^{8,9}
- 3.3. According to the Office for National Statistics, between 1993 and 2013, there were 11 drug related deaths reported which only mentioned an alkyl nitrite on the death certificate.¹⁰

Enquiries related to alkyl nitrites¹¹

- 3.4. The National Poisons Information Service (NPIS) reported that there had been 8,497 TOXBASE accesses related to alkyl nitrites since the 2007/8 reporting year. TOXBASE accesses were more common at the beginning of this study period than at the end but there has been no major change in annual access numbers since 2010-11.
- 3.5. Over this study period there had also been 494 telephone enquiries. There has been no consistent change in annual telephone enquiry numbers over this study period. The majority of telephone enquiries since April 2012 have concerned males (78% males, 22 % females from 182 telephone enquiries). Furthermore 36% of the enquiries concerned people aged 18-30 years and 57% aged 31-59 years.

Harms associated with “poppers”

3.6. The ACMD report “Consideration of the Novel Psychoactive Substances (‘legal highs’)” (2011) stated: ¹²

“Poppers are not subject to the controls in the Misuse of Drugs Act 1971 and there are no plans to bring them under the control of the 1971 Act as, at present – unlike other substances of abuse – their misuse, within the terms of section 1 of the Act, is not seen to be capable of having ‘harmful effects sufficient to constitute a social problem’”

3.7. The harms associated with “poppers” have been reviewed in “fact sheets” by DrugWise, DrugScience and The Site.org. ^{6, 13, 14}

“Poppers” can cause a chemical burn on the skin.

3.8. People who use “poppers” heavily may develop crusty skin lesions with a distinctive yellow tint around exposure areas, including the nose, mouth, lips, and face. ^{2, 13}

There are reports which show that use of “poppers” can cause impaired or loss of sight.

3.9. “Poppers” are a cause of concern in a small number of cases of maculopathy/retinopathy (eye damage) in recent case reports from UK (2012 and 2014) and France (2010 and 2016). ^{15, 16, 17, 18, 19, 20, 21} There have been around 30 published cases. ¹⁷

3.10. One study described foveal (“centre-of-gaze”) damage in six habitual “poppers” users. ²² In 2014 optometrists and ophthalmologists reported having noticed an increase in vision loss in chronic “poppers” users in the UK associated with isopropyl nitrite being substituted for isobutyl nitrite. ^{16, 23} The authors suggest that this may be related to the switch to using isopropyl nitrite in recent years, although a transient loss of vision was reported in a subject who had inhaled isobutyl nitrite. ^{15, 24, 25}

3.11. There is evidence that “poppers”-induced retinopathy and loss of sight may be reversible on termination of “poppers” use. ²⁶

“Poppers” are very flammable.

3.12. People sometimes dip cigarettes in “poppers” to inhale through the unlit cigarette. Some have been burnt after mistakenly lighting the cigarette. ¹³

“Poppers” lower blood pressure and increase heart rate.

- 3.13. Their use may be more risky for people with heart conditions or abnormal blood pressure. There could also be added risks for people with glaucoma or anaemia, and those with enzyme deficiencies that make them more prone to methaemoglobinaemia.^{7, 24} Similarly, “poppers” taken in combination with other vasodilators such as sildenafil (Viagra) are potentially life-threatening. The combination could lead to dangerously low blood pressure and heart rate, causing a person to faint, or even have a heart attack or stroke.^{13, 24}

“Poppers” can cause headaches

- 3.14. The most common after-effect of using “poppers” is headache. People have also reported feeling nauseous and sick after using “poppers”. People may also feel very dizzy and can faint.^{13, 27}

Other Potential Concerns

- 3.15. Considering the use of “poppers” by gay men, it is reported that there is no good evidence for “poppers” causing immune suppression, Kaposi’s Sarcoma or AIDS.^{2, 5} However, the use of “poppers” during receptive unprotected anal intercourse has been found to be associated with an increased transmission of HIV infection; in a multi-centre case control study the risk was doubled.²⁸ The authors of this study note that this may be because “poppers” increase the risk of transmission, or because the use of “poppers” is associated with other behaviours that may cause increased transmission. These potential concerns are relatively rare.

Conclusion on harms

- 3.16. The ACMD’s opinion given in 2011 (see para 3.6) remains valid. However, although reports of ocular damage caused by alkyl nitrites remain rare, they are serious and should be carefully monitored.
- 3.17. Methaemoglobinaemia is a severe and potentially life threatening adverse effect associated with the use of “poppers”.

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