Public Consultation on the Proposed Amendments to the Poisons Standard

Notice under subsections 42ZCZL of the Therapeutic Goods Regulations 1990 (the Regulations)

The delegate of the Secretary to the Department of Health publishes herein all valid public submissions made in response to the invitation for public submission on the proposed amendments to the Poisons Standard. These submissions were considered by the November 2016 meeting of the Joint Advisory Committee on Chemicals and Medicines Scheduling (ACCS-ACMS).

In accordance with the requirements of subsection 42ZCZL of the Regulations these submissions have had their confidential information removed.

Materials claimed to be commercial-in-confidence was considered against the guidelines for the use and release of confidential information set out the Chapter 6 of the Scheduling Policy Framework for Medicines and Chemicals (SPF, 2015), issued by the Australian Health Ministers' Advisory Council. The SPF is accessible at https://www.tga.gov.au/publication/ahmac-scheduling-policy-framework-medicines-and-chemicals.

[redacted]

Unfortunately there are some aspects of the current situation that put many smokers off:

1. That possession of nicotine is illegal. [redacted] Some even fear their employment will be terminated if they should be charged with nicotine possession.
2. Ordering over the internet. [redacted]
3. The cost of postage from the United States, China or more recently, New Zealand.
4. Either the expense & uncertainty of buying pre-mixed nicotine (a), or the complexity of mixing it at home (b)).
    a. This problem stems from uncertainty as to what nicotine strength will be needed, which flavours and the ratio of PG/VG diluent will work best. Which can be solved by buying more concentrated, unflavoured nicotine and mixing it yourself, unfortunately..
    b. Mixing your own involves doing calculations as to the amounts of flavour (many new users prefer 'cigarette flavour' - but quickly move on to more delicious flavours), nicotine (I was a heavy smoker & made the initial e-liquid at 33 mg/mL - but soon dropped the concentration and am now using 12 mg/mL), PG & VG are needed (PG provides a good 'throat hit', while VG makes that vapor more cloudy) for a particular effect. To ease this problem, Being a programmer by trade, I wrote a small application to do the calculations for the amounts of each component, though there are also on-line calculators. This requires counting drops, or weighing the developing mix on a scale. As you might appreciate, this is not a method for obtaining e-liquid that is open to many people & is largely restricted to enthusiasts.

Counterpoints to the opponents

There will undoubtedly be opponents to this proposal - from public health advocates, representatives of pharmaceutical companies or tobacco companies (who typically argue for

closed systems of limited flavour choice and strength, that lock consumers to their hardware & refill cartridges).

These arguments might take any of the following forms, plus more that don't immediately spring to mind:

- Think of the children! E-cigs might be a gateway to smoking.
- E-cigs allow Big Tobacco to circumvent advertising bans.
- Use of e-cigs renormalises smoking.
- Use of e-cigs encourages dual use of cigarettes and e-cigs, thereby delaying smokers making a successful attempt to quit smoking.
- The long term safety of e-cigarettes has not been proven.
- …

The Prime Minister & Health Minister call you to a meeting on e-cigarettes:

PM: Great news! We can get bipartisan support for legislation to allow access to e-cigarettes to smokers as a consumer product as long as we can get your official 'tick of approval'. The legislation puts a variety of conditions on success, and if it fails to meet any one of them, it will be *automatically* cancelled. Further, it will expire after 12 months unless it is explicitly renewed. The conditions are as follows:

- It leads to a net increase in smokers successfully quitting smoking completely. I.E. unless it *accelerates* the rate at which the smoking rate is falling, it will have failed.
- For every person who has never smoked & takes up e-cigarettes then goes on to smoke conventional cigarettes, there will be at least 100 smokers who convert completely to vaping using e-cigarettes.
- That advertising is not targeted at children and non smokers.
- That big tobacco companies cannot use e-cigarettes to get around falling profits, and further, that they will be de facto excluded from the e-cigarette market in a way that is easily defensible in a court of law.
- That no long term, significant dangers (that e.g. make e-cigs more than 5% as harmful as smoking) become apparent.
- That no quantifiable harms come to those in the vicinity of vaping.

Do we have your approval for this legislation to allow nicotine containing e-cigarettes to be sold to consumers through licenced retail outlets?

If a public health professional truly wants to lower smoking rates and thereby increase the level of public health, it should get their enthusiastic approval. But I'd bet my bottom dollar that **most of the dissenters would still resist approving e-cigarettes**.

As an aside, [redacted]

[redacted]

On the WHO FCTC & Harm Reduction

Australia is a signatory to the Framework Convention on Tobacco Control. Article 1(d) of the FCTC states:

"tobacco control" means a range of supply, demand and **harm reduction strategies** that aim to **improve the health of a population** by eliminating or reducing their consumption of tobacco products and **exposure to tobacco smoke**;

Australia has implemented the strategy to 'reduce the motivation' to consume tobacco using the stick. I would like to say 'using the carrot & the stick' [redacted] There was:

- Banning smoking indoors, and more recently, outdoors (for which there is absolutely no health justification).
- Demonisation of tobacco smoke, and more importantly, of smokers themselves.
- Scare messages on cigarette packs.
- Increasing the price of tobacco products.

[redacted]

[redacted]

[redacted] The supply of smokers who can be shamed, bludgeoned or cajoled into giving up is quickly becoming depleted. Each smoker will concede that they feel the harm smoking is doing them, yet they still smoke.

It is for the sake of the health of **those** people that I implore Australian Tobacco Control to forge a new path. Embrace e-cigarettes and offer the current smokers a carrot. A (much) reduced harm alternative to smoking, that is also ***enjoyable***, could go a long way to dropping smoking rates below the magic 5% figure quoted as being the smoking 'end-game'. It is long overdue.

I'll close with a quote from the Royal College of Physicians report Nicotine Without Smoke: Tobacco Harm Reduction:

A risk-averse, precautionary approach to e-cigarette regulation can be proposed as a means of minimizing the risk of avoidable harm, e.g. exposure to toxins in e-cigarette vapour, renormalisation, gateway progression to smoking, or other real or potential risks. However, if this approach also makes e-cigarettes less easily accessible, less palatable or acceptable, more expensive, less consumer friendly or pharmacologically less effective, or inhibits innovation and development of new and improved products, then it **causes harm by perpetuating smoking**. (Section 12.10 page 187)

DECLARATION: [redacted] has NO financial interest or vested commercial interest in the tobacco industry nor in the electronic cigarette manufacturing/import/distribution industry. [redacted]

[redacted]

The main emphasis is how there may be reduction from harm from tobacco smoking through the use of nicotine containing e-cigarettes (ENDS). [redacted]

[redacted]

BACKGROUND: It is of paramount importance to keep the concept of "good science" in mind when deciding which studies are best for evidence to address the concerns that are presented in the policy that surrounds nicotine e-liquid and nicotine containing ENDS. Research on ENDS that comes from the United States and the EU, especially from the former - needs to be approached cautiously for its veracity and its ethical underpinnings due to the possibility of it being unduly influenced by commercial interests and profits – the

protection thereof, as well as professional investment (scientists, some not all) and government revenue (protection of same) are the driving force behind much of the "science" as it relates to ENDS. There are quite a few researchers in both the United States (Michael Siegel, PhD from Boston University) and the EU (Konstantinos Farsolinos, MD and his team at the Onassis Research institute in Athens) that not only conduct their own research, but review the research from around the world for its validity based on scientific method, ethical standards and process of funding.

[redacted]

There is no evidence of increased nicotine intake from dual use. Smokers regulate their smoking behaviour in order to maintain the blood concentrations of nicotine within a comfortable range. If those levels get too high, symptoms of nicotine toxicity – such as nausea, headache and dizziness can occur and smoking is then reduced. A recent study found that smokers using ENDS maintain their intake of nicotine, but reduce their smoke and toxin intake, which results in an overall health benefit, therefore reducing harm through reducing exposure to the toxicants in combustible tobacco [10]. It is extremely difficult for

someone to have a fatal overdose of nicotine through either ENDS use or through ingesting nicotine containing e-liquid due to nicotine's inherent emetic qualities.

Promotion to young people: *Overseas evidence shows that promotion of e-cigarettes targeting young people through flavours, packaging may appeal to young people.*

The main issue with youth is harm reduction. One cannot, in an unequivocal manner state that they can prevent youth from uptake or experimentation with any harmful substance of behaviour with 100% guarantee. [redacted]

With regards to the uptake of "vaping" in previously non-smoking youth, the available evidence does not support the "gateway hypothesis" that ENDS encourages nicotine addiction or uptake by youth. [redacted]

As far as the argument that "vaping clouds could be a nuisance to others especially in enclosed spaces", unless the government also wishes to regulate the use of body sprays, perfumes, and deodorants which are also a nuisance – and can be a health hazard to those

who have respiratory difficulties and disease (unlike second hand vapour which has NO health harms associated with it [15,16] therefore this argument is not valid.

CONCLUSION:

When looking at the research and information on ENDS from a Public Health perspective, one needs to weigh the same five criteria that we mentioned in our introduction: Harm Prevention, Harm Reduction, Proportionality, Ease of Implementation and Cost Effectiveness.

[redacted]

REFERENCES:

1. Bell K, Keane H. All gates lead to smoking: the 'gateway theory', e-cigarettes and the remaking of nicotine. Soc Sci Med. 2014;119:45-52.

2. Zwar N, Bell J, Peters M, Christie M, Mendelsohn C. Nicotine and nicotine replacement therapy – the facts. Australian Pharmacist. 2006;25(12):969-73

[redacted]

11. Bell K, Keane H. All gates lead to smoking: the 'gateway theory', e-cigarettes and the remaking of nicotine. Soc Sci Med. 2014;119:45-52.

12. Bauld L, MacKintosh AM, Ford A, McNeill A. E-Cigarette Uptake Amongst UK Youth: Experimentation, but Little or No Regular Use in Non-smokers. Nicotine Tob Res. 2016;18(1):102-3.

13. Use of electronic cigarettes among children in Great Britain. Action on Smoking and Health, UK, 2015 Contract No.: Fact sheet 34. Available at

http://www.ash.org.uk/information/facts-and-stats/fact-sheets (accessed August 2016).

14. McNeill A, Brose LS, Calder R, Hitchman SC, Hajek P, McRobbie H. E-cigarettes: an evidence update. A report commissioned by Public Health England. PHE publications gateway number: 2015260 2015. Available at https://www.gov.uk/government/publications/e-cigarettes-an-evidence-update (accessed July 2016).

[redacted]

[redacted] [redacted]

To: Medicines Scheduling
Subject: Consultation: Proposed amendments to the Poisons Standard - ACMS meeting, November 2016
Date: Thursday, 18 August 2016 1:46:02 PM

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https://www.tga.gov.au/consultation-invitation/consultation-proposed-amendments-poisons-standard-acms-meeting-november-2016#.V7UuMS1eptQ.mailto

Id like to see nicotine replacements available for self administering. [redacted]

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Sent from my Android phone with mail.com Mail. Please excuse my brevity.

Submission for the Scheduling medicines and poisons

Date of submission invitation 4th August 2016
Submission with regard to the application for the proposal to exempt nicotine from Schedule 7 at 3.6% or less for self administration, with a personal vapouriser or electronic cigarette, for the purpose of tobacco harm reduction.

I [redacted] residing at [redacted] am submitting the following in support of the afore mentioned application.

[redacted]

2/

[redacted]

In closing my submission is to:
Decriminalise the possession of e-liquid containing nicotine, and make it available as a consumer product, in the strength applied for in the application.

I support making e-liquid available as a consumer product through responsible retail outlets.
I feel very strongly that hardware and e liquids should not be taxed as tobacco products. 10% GST would be a fair compromise.

I consent for this submission to be posted on any website with the parts highlighted not for publication omitted
I make this submission in accordance with relevance to the aforementioned proposed amendment and feel addresses the matter mentioned in section 52E of the *Therapeutic Goods Act 1989*.

Signed and Dated this the 22nd day of August 2016

[redacted]

22 August 2016

Advisory Committee On Medicine Scheduling
RE: Nicotine Rescheduling November 2016

Via: medicines.scheduling@tga.gov.au

KEY POINTS:

1. Low concentration nicotine should be rescheduled for use in E Cigarettes and made available to persons aged 18 and over as a consumer product.
2. Low concentration nicotine has a proven safety record and is currently widely available as Nicotine Replacement Therapy.
3. Current restrictions place nicotine E Cigarette users unnecessarily outside the law.
4. Anti tobacco restrictions should not be extrapolated to low concentration nicotine use.
5. My personal journey would not have been possible without the outlaw use of low concentration nicotine liquid.

[redacted] I welcome the opportunity for the Therapeutic Goods Administration to reschedule nicotine from a schedule 7 poison and make it available as a consumer product for appropriate use in E-Cigarettes.

Low concentration nicotine is currently widely available in Australia as nicotine replacement therapies. It is available in many formats including aerosols and is generally considered safe. The sale of nicotine in this format is unrestricted in any supermarket across the country.

As a replacement therapy, low concentration nicotine has been separated from tobacco into a safer mechanism for delivery. E-Cigarettes containing low level nicotine apply the same principles to displace use of combustible tobacco products for adults who smoke.

The circumstances for E-Cigarette users who must flout the law when using nicotine is disadvantageous in allowing another avenue of ending tobacco reliance and is largely unenforceable.

No one can argue that tight tobacco control is not to the greater benefit of public health, but these principles should not be used to limit the supply of low level nicotine for use by adults in E-Cigarettes. Anything that significantly reduces the risks from smoking tobacco should be celebrated as a victory for public health.

[redacted] recommend people who smoke try E-Cigarettes to quit but this cannot be achieved without the addition of nicotine.

I sincerely hope that the health gains I have achieved can be offered to others when low concentration nicotine is rescheduled, regulated and available for consumers as it is in many countries worldwide.

I am happy to support my submission further if required.

[redacted]

[redacted]

8/27/2016

Dear Sir/Madam,

I am writing to regarding the proposed amendment to the poisons act regarding the availability of low strength liquid nicotine in Australia.

[redacted]

[redacted]

[redacted]

Pre-meeting submission consultation: Proposed amendments to the Poisons Standard, ACMS meeting, November 2016:

Nicotine	An applicant has proposed to exempt nicotine from Schedule 7 at concentrations of 3.6 per cent or less of nicotine for self-administration with an electronic nicotine delivery system ('personal vaporiser' or 'electronic cigarette') for the purpose of tobacco harm reduction.

I wish to comment in support of this proposed amendment.

[redacted]

I support the proposed amendment for many reasons:

- Nicotine is already readily available in many, many places.

  Unfortunately, it is only available when accompanied by the many known carcinogens in the smoke from tobacco products, or in NRT products [redacted]

- [redacted]

- Nicotine toxicity has been exaggerated.

  Although nicotine should be treated with care, [redacted]

  E-cigarettes: an evidence update

  Nicotine without smoke: Tobacco harm reduction

  How much nicotine kills a human? Tracing back the generally accepted lethal dose to dubious self-experiments in the nineteenth century

- [redacted]

  From speaking to other vapers, it is clear that there is a wide variation in what works for each individual. It is important that vapers have control over the type of equipment they use, the e-liquid they use, and the strength of the nicotine. A maximum of 3.6% would seem to be a reasonable compromise.

- By virtue of being in Schedule 7, possessing even very low concentrations of nicotine is currently illegal in many states.

  This relates back to my first point. [redacted]

- The inability to buy low-strength nicotine for personal vaporisers locally has some unfortunate side-effects:
  - It is far easier to just go to the nearest store and buy cigarettes.
  - Higher concentrations are being imported and used to mix down to lower, usable levels.
  - Those without internet access and those uncomfortable with buying online are excluded from a harm reduction strategy which has been very successful for many people. As "disadvantaged groups in the population [are] more likely to take up and continue smoking" (Trends in the prevalence of smoking by socio-economic status), the very people who could be most helped by having low-strength nicotine available are those least likely to be able to access it.

For all these reasons, [redacted] I write in favour of the proposal to exempt from the SUSMP nicotine at concentrations of 3.6% or less for use in an ENDS being accepted. ☐

[redacted]

[redacted]

I submit the following in support of the application to remove preparations of e-liquid containing up to <=36mg/ml of nicotine from schedule 7

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

The removal of <=36mg/ml nicotine preparations (e-juice) from schedule 7 would be an amazing step in the right direction, making it available not only to existing vapers but to the millions of tobacco addicted still fighting to quit.

The Royal College of Physicians (UK) have stated that vaping is at “least” 95% safer than smoking, also despite claims to the contrary reports to the poisons centre (US) due to e-juice have also dropped dramatically in the US with normal “household” chemicals outstripping e-juice by the thousands.

Of course some regulation is necessary eg: Child Proof Caps, prohibit sales to under 18 even though a twelve year old can freely access nicotine through NRT I would not support this product for under 18 year olds.

Please I beg the TGA to allow commonsense to prevail and move to the forefront in the fight against tobacco addiction by allowing the removal of <=36mg/ml nicotine e-juices from schedule 7 allowing Australia to maintain its international standing as a ground breaker in the fight against traditional cigarettes.

27 August 2016

Dear Sir/Madam

[redacted] I am writing regarding the change of scheduling of eliquids containing nicotine up to 36mg/ml.

- [redacted]
- [redacted]
- I feel that the current situation is ridiculous. The only source of legal nicotine is either deadly cigarettes or ineffective NRTs. The simple fact is that you can have the safest quit product in the world but if smokers don't like it, it is completely useless.
- I think that a lot of older people and poorer people who smoke cannot access it via the internet at the moment. This is a massive shame when 15 000 Australians die every year of smoking related illness. Many more people are incapacitated by smoking and live quite unpleasant lives due to smoking.
- I feel that Australia is well able to regulate sensibly the sale of eliquids containing no more than 36mg/ml in a manner that is safe, i.e. childproof caps, sensible warnings on the labels etc.

Thank you for taking the time to read my submission.

To whom it may concern,

I am writing in relation to the recent application to have nicotine eliquid made exempt from being a Schedule 7 poison in the same way that cigarettes are exempt.

First let me state that I fully support this application.

I feel very strongly about this issue because I do not want my loved ones to go back to smoking. I get angry when I read comments by the Cancer Council and politicians saying ecigarettes are 'insidious', 'a gateway to smoking', 'a ploy by big tobacco to get their claws into children'. . I know many people who have stopped smoking thanks to ecigarettes, I don't know anybody who has started using ecigarettes who was not already a smoker.

To summarise I think it is important that:
- nicotine ejuice be made legal for personal use
- it be legal in high strengths (I needed 36mg to seem equivalent to cigarettes)
- have no restriction on flavours (as finding the right flavour can make all the difference)
- remain significantly cheaper than smoking (so the unconvinced at least give it a try)

Thankyou for reading my submission.

Yours Sincerely

Submission on proposal received by the TGA to "exempt nicotine from Schedule 7 at concentrations of 3.6 per cent or less of nicotine for self-administration with an electronic nicotine delivery system ('personal vaporiser' or 'electronic cigarette') for the purpose of tobacco harm reduction."

[redacted]

26 August 2016

[redacted]

I write to set out concerns about proposals to allow nicotine to be freely accessed by users of electronic nicotine delivery systems (ENDS).

1. Is nicotine carcinogenic?

E-cigarette advocates argue that nicotine is almost benign as it is consumed by smokers and ENDS users. They repeatedly argue that the deleterious effects of smoking derive almost entirely from the inhalation of the particulates and gases emitted by combusted tobacco, arguing that people "smoke for the nicotine but die from the smoking." A 2014 paper reviewed the historic origins of the 30-60mg LD_{50} for nicotine in adults and argued that this is far too low. (1)

Concerns about the toxicity of nicotine however, go far beyond concern about lethal poisoning of an adult. The glib argument that nicotine is all but benign is often advanced by those highly conflicted by commercial interests involved in selling ENDS. Such arguments seldom note the findings of a large body of research into possible adverse effects arising from consumption of nicotine. Nicotine's possible role as a cancer promoter is of particular concern.

In 2014, the WHO's International Agency for Research in Cancer published lists of agents intended for investigation between 2015-2019 for their carcinogenicity, with these assessments planned for publication in the authoritative IARC Monograph series(2). Nicotine was listed as a "high" priority agent, with IARC noting "increasing population exposure via electronic nicotine delivery systems; recent mechanistic data suggest an association with DNA damage and other pathways of carcinogenesis."

No IARC report has yet appeared. Appendix 1 provides examples of research and reviews that have been published in recent years which are indicative of the associations of nicotine with harm to which IARC would have been referring.

2. Human development and nicotine: including impaired fetal brain and lung development, and altered development of cerebral cortex and hippocampus in adolescents

Researchers from the US Office on Smoking and Health within the Centers for Disease Control(3) reviewed concerns about nicotine's role in human development. Their review concluded that:

> "Human and animal data support that nicotine exposure during periods of developmental vulnerability (fetal through adolescent stages) has multiple adverse health consequences, including impaired fetal brain and lung development, and altered development of cerebral cortex and hippocampus in adolescents. Measures to protect the health of pregnant women and children are needed and could include (1) strong prohibitions on marketing that increase youth uptake; (2) youth access laws similar to those in effect for other tobacco products; (3) appropriate health warnings for vulnerable populations; (4) packaging to prevent accidental poisonings; (5) protection of non-users from exposure to secondhand electronic cigarette aerosol; (6) pricing that helps minimize youth initiation and use; (7) regulations to reduce product addiction potential

and appeal for youth; and (8) the age of legal sale."

3. Nicotine and mental health concerns

It has long been observed that people living with psychosis have far high smoking rates than those found in the wider population. For many years, this observation was explained by a "self medication" hypothesis that assumed that people with psychosis found smoking to be in some way comforting, calming or pleasurable. This traditional explanation of the higher smoking of people with psychosis has always been that people with psychosis self-medicate with nicotine: as a Lancet review summarises: "smoking corrects a pharmacological abnormality (such as excessive dopamine blockade induced by antipsychotics), counteracts negative or cognitive symptoms of schizophrenia, or relieves boredom or distress."

Two recent studies published in high impact factor research journals provide evidence that suggest that exposure to nicotine early in life, including in utero may rather be causative for psychosis (including schizophrenia) in some individuals.

A 2016 Lancet systematic review of tobacco use and psychosis found that in five longitudinal prospective studies, the risk of psychotic disorder was increased modestly by daily smoking.(4)

In 2016 a case control study was published in the American Journal of Psychiatry (5) examining the association between maternal blood cotinine levels (a metabolite of nicotine) drawn twice during pregnancy and subsequent diagnosis of schizophrenia in all children born in Finland from 1983-1998.

Finland has long had highly advanced record linkage for all citizens, and 98% of all mothers who had live births across this 16 year period gave serum samples. 977 cases of diagnosed schizophrenia in this birth cohort were identified and these were matched with controls (without schizophrenia) for date of birth (within 1 month), sex, and residence in Finland at the time of case schizophrenia diagnosis.

The study found that heavy maternal nicotine exposure was related to a 38% increased odds of schizophrenia in offspring and these findings were not explained by maternal age, maternal or parental psychiatric disorders, socioeconomic status, or other covariates.

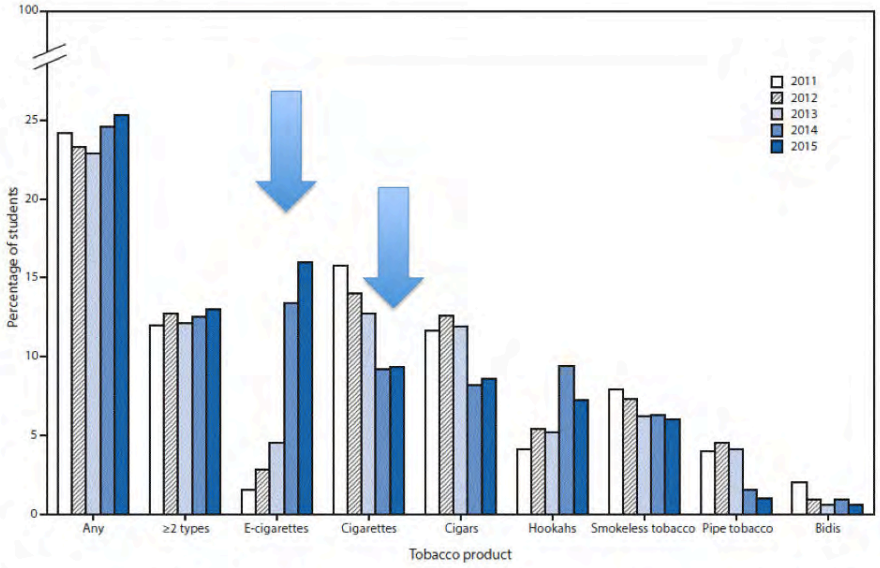
4. Youth uptake of ENDS

ENDS are a relatively recent phenomenon. Several nations, particularly the USA, have seen dramatic uptake of ENDS use among youth (middle and high school students). The most recent Centers for Disease Control data on tobacco and ENDS use by US youth shows that a continual fall in cigarette smoking that has been occurring since at least 1998 (6), has stopped in 2014 and 2015(7). The figure below, taken from the CDC report shows this decline and the halt in 2014.

It also shows the dramatic increase in ENDS use between the years 2011-2015.

It is clear that since the advent of ENDS, far more US youth are now using nicotine than at any time in the past decade. Much of this can be attributed to the spectacular rise in the use of e-cigarettes by youth.

FIGURE 1. Estimated percentage of high school students who currently use any tobacco products,* ≥2 tobacco products,† and select tobacco products§ — National Youth Tobacco Survey 2011–2015



* Any tobacco product use is defined as past 30-day use of cigarettes, cigars, smokeless tobacco, electronic cigarettes (e-cigarettes), hookahs, pipe tobacco, and/or bidis.

The relationship between ENDS use and subsequent uptake of smoking is both complex and highly contested. The so-called "gateway" hypothesis when applied to ENDS would product that there would be some non-smoking young people who would begin to use ENDS and who would then go onto start smoking, who in the absence of having used ENDS would be unlikely to have ever smoked. Refinements of this hypothesis have suggested that ENDS might serve as a "catalyst"(8) for smoking uptake. The authors of this paper stated that

> "Our results indicate that the perceived [lower] health risks, specific product characteristics (such as taste, price and inconspicuous use), and higher levels of acceptance among peers and others potentially make e-cigarettes initially more attractive to adolescents than tobacco cigarettes. Later, increasing familiarity with nicotine could lead to the reevaluation of both electronic and tobacco cigarettes and subsequently to a potential transition to tobacco smoking."

Hall and Lynskey(9) reviewed the gateway hypothesis literature on whether cannabis use "led" to other illicit drug use and concluded:

> "The available evidence indicates that the association reflects in part but is not wholly explained by: (1) the selective recruitment to heavy cannabis use of persons with pre-existing traits (that may be in part

> genetic) that predispose to the use of a variety of different drugs; (2) the affiliation of cannabis users with drug using peers in settings that provide more opportunities to use other illicit drugs at an earlier age; (3) supported by socialisation into an illicit drug subculture with favourable attitudes towards the use of other illicit drugs. Animal studies have raised the possibility that regular cannabis use may have pharmacological effects on brain function that increase the likelihood of using other drugs."

The 2014 Shattuck Lecture by Nobel prize winning neuro-psychiatrist Eric Kandell (https://en.wikipedia.org/wiki/Eric_Kandel)(published in the New England Journal of Medicine(10)) set out the molecular biological evidence for the proposition that nicotine may be a gateway drug.

Critics tend to blithely dismiss this possibility with the soundbite that "some kids will experiment with drugs", implying that all who started nicotine use with vaping and who later smoked would have done so regardless.

A very recent cohort study with 12 months follow up (T1 to T2) from Hawaii(11) provides important evidence against this hypothesis.

> "assessed e-cigarette use, propensity to smoke based on 3 psychosocial factors known to predict smoking (rebelliousness, parental support and willingness to smoke), and cigarette smoking status. Analyses based on T1 never-smokers tested the relation of T1 e-cigarette use to T2 smoking status for participants lower versus higher on T1 propensity to smoke. RESULTS: The relation between T1 e-cigarette use and T2 smoking onset was stronger among participants with lower levels of rebelliousness and willingness and higher levels of parental support. A multiple logistic regression analysis with T2 smoking as the criterion tested the cross-product of T1 e-cigarette use and T1 smoking propensity score; the interaction (OR=0.88, p=0.01) indicated a significantly larger effect for smoking onset among lower risk youth. CONCLUSIONS: The results indicate e-cigarette use is a risk factor for smoking onset, not just a marker of high risk for smoking. This study provides evidence that e-cigarettes are recruiting lower risk adolescents to smoking, which has public health implications."

Australia today has the lowest ever recorded rates of smoking by youth. Much of the discussion about the potential benefits of ENDS use accelerating in Australia concerns smokers who might switch completely ENDS. But such potential benefits need to be balanced against the possibility of non-smokers (particularly youth and ex-smokers) acquiring a nicotine dependency via ENDS and the possibility that this might have a gateway effect in some.

Here, policy about how current smokers might be able to access nicotine for ENDS use while maximizing the possibility that youth might also access it, remains a question of critical importance.

One suggestion that has been made by veteran drugs policy researcher Professor Wayne Hall and Dr Coral Gartner (University of Queensland)(12) has been to introduce a nicotine users licensing scheme to regulate access to nicotine for use in ENDS. Their proposal is adapted from a scheme described in PLoS Medicine for the licensing of smokers(13).

Is ENDS use harm-reducing compared with cigarettes?

A significant majority of those who use ENDS continue to smoke. The Figure below from the Smoking In England study, illustrates this. Good cohort data are not yet available showing the proportions of ENDS users who, over time, stop smoking altogether, relapse back to smoking, continue to "dual use" into the long term, and estimations of what proportions of these might have been expected ro quit smoking in the absence of the availability of ENDS.

There is a widespread assumption among ENDS users that any reduction in cigarette use associated with the concurrent use of ENDS is self-evidently harm-reducing. However, there is large-scale research on this question and it is not good news for the "cutting down obviously reduces risk" belief. Four cohort studies published since 2006 have reported on whether reducing smoking, as opposed to stopping smoking altogether, confers any mortality benefit.

A Norwegian cohort of 51,210 people followed from the 1970s until 2003 found "no evidence that smokers who cut down their daily cigarette consumption by >50% reduce their risk of premature death significantly." (14)

A Scottish study of two cohorts followed from the 1970s to 2010 also found no evidence of reduced mortality in reducers, but clear evidence in quitters and concluded "that reducing cigarette consumption should not be promoted as a means of reducing mortality." (15)

The largest study, from Korea involving nearly half a million men followed for 11 years, found no association between smoking reduction and all cancer risk but a significant decrease in risk of lung cancer, but with the size of risk reduction being "disproportionately smaller than expected".(16)

There seems little doubt that smokers who stop smoking completely and switch to ENDS will reduce their risk of early death

Allowing open access to ENDS nicotine supplies will also result in large-scale respiratory exposure to thousands of flavouring chemicals never assessed for safety via inhalation

Nicotine used in vapourised form is sold in preparations that are flavoured. A 2014 study in the US of 466 ENDS brands being advertised on the www noted 7,764 different flavor descriptors being advertised.(17)

The Flavor and Extract Manufacturers Association of the United States(18) has warned in an e-cigarette advisory (updated in 2016) that flavouring chemicals

used in e-cigarettes have been assessed only for their safety when used in foods.

None have been assessed for their safety when being inhaled in vapourised form. One study(19) noted that "A significant number of the flavour chemicals were aldehydes, a compound class recognised as 'primary irritants' of mucosal tissue of the respiratory tract." Cytotoxic cinnamon flavours are also used(20) and cherry flavor exposes users to the inhalation irritant benzaldehyde(21). Given that ENDS users inhale these vapourised mixtures between 200-600 times per day(22) (73,050 – 219,150 times per year), allowing free access to nicotine for use in ENDS in Australia (with the accompanying widespread promotional activities that would inevitably accompany such deregulation) would see large numbers of Australians exposed to the unknown but plausibly harmful array of

Research about the short term impact of such exposure is in its infancy eg:(23-25) and long-term consequences are of course unable to be assessed because of the short number of exposure-years ENDS users have experienced.

Appendix 2 (attached) shows the introductory summary of areas for a proposed cross-examination provided by lawyers for the US Food and Drug Administration in its defense in a case being currently brought by an ENDS producer Nicopure Labs. This summary contains considerable material that will be of interest to the TGA, coming from its counterpart in the United States.

Summing up

ENDS advocates wish to have much easier access to nicotine for use in vapourisers because they are convinced that they are significantly reducing harm compared to that caused by their previous use of cigarettes. They are almost certainly correct in this belief, although the factoid of ENDS being "95% less harmful" than smoking (derived from the guesses of a consensus group(26) whose provenance has been heavily questioned(27))has been justly criticized as being untethered from any evidence about what the true level of reduced harm will be(28) because that information will only be available in strong form in decades to come.

Smoking is the "Mt Everest" of harm, with two in three long term Australian users dying of smoking caused diseases(29). We do not know the size of the "mountain" that ENDS-caused mortality will turn out to be, but its population-wide impact might still be very considerable.

If a rescheduling of nicotine were to occur in such a way that would make it very easy for many young people to access liquid nicotine for vaping, this may have

important adverse consequences for Australia's goals of continuing to reduce smoking throughout the population. The long term business model for the ENDS industry must involve seeing cohorts of young people take up vaping, regardless of protests from that industry to the contrary(30). In the UK where it is illegal to sell ENDS supplies to children, a recent report found that 40% of ENDS retailers did so (http://www.localgov.co.uk/Retailers-flout-laws-on-selling-e-cigarettes-to-children/41409).

I hope the information I have provided will be of assistance to the TGA in developing its response to the application. I do not support the rescheduling as proposed by the applicant(s).

References

1. Mayer B. How much nicotine kills a human? Tracing back the generally accepted lethal dose to dubious self-experiments in the nineteenth century. Arch Toxicol. 2014;88(1):5-7.
2. Straif K, Loomis D, Guyton K, Grosse Y, Lauby-Secretan B, El Ghissassi F, et al. Future priorities for the IARC Monographs. The Lancet Oncology.15(7):683-4.
3. England LJ, Bunnell RE, Pechacek TF, Tong VT, McAfee TA. Nicotine and the Developing Human: A Neglected Element in the Electronic Cigarette Debate. American journal of preventive medicine. 2015;49(2):286-93.
4. Gurillo P, Jauhar S, Murray RM, MacCabe JH. Does tobacco use cause psychosis? Systematic review and meta-analysis. Lancet Psychiatry. 2015;2(8):718-25.
5. Niemela S, Sourander A, Surcel HM, Hinkka-Yli-Salomaki S, McKeague IW, Cheslack-Postava K, et al. Prenatal Nicotine Exposure and Risk of Schizophrenia Among Offspring in a National Birth Cohort. Am J Psychiatry. 2016;173(8):799-806.
6. Ahern C, Batchelor S, Blanton C, al e. Youth Tobacco Surveillance --- United States, 1998--1999. MMWR Morb Mortal Wkly Rep. 2000(49(SS10)):1-93.
7. Singh T, Arrazola RA, Corey CG, Husten CG, Neff LJ, Homa DM, et al. Tobacco use among middle and high school students - United States, 2011-2015. MMWR Morb Mortal Wkly Rep. 2016;65(14):361-7.
8. Schneider S, Diehl K. Vaping as a Catalyst for Smoking? An Initial Model on the Initiation of Electronic Cigarette Use and the Transition to Tobacco Smoking Among Adolescents. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2016;18(5):647-53.
9. Hall WD, Lynskey M. Is cannabis a gateway drug? Testing hypotheses about the relationship between cannabis use and the use of other illicit drugs. Drug Alcohol Rev. 2005;24(1):39-48.
10. Kandel ER, Kandel DB. Shattuck Lecture. A molecular basis for nicotine as a gateway drug. N Engl J Med. 2014;371(10):932-43.
11. Wills TA, Sargent JD, Gibbons FX, Pagano I, Schweitzer R. E-cigarette use is differentially related to smoking onset among lower risk adolescents. Tob Control. 2016.

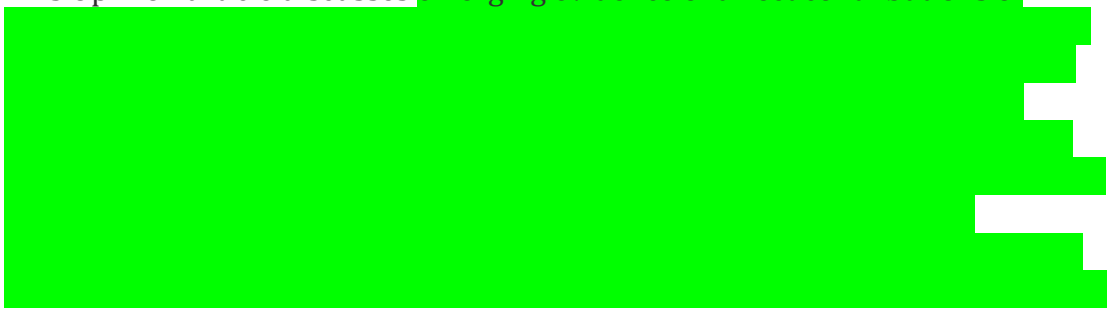
12. Gartner C, Hall W. A licence to vape: Is it time to trial of a nicotine licensing scheme to allow Australian adults controlled access to electronic cigarettes devices and refill solutions containing nicotine? The International journal on drug policy. 2015;26(6):548-53.
13. Chapman S. The case for a smoker's license. PLoS Med. 2012;9(11):e1001342.
14. Tverdal A, Bjartveit K. Health consequences of reduced daily cigarette consumption. Tob Control. 2006;15(6):472-80.
15. Hart C, Gruer L, Bauld L. Does smoking reduction in midlife reduce mortality risk? Results of 2 long-term prospective cohort studies of men and women in Scotland. American journal of epidemiology. 2013;178(5):770-9.
16. Song YM, Sung J, Cho HJ. Reduction and cessation of cigarette smoking and risk of cancer: a cohort study of Korean men. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2008;26(31):5101-6.
17. Zhu S-H, Sun JY, Bonnevie E, Cummins SE, Gamst A, Yin L, et al. Four hundred and sixty brands of e-cigarettes and counting: implications for product regulation. Tobacco Control. 2014;23(suppl 3):iii3-iii9.
18. Flavor and Extract Manufacturers Association of the United States. The safety assessment and regulatory authority to use flavors – focus on e-cigarettes. Flavor and Extract Manufacturers Association of the United States, 2015.
19. Tierney PA, Karpinski CD, Brown JE, Luo W, Pankow JF. Flavour chemicals in electronic cigarette fluids. Tob Control. 2016;25(e1):e10-5.
20. Behar RZ, Davis B, Wang Y, Bahl V, Lin S, Talbot P. Identification of Toxicants in Cinnamon-Flavored Electronic Cigarette Refill Fluids. Toxicol In Vitro. 2013.
21. Kosmider L, Sobczak A, Prokopowicz A, Kurek J, Zaciera M, Knysak J, et al. Cherry-flavoured electronic cigarettes expose users to the inhalation irritant, benzaldehyde. Thorax. 2016;71(4):376-7.
22. Martin EM, Clapp PW, Rebuli ME, Pawlak EA, Glista-Baker E, Benowitz NL, et al. E-cigarette use results in suppression of immune and inflammatory-response genes in nasal epithelial cells similar to cigarette smoke. Am J Physiol Lung Cell Mol Physiol. 2016;311(1):L135-44.
23. Sherwood CL, Boitano S. Airway epithelial cell exposure to distinct e-cigarette liquid flavorings reveals toxicity thresholds and activation of CFTR by the chocolate flavoring 2,5-dimethypyrazine. Respir Res. 2016;17(1):57.
24. Wang MP, Ho SY, Leung LT, Lam TH. Electronic Cigarette Use and Respiratory Symptoms in Chinese Adolescents in Hong Kong. JAMA Pediatr. 2016;170(1):89-91.
25. Lerner CA, Rutagarama P, Ahmad T, Sundar IK, Elder A, Rahman I. Electronic cigarette aerosols and copper nanoparticles induce mitochondrial stress and promote DNA fragmentation in lung fibroblasts. Biochem Biophys Res Commun. 2016;477(4):620-5.
26. Nutt DJ, Phillips LD, Balfour D, Curran HV, Dockrell M, Foulds J, et al. Estimating the harms of nicotine-containing products using the MCDA approach. Eur Addict Res. 2014;20(5):218-25.
27. Gornall J. Public Health England's troubled trail. BMJ. 2015;351:h5826.
28. Combes RD, Balls M. On the safety of e-cigarettes: "I can resist anything except temptation". ATLA. 2015;43:417-25.

29. Banks E, Joshy G, Weber MF, Liu B, Grenfell R, Egger S, et al. Tobacco smoking and all-cause mortality in a large Australian cohort study: findings from a mature epidemic with current low smoking prevalence. BMC Med. 2015;13:38.
30. Chapman S. The future of electronic cigarette growth depends on youth uptake. Med J Aust. 2015;202(9):467-8.

Appendix 1:

The elimination of cigarettes and other combusted tobacco products in the U.S.

This Opinion article discusses emerging evidence of direct contributions of



have tumorigenic effects, and these receptors might be able to be targeted for

Nilsson PJ, Ye W, Andersson TM, Nyrén O.

Bavara JH, Tae H, Settlage RE, Garner HR. Characterizing the Genetic Basis for

regulated by -2.73 fold); both are genes that have not been previously implicated

Cardinal A, Nastrucci C, Cesario A, Russo P. Nicotine: specific role in angiogenesis, proliferation and apoptosis. *Critical Reviews in Toxicology*, 2012; 42(1): 68–89 http://www.ncbi.nlm.nih.gov/pubmed/22050423

Momi N, Kaur S, Ponnusamy MP, Kumar S, Wittel UA, Batra SK. Interplay between smoking-induced genotoxicity and altered signaling in pancreatic carcinogenesis. Carcinogenesis. 2012 Sep;33(9):1617-28. doi: 10.1093/carcin/bgs186. Epub 2012 May 23.

Despite continuous research efforts directed at early diagnosis and treatment of pancreatic cancer (PC), the status of patients affected by this deadly malignancy remains dismal. Its notoriety with regard to lack of early diagnosis and resistance to the current chemotherapeutics is due to accumulating signaling abnormalities. Hoarding experimental and epidemiological evidences have established a direct correlation between cigarette smoking and PC risk. The cancer initiating/promoting nature of cigarette smoke can be attributed to its various constituents , which is the major psychoactive component, and several other toxic constituents, such as nitrosamines, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone, and polycyclic aromatic hydrocarbons. A better

understanding of the molecular mechanisms underpinning these events is crucial for the prevention and therapeutic intervention against PC. This review presents various interconnected signal transduction cascades, the smoking-mediated genotoxicity, and genetic polymorphisms influencing the susceptibility for smoking-mediated PC development by modulating pivotal biological aspects such as cell defense/tumor suppression, inflammation, DNA repair, as well as tobacco-carcinogen metabolization. Additionally, it provides a large perspective toward tumor biology and the therapeutic approaches against PC by targeting one or several steps of smoking-mediated signaling cascades.

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3514894/

Petros WP, Younis IR, Ford JN, Weed SA. Effects of tobacco smoking and nicotine on cancer treatment. Pharmacotherapy. 2012 Oct;32(10):920-31. doi: 10.1002/j.1875-9114.2012.01117.
http://www.ncbi.nlm.nih.gov/pubmed/23033231

A substantial number of the world's population continues to smoke tobacco, even in the setting of a cancer diagnosis. Studies have shown that patients with cancer who have a history of smoking have a worse prognosis than nonsmokers. Modulation of several physiologic processes involved in drug disposition has been associated with long-term exposure to tobacco smoke. The most common of these processes can be categorized into the effects of smoking on cytochrome P450-mediated metabolism, glucuronidation, and protein binding. Perturbation in the pharmacokinetics of anticancer drugs could result in clinically significant consequences, as these drugs are among the most toxic, but potentially beneficial, pharmaceuticals prescribed. Unfortunately, the effect of tobacco smoking on drug disposition has been explored for only a few marketed anticancer drugs; thus, little prescribing information is available to guide clinicians on the vast majority of these agents. The carcinogenic properties of several compounds found in tobacco smoke have been well studied; however, The implications of these data are still unclear but may lead to important questions regarding approaches to smoking cessation in patients with cancer.

Catassi A, Servent S, Paleari L, Cesario A, Russo P. Multiple roles of nicotine on cell proliferation and inhibition of apoptosis: implications on lung carcinogenesis. Mutat Res. 2008 Sep-Oct;659(3):221-31. doi: 10.1016/j.mrrev.2008.04.002. Epub 2008 Apr 11.

The genotoxic effects of tobacco carcinogens have long been recognized, the contribution of tobacco components to cancerogenesis by cell surface receptor signaling is relatively unexplored. nAChR are functionally present on human lung airway epithelial cells, on lung carcinoma [SCLC and NSCLC] and on mesothelioma and Different nAChR subunit

gene expression patterns are expressed between NSCLC from smokers and non-smokers. These observations led to the hypothesis that Here, we briefly overview the role and the effects of nicotine on pulmonary cell growth and physiology and its feasible implications in lung carcinogenesis.

Slotkin TA. If nicotine is a developmental neurotoxicant in animal studies, dare we recommend nicotine replacement therapy in pregnant women and adolescents? Neurotoxicol Teratol. 2008 Jan-Feb;30(1):1-19.

Tobacco use in pregnancy is a leading cause of perinatal morbidity and contributes in major ways to attention deficit hyperactivity disorder, conduct disorders and learning disabilities that emerge in childhood and adolescence. Over the past two decades, Importantly, the long-term alterations include effects on reward systems that reinforce the subsequent susceptibility to nicotine addiction in later life. There are also serious questions as to whether NRT is actually effective as an aid to smoking cessation in pregnant women and adolescents. This review considers the ramifications of the basic science findings of nicotine's effects on brain development for NRT in these populations.

Egleton RD, Brown KC, Dasgupta P. Nicotinic acetylcholine receptors in cancer: multiple roles in proliferation and inhibition of apoptosis. Trends Pharmacol Sci. 2008 Mar;29(3):151-8. doi: 10.1016/j.tips.2007.12.006. Epub 2008 Feb 11.

Nicotinic acetylcholine receptors (nAChRs) constitute a heterogeneous family of ion channels that mediate fast synaptic transmission in neurons. They have also been found on non-neuronal cells such as bronchial epithelium and keratinocytes, underscoring the idea that they have functions well beyond neurotransmission. Components of cigarette smoke, and NNK [4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone], are agonists of nAChRs.

Given the association of tobacco use with several diseases, the non-neuronal nAChR signaling pathway has considerable implications for cancer and cardiovascular disease. As a result, alpha7 nAChR might be a valuable molecular target for therapy of cancers such as lung cancer and mesothelioma. Future studies involving the design of nAChR antagonists with improved selectivity might identify novel strategies for the treatment of tobacco-related cancers.

Zeilder R, Albermann K, Lang S. Nicotine and apoptosis. Apoptosis. 2007 Nov;12(11):1927-43.

Cigarette smoking is associated with a plethora of different diseases. is the addictive component of cigarette but also This review provides an overlook how nicotine influences apoptotic processes and is thus directly involved in the etiology of pathological conditions like cancer and obstructive diseases.

Wickström R. Effects of nicotine during pregnancy: human and experimental evidence. Curr Neuropharmacol. 2007 Sep;5(3):213-22. doi: 10.2174/157015907781695955.

Prenatal exposure to tobacco smoke is a major risk factor for the newborn, increasing morbidity and even mortality in the neonatal period but also beyond. As nicotine addiction is the factor preventing many women from smoking cessation during pregnancy, nicotine replacement therapy (NRT) has been suggested as a better alternative for the fetus. However, the safety of NRT has not been well documented, and . As exposure to pure nicotine is quite uncommon in pregnant women, very little human data exist aside from the vast literature on prenatal exposure to tobacco smoke. The current review discusses recent findings in humans on effects on the newborn of prenatal exposure to pure nicotine and non-smoke tobacco. It also reviews the neuropharmacological properties of nicotine during gestation and findings in animal experiments that offer explanations on a cellular level for the pathogenesis of such prenatal drug exposure.

leads to apoptosis and mitotic abnormalities, a total abstinence from all forms of

Full text here http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2656811/

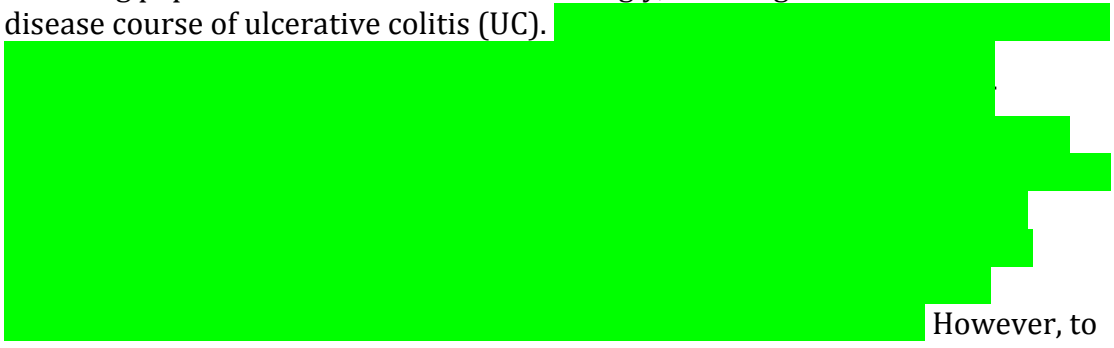
Grozio A, Catassi A, Cavalieri Z, Paleari L, Cesario A, Russo P.
Nicotine, lung and cancer. Anticancer Agents Med Chem. 2007 Jul;7(4):461-6.

The respiratory epithelium expresses the cholinergic system including nicotinic receptors (nAChRs). It was reported that normal human bronchial epithelial cells (BEC), which are the precursor for squamous cell carcinomas, and small airway epithelial cells (SAEC), which are the precursor for adenocarcinomas, have slightly different repertoires of nAChRs.

This is supported by the findings that nicotine can prevent apoptosis induced by various agents - such as chemotherapeutic in NSCLC, conferring a survival advantage as well.

Wu WK, Cho CH. The pharmacological actions of nicotine on the gastrointestinal tract. J Pharmacol Sci. 2004 Apr;94(4):348-58.

Increasing use of tobacco and its related health problems are a great concern in the world. Recent epidemiological findings have demonstrated the positive association between cigarette smoking and several gastrointestinal (GI) diseases, including peptic ulcer and cancers. Interestingly, smoking also modifies the disease course of ulcerative colitis (UC).



However, to elucidate this complex pathogenic mechanism, further study at the molecular

level is warranted. In contrast, findings of clinical trials give promising results on the use of nicotine as an adjuvant therapy for UC. The beneficial effect of nicotine on UC seems to be mediated through multiple mechanisms. More clinical studies are needed to establish the therapeutic value of nicotine in this disease.

Zhu B-Q, Heeschen C. Sievers RE, Karliner JS, Parmley WW, Glantz SA, Cooke JP. Second hand smoke stimulates tumor angiogenesis and growth. Cancer Cell 2003; Sept 191-196.

http://ac.els-cdn.com/S1535610803002198/1-s2.0-S1535610803002198-main.pdf?_tid=ad1f8084-a439-11e5-b823-00000aab0f6c&acdnat=1450300512_9ba5bb948ad346910e374692a9b5715a (full text)

Exposure to second hand smoke (SHS) is believed to cause lung cancer. Pathological angiogenesis is a requisite for tumor growth. Lewis lung cancer cells were injected subcutaneously into mice, which were then exposed to sidestream smoke (SHS) or clean room air and administered vehicle, cerivastatin, or mecamylamine. ,
Cerivastatin (an inhibitor of HMG-coA reductase) or mecamylamine (an inhibitor of nicotinic acetylcholine receptors) suppressed the effect of SHS to increase tumor size and capillary density. Cerivastatin reduced MCP-1 levels, whereas mecamylamine reduced VEGF levels and EPC.

with increases in plasma VEGF and MCP-1 levels, and EPC, mediated in part by isoprenylation and nicotinic acetylcholine receptors.

Submission for the Scheduling medicines and poisons

Date of submission invitation 4th August 2016

Submission relating to the application for the proposal to exempt nicotine from Schedule 7 at concentrations of 3.6 per cent or less of nicotine for self-administration with an electronic nicotine delivery system ('personal vaporiser' or electronic cigarette') for the purpose of tobacco harm reduction

I, [redacted] in the state of New South Wales, would like to submit the following in support of the above mentioned application.

[redacted] to smoking, and prevent access to this alternative to many current smokers.

In closing my submission is to:

Decriminalise the possession of e-liquid containing nicotine, and make it available as a consumer product, in the strength applied for in the application.

- I support making e-liquid available as a consumer product through responsible retail outlets.
- I support limited regulation that is proportionate to the risk. This may include ensuring it is made to a standard of quality, is correctly labelled, has child-proof caps and is not available to minors under the legal smoking age.

I give my consent for this submission to be posted on any website with the parts highlighted not for publication omitted

I make this submission in accordance with relevance to the aforementioned proposed amendment and feel addresses the matter mentioned in section 52E of the *Therapeutic Goods Act 1989.*

Signed and Dated this the 19th day of August 2016

[redacted]

For reasons outlined above I urge the TGA to reconsider the Schedule 7 Poisons Standard to allow nicotine at concentrations of 3.6% or less for the purpose of tobacco harm reduction.

Comment For The Scheduling Of Nicotine Regarding The Proposed amendments to the Poisons Standard

[redacted] In 2009 I discovered that E Cigarettes were available, along with the 'e-Juice' which contains various quantities of nicotine. I sourced the hardware and E liquid from internet vendors and researched which ones were the best quality.

[redacted]

[redacted]

The U.K government has been accepting of e-cigarettes, and the popularity of ecigs is now an everyday accepted phenomenon.

[redacted] I request the council goes ahead and permits the sale of nicotine liquids for use in personal vaporizers in Australia-the liquids can be sourced online and will be used anyway, so the official acceptance of this will make life that much easier for those who wish to quit the harmful Tobacco habit, if we can just go to a local shop and buy it.

Hello and thank you for the chance to have my say on this important topic.

I would welcome this application to have low strength nicotine be exempt from the poisons schedule and be available for people to use in personal vaporisers .

[redacted]

[redacted]

Through research it is obvious to me that nicotine is not as addictive as once was believed otherwise nicotine replacement therapies like gum and patches would not be available to anyone twelve years or older for as long as they like. By the way nicotine gums and patches are available at your nearest supermarket! Latest research also suggests it is nowhere near as deadly as was originally believed.

The Royal College of Physicians Uk has released a report Nicotine Without Smoke in which this highly regarded body recommends doctors advising patients to switch to vaping!

https://www.rcplondon.ac.uk/projects/outputs/nicotine-without-smoke-tobacco-harm-reduction-0

Public Health England has also endorsed vaping as far safer than smoking.

I fear that here in Australia we will be put many years behind places like the UK because our government and health organisations tend to listen to a few rusted on geriatric “health people” who are way out of touch with modern day harm reduction principles.

Every time people like Simon Chapman and Mike Daube release a report damning vaping they are immediately shot down by people who actually know how to research and read reports correctly without bias or conflicts of interest.

Please start to listen to people who do vape and not solely rely on people who will not engage in discussions with vapers and who consider our stories as being only anecdotal.

I suppose over six million vapers in Europe are anecdotal ?

[redacted]

30-8-16

Comment on the proposal to exempt nicotine from Schedule 7 at concentrations of 3.6 per cent or less of nicotine for self-administration with an electronic nicotine delivery system ('personal vaporiser' or 'electronic cigarette') for the purpose of tobacco harm reduction.

To TGA,

I write to comment on the proposal to exempt nicotine from Schedule 7 at concentrations of 3.6% or less for self-administration via electronic cigarettes or personal vaping devices. for the purposes of tobacco harm reduction.

[redacted]

[redacted] People with mental illness smoke in much higher rates than the general population, and the poor health outcomes reported in research are typically associated with smoking related harms. In my opinion, people with mental illness should be offered the opportunity to reduce or quit smoking using e-cigarettes. Exisiting nicotine replacement therapies have very poor efficacy and they are often costly, not at all affordable for people on a disability pension. E-cigarettes by comparison are very low cost, which increases the likelihood of their uptake by this population. I believe it is ethically wrong to withhold this potentially life saving intervention from people with mental illness, and the general population of smokers.

Nicotine on its own is a relatively benign drug, equivalent to caffeine in its effect and physiological impact. It is illogical to permit the sale and use of nicotine for other nicotine replacement therapies, yet ban nicotine use in e-cigarettes. The use of vaporizing as a safe and effective drug delivery system is well established, for example Ventolin pumps and puffers work in a similar way to deliver drugs to asthma patients. 'Vapor' has also been used widely since the 1970s in 'smoke machines' at concerts and nightclubs, and if there was any risk to health associated with vapor it would have been outlawed by Australia's stringent OH&S legislations many years ago. The most difficult and illogical position to understand with respect to this matter, however, is that cigarettes (proven lethal) are legal and available for sale at any corner store, yet nicotine use in e-cigarettes, which have helped millions of people to quit smoking, are illegal.

I believe that Australian adult consumers should be afforded the right to make an informed choice about how (and using what products) they wish to quit smoking. Every effort should be made to support the public in reducing smoking related harms, and permitting the use of nicotine in e-cigarettes provides greater choice for smokers wishing to quit.

Sincerely

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

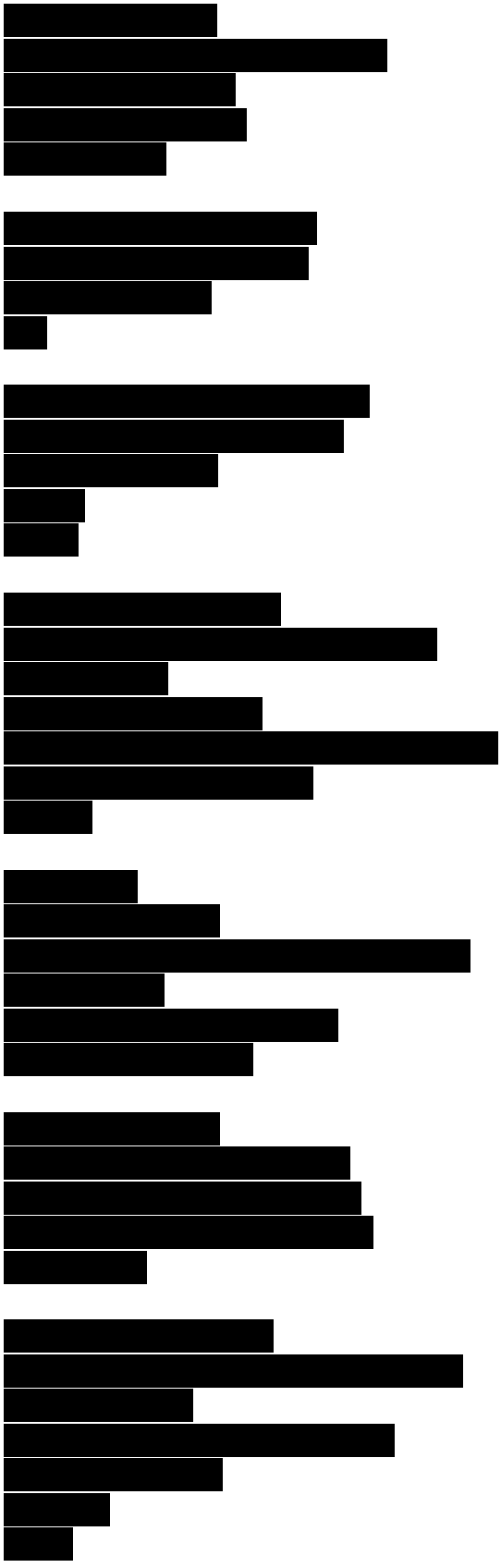
[redacted]

I would love to see nicotine e-liquid available in Australia even if it was limited to 24 - 36 mg for safety reasons, not just for my benefit but for the benefit of every smoker in Australia. Everyone deserves the chance to quit smoking in a safe and effective manner and experience life without the smokes, I believe if nicotine e-liquid was available in Australia a lot more people would quit smoking which would have huge benefits for our great country and stop so much suffering.

30/08/2016

Proposed Amendments to the Poisons Standard

America



Proposed Amendments to the Poisons Standard

Summary

The signatories above submit this comment in support of the application to amend Schedule 7 of the Poisons Standard to exempt nicotine in preparations with concentrations under 3.6 percent, the levels typically used in electronic nicotine delivery systems (ENDS). The comment is organised under the six headings covering matters the Minister should take into account when considering an application to amend Schedule 7.

(a) the risks and benefits of the use of a substance

The exemption would beneficially mitigate two important risks. Firstly, it would allow many more of Australia's 2.8 million smokers to legitimately switch from cigarettes to ENDS use ('vaping') and so substantially reduce their health risks. The Royal College of Physicians (London) recently stated that the risk of vaping is unlikely exceed 5 percent of the risk of smoking and may be substantially lower than that. However, the Poisons Standard creates a *de facto* prohibition on smokers adopting this option in Australia. Secondly, it would mean that Australians could purchase regulated nicotine liquids for vaping legitimately from Australian business and so avoid risks associated with a grey or black market supply chain and risks associated with handling and mixing of higher strength liquids.

(b) the purposes for which a substance is to be used and the extent of use of a substance

Nicotine liquids are used for the purpose of "tobacco harm reduction" – an approach that is proving popular and successful with smokers in the Europe and the United States without any major adverse consequences. Use of these products is making substantial inroads into the cigarette market and adult and adolescent smoking trends are consistent with ENDS use displacing smoking.

(c) the toxicity of a substance

The toxicity of nicotine liquids at the low concentrations proposed presents no significant risks beyond those already widely present in the home, for example from medicines or cleaning products, and these can be mitigated through straightforward packaging and labelling obligations.

(d) the dosage, formulation, labelling, packaging and presentation of a substance

An amendment to the schedule should include some supporting safeguards and standards that would be based on consumer protection concepts, such as clear labelling, accurate description of contents and secure packaging. Australia has the opportunity to assume leadership in regulation of nicotine products to optimise their potential for public health.

(e) the potential for abuse of a substance

Nicotine use through cigarette smoking can cause dependence. Nicotine liquids would be primarily used to reduce harm to smokers who cannot easily quit nicotine use or choose not to. If the harms associated with ENDS use are much lower, then the negative consequences of any residual nicotine dependence are greatly reduced.

(f) any other matters that the Secretary considers necessary to protect public health

There is a strong public health, ethical and pragmatic case to amend the schedule and to allow Australians access to much less risky ways to consume nicotine than smoking. The case for a *de facto* prohibition and denying Australians this option is very weak.

Proposed Amendments to the Poisons Standard

Comment on a proposal to amend the Poisons Standard Schedule 7 entry for nicotine

Introduction

This is a comment on the proposal to amend Schedule 7 of the Poisons Standard[1] to exempt nicotine in preparations for use as a substitute for tobacco in concentrations up to 3.6 percent - the concentrations commonly used in personal vaporisers or e-cigarettes.

We strongly support an amendment to exempt nicotine in low-concentrations for use in Electronic Nicotine Delivery Systems (ENDS) from Schedule 7 of the Poisons Standard.

Under Section 52E of the Therapeutic Goods Act, in exercising the power to amend Schedule 7, the Secretary (minister for health) must take the following matters into account (where relevant)[2]:

(g) the risks and benefits of the use of a substance;
(h) the purposes for which a substance is to be used and the extent of use of a substance;
(i) the toxicity of a substance;
(j) the dosage, formulation, labelling, packaging and presentation of a substance;
(k) the potential for abuse of a substance;
(l) any other matters that the Secretary considers necessary to protect public health.

This comment follows the structure of this section of The Act.

(a) The risks and benefits of the use of nicotine

a.1 Benefit of clean nicotine availability: mitigation of smoking-related risks

In 2014-15, 16 percent of Australian adults aged 18 years and over, 2.84 million people, were current smokers[3]. These are people using the mildly psychoactive drug nicotine via its most harmful and its least regulated and controllable delivery system – that is by inhaling tobacco smoke, mainly from cigarettes. The harms associated with nicotine use are overwhelmingly caused by its delivery to the lungs via toxic particles and gases that contain products of combustion of tobacco leaf, not the nicotine itself. The harms are significant and well documented[4] – smoking is a major cause of cancer, cardiovascular disease and respiratory illness, as well as degraded welfare and wellbeing. Each year, smoking kills an estimated 15,000 Australians and costs Australia $31.5 billion in social (including health) and economic costs[5].

In addition to the harms caused directly by smoking, there are additional harms to continuing smokers arising from the *policy response* that aims reduce smoking – for example through high and regressive tobacco taxation or the stigma or alienation that many smokers feel through the public

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1 Government of Australia, Therapeutic Goods Administration, The Poisons Standard July 2016. Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) [link] made under 52D(2)(b) of the *Therapeutic Goods Act* 1989 [link]
2 Therapeutic Goods Act, 1989 section 52E [link]
3 Australian Bureau of Statistics, National Health Survey: First Results, 2014–15 — Australia. Table 9. [link]
4 Surgeon General of the United States. The Health Consequences of Smoking—50 Years of Progress. Centers for Disease Control and Prevention (US) 2014. [link]
5 Australian Government, Department of Health, Tobacco Control key facts and figures, accessed 16 August 2016 [link]

health strategy of 'denormalising' smoking. While these policy impacts may be considered a price worth paying to reduce smoking, they are nevertheless a significant detriment to those who continue to smoke.

While nicotine is not entirely benign, it accounts for a very small fraction of the direct harm caused by smoking. Studies of the health effects of prolonged NRT use and smokeless tobacco have allowed the nicotine health effect to be isolated from the overall smoking health effect. The Royal College of Physicians (2016) describe the effects of nicotine alone as follows[6]:

Nicotine is the main reason why people smoke, but not the direct cause of harm. To summarise[7]:

In its extensive April 2016 report[8], the Royal College of Physicians (London) characterised the relative risk of smoking and e-cigarette use as follows:

At present, Australia's legal recreational nicotine market is dominated by cigarettes. There is no justification for purposefully denying smokers access to products that are a much safer way of using nicotine than smoking. The proposed amendment allows for significant individual and population *risk reduction* that is currently blocked by the Poisons Standard.

a.2 Benefit of clean nicotine availability: mitigation of supply chain risks

Australia's *de facto* prohibition of nicotine liquids for harm reduction does not mean there is no use for this purpose in Australia. In fact, there is a thriving, though unquantified, consumer base of people who are using these products to mitigate their smoking-related risks and to take control of their health outcomes. In doing so, they are forced to circumvent the restrictions of the Therapeutic Goods Act and to purchase internationally from many legitimate websites that cater for this trade or through an unregulated black market.

The economics of the international trade incentivises users to purchase nicotine at higher concentrations (as high as 99 percent), and higher than they would generally use (typically up to 3.6 percent) and then handle, mix and dilute the high strength liquids down to their preferred mix with obvious handling risks. Purchases can be made from many high quality web sites, with prices in multiple currencies, secure payments systems, reputable couriers and paperwork and certification, yet with uncertain quality, ingredients and safety[9]. The example below is a marketing email from a Chinese supplier provided for illustrative purposes.

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6 Royal College of Physicians (London) Nicotine without smoke: tobacco harm reduction 28 April 2016 [link]

7 Russell MJ. Low-tar medium nicotine cigarettes: a new approach to safer smoking. BMJ 1976;1:1430–3. [link]

8 Royal College of Physicians (London) Nicotine without smoke: tobacco harm reduction 28 April 2016 [link] Section 5.5.

9 See test purchase experience: Bates C. Regulators and the compliance fallacy - buying 99% nicotine e-liquid from China, The Counterfactual [link]

Example of unsolicited promotional email for Chinese-supplied e-liquids
We are specializing in 99.95% pure nicotine, PG VG based nicotine liquid from 36mg/ml-600mg/ml and about 500 kinds flavors in China. **About Product details:** **Pure nicotine is 99.95% USP grad, 1000mg/ml.** **Price is :** USD $196/1.15L 500ml is $100 (20ml sample for free test) **Flavor is USP grade, pure concentrate liquid.** **Flavor Price:** Tobacco series & Mint series USD $75 per liter, 500ml is $38 Fruit series & Herb & Flowers USD $62 per liter, 500ml is $31 **Flavor sample:** 125ml sample is $10 per one. **Certificate**: COA and MSDS. **Packing:** Fluorinated bottle and aluminum foil bag. **Delivery:** We always send by FedEx, DHL, TNT, UPS.

The offer of 500ml of 99.95% e-liquid for US$100 makes this purchasing option *extremely* cost effective. Assuming 99.95% is equivalent to pure nicotine in in the calculation below:

- ~100% nicotine liquid = 1000mg/ml
- Half litre = 500ml = 500,000mg nicotine
- Typical daily vaper nicotine consumption = 36mg nicotine[10]
- 500,000 mg = 13,889 day supply = 38 years supply or one-year supply for 38 people
- Cost = $2.60 per person-year

We believe that a regulated domestic market for these liquids would be a preferable way to meet the rational and legitimate expectations of Australians to be able to use products that can dramatically reduce their risks. These products are widely available in Europe and the United States with no material harms arising. The proposed amendment would extend a safe supply to Australians: nicotine liquids could be prepared by local manufacturers and made available locally.

(b) The purposes for which nicotine is to be used and extent of use of nicotine

The primary purpose of the amendment would be to allow Australian smokers to use nicotine through technologies that cause much lower risk to health than through smoking, for example through use of e-cigarettes or personal vaporisers – so called Electronic Delivery Systems (ENDS). These technologies rely on electricity to heat a liquid to create an inhalable aerosol rather than combustion of tobacco to create smoke. These technologies have grown rapidly over the last five years primarily because advances in battery technology have allowed for small devices with sufficient power and battery life to make viable consumer alternatives to cigarettes. Experience from other countries suggests that the products in their current state of advancement can reach many smokers – and given continuing innovation will reach many more in future if the regulation and risk communications are fair and proportionate.

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[10] Farsalinos KE, Romagna G, Tsiapras D, *et al.* Characteristics, Perceived Side Effects and Benefits of Electronic Cigarette Use: A Worldwide Survey of More than 19,000 Consumers. *Int J Environ Res Public Health* 2014;**11**:4356–73. Table 2 [link]

b.1 United Kingdom experience

We do not have recent detailed data for e-cigarette use in Australia. In 2013, an international survey found that among Australian smokers 9 percent were current users and 24 percent had tried e-cigarettes[11]. In the United Kingdom where ENDS are widely available, the use of these alternatives is now at a material scale relative to smoking. The Office of National Statistics reported data for 2015[12]

Smoking and e-cigarette users 2015	British adults
Current smokers	8,843,000
Current e-cigarette users	2,201,000
Of the current e-cigarette users:	
Current smokers	1,297,000
Ex-smokers	849,000
Never smokers	56,000
Ex-smokers and ex-e-cigarette users	717,000

Figures rounded to nearest 1,000

The use of ENDS by never-smokers in the UK is very low (0.2 percent of never smokers use e-cigarettes) and even among this group, 39% said they had used e-cigarettes to help them quit smoking. This means the appropriate comparator is with the risks to nicotine users who are smoking. Many of those who are both smoking and using e-cigarettes may be on a path to eventual exclusive use and some evidence suggests that these 'dual users' are more likely to go on to quit[13]. The 849,000 current ENDS users and 717,000 former ENDS users who have stopped smoking represent a substantial inroad into the smoking population, though it is not possible to attribute their smoking cessation directly to ENDS use. However, the trend in smoking prevalence is also encouraging. The 8.8m current smokers represents current *record low* adult smoking prevalence of 17.5 percent[14]. After stalling in the late-2000s smoking prevalence has been falling rapidly as e-cigarette use has increased from negligible levels in 2011. Throughout this period of widespread ENDS use there have been no major health problems or any other problems – though many ENDS users are now no longer smoking and will be gaining significant benefit from smoking cessation.

b.2 United States experience

Similar patterns are seen in the United States. The National Health Interview Survey[15] shows that U.S. adult smoking prevalence (18 years and over) has fallen from 18.9 percent in 2011 to a record low of 15.1 percent in 2015 – below that of Australia – with an especially sharp decline between 2014 and 2015 – see figure below. As with Britain, the impact of ENDS on the cigarette trade is substantial: in 2015, there were approximately 37.5m smokers, but there were 8.3m e-cigarette users of whom 2.5m were ex-smokers[16].

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11 Gravely S, Fong G, Cummings K, *et al.* Awareness, Trial, and Current Use of Electronic Cigarettes in 10 Countries: Findings from the ITC Project. *Int J Environ Res Public Health* 2014;**11**:11691–704. [link]

12 Office of National Statistics (UK), E-cigarette use in Great Britain, 2015 Dataset. 18 February 2016 [link] Table 2a.

13 Manzoli L, Flacco ME, Ferrante M, Vecchia CL, Siliquini R, Ricciardi W, et al. *Cohort study of electronic cigarette use: effectiveness and safety at 24 months.* Tobacco Control. 2016 [link]

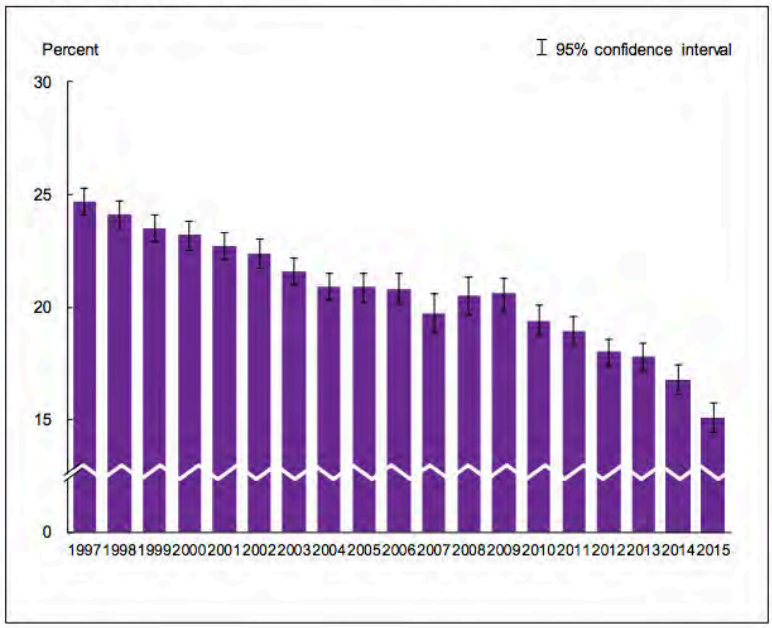
14 Office of National Statistics (UK), Adult Smoking Habits in Great Britain1974-2014. 18 February 2016 [link] Table 1.

15 National Center for Health Statistics, *National Health Interview Survey, 1997–2015*, Sample Adult Core component. Figure 8.1. Prevalence of current cigarette smoking among adults aged 18 and over: United States, 1997–2015. [link]

16 CDC, *National Health Interview Survey, 2015 Data Release* [link]; Cited in Rodu B. *How Many Americans Vape? CDC Data Show Fewer Vapers & Smokers in 2015*, Tobacco Truth 17 July 2016 [link]

Current smoking

Figure 8.1. Prevalence of current cigarette smoking among adults aged 18 and over: United States, 1997–2015



Source: National Center for Health Statistics, *National Health Interview Survey, 1997–2015*

b.3 Adolescent ENDS use

There have been concerns expressed that adolescent uptake of ENDS may be 'addicting future generations'. However, the data suggest a different pattern. Most use is by teenage smokers and data is consistent with ENDS use displacing smoking.

In the UK, use of ENDS among adolescents is low and confined mainly to young smokers. A March 2015 survey found 2.4 percent of 11-18 year olds had used e-cigarettes in the last month, and these were mainly smokers[17].

In the United States, almost all adolescent users of ENDS are former or current smokers, and therefore ENDS represents a *change* in the way nicotine is used for most. Analysis of CDC 2014 data shows that 90 percent of the 1.96m current e-cigarette high school users are current or former users of other tobacco products[18]. Some of the remaining 10 percent may have become smokers in the absence of e-cigarettes. There is no evidence supporting a gateway from ENDS to smoking[19].

In fact, smoking among American adolescents has been falling rapidly. The National Youth Tobacco Survey (CDC)[20] shows that between 2011 and 2015, current use of cigarettes by high school students fell from 15.8 percent to 9.3 percent, and use of cigars and pipes also fell. The data are consistent with a decline in smoking partly due to displacement by much lower risk ENDS (an 'exit gateway'), though it is not possible to attribute causation from this type of survey.

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17 YouGov for Action on Smoking and Health (UK) Smokefree GB Youth Survey. Published in ASH Fact sheet [link]

18 Rodu, B. Analysis of CDC National Youth Tobacco Survey 2014, The CDC Buries the Lead: Teen E-cigarette Use Rises as More Dangerous Cigarette Use Plummets, 13 October 2015 [link]

19 McNeill A, Brose LS, Calder R, *et al.* E-cigarettes: An Evidence Update. A Report Commissioned by Public Health England. London: 2015. [link] Section 4 *Gateway* page 37

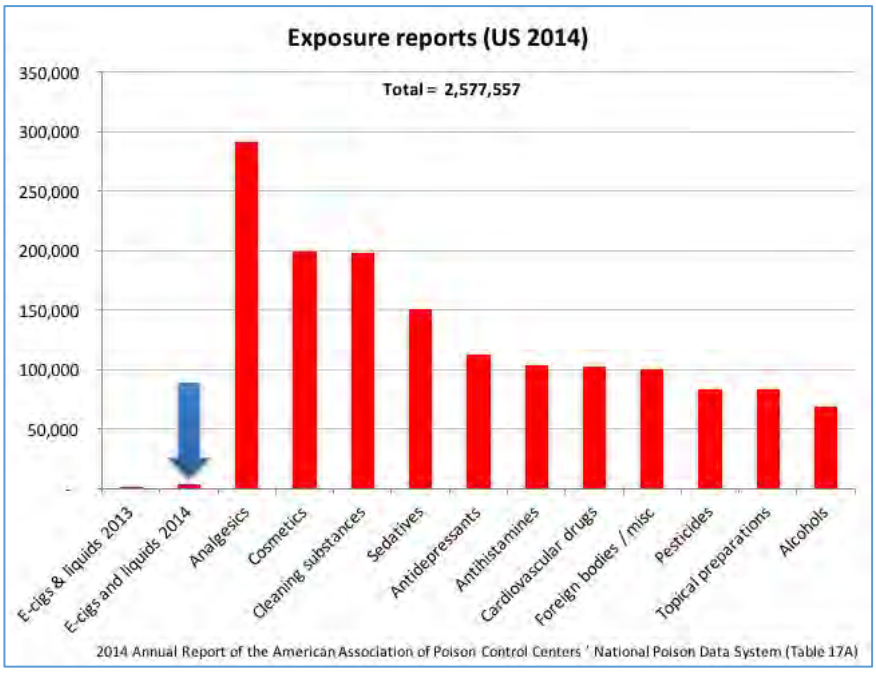
20 Singh T, Arrazola RA, Corey CG, et al. *Tobacco Use Among Middle and High School Students — United States, 2011–2015*. MMWR Morb Mortal Wkly Rep 2016;65:361–367. [link]

(c) The toxicity of nicotine

Public Health England's expert review addressed the toxicity risks of nicotine liquids used for personal vaporisers[21]. The review noted that:

- fatal nicotine poisoning is extremely rare
- conventional estimates of LD_{50} for humans (30-60mg ingestion) are grounded in 'dubious' 19th Century experiments and the likely lethal dose is much higher[22]
- that individuals attempting suicide with nicotine have survived very high doses
- nicotine inhalation is self-regulating as users become nauseous
- that nicotine is an emetic and swallowing a significant dose ends in vomiting.

American activists have publicised rapidly rising calls to poison centers as though it a proxy for poisoning risks[23]. However, these calls are from a low base, rise in line with growth in the product from 2011 and refer to 'exposures' (any contact) rather than poisoning or harm. E-liquid or e-cigarette related calls to poison centers rose from 271 in 2011 to 3,783 in 2014, though have been declining since[24]. However, these figures are small compared to other normal household risks[25].



Data source: American Association of Poison Control Centers 2014 Annual Report

The approach to poisoning risks with nicotine liquids should be as with other moderate household hazards: child-resistant containers, labelling, and advice on what to do in the event of contact. This can be specified through ordinary consumer regulation, and is done for a large number of consumer products.

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21 McNeill A, Brose LS, Calder R, *et al.* E-cigarettes: An Evidence Update. A Report Commissioned by Public Health England. London: 2015. [link] Section 9 page 63-67

22 Mayer B. How much nicotine kills a human? Tracing back the generally accepted lethal dose to dubious self-experiments in the nineteenth century. *Arch Toxicol* 2014;**88**:5–7. doi:10.1007/s00204-013-1127-0 [link]

23 Campaign for Tobacco Free Kids, Poisoning Cases Related to E-Cigarettes Keep Spiraling Upward, September 2014 [link]

24 American Association of Poison Control Centers, E-Cigarettes and Liquid Nicotine, viewed 21 August 2106 [link]

25 Mowry JB, Spyker DA, Brooks DE, *et al.* 2014 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 32nd Annual Report. *Clin Toxicol* 2015;**53**:962–1147.(Table 17A) [link]

(d) The dosage, formulation, labelling, packaging and presentation of nicotine

We support the proposal to exempt nicotine preparations up to 3.6 percent nicotine from schedule 7 of the Poisons Standard for use in ENDS for harm reduction. Given that nicotine "*in tobacco prepared and packed for smoking*" is exempted from Schedule 7, it is discriminatory and 'anti-proportionate' to continue to include the much lower-risk commercial alternative.

d.1 Standards to build into the Schedule 7 exemption

Exempting these nicotine liquids from Schedule 7 would approximately recreate the regulatory regime that has worked well in Europe and the United States prior to introduction of the European Union Tobacco Products Directive on 20 May 2016 and FDA Deeming Regulation on 8 August 2016 respectively. Though specifying the exemption provides the TGA with opportunities to specify some conditions regarding the packaging:

- Intended for recreational use in electronic cigarettes, personal vaporizers or other nicotine delivery systems that do not include tobacco prepared and packed for smoking.
- Where no therapeutic claim is made by the manufacturer
- That do not exceed 3.6 percent nicotine concentration (by mass)
- In a child resistant container specified to ISO standard 8317[26]
- Accurately labelled with nicotine content usually specified as mg/ml
- List of ingredients
- Appropriate warnings regarding children

The threshold of 3.6 percent is sensible and cautious. Though the large majority (>90 percent) of consumers are likely to use liquids under 2.0 percent[27], the stronger liquids are important for the more highly dependent nicotine users (and hence more at-risk smokers); for novice users while they learn to use the products; and to support future innovations.

d.2 Towards a world-leading regulatory regime for ENDS

An amendment as proposed also gives Australia an opportunity to define a world-leading proportionate public-health orientated regulatory framework for ENDS. The regime defined in the United States is built on legislation designed for tobacco products before ENDS existed. The European Union Tobacco Products Directive is based on pre-2012 understanding of the risks and potential benefits. Neither provides a model for Australia, or anywhere.

Such an approach would be based on industry-wide standards for ENDS and e-liquids – and could be variations on those developed by British Standards Institute (BSI)[28] and in France under the equivalent body, AFNOR[29], or a forthcoming European CEN standard.

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[26] ISO 8317 Child resistant packaging [link][guide]

[27] Action on Smoking and Health, Fact sheet: ASH Fact Sheet on the use of electronic cigarettes among adults in Great Britain [link]

[28] BSI PAS 54115:2015 Vaping products, including electronic cigarettes, e-liquids, e-shisha and directly-related products - Manufacture, importation, testing and labelling - Guide [link] July 2015

[29] AFNOR (France) Electronic cigarettes and e-liquids Part 1: Requirements and test methods for e-cigarettes XP D90-300-1 March 2015 [link] and Part 2: Requirements and test methods for e-cigarette liquid XP D90-300-2 [link] March 2015

(e) The potential for abuse of nicotine

e.1 Psychoactive properties of nicotine

Nicotine is a mildly psychoactive drug with few side effects or direct harms, and, unlike alcohol, it does not cause intoxication and resulting accidents, violence and vulnerability. According to Benowitz[30].

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mance

It may be that these benefits are in fact manifestations of relief from withdrawal or craving – i.e. there no additional benefits compared to being a non-user. However, this interpretation is controversial and for those already dependent on nicotine it is of academic interest only – these are rewards that are experienced directly and contribute to continued use.

e.2 Dependence on smoking

Nicotine is dependence-forming when smoked on account of its activation of reward systems in the brain; the speed with which a peak nicotine blood concentration is reached through lung delivery; the presence of other substances in tobacco smoke (for example, monoamine oxidase inhibitors) that contribute to dependence; sensory effects such as 'throat hit'; conditioning behaviours and cues that trigger craving.

e.3 Dependence on ENDS

The use of nicotine liquids has been overwhelmingly concentrated in current or former smokers who are already exposed to nicotine and may be dependent on nicotine through smoking. It is likely that nicotine delivered through electronic delivery systems (ENDS) is less dependence-forming than through smoking: there are other agents present in cigarette smoke that contribute to dependence and the pharmacokinetics of nicotine delivery by ENDS is 'slower'. However, that is not a reliable assumption for the longer term – the success of ENDS as a public health intervention depends on replacing the experience of smoking with a satisfying way to take nicotine that is less harmful.

(f) Any other matters necessary to protect public health

f.1 The value of lifting Australia's *de facto* prohibition on e-liquids

Policymakers must base decisions with real-world life-or-death consequences on a dispassionate view of the evidence, and the scientific evidence now suggests that electronic nicotine delivery systems (ENDS) could be a benefit to millions of smokers.

- Smokers who switch to ENDS are likely to avoid at least 95% of the major smoking-related risks for cancer, heart disease and respiratory illness. They will also experience significant short-term gains in health and wellbeing and, in high tobacco tax jurisdictions like Australia they are likely to be financially better off. No government should deliberately try to deny smokers this option – now adopted by millions of smokers world-wide.

[30] Benowitz NL. Nicotine addiction. *N Engl J Med* 2010;**362**:2295–303. [link]

- It is unethical to deny a smoker access to products that are much safer than the dominant product on the market, cigarettes[31]. Outside the field of tobacco and illicit drugs, there are no precedents for banning safer alternatives to widely used products.
- The availability of ENDS is not an alternative to conventional anti-smoking policy but complementary. By providing smokers with an easier way of responding to the pressures of high taxes and other measures, the overall tobacco control policy will become both more responsive and more humane.
- There is no credible evidence to suggest that ENDS undermine tobacco control, induce young people to smoke, or reduce the rate that adults quit smoking. The evidence, when examined dispassionately, shows what a neutral observer would expect unless presented with evidence to the contrary: people use much safer products to reduce their health risks or quit smoking.
- ENDS are an effective tool for switching from smoking at no cost to the public purse – the individual smokers bear the costs.
- A widespread switch to ENDS would reduce exposure to second-hand tobacco smoke. E-cigarettes pose no material risk to bystanders[32].
- The quality of products available from reputable manufacturers is now very high and they are on widespread sale in the European Union, North America and throughout Asia without any major problems.
- There is a growing international experience with the regulation of ENDS as consumer products, and, by changing its approach, Australia has the opportunity to take a leadership role in these developments.
- It would be better for Australia to have its own legitimate and properly regulated supply chain and to have responsible producers contributing corporate and sales taxes as appropriate, and less international internet trade in high strength liquids.
- There is no reason to protect the cigarette trade in Australia from competition from superior low-risk products or erect regulatory barriers to entry that are so severe that only tobacco companies have the resources to enter the market, if any company does.

Misrepresentation of scientific findings by some academics and the media have combined to exaggerate risks but understate the benefits of e-cigarettes. There are no precedents for banning safer products while leaving the most dangerous products widely available. On the contrary, ENDS will *support* a tobacco control agenda by giving smokers options to respond to increasing taxes and other controls on smoking. ENDS offer far safer options to smokers than coping with high taxes by switching to buying cigarettes on the black market.

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31 Hall W, Gartner C, Forlini C. Ethical issues raised by a ban on the sale of electronic nicotine devices. *Addiction* 2015; **110**:1061–7 [link]

32 Burstyn I. Peering through the mist: systematic review of what the chemistry of contaminants in electronic cigarettes tells us about health risks. *BMC Public Health*, 2014 [link]

f.2 The experience of users

Ministers, officials and regulators should be mindful of the human consequences of their decisions and avoid dehumanising the 2.8 million Australians who smoke. Vapers in Australia[33], the United Kingdom[34] and the United States[35] provide moving and inspiring testimony of their experience in using ENDS to quit smoking. Three examples of thousands of user testimonials are included below in their own words:

Example of experience from Australia

[redacted]

Example of experience from the UK

[redacted]

Example of experience from the United States

[redacted]

f.3 The preferences of users

A 2014 survey of Australian vapers[36], an important group of notional beneficiaries of Australia's policy approach, drew the following conclusion about attitudes to regulation:

[redacted]

The Secretary should reflect on the justification for state intervention to *prevent* smokers adopting vaping. There is now every reason to encourage rather than discourage these user experiences in Australia. There is no reason for any government to place obstacles in the way of smokers making the life-saving transformations described in the testimonials above and thousands of others.

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33 AussieVapers forum, Your story. [link]

34 Counterfactual. UK vaping testimonies. clivebates.com. [link]

35 Consumer Advocates for Smoke-free Alternatives Association (CASAA), E-cigarette user testimonials. [link]

36 Fraser D, Weier M, Keane H, *et al.* Vapers' perspectives on electronic cigarette regulation in Australia. *Int J Drug Policy* 2015;**26**:589–94. [link]

This submission is in support of the proposal to exempt liquid nicotine at a concentration of 3.6% and below from the Poisons Schedule. I have no financial, or other interests, in either the electronic cigarette industry or the tobacco industry.

This submission will examine current recommendations from the United Kingdom; the toxicity of nicotine; risk to children and youth; efficacy for smoking cessation; risk to bystanders; and long-term effects of vaping.

"Bans of e-cigarettes based on harms that are minor compared to smoking are likely to perversely protect tobacco sales from competition." – Dr Murray Laugesen.

"We have such a massive opportunity here. It would be a shame to let it slip away by being overly cautious. E-cigarettes are about as safe as you can get." – Professor Peter Hajek.

"It is absolutely irresponsible and dangerous behaviour to ban e-cigarettes." – Dr Konstantinos Farsalinos.

Recommendations from the United Kingdom

The Australian Government has an opportunity to embrace tobacco harm reduction to enable many Australians to stop smoking. The use of electronic cigarettes/personal vaporisers has been embraced by Public Health England and the Royal College of Physicians as an effective way for people to stop smoking. Both of these groups have estimated that vaping is at least 95% safer than smoking and both groups recognise that the electronic cigarette industry is not some ploy by the tobacco industry to addict young people to nicotine.
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/457102/Ecigarettes_an_evidence_update_A_report_commissioned_by_Public_Health_England_FINAL.pdf

https://www.rcplondon.ac.uk/projects/outputs/nicotine-without-smoke-tobacco-harm-reduction-0

"Saying e-cigs are 95% safer is not a medical claim it's a truth." – Professor Linda Baud.

Toxicity

It is widely accepted that people smoke for the nicotine but die from the tar. Nicotine is an essential ingredient in electronic cigarette liquid for people who want to stop smoking. (http://www.la-press.com/evaluating-nicotine-levels-selection-and-patterns-of-electronic-cigare-article-a3858-abstract). Nicotine, at the level used in personal vaporisers, is of no more concern as a poison than many household cleaning products and cosmetics. Oral Ingestion of enough nicotine to be of concern leads to vomiting and therefore, it is expelled from the body. There are also questions around the currently accepted toxicity levels (see link below).

http://link.springer.com/article/10.1007%2Fs00204-013-1127-0/fulltext.html

"It seems very safe even in non-smokers. In our studies we find it actually reduces blood pressure chronically. And there were no addiction or withdrawal problems, and nobody started smoking cigarettes. The risk of addiction to nicotine alone is virtually nil." – Dr Paul Newhouse, Director, Vanderbuilt University Center for Cognitive Medicine.

The Children

Many people have asserted that children and young people will take up vaping in large numbers and then progress to smoking cigarettes. There is no evidence of large numbers of children and young people taking up vaping (the few who do are largely smokers) and there is no evidence that a so

called ‘gateway effect’ occurs whereby non-smokers start vaping and progress to smoking. Most electronic cigarette use by young people does not involve nicotine. Therefore, there is no potential for an addiction to be created.

http://tobaccocontrol.bmj.com/content/early/2016/07/21/tobaccocontrol-2016-053014.full

Please also see the Public Health England and Royal College of Physicians reports linked above.

Electronic Cigarette use for Cessation

Some submissions about this subject may assert that people who use personal vaporisers are less likely to quit smoking than those who do not. This assertion was based on a flawed meta-analysis undertaken in the USA which was subsequently debunked by many subject matter experts (see link below for one example).

http://www.clivebates.com/?p=3560

Likewise, some submissions about this subject may assert that there is little evidence that people who use personal vaporisers quit smoking at any great rate due to most of the studies being conducted on convenience samples of vapers. However, evidence of people quitting smoking using these devices does continue to grow. Recently, scientists from the University of Patras-Greece, Onassis Cardiac Surgery Centre-Greece, and the French National Institute for Health and Medical Research analysed the data from the 2014 Eurobarometer on smoking and the use of electronic cigarettes. They found that among the current 27460 e-cigarette users surveyed that 35.1% had quit smoking and 32.2% had reduced their cigarette consumption. (http://www.ncbi.nlm.nih.gov/pubmed/27338716) They also found that use by non-smokers was minimal. The Eurobarometer is a survey performed by the European Commission which enrolled a large number of Europeans representative of the European Union so it can be generalised to the population, which means that 6.1 million Europeans have quit smoking by using electronic cigarettes.

“It’s pretty clear to me that e-cigarettes have helped more people quit smoking than the 2009 Tobacco Control Act, all the FDA approved smoking cessation drugs and all the government anti-tobacco propaganda programs combined.” – Bill Godshall, Executive Director, Smokefree Pennsylvania.

Air Quality

Some submissions about this subject may assert that there is not enough evidence about what is in the vapour and that it may harm others. This has been extensively studied and no evidence has been found of any harmful chemicals in the vapour and ambient air at a level that would harm bystanders. Two such studies are linked below for your perusal.

http://www.ncbi.nlm.nih.gov/pubmed/23033998

http://bmcpublichealth.biomedcentral.com/articles/10.1186/1471-2458-14-18

“A considerable advantage to vaping is that there is no risk to bystanders.” – ASH, UK.

Long Term Data

Whilst it is true that there have been no long term studies (50+ years) regarding the use of electronic cigarettes due to the newness of these devices, there is a growing body of evidence that suggests negative effects of use in the long term are unlikely. A recently published longitudinal study which

analysed the biomarkers of smokers who switched to vaping found significant drops, similar to what occurs in smokers who stop smoking cold turkey.
http://ntr.oxfordjournals.org/content/early/2016/08/16/ntr.ntw160

Stable, long term improvements in asthma symptoms have been found in smokers who switch to electronic cigarettes which demonstrates a significant level of harm reversal.
http://www.discoverymedicine.com/Riccardo-Polosa/2016/02/persisting-long-term-benefits-of-smoking-abstinence-and-reduction-in-asthmatic-smokers-who-have-switched-to-electronic-cigarettes/

"If we could get all of those people [who smoke] to completely switch all of their cigarettes to non-combustible cigarettes, it would be good for public health." – Mitch Zeller, Director, Center for Tobacco Products, FDA.

Conclusion

The Australian Government has an opportunity to drastically reduce smoking rates by exempting liquid nicotine at a concentration of 3.6% and below from its poisons schedule. Vaping is at least 95% safer than smoking. Nicotine is an essential ingredient for smokers to switch to vaping and it is not particularly dangerous at the concentrations used by vapers. Uptake of electronic cigarettes by children, young people and non-smokers has been low in other countries. Vaping is an effective way for people to stop smoking with no known harms to themselves or others.

The World Health Organisation estimates than a billion lives will be lost to smoking this century. I implore the Australian Government to ensure that Australian smokers are not over represented in the death rates caused by smoking by exempting liquid nicotine at concentrations of 3.6% and below from the poisons schedule.

Pre-meeting submission consultation: Proposed amendments to the Poisons Standard, ACMS meeting, November 2016:

Nicotine	An applicant has proposed to exempt nicotine from Schedule 7 at concentrations of 3.6 per cent or less of nicotine for self-administration with an electronic nicotine delivery system ('personal vaporiser' or 'electronic cigarette') for the purpose of tobacco harm reduction.

I wish to comment in support of this proposed amendment.

[redacted]

[redacted]

[redacted]

I am writing in favour of the proposal to exempt from the SUSMP nicotine at concentrations of 3.6% or less for use in an ENDS being accepted.

[redacted]

August 31, 2016

Therapeutic Goods Administration, TGA
Advisory Committee on Medicines Scheduling (ACMS)
Medicines.scheduling@tga.gov.au

RE: Proposed amendments to the Poisons Standard (Medicines)

Dear Advisory Committee on Medicines Scheduling (ACMS):

[redacted] welcomes the opportunity to provide a submission on a proposal to amend the Poisons Standard to exempt nicotine from Schedule 7 at concentrations of 3.6% or less for self-administration with an electronic nicotine delivery system (i.e. a personal vaporiser or electronic cigarette), for 'tobacco harm reduction' purposes.

[redacted]

[redacted] considers the submission [redacted] be high quality and comprehensive that addresses the main issues relevant to this consultation. There is little purpose to be served in replicating this submission, so [redacted] wishes to support and endorse its conclusions. While endorsing and supporting the submission [redacted] respectively requests that the TGA register this communication from [redacted] as a separate submission.

[redacted] **does not** support the proposed amendment to the Poisons Standard to exempt nicotine from Schedule 7 at any concentration for self-administration with electronic nicotine delivery systems for the following reasons:

- Nicotine is a toxic and addictive substance; there is strong scientific evidence showing that nicotine poses a number of health hazards and can cause adverse biological effects on various systems of the body, including cardiovascular, respiratory, renal and reproductive[i]. Nicotine can directly contribute to both the onset and growth of various forms of cancer[ii], and recent research demonstrated the immediate and substantial adverse effects of using electronic cigarettes on the cardiovascular system by stiffening major blood vessels[iii]. Despite the lower dose of toxins, the effects on the cardiovascular system are nearly as large as those caused by the smoking traditional tobacco products. In addition, the use of nicotine during pregnancy can effect fetal brain development[iv], and also appears to have mental health implications following exposure during the prenatal period[v].

- There is good evidence that nicotine is combined with other substances when delivered by the use of electronic cigarettes. Various studies have confirmed that the chemical combinations used in electronic cigarettes have an adverse impact on pulmonary function and the cardiovascular system. Second-hand electronic cigarette vapour is also associated with potential negative health effects as it contains pollutants at levels above background levels[vi vii].

[redacted]