

## Overview

I disagree with the proposed amendment to reschedule alkyl nitrites. The Advisory Committee on Medicines Scheduling (ACMS) has failed to adequately assess the probability of risk in the reasons it gave for its decision to reschedule alkyl nitrites from Schedule 4 to Schedule 9. Further, an extremely low probability of harm does not justify highly restrictive regulation. Additionally, regulation would have a punitive impact on the gay community - a community that has already suffered stigmatisation, marginalisation and criminalisation. ACMS has failed to differentiate the risks involved in the different types of alkyl nitrites. Most of the toxicities identified are rather minor and do not justify such a highly restrictive regulation. ACMS has also failed to consider if changes to packaging and labelling could not by themselves mitigate any risks identified. Further, ACMS has not considered the benefit and importance that alkyl nitrites have for gay and bisexual men.

*The matters under subsection 52E (1) of the Therapeutic Goods Act 1989 considered relevant by the delegate for the decision include:*

*a. The risks and benefits of the use of a substance:*

*There are numerous risks of harm associated with alkyl nitrites.*

*Risks associated with the use of alkyl nitrites include illicit use for euphoric (perceived due to dilation of blood vessels in brain and periphery), analgesic and muscle relaxant effects.*

Alkyl nitrites have been used by the gay community for around 50 years and are generally considered low risk to general and mental health.<sup>1</sup> The effects described as euphoric, analgesic and muscle relaxant do not themselves make the use of alkyl nitrites risky. ACMS's description of them as such, appears to be a moral judgment. In fact, these effects should be considered therapeutic benefits. The muscle relaxant effects allow for easier and less painful anal sex; this is a benefit to gay men who may otherwise find anal intercourse painful. Contrast the ACMS's attitude to alkyl nitrites with their attitude to phosphodiesterase type 5 (PDE-5) inhibitors; here, helping men achieve an erection is considered a therapeutic benefit.

ACMS has also failed to consider that the effects of alkyl nitrites are very short-acting and the feeling of euphoria is brief. ACMS has also not considered that nitrites are not addictive, one of the factors the committee needs to consider in evaluating a Schedule 9 listing.

*Adverse events associated with the use of alkyl nitrites include methaemoglobinaemia and maculopathy.*

ACMS has failed to properly assess the probability of the risks. ACMS has also failed to examine the differing risks for each of the different types of alkyl nitrites sold in Australia.

ACMS appears to have ignored the fact that there were no reports of "poppers maculopathy" before 2007<sup>2</sup>. In 2007 the European Union banned the sale of isobutyl nitrite, at the time the most commonly used compound in "poppers". Manufacturers changed their production to meet the new laws and the most common compound now sold is isopropyl nitrite. The reports of "poppers maculopathy" emerged a few years later.<sup>3</sup> Australian ophthalmologist Dr Michael Chilov noted, "A change in compound from isobutyl nitrite to isopropyl nitrite to escape legislative measures preventing their sale is thought to be responsible for the increase in the number of cases of macula damage"<sup>4</sup>

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<sup>1</sup> Davies A, Kelly S, Naylor S, Bhatt P, Matthews J, Sahini J, Haslett R, McKibbin M. Adverse ophthalmic reaction in poppers users: case series of 'poppers maculopathy' The Scientific Journal of The Royal College of Ophthalmologists.

<sup>2</sup> Ibid

<sup>3</sup> Ibid

<sup>4</sup> Carter Helen. Poppers on the program at Super Sunday (2015, March 24) Australian Ophthalmology. Retrieved 6 October, 2018 from <http://www.optometry.org.au/blog-news/2015/3/24/poppers-on-the-program-at-super-sunday/>

ACMS has failed even to examine the difference between the differing alkyl nitrites sold in Australia. ACMS has erred in failing to consider different scheduling for different alkyl nitrite compounds. ACMS's proposal to reschedule all alkyl nitrites as Schedule 9 substances is overkill. A more nuanced approach may see only isopropyl nitrite rescheduled.

ACMS's report claims, "Ophthalmologists in Australia are reporting an increase in the number of cases of [poppers] maculopathies", but ACMS have failed to provide evidence of this, such as a study into poppers maculopathy in Australia that may identify the number of cases and how much they have increased over time.

ACMS's Substance Summary claims, "Ophthalmologists believe that chronic use could lead to irreversible damage." Dr Michael Chilov also claims "poppers maculopathy" is seen in chronic users of alkyl nitrites' but neither he nor ACMS define the term "chronic user". ACMS has also failed to identify who these chronic users are. A 2017 study of ecstasy users found: "*Frequency of amyl nitrite use was generally low, with participants reporting a median of three days of use in the last six months (range: 1–100 days). Over two-thirds (68%) of participants who had recently used amyl nitrate (n=197) [sic] had used less than once per month in the preceding six months. No participants reported daily use.*"<sup>5</sup> It appears even ecstasy users are not "chronic users" (in any obvious sense of the term) of alkyl nitrites and ACMS does not provide any evidence to identify who is.

ACMS cannot justify rescheduling all alkyl nitrites as Schedule 9 when they have failed to provide any substantial evidence as to the risk of maculopathy.

In regards to methaemoglobinaemia, ACMS has failed to properly examine and assess the risks in the report it mentions. The report lists 21 cases of methaemoglobinaemia. 10 of the cases involved amyl nitrite<sup>6</sup>. Despite "amyl" being the colloquial name for "poppers" in Australia almost none of the compounds sold in Australia use amyl nitrite, in fact, ACMS's own report states that the nitrites sold in Australia are not usually amyl nitrite. Another 5 cases involved isobutyl nitrite. Since the banning of isobutyl nitrite by the European Union this compound is no longer commonly used in the manufacture of alkyl nitrites. In another two cases butyl nitrite was used and no treatment for methaemoglobinaemia was required. This leaves one case where "Liquid Gold" was ingested orally and another case where the type of nitrite was not known. Thus ACMS has failed to adequately assess the risks involved in relation to alkyl nitrite use and methaemoglobinaemia, and failed to justify the rescheduling of all alkyl nitrites under Schedule 9.

*Alkyl nitrites are toxic via inhalation. Toxicity includes tachycardia, hypotension, headache, flushing, dizziness, nausea, and syncope. Co-use with phosphodiesterase type 5 (PDE-5) inhibitors can lead to severe hypotension. Increased risk of cardiovascular harm when used in conjunction with other vasodilators.*

These health risks are relatively minor when one considers that they are very brief in duration. The ACMS report does not provide any medical evidence that any of these health risks lead to serious or long-lasting health issues. The majority of users do not experience these effects beyond flushing and light-headedness, for a few minutes at most. A warning label that alkyl nitrites should not be used in conjunction with PDE-5 inhibitors could mitigate most of such risks as exist.

The health risks of tobacco and alcohol are well documented and appear considerably worse than any associated with nitrites. In fact, a recent study by the Bill and Melinda Gates Foundation concluded that there is no safe level of alcohol use. There are also many social problems caused by alcohol (e.g., violence, family breakdown, loss of employment, drunk driving, homelessness). Alcohol is the cause of over

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<sup>5</sup> Uporova J, Karlsson A, Sutherland R, and Burns L. AUSTRALIAN TRENDS IN ECSTASY AND RELATED DRUG MARKETS 2017: Findings from the Ecstasy and Related Drugs Reporting System (EDRS)

<sup>6</sup> Hunter, L. et al., (2011) 'Methaemoglobinaemia associated with the use of cocaine and volatile nitrites as recreational drugs: A review', British Journal of Clinical Pharmacology, 72(1), pp.18-26

5,000 deaths a year in Australia<sup>7</sup> ; by contrast, ACMS has not provided evidence of any deaths in Australia caused by alkyl nitrites. As the risks of alcohol appear far worse than those of alkyl nitrites and as alcohol is not listed under Schedule 9, it would be inconsistent to reschedule alkyl nitrites under Schedule 9.

It is of interest that the UK Government Advisory Body on the Misuse of Drugs found the use of poppers was “not seen to be capable of having harmful effects sufficient to constitute a societal problem.”<sup>8</sup> ACMS is wrong to recommend the rescheduling of nitrites under Schedule 9, the same category as addictive illicit drugs as heroin, crystal methamphetamine and cocaine.

*Alkyl nitrites are sweet-smelling liquids and pose a risk to child safety through cases of accidental ingestion.*

Most people would consider the odour of alkyl nitrites to be unpleasant; indeed, they have been described as smelling like “stinky socks”.<sup>9</sup> Further, nail polish remover is also sweet-smelling but is not considered to attract children to ingest it. If this is a real issue, then ACMS could recommend alkyl nitrites be sold with child-proof lids. ACMS is wrong to use this as a reason to reschedule alkyl nitrites under Schedule 9.

*Over an eleven year period (2004-2014), Australian Poisons Information Centres received 273 calls about alkyl nitrite exposures:*

- *3.7% of calls (10 cases) which involved accidental paediatric exposures.*
- *Hospitalisation was required in 72.5% of all cases with almost all of these requiring a clinical toxicology consultant, indicating high perceived risk or severity.*
- *15% (41 cases) of the hospital admitted patients presented with methaemoglobinaemia, with 14 requiring treatment with the antidote, methylene blue.*

The raw figures ACMS cites do not provide enough information to correctly assess the risks of alkyl nitrites. The submission by NSW Poisons Information Centre dated 10 May 2018 states: ‘Australian PICs do not routinely conduct follow up calls and thus we lack complete outcome data.’ This means ACMS is unable to say if any calls resulted in any severe or permanent harm.

The raw numbers do not provide any indication of how common or rare these cases are. In particular, it is not clear what proportion of total alkyl nitrite use the 273 calls represented. Might they have come from a very much larger number of instances of use? Without this context ACMS has failed to assess the risk of alkyl nitrites and should not use the figures as justification for listing alkyl nitrites as Schedule 9 substances.

The submission by NSW Poisons Information Centre shows that, over 11 years, only 89 alkyl nitrite – related calls involved inhalation and 169 ingestion. This may indicate that better labelling and child-proof lids should be required, rather than a Schedule 9 listing. The figures from the calls do not provide any information on the type of nitrites or brands involved in the cases. As discussed above, such figures are needed to provide an accurate risk assessment.

Also of note is that, of the 41 cases of methaemoglobinaemia, only 14 required treatment. One assumes that the other cases were minor. The need for treatment by just 14 people over an 11-year period does not warrant listing all alkyl nitrites as Schedule 9 substances.

*There are no therapeutic benefits associated with the use of alkyl nitrites other than amyl nitrite...*

As noted, alkyl nitrites relax the anal sphincter and facilitate anal intercourse. ACMS may not consider this a therapeutic benefit. In fact, however, it is an important benefit to many gay couples who may otherwise find anal intercourse painful. In failing to consider this, ACMS appears to have exercised a (questionable) moral judgement. As stated above, the contrast with attitudes towards failure to achieve an erection is very

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<sup>8</sup> Home Affairs Committee, Psychoactive Substances (report), London: Stationery Office, 23 Oct 2015, p. 14

<sup>9</sup> Upfal, J. (2016). *Australian Drug Guide* (8th Edition ed.). Melbourne: Black Inc.

striking. ACMS is thus wrong to conclude that there is no therapeutic benefit associated with the use of alkyl nitrites and to use that as justification for rescheduling them under Schedule 9.

*Industry stakeholders have not identified any current use of alkyl nitrites and have indicated that the proposed changes to the Poisons Standard with respect to alkyl nitrites and lubricants will therefore not impact their current products.*

It is not clear which industry stakeholders were consulted. (for instance, did they consult with the Alcohol and Drug Foundation, which considers the level of harm from the long-term use of nitrites as generally low.<sup>10</sup>)? It is worth noting that while ACMS consulted with unnamed “industry stakeholders”, it did not see fit to consult with the gay community, arguably the major user of alkyl nitrites.

*b. the purposes for which a substance is to be used and the extent of use of a substance:*

*Commonly misused alkyl nitrites include amyl nitrite, butyl nitrite and isobutyl nitrite, with more recent variations including isopropyl and cyclohexyl nitrite.*

*Alkyl nitrites have little to no therapeutic use. There are no products on the Australian Register of Therapeutic Goods (ARTG) that contain alkyl nitrites. There are no agricultural products or veterinary medicines containing any nitrite listed on the Australian Pesticides and Veterinary Medicines Authority's PubCRIS database.*

The ACMS report fails to acknowledge the role nitrites play in sexual relations between gay and bisexual men and how this is a benefit in many gay relationships.

*Alkyl nitrites are largely used recreationally as 'party drugs'. There has been an increase in the use and abuse of alkyl nitrites in Australia over recent years. According to the most recent 2017 report of the Ecstasy and Related Drugs Reporting System (EDRS)[28] recent users of alkyl nitrites was reported in 25% of study participants.*

The report referenced also does not assess the health risks but only identifies the percentage of users. Further, the report also indicates that alkyl nitrite use by ecstasy users declined from 2016 to 2017; this was not mentioned by ACMS. Importantly, ACMS has failed to assess actual health risks in regards to use of alkyl nitrites and ecstasy. Also, there is a blatant inconsistency here: If ecstasy users' taking a substance is a reason for listing under Schedule 9, then other “party drugs”, notably alcohol and tobacco, should also be banned.( The report shows alcohol was recently used by 99% of ecstasy users and tobacco by 87%).<sup>11</sup>

*c. the toxicity of a substance:*

*Alkyl nitrites are toxic via inhalation. Toxicity includes tachycardia, hypotension, headache, flushing, dizziness, nausea, and syncope. Co-use with phosphodiesterase type 5 (PDE-5) inhibitors can lead to severe hypotension.*

As discussed above, most of these health risks are relatively minor and a warning on labels (like those on cigarette packets) could be used. These risks do not justify scheduling alkyl nitrites under Schedule 9.

*Increased risk of cardiovascular harm when used in conjunction with other vasodilators.*

As above, a health warning on labels could reduce this harm.

*Inhalation of alkyl nitrites can lead to methaemoglobinaemia and even death, with significantly increased risk if ingested. Methaemoglobinaemia is potentially life threatening if not treated appropriately.*

As discussed above, ACMS's interim decision fails to differentiate between the different nitrite compounds in the risk of leading to methaemoglobinaemia. ACMS also failed to provide evidence as to how commonly methaemoglobinaemia occurs among nitrite users in Australia. Also ACMS's interim decision fails to

<sup>10</sup> Alcohol and Drug Foundation; Drug Facts: Amyl Nitrite retrieved 30 September 2018.

<sup>11</sup> Ibid

recognise that nitrites have been commonly used in the gay community for 50 years and are generally considered low-risk to general and mental health.<sup>12</sup>

Alkyl nitrites can cause chemical burns to the skin and eyes on direct contact. Other risks of alkyl nitrites include maculopathy and skin lesions.

As discussed; the ACMS report does not assess the risks and provide evidence as to how common these conditions are.

Chemical burns, if they occur, are likely to be superficial; no evidence has been provided that they are severe.

In regards to maculopathy ACMS has failed to assess the risks and also failed to differentiate between the risks from different nitrite compounds. ACMS has failed to identify isopropyl nitrite as the most likely reason for poppers maculopathy and that the increase in use of isopropyl nitrite was most likely due to regulatory interference (see above). ACMS claims the risk is to chronic users but fails to define "chronic use". The risks identified do not justify scheduling all alkyl nitrites as a Schedule 9 substances.

e. the potential for abuse of a substance:

- There is a high potential for misuse and abuse of alkyl nitrites for euphoric properties, and as sex aids due to their muscle relaxant properties.
- The misuse and abuse of alkyl nitrites appears to be in particular sections of the community rather than widespread.

It is interesting that here ACMS has failed to state openly that nitrites are commonly used as a sex aid by the gay community. This smacks of homophobia; ACMS's decision appears to use moral judgement rather than evidence.

f. .any other matters that the Secretary considers necessary to protect public health:

- Exemptions from scheduling for lubricants were first proposed in 1965 and in 1969 and 'motor fuels and lubricants' were included in the list of exemptions at this time. Amendments to the Appendix A lubricant entry will clarify its intent, restricting the Appendix A exemption under the Poisons Standard to machinery use, not personal care use.
- Feedback from those supplying industrial machinery lubricants did not identify any problems with the proposed new wording for the Appendix A entry.

ACMS has failed to consider S52E (1)(d) of The Therapeutic Goods Act 1989. This section specifies "(d) the dosage, formulation, labelling, packaging and presentation of a substance". As noted, the use of childproof lids would mitigate any risk to children's access to the product and warning labels could be used to indicate any risks to adults.

ACMS has failed to take into account the fact that that alkyl nitrites do not present a high risk of dependency, one of the factors ACMS needs to consider in listing a substance under Schedule 9.

ACMS has failed to differentiate the risks posed by different alkyl nitrite compounds.

ACMS is wrong to state that: "*it is unclear if the United Kingdom (UK) Government will include alkyl nitrites in a list of banned psychoactive substances.*" [emphasis added] The UK decided in 2016 not to include alkyl nitrites on this list and they are still available for purchase.<sup>13</sup>

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<sup>12</sup> Davies A, Kelly S, Naylor S, Bhatt P, Matthews J, Sahini J, Haslett R, McKibbin M. Adverse ophthalmic reaction in poppers users: case series of 'poppers maculopathy' The Scientific Journal of The Royal College of Ophthalmologists.

ACMS claims, "The international legal status of alkyl nitrites is unclear", but failed to identify any country where all alkyl nitrites have been scheduled as prohibited substances after previously being available. The availability of alkyl nitrites in countries similar to Australia is an argument against a Schedule 9 listing.

ACMS has failed to consult any Australian police forces. In fact, former Australian Federal Police Commissioner, Mick Palmer, recently stated that making "amyl nitrite an illegal drug would be ineffective."<sup>14</sup>

For all the reasons I have identified, I submit that the ACMS's interim decision to move all alkyl nitrites from Schedule 4 to Schedule 9 was ill-founded and unwarranted. ACMS should leave alkyl nitrites listed under Schedule 4, but recommend changes to labelling and packaging. If after a proper risk assessment it is found that isopropyl nitrite is a risk in causing maculopathy, then isopropyl nitrite, but not other alkyl nitrites, should be rescheduled.

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<sup>13</sup> BBC website. Poppers not part of legal highs ban (2016 March 16) Retrieved, 2018 October 6 from <https://www.bbc.com/news/uk-35826369>

<sup>14</sup> The Guardian Australia website, "Making amyl nitrite an illegal drug would be ineffective, warns former AFP chief" article by Paul Karp, published 25 September 2018.