Discussion paper: Options to minimise the risks associated with the marketing and use of electronic nicotine delivery systems [ENDS] in Australia

This discussion paper is provided for the purposes of informing the consultation **by invitation only**, please do not distribute or circulate this paper to other parties.

Prepared by Dr Becky Freeman, James Kite, Prof Nicholas Buckley, Dr Blythe O'Hara, Prof Simon Chapman, Scott Walsberger, Prof Bill Bellew, and Prof Adrian Bauman for the Intergovernmental Committee on Drugs

EXECUTIVE SUMMARY

Electronic nicotine delivery systems [ENDS] are products that heat a solution, typically including nicotine, to form an aerosol, which is then inhaled by the user. For the purposes of this discussion paper we use the term 'ENDS' to mean all products that are designed to generate or release an aerosol or vapour (whether or not containing nicotine) by electronic means for inhalation by its user, unless specified otherwise. For specific reference to non-nicotine containing versions the term 'non-nicotine ENDS' is used. Sale of ENDS is not currently permitted in Australia if they contain liquid nicotine and no ENDS have to date been approved by the Therapeutic Goods Administration (TGA) for sale as a therapeutic good. Sale of non-nicotine ENDS is treated differently by jurisdictions.

This discussion paper was prepared to inform a consultation process with technical experts in ENDS, tobacco control or public health. The paper has four key sections: 1) introduction, 2) a literature/evidence review, 3) an analysis of current ENDS policy development, legal issues, and prevention and control activities in Australia and internationally, and 4) possible policy options to minimise risks and harms from ENDS use and marketing.

Prevalence of the use of ENDS in Australia currently appears to be lower than in the US and UK and similar to that in Canada. In Australia, from data collected in 2013, daily smokers were most likely to have used an ENDS in the last 12 months, with 15.3% using. 1.8% of former smokers reported using an ENDS in the last 12 months and use among non-smokers was low, with 0.8% having used an ENDS in the last 12 months. ENDS use among all youth age 14-17 years was 4.3% in the previous 12 months. While there is limited data available, awareness, trial and regular use of ENDS appears to have increased amongst adult smokers and former smokers between 2010 and 2013.

The global ENDS market was worth US$3 billion in 2013. All major international tobacco companies have invested in the ENDS market. A significant portion of ENDS business is conducted online. The number of ENDS brands and available flavours has substantially increased in recent years.

As these products are relatively new, there are insufficient data available to determine the long-term health effects of ENDS use or of second-hand vapour exposure, in either adults or children. There is substantial variation in the components and operation of different ENDS products. ENDS may contain nicotine; the nicotine content varies considerably, both across different ENDS products and within the same product. Acute nicotine poisoning is possible, particularly if children swallow the liquid. Nicotine may also play a role in tumour promotion and growth and is being investigated as a possible cancer-causing agent. There is inadequate research to determine the safety of inhaling stabilising agents used in ENDS, such as propylene glycol. There is evidence that flavourings used in ENDS may be harmful to users. There are also concerns about particulate matter in ENDS emissions.

Definitive evidence is lacking that ENDS users are more likely than smokers using other methods (including cold turkey) to quit all cigarette use. Outcomes of cessation research are highly mixed, with some studies reporting increased smoking cessation with ENDS use and others reporting less smoking cessation with ENDS use. The high potential dependence risk associated with the inhalation of nicotine aerosols compared with NRT products is also an important consideration.

Online advertising of ENDS, particularly by vendors, is accessible in Australia. Point-of-sale displays are common in some regions of Australia among the small number of retailers that sell ENDS. ENDS

ads can also be found in some Australian print media. ENDS ads often contain potentially misleading information about unproven health benefits. ENDS ads appear to increase the desire to try products and if ads include vaping imagery, they may increase the urge to smoke traditional cigarettes. Further information about claims by ENDS retailer websites can be found in section 2.6 of the Appendix.

In Australia, regulation of ENDS is shared between Commonwealth, and state and territory governments. John Hopkins Bloomberg School of Public Health has summarised ENDS regulation of 123 countries in a comprehensive website. This summary reported that the sale of all types of e-cigarettes is banned in 26 countries, eighteen countries regulate ENDS as medicinal products, 26 countries regulate ENDS as tobacco products (or imitation/derivative/substitute products) and 4 countries regulate ENDS containing nicotine as poisons. Use of e-cigarettes is banned in three countries (Cambodia, Jordan and the United Arab Emirates). As of February 2016, 71 countries have been identified that regulate e-cigarettes.

Seven policy approaches for expert consultation are outlined in Section 4. These policy options are not meant to be mutually exclusive.

The seven possible policy approaches are as follows:

Policy approach 1: Maintain the status quo
Policy Approach 2: Increase awareness and enforcement of and compliance with existing legislation
Policy approach 3: Regulate ENDS as consumer products
Policy approach 4: Regulate ENDS as tobacco products
Policy approach 5: Regulate ENDS as medicines
Policy approach 6: Develop an ENDS regulatory framework
Policy approach 7: Adopt measures to ban ENDS

CONTENTS

EXECUTIVE SUMMARY 2

SECTION 1 INTRODUCTION 5

1.1 Background and strategic context 5

1.2 What are ENDS? 5

1.3 Health claims and health concerns 5

SECTION 2 LITERATURE REVIEW 6

2.2 Prevalence of ENDS use 6

2.3 International ENDS market 7

2.4 Health effects of use and second-hand exposure to ENDS 7

2.5 Risk of dependence, cessation and reducing consumption of conventional tobacco products 8

2.6 Marketing 10

SECTION 3 SITUATION ANALYSIS 12

3.1 ENDS policy - situation analysis for Australia 12

3.2 ENDS policy - situation analysis for other jurisdictions 19

SECTION 4 POLICY OPTIONS 20

4.1 WHO FCTC and international guidance on ENDS policy objectives 20

4.2 National guidance on tobacco control and ENDS policy objectives 21

4.3 Possible policy approaches to minimise the risks associated with the marketing and use of ENDS 22

AUTHOR DISCLOSURE STATEMENT 31

REFERENCES 31

APPENDIX 35

SECTION 1 INTRODUCTION

1.1 Background and strategic context

This discussion paper was prepared to inform a consultation process with technical experts in electronic nicotine delivery systems (ENDS), tobacco control and public health. This paper has four key sections: 1) an introduction 2) a literature/evidence review; 3) an analysis of current ENDS policy development, legal issues, and prevention and control activities in Australia and internationally; and 4) an outline of possible policy options to minimise risks and harms from ENDS use and marketing. The overarching assumption when outlining the possible policy options for minimising the risk posed by ENDS will be that policies must, as much as is possible to determine, be consistent with the objectives of the *National Tobacco Strategy 2012-2018*.

In October 2014, at the 6th session of the Conference of the Parties (COP) of the World Health Organization [WHO] Framework Convention on Tobacco Control (FCTC), to which Australia is a Party, a decision on ENDS(1) was accepted and endorsed.(2) The COP decision was to invite Parties to consider prohibiting or regulating ENDS, including as tobacco products, medicinal products, consumer products, or other categories, as appropriate, taking into account a high level of protection for human health.

1.2 What are ENDS?

ENDS are products that heat a solution, usually including nicotine but not necessarily, to form an aerosol, which is then inhaled by the user. For the purposes of this report we use the term 'ENDS' to mean all products that are designed to generate or release an aerosol or vapour (whether or not containing nicotine) by electronic means for inhalation by its user unless specified otherwise. For specific reference to non-nicotine versions the term 'non-nicotine ENDS' is used. (See Appendix for additional information.) Where terms such as e-cigarettes or electronic cigarettes have been used in surveys, legislation, or other key sources in this discussion paper, these terms have been retained.

While ENDS are the focus of this discussion paper, the term does not necessarily capture all products which deliver an aerosol and/or vapour via inhalation, including but not limited to the Philip Morris's Marlboro iQOS system (which has tobacco as an ingredient), or British American Tobacco's Voke Inhaler (which does not use electrical power to generate an aerosol). The *Tobacco and Other Smoking Products Act 1998* (Qld) was recently updated to include the term 'personal vapouriser'. Further information about these products is provided in sections 1.2 and 2.3 in the Appendix, respectively.

1.3 Health claims and health concerns

Three central health benefits claimed for ENDS are that:

1. they are far less hazardous to health than combustible tobacco products;(3-9)
2. they are an effective means of stopping smoking, comparable to or more effective than other smoking cessation strategies;(3, 8, 9) and
3. smokers who also use ENDS ("dual users") reduce the number of cigarettes they smoke and that this is likely to be harm reducing.(8, 9)

Four central health concerns expressed for ENDS are that:

1. smokers who might otherwise have quit smoking, may continue smoking and vaping (dual-using) in the belief that their reduced smoking is significantly harm reducing;(10)
2. non-smokers (especially youth) who may have never used any nicotine product, may take up vaping in the belief that ENDS are risk-free;(11)
3. a proportion of non-smokers may commence smoking in addition to vaping (the so-called gateway effect)(12); and
4. The longer term health effects of use are unknown(13)

SECTION 2 LITERATURE REVIEW

See Appendix for section 2.1 Methods and for the additional, detailed literature review content.

2.2 Prevalence of ENDS use

Australia

Data from the 2013 National Drug Strategy Household Survey (NDSHS) show that 14.8% of **current smokers** had ever used 'battery-operated electronic cigarettes' or ENDS in the last 12 months.(14) The 2013 survey was the first time that respondents were asked about their use of ENDS. In 2013:

- 1 in 7 (14.8%) smokers aged 14 or older had used ENDS in the last 12 months;
- younger smokers were more likely to have ever used an ENDS in the last 12 months than older smokers: 27% for smokers aged 18–24 compared with 7.2% for those aged 60–69 ;
- daily smokers were most likely to have ever used an ENDS in the last 12 months (15.3%), with only 1.8% of ex-smokers reporting use in the last 12 months;
- male smokers aged 14 or older were generally more likely than females to have ever used ENDS, except among those aged 50–59 where 13.5% of female smokers had used this product compared with 6.7% of male smokers;
- Ever use of ENDS among non-smokers was low, with 0.8% having used an ENDS in the last 12 months, and an additional 0.5% having used an ENDS, but not within the last 12 months;
- Ever having used an ENDS among all youth aged 14-17 years was 4.3% in the last 12 months, and a further 1.7% of youth having ever used an ENDS but not in the last 12 months; and
- ENDS use in the past 12 months was highest in the Northern Territory at 6% and lowest in NSW at 2.8%.

Information regarding ENDS use among vulnerable populations is provided in section 2.2 of the Appendix.

Data from the Cancer Institute NSW's Tobacco Tracking Survey of adult smokers and recent quitters, which included 9% current ENDS users, found that the most common places of purchase of ENDS were the internet (30%) and tobacconists (28%).(15)

Evidence of gateway and renormalisation concerns

Concern has been expressed about whether ENDS use might be a possible gateway into smoking. A 2014 WHO report on ENDS noted that experimentation with ENDS is increasing among adolescents and young adults and is highest among those who also smoke tobacco; this is true both in Australia and internationally.(1) Smoking rates among youth have also declined during these same time periods. The data currently available on youth ENDS use patterns in Australia do not allow

conclusions to be made as to whether youth who try ENDS are more or less likely to go on to use tobacco; if youth who smoke are switching to ENDS; or if youth are experimenting with ENDS in lieu of tobacco. The data show that dual use of tobacco and ENDS is the most likely scenario, as current smokers are also the most likely to be current users of ENDS. As most existing prevalence studies of youth are cross-sectional, it is not possible to determine which users started with cigarettes and which users started with ENDS.(11)

The daily smoking rate among Australian youth aged 12-17 is 3.4% and 13.4% among young adults aged 18-24.(16) ENDS ever use and current use is also low among Australian youth age 14-17. By contrast, ENDS use has rapidly risen among youth in nations with less stringent ENDS regulations and less comprehensive tobacco control laws,(17) including among adolescent never smokers.(11) Further information regarding ENDS awareness, trial and/or use in Australia when compared to other countries is provided in section 2.2 of the Appendix.

2.3 International ENDS market

Euromonitor estimates that the global ENDS market was worth US$3 billion in 2013.(18) This is a very small market when compared to the global tobacco market; one of the most valuable fast moving consumer goods industries, worth an estimated annual US$800 billion – more than 260 times the size of the ENDS market.(19) This reflects the fact that ENDS use is not as widespread geographically as cigarette use. Euromonitor estimates that the vapour products market could be worth 4% of the total global tobacco market by 2030, for a value of about US$50 billion.

Outside of China, the global tobacco market is dominated and controlled by five major players: Japan Tobacco International (JTI), Imperial Tobacco (IT), British American Tobacco (BAT), Philip Morris International (PMI), and Altria/Philip Morris USA. All of these major global tobacco companies now have a stake in the ENDS market, with most buying up independent ENDS companies.(20)

2.4 Health effects of use and second-hand exposure to ENDS

ENDS have been suggested by some as presenting a significant opportunity to address the burden of tobacco use through harm reduction.(3-6) The current ENDS on the market are relatively new products, so regulators are making decisions on the basis of very limited evidence.

ENDS are often marketed as a less dangerous alternative to smoking and there is evidence that one of the primary reasons for the increasing popularity of ENDS is that users perceive them as being less harmful.(8, 9, 21) The short-term toxicity of ENDS use appears to be comparatively low and, further, ENDS aerosol does not stay in the air for long, reducing the risk of exposure to second-hand vapour by non-users.(10, 22-24) However, while we identified several reviews of the health effects of ENDS, most concluded that there are insufficient data available to determine the long-term health effects of ENDS use or of second-hand exposure, in either adults or children.(5, 10, 13, 22, 23, 25-27) Further, Pisinger and Døssing found that of the 76 articles included in their review many were small, short-term studies with major methodological flaws and authors with significant conflicts of interest, making it difficult to draw firm and reliable conclusions as to the health effects of ENDS.(27)

The lack of product standards and international differences in regulation has meant that there is substantial variation in the components and operation of the different ENDS products and even within the same products.(10, 13, 22, 23, 28) Complicating matters further, recent evidence suggests that differences in the mechanical components, as opposed to the chemical components, of ENDS have implications for potential health effects of ENDS use.(29) It is therefore difficult to determine the health effects of ENDS as a homogenous product class.(30)

ENDS aerosols deliver ultrafine particles. While it is unclear what effect ultrafine particles in ENDS aerosols have on health, frequent, low-level exposure to fine and ultrafine particles from tobacco smoke or air pollution has been shown to contribute to inflammation and increased risk of cardiovascular and respiratory morbidity and mortality.

While ENDS use has not been linked to any serious adverse respiratory events,(30) it may constrict airways, creating a potential risk particularly for those with asthma and other respiratory conditions.(5, 26, 31, 32) There is limited evidence that suggests that ENDS use has no impact on lung function in the short-term but there is also emerging evidence that it may cause pulmonary inflammation.(33) If confirmed, this would have significant implications for public health, particularly in relation to rates of chronic obstructive pulmonary disease (COPD).

ENDS have been linked to occasional explosions, fires, and poisonings.(5, 26) Indeed, the number of ENDS-related reports to poison centres in the USA has been increasing in line with the increasing popularity of ENDS. (13, 25) The potential risk for poisoning is high for liquid nicotine compared with tobacco products and nicotine replacement therapies.(34) The Centers for Disease Control reported that in the United States in the period September 2010 and February 2014 more than half (51%) of the calls to poison centres on ENDS exposures (2,405 calls) related to children aged 0 to 5 years. ENDS poisonings were more likely to be as a result of inhalation, eye and skin contact, and less likely to be as a result of ingestion, compared to conventional cigarettes.(35) Hajek et al. note that such reports remain at lower levels than those related to conventional tobacco products (5) as would be expected given the significantly lower levels of ENDS use.

ENDS contain a number of potentially harmful compounds, albeit at orders of magnitude lower levels than those found in conventional cigarettes.(10) These include both compounds that are purposefully added to ENDS and those that result from the process of using ENDS (i.e. through vaporising or inhalation/exhalation). There is ongoing debate about the absolute toxicity of ENDS relative to tobacco products.(36) There is evidence that nicotine is toxic to the foetus and impacts on the development of the adolescent brain. Further information about the health effects of nicotine, flavourings and other ingredients typically found in ENDS is provided in section 2.4 of the Appendix.

Combes and Balls (2015) state that there is insufficient toxicological data to perform a hazard assessment for electronic cigarettes. They also state that due to the inadequate research, the relative safety of electronic cigarettes has not been scientifically established.(37)

2.5 Risk of dependence, cessation and reducing consumption of conventional tobacco products

Risk of dependence for inhaled nicotine aerosols

The high potential dependence risk associated with the inhalation of nicotine aerosols compared with NRT products is an important issue. Some ENDS have been shown to have a similar nicotine absorption profile to conventional cigarettes (i.e. very rapid absorption and a subsequent rapid fall) in experienced users.(38, 39)

Smoking cessation

A summary of the systematic reviews which were identified in our literature review are provided below. A summary of additional primary studies are provided in Section 2.5 of the Appendix.

Grana et al's review combined the results of four longitudinal and one cross-sectional study in a random-effects meta-analysis and concluded "that ENDS use in the real world is associated with significantly lower odds of quitting smoking cigarettes."(26) While Grana et al describe these studies as longitudinal, the Cochrane review (see below) notes that, for the purposes of evaluating efficacy of ENDS, two of these were not longitudinal studies: one was essentially a cross-sectional design (because participants were only asked about ENDS use at follow up) and one was a retrospective survey 7 months after enrolment into a quitline service. Herzig, in a critique of Grana et al.'s review, notes that a limitation of this review is that some of the included studies did not control for level of nicotine dependence. (40) This may have adversely impacted the results because it may be that more heavily addicted smokers who are less likely to succeed in quitting are more likely to use ENDS as a cessation aid. In their reply to Herzig, Grana et al noted that an additional two studies had been published since their original review, both of which supported their conclusion that "ENDS use is associated on balance with less cigarette smoking cessation" than among smokers not using ENDS.(41)

The Cochrane Collaboration published a review that considered both cessation and smoking reduction in 2014.(42) Based principally on the only two randomised controlled trials, the review found that participants using ENDS were more likely to have abstained from smoking for at least six months compared with participants using a placebo. One study compared ENDS to nicotine patches and found no significant difference in six-month abstinence rates. The review also included a further 10 prospective cohort studies. The reviewers deemed that all these cohort studies were at high risk of bias. The review authors noted that the overall quality of the evidence included in their review was weak to very weak due to the small number of trials. Consequently their confidence in the estimates of effects was low.

Rahman et al meta-analysed results from six studies on cessation and reduction and concluded that ENDS containing nicotine were more effective for cessation than those without nicotine.(43) The analysis also reported that use of ENDS was associated with a reduction in use of conventional cigarettes. However, the authors noted the heterogeneity of the studies they pooled for their analysis. In particular, one of the included studies was highlighted as having significant problems for generalizability of findings because the study participants were recruited only from notices in community newspapers. Further, the authors noted that they were unable to assess the efficacy of ENDS compared to other cessation interventions due to a lack of evidence.

A **2016 review and meta analysis** assessed the association between e-cigarette use and cigarette smoking cessation among adult cigarette smokers, irrespective of their motivation for using e-

cigarettes and found that e-cigarettes, as currently being used, are associated with significantly less quitting among smokers.(44)

In addition to the systematic reviews highlighted above, we identified four significant primary studies. A summary of the findings from these studies is provided in Section 2.5 of the Appendix.

Reducing consumption of conventional tobacco products

The previously noted Cochrane review found that a greater proportion of ENDS users were able to reduce cigarette consumption by at least half, compared with both those using a placebo and those using nicotine patches.(42) As with cessation, these findings are weakened by the overall poor quality of the available evidence. Further, the authors noted that unlike smoking cessation outcomes reduction results were not biochemically verified.

In addition, large declines in daily consumption of conventional cigarettes in ENDS users have been noted in some primary studies. (45, 46) However, available evidence suggests that the health benefits of reducing consumption of conventional tobacco products are minimal at best. For instance, a 2007 systematic review of the evidence on the health impact of smoking reduction noted that most studies available for review were small and had limited follow-up. (47) It found that while there may be a small health benefit in substantially reducing consumption, more studies were needed.

Since that review, three papers involving four cohorts – two being very large – have been published that substantially increase evidence about the health implications of smoking reduction. Note that these studies report mortality but not morbidity and that the use of ENDS was absent or negligible at the time these studies were conducted. A Norwegian cohort of 51,210 people followed from the 1970s until 2003 found no evidence that smokers who reduced their consumption by 50% or more reduced their risk of premature death significantly. (48) Similarly, a Scottish study of two cohorts followed from the 1970s to 2010 found no evidence of reduced mortality in smokers who reduced their consumption.(49) The largest study, from Korea and involving 479,156 men followed for 11 years, found an association between smoking reduction and a significant decrease in risk of lung cancer, but with the size of risk reduction "disproportionately smaller than expected".(50) Moreover, there was no association between smoking reduction and a decline in all-cancer risk.

The Korean study authors were painstaking in noting any limitations in their own research. The study did not include a biological validation of self-reported smoking status; data on smoking status at multiple time points up to the time of cancer occurrence were not available which the authors state leaves a possibility of underestimating the effect of smoking reduction on lung cancer risk.(50)

2.6 Marketing

Australia has one of the most comprehensive bans on tobacco advertising in the world, being the only country to have thus far enacted standardised, plain packaging laws. (Point of sale tobacco advertising laws differ by jurisdiction.) Equally, advertising of over-the-counter medicines and

prescription drugs is tightly regulated. In contrast, marketing of ENDS is not as tightly regulated and ENDS marketing is occurring in Australian social media, email promotions, online group purchasing coupons, television, print media and at retail point-of-sale.

There is limited published evidence on the availability and promotions of ENDS in Australia. It is likely that there is wide variety across states given the differing regulatory environments. A study on the availability and promotion of ENDS undertaken by the Cancer Council NSW in 2014 found that in an audit of 1519 tobacco retail outlets across 85 postcodes in NSW(51):

- ENDS were observed for sale in 5.1% (n=77) of outlets sampled;
- Of the 5.1% of outlets where ENDS were observed for sale: Availability of ENDS varied by outlet type, with ENDS most often observed by auditors in tobacconists (45.5%), convenience stores (33.8%) and petrol stations (1.7%). No ENDS were observed in supermarkets or newsagents;
- Auditors in Sydney and suburbs observed ENDS in outlets more often (7.7%) than auditors in other areas of NSW (1.5%); ENDS display boxes were observed in most outlets (81.8%) where ENDS were sold; and ENDS promotional posters were observed in only a few outlets (5.2%) where ENDS were sold.

Photographs of the ENDS displays taken during the audit show: the use of packaging colours, emphasis on flavours, and the positioning of products next to confectionery items (Figure 1).

Figure 1 Sample images of ENDS displays collected in NSW tobacco retail outlet audit

One systematic content analysis of ENDS website marketing reported numerous misleading claims.(52) Additionally, some evidence suggests that the widespread promotion of ENDS may increase the urge to smoke among existing smokers, and may reduce former smokers' confidence in their ability to refrain from smoking.(53) There is also evidence that young non-smokers may be more interested in trying ENDS after exposure to ENDS advertisements.(54) Further information on the marketing of ENDS is provided in Section 2.6 of the Appendix.

SECTION 3 SITUATION ANALYSIS
ENDS policy development, legal issues, and prevention and control activities

3.1 ENDS policy - situation analysis for Australia

With the exception of Queensland and NSW, there are no laws specifically addressing the regulation of ENDS in Australia. Instead, poisons, therapeutic goods, consumer law and tobacco control/product laws apply to ENDS.(55)

The regulatory arrangements applicable to ENDS are shared between the Commonwealth and the states and territories. Broadly, the Commonwealth has responsibility for approving the marketing

and supply of therapeutic goods and requiring suppliers to ensure that consumer products are safe and fit for purpose and that all representations or claims made in relation to the supply of products are truthful. States and territories have responsibility for restrictions on the sale and supply of nicotine, and may also be able to place restrictions on the sale and supply of ENDS devices and on their use in smoke free areas.

The following sections outline the current laws that apply to ENDS sales and possession. Following a description of the existing laws, we outline potential regulatory impacts and effects.

Australia – Existing Regulation Frameworks

Consumer law

Under the Commonwealth Competition and Consumer Act 2010 (CCA), suppliers of consumer goods such as ENDS are responsible for ensuring the products they supply are safe, fit for purpose and comply with all applicable legal requirements. Potential suppliers of ENDS should ensure that ENDS, as well as the chemicals that their users are exposed to, are safe before they market the product. The CCA also requires that all representations or claims made in relation to the supply of consumer goods are truthful. Further, the Australian Competition and Consumer Commission (ACCC) advises consumers that the quality and safety of electronic cigarettes is not known.

Therapeutic goods regulation

The Therapeutic Goods Administration (TGA) is Australia's regulatory authority for therapeutic goods. No ENDS products have, to date, been approved as a medical device under the *TGA*.(55) The importation and supply of ENDS (with or without nicotine) that make therapeutic claims is illegal in Australia unless authorised by the TGA.

Nicotine regulation

The Commonwealth *Standard for the Uniform Scheduling of Medicines and Poisons* classifies nicotine as a schedule 7 poison that can only be included in products for therapeutic use or in tobacco products.(56) Nicotine for human consumption is then also listed as a schedule 4, prescription-only medicine, with exceptions given for approved therapeutic nicotine replacement products [NRT] that are absorbed through the skin or lining of the mouth. These approved NRT products are unscheduled and can be sold at retail outlets.(57)

The commercial supply (including sale) of nicotine for use in ENDS is illegal in Australia under state and territory poisons legislation. In specific circumstances, it may be lawful for individuals to import ENDS and/or liquid nicotine for personal therapeutic use via the TGA's Personal Importation Scheme (PIS). Where ENDS users want to import liquid nicotine for this purpose, the importer must comply with the requirements of the PIS. This includes having a prescription from a medical practitioner registered in Australia, and ensuring that the nicotine when used for this specific purpose is legal under state or territory law. While the PIS may be used to import unapproved therapeutic goods into Australia, the TGA advises that these goods may not be approved for supply in Australia and

therefore there are no guarantees about their safety or quality. Further information about the PIS is available at: https://www.tga.gov.au/personal-importation-scheme.

Australia – State and Territory Laws that apply to ENDS

ENDS devices are subject to different regulations across Australian States and Territories.

State and Territory laws that specify personal vaporisers/ENDS

Queensland

As of 1 January 2015, laws took effect in Queensland that specify that ENDS, referred to as, "personal vaporisers" are included in existing tobacco control laws as smoking products. This means that in Queensland, ENDS are:

- prohibited from being sold to minors;
- restricted from advertising, promotion or display at retail outlets; and
- prohibited from use in smoke-free areas including indoor and outdoor smoke-free public places and in vehicles with children under 16 present;
- prohibited from sale in vending machines.

NSW

On 24 June 2015, a Bill to amend the Public Health (Tobacco) Act 2008 was passed in the Upper House, placing restrictions on the sale to minors, display and advertising of ENDS. The key points in this legislation are:

- it is an offence to sell ENDS and accessories to minors;
- it is an offence for adults to buy ENDS and accessories on behalf of minors;
- it is an offence to use ENDS in cars with children under 16 present;
- police have the power to seize an ENDS that is in the possession of a person under the age of 18;
- new restrictions apply to the display and advertising of ENDS;
- a person is not able to operate or use a vending machine that dispenses ENDS on behalf of a minor;
- ENDS vending machines are only able to be located in areas restricted to adults over 18, such as licensed premises; and
- the sale of ENDS to a minor is subject to the same maximum penalty as the sale of a tobacco product to a minor in NSW - that is, $11,000 for an individual or $55,000 for a corporation and, for repeat offenders, $55,000 for an individual and $110,000 for a corporation.

The Act was implemented in two stages; the restrictions relating to sales to and on behalf of a minor commenced on the 1 September 2015, the remaining provisions relating to the display and advertising of products and the use of ENDS in cars with children under 16 present commenced on 1 December 2015.

ACT

The ACT Government has announced a proposal to prohibit the sale, use and promotion of personal vaporisers in the same way as tobacco products in the ACT. Legislation scheduled to be introduced in 2016 will prohibit personal vaporiser sales to under-18s, ban sales by vending machine, and restrict in-store and point-of-sale advertisements and displays. Personal vaporiser promotions, inclusion in customer reward schemes, sponsorships and product giveaways will also be banned. To prevent the renormalisation of tobacco smoking, e-cigarette use will be prohibited in smoke-free areas.

This approach follows a discussion paper in late 2014 that outlined policy options to protect the community from potential harms associated with personal vaporisers. The purpose of the discussion paper was to seek views on the range of options under consideration, including feedback on the associated costs and benefits. A summary of outcomes from the consultation has been published on the ACT Health website (www.health.act.gov.au). All non-confidential submissions to the consultation have also been made available on the site.

Tasmania

In June 2015, the Tasmanian Government issued a discussion paper outlining options for a public health response to electronic cigarettes. The consultation process closed on 24 July 2015 and information gathered will contribute to the Tasmanian Government decision-making process. The policy options included in the discussion paper were:

Options to prevent uptake:

1. continue with the status quo
2. public education;
3. part-regulation – restrictions on sale and advertising;
4. part-regulation - sale to people under 18 years of age;
5. part-regulation – sale of flavoured e-liquids; or
6. full-regulation of electronic cigarettes in the same way as tobacco.

Options to prevent renormalisation of smoking and protection from second-hand vapour:

1. continue with the status quo
2. prohibit use of electronic cigarettes in existing smoke free public places

South Australia

In June 2015 the South Australian House of Assembly established a Select Committee to investigate and report on e-cigarettes and any legislative and regulatory controls that should be applied to the advertising, sale and use of personal vaporisers. The South Australian Select Committee invited and received public submissions from July to August 2015 addressing the terms of reference. The final report of the Select Committee was tabled in Parliament on 24 February 2016 and contains 20 recommendations across the following seven areas:

- Sale
- Use
- Promotion
- Product safety and quality control
- Enforcement
- Research
- Taxation

The final report of the Select Committee on e-cigarettes is available from the Parliament of South Australian website - www.parliament.sa.gov.au.

Victoria

In November and December 2015, as part of a broader Review of the *Tobacco Act 1987*, targeted consultation was undertaken with key stakeholders on regulating electronic cigarettes. The Victorian Government is considering the findings and will make announcements in due course.

Sale of ENDS

Currently, in Queensland, South Australia, Western Australia, and New South Wales, tobacco control laws prevent the sale of products that "resemble tobacco products". In NSW however these laws apply to toys and food products. Queensland specifically exempts "personal vaporisers" (ENDS) from the ban on sales of goods that resemble tobacco products.

In WA, a vendor of non-nicotine e-cigarettes was charged with being in breach of section 106(a) of the *Tobacco Products Control Act 2006* (WA), which states that "a person must not sell any food, toy or other product that is not a tobacco product but is (a) designed to resemble a tobacco product." Initially, the Defendant was acquitted but this was overturned on appeal in the WA Supreme Court.

The Defendant subsequently made application to the Full Court of the Supreme Court to appeal the decision. The matter was heard by the WA Supreme Court on 23 November 2015 and the appeal was unanimously dismissed in a decision handed down on 10 March 2016.

Under the South Australian *Tobacco Products Regulation Act 1997*, 'A person must not sell by retail any product (other than a tobacco product) that is designed to resemble a tobacco product'. This carries a maximum penalty of $5,000. Enforcement action in South Australia related to this provision has been based largely on the appearance of the e-cigarette being comparable to a normal cigarette or other tobacco product.

In Victoria, there are provisions in the *Tobacco Act 1997* to ban products that resemble a tobacco product, but no such ban order on ENDS has been issued. In the ACT and Tasmania, laws prevent the sale of a 'toy or food' that resemble, or is intended to represent, a tobacco product. Similarly in the Northern Territory, the law prevents the sale of a product designed for consumption by children if it resembles, or is packaged to resemble, a tobacco product; or it has, or is likely to have, the effect of encouraging children to smoke.(57) To date, these laws have not been applied to ENDs.

Potential regulatory impacts under current regulatory framework

Australia's regulatory framework

Overall Australia's existing regulatory framework appears to have limited the marketing and prevalence of use of ENDS compared to countries with more liberal regulatory frameworks such as the USA and the UK. However, there is some evidence that the rate of increase of use of ENDS in Australia may be comparable to the UK over the period 2010-2013.

However, there is not currently a consistent approach to ENDS regulation across Australia, which may be serving as a source of confusion to users, retailers, employers and the general public. Of particular note, are differences as to whether ENDS/personal vaporisers are included under laws that ban the sale of products that resemble tobacco products and how such laws are applied.

ENDS containing nicotine

Although it is illegal to sell ENDS containing nicotine in every Australian jurisdiction, testing of products available at retail outlets reveals that many do in fact contain nicotine and are mislabelled and being sold in direct violation of existing laws. In NSW for example, tests of e-liquid samples collected by NSW Health in 2013 showed that 70 per cent of the samples contained high levels of nicotine even though the label did not state nicotine as an ingredient.(58) ENDS product testing in Tasmania found similar results.(59) If consumers are unaware of the contents, mislabelling has additional impacts, such as increasing exposure to an addictive substance and increasing the risk of inadvertent poisoning.

Medical prescription

While the TGA has clarified that a medical prescription is considered a valid authority to import ENDS containing nicotine for personal therapeutic use, it may be unclear for consumers whether some state and territory poisons legislation allows the lawful possession of liquid nicotine (being a Schedule 4 poison) for therapeutic use in ENDS when obtained via the TGA's personal importation scheme. Requiring a medical prescription may pose a practical barrier for people who wish to legally

purchase ENDS containing nicotine online for smoking cessation, as some medical practitioners may be unwilling or unable to provide a prescription for a product that has not been approved by the TGA. Additionally, ENDS users may be uninclined to obtain a valid prescription given how readily available products are both online and in local retail outlets. Additionally, it is currently unknown how many, if any, Australian doctors are providing prescriptions.

Labelling and packaging

Unlike for tobacco products and for therapeutic goods, Australia has not adopted any standardised labelling, packaging, or health warnings for ENDS. E-liquid bottles are often not labelled correctly. Even if a bottle says it does not contain nicotine it may still contain nicotine. Also, the risk of poisoning among children can increase if e-liquid bottles do not have child resistant packaging.

Standards

An unknown number of ENDS users are purchasing their supplies from the Internet and overseas markets, despite poor controls on quality, nicotine content, and consistency of nicotine dose. The TGA advises that goods imported via the PIS may not be approved for supply in Australia and therefore there are no guarantees about their safety or quality.

While ENDS that make therapeutic claims, and/or are supplied with nicotine require approval from the TGA prior to marketing in Australia, those controls do not currently apply to non-nicotine containing devices if no therapeutic claims are made. This may impact on consumer safety. Finally, there is also some uncertainty regarding the nature and extent of standards that should be in place due to the limited state of the evidence.

Flavours

Again, unlike for traditional cigarettes, where fruit or confectionery flavours that may have increased appeal to children are banned in most Australian states and territories, ENDS are sold in a multitude of flavours, including many which may be appealing to young consumers. There are potential inhalation risks related to flavourings used in ENDS. Further information about the health effects of flavourings in ENDS can be found in section 2.4 of the Appendix.

Advertising

ENDS advertising modalities include print media, television, social media, and at retail point-of-sale. As a result, responsibility for the marketing of ENDS is shared between the Commonwealth and states and territories. The following legislation may apply: the *Therapeutic Goods Act 1989*, the *Competition and Consumer Act 2010*, the *Tobacco Advertising Prohibition Act 1992*, and relevant state and territory tobacco regulations. Overall, controls on advertising of ENDS are limited and laws banning therapeutic claims are ambiguous. ENDS displays at retail outlets that sell these products are common and may appeal to young people. Additionally, ENDS print ads have appeared in magazines and free entertainment newspapers that, again, have high youth appeal. While current laws ban ENDS ads from making therapeutic claims or promoting tobacco use, people continue nonetheless to be exposed to these promotions.

Smoke-free laws

It is possible that employees and non-users could be exposed to potentially harmful particulates and constituents in second-hand vapour from ENDS, especially in enclosed areas, should ENDS users

congregate in large numbers as well as from nearby co-workers if ENDS are used in a workplace. Additionally, as some ENDS look very similar to traditional cigarettes and emit a vapour that may appear to be second-hand smoke, using these devices in smoke-free areas may cause confusion and conflict unless laws are clarified. As of February 2016, Queensland is the only state that includes ENDS under smoke-free environment laws. Currently, outside of Queensland, individual workplaces and companies have adopted policies banning ENDS use. Qantas Airlines, for example, does not allow the use of ENDS while on board, but does permit them to be transported in carry-on luggage, but not in checked bags.(60)

3.2 ENDS policy - situation analysis for other jurisdictions

WHO Survey of ENDS regulation in Member States

In 2014, the WHO conducted a tobacco products survey on ENDS, as well as smokeless tobacco, reduced ignition propensity cigarettes, and novel tobacco products. (1) A total of 90 WHO Member States responded to the survey.

The survey found that the sale of ENDS with nicotine is banned in 13 of the 59 countries that regulate them. The majority of these 13 countries report that ENDS are still available to the public, either through illicit trade or cross-border Internet sales. Comprehensive advertising, promotion and sponsorship bans on ENDS are in place in 39 countries, use of ENDS in enclosed public places is banned in 30 countries, premarket review is required by 19 countries, vendor licences are required by nine countries, and sales to minors laws were in place in 29 countries.

Table 1 WHO Survey ENDS regulation

Type of ENDS	ENDS regulated as					Not regulated or unknown
	consumer product	therapeutic product	tobacco product	other	total	
With nicotine	14 (27%)*	12 (6%)	22 (10%)	11 (6%)	59 (49%)	135 (51%)
Without nicotine	23 (35%)	0 (0%)	18 (7%)	12 (2%)	53 (44%)	141 (56%)

* The figure in parentheses after the number of countries indicates the percentage of the world population living in these countries

Source: Electronic nicotine delivery systems. Report by WHO.(1)

John Hopkins Bloomberg School of Public Health has summarised ENDS regulation of 123 countries in a comprehensive website.(61) Eighteen countries regulate ENDS as medicinal products, 26 countries regulate ENDS as tobacco products (or imitation/derivative/substitute products) and four countries regulate nicotine-containing ENDS as poisons.(61) Sale of all types of e-cigarettes is banned in 26 countries and three countries ban the use of e-cigarettes (Cambodia, Jordan and the United Arab Emirates).

Togo taxes ENDS at a ceiling of 45% and South Korea applies a special tax to ENDS.

The John Hopkins Bloomberg School of Public Health also reported that use of ENDS is banned in enclosed public spaces, including bars, restaurants and other workplaces in: Bahrain, Belgium,

Colombia, Croatia, Ecuador, Greece, Honduras, Malta, Nepal, Nicaragua, Panama, Philippines, Serbia, South Korea and Turkey.

A selection of country case study regulations is outlined in the Appendix. This literature review found little in the way of regulatory evaluation of these policies and any impact they have on population-level smoking rates.

SECTION 4 POLICY OPTIONS

Noting the evidence presented in the literature summary (section 2) and the regulatory review (section 3) of this document, this section sets out for consideration possible policy options to minimise the risks associated with the marketing and use of ENDS in Australia.

4.1 WHO FCTC and international guidance on ENDS policy objectives

The World Health Organization (WHO) Framework Convention on Tobacco Control (FCTC), to which Australia is a Party, aims to advance international cooperation to protect present and future generations from the preventable and devastating health, social, environmental and economic consequences of tobacco consumption and exposure to tobacco smoke. Further information about the WHO FCTC is available at: http://www.who.int/fctc/WHO_FCTC_summary_January2015_EN.pdf?ua=1.

In mid-October 2014, the sixth session of the Conference of the Parties (COP 6) to the WHO FCTC discussed the WHO Report on ENDS. The report states that there is limited evidence on the health risks of ENDS to users and non-users; the efficacy of ENDS in helping smokers to quit smoking; and the effect of widespread ENDS use on nicotine dependence. The report, in items 12 through to 17, identifies a number of health risks of ENDS to users and non-users. The report identifies a number of regulatory objectives to minimise the risks related to ENDS and outlines a range of specific regulatory options for consideration. These options include addressing health claims, the use of ENDS in public places, advertising promotion and sponsorship, protection from vested commercial interests, product design and information, health warnings, surveillance and monitoring and sale to minors. The WHO report on ENDS also states that *'…Parties will need to consider the available national regulatory frameworks that could best provide solid regulatory grounds. Nevertheless, it is likely that a two-pronged regulatory strategy – regulating ENDS as both a tobacco product, in accordance with the provisions of the WHO FCTC, and as a medical product – would be necessary.'*

Noting the findings of the WHO Report on ENDS, Parties agreed to a decision pertaining to ENDS/ENNDS.(2) The decision invites Parties to consider a range of measures to address the challenges posed by ENDS/ENNDS, including prohibition or regulation '*as tobacco products, medicinal products, consumer products, or other categories, as appropriate, taking into account a high level of protection for human health*'. The decision also invites Parties to *'protect tobacco-control activities from all commercial and other vested interests related to ENDS/ENNDS, including interests of the tobacco industry'.*

4.2 National guidance on tobacco control and ENDS policy objectives

All policy options canvassed in this section should be seen within the overarching strategic context of *harm minimisation* as defined in the Australian National Drug Strategy 2010–2015.(62) This encompasses the three pillars of *demand reduction, supply reduction and harm reduction* being applied together in a balanced way. From a tobacco control perspective, demand reduction means strategies and actions that prevent the uptake and reduce the use of tobacco and support people to quit smoking. Supply reduction means strategies and actions that control, manage and/or regulate the availability of tobacco. Harm reduction means strategies and actions that primarily reduce the adverse health consequences of tobacco use.

The overarching assumption when outlining the possible policy options for minimising the risk posed by ENDS will be that policies must, as much as is possible to determine, be consistent with the objectives of the *National Tobacco Strategy 2012-2018*. These are to:

- prevent uptake of smoking;
- encourage and assist as many smokers as possible to quit as soon as possible, and prevent relapse;
- reduce smoking among Aboriginal and Torres Strait Islander people, groups at higher risk from smoking, and other populations with a high prevalence of smoking;
- eliminate harmful exposure to tobacco smoke among non-smokers reduce harm associated with continuing use of tobacco and nicotine products;
- ensure that tobacco control in Australia is supported by focused research and evaluation; and
- ensure that all of the above contribute to the continued denormalisation of smoking.

In March 2015, the Australian National Health and Medical Research Council [NHMRC] issued a statement on e-cigarettes citing that there is insufficient evidence to conclude whether e-cigarettes can benefit smokers in quitting, or about the extent of their potential harms. The NHMRC recommended that health authorities act to minimise harm until evidence of safety, quality and efficacy can be produced.

A detailed policy situation analysis for Australia is set out earlier (refer to section 3.1). Key summary points of the status quo are provided here for ease of reference.

Current nicotine regulation

- Except when used in approved therapeutic preparations, or where it is present in tobacco prepared and packed for smoking, nicotine is a schedule 7 poison and cannot be manufactured, sold, or supplied without a valid licence;
- The TGA permits ENDS users in Australia who wish to legally use nicotine in their vaping devices, for therapeutic purposes such as quitting smoking, to obtain a valid prescription from a medical practitioner. However, the nicotine for use in ENDS must also be legal under state or territory law, the medical practitioner must be willing to prescribe it and the importer must comply with the conditions of the TGA PIS;
- Where therapeutic claims are made in relation to nicotine free ENDS, importers must comply with the conditions of the TGA PIS;
- It is legal to possess an ENDS that is nicotine-free in all states and territories; and

- Regulation of the sale of ENDS that are free of nicotine and do not make therapeutic claims varies across Australian states and territories.

Some potential ENDS regulation impacts from the current regulatory framework

- Australia regulatory framework for ENDS appears to have helped to limit the marketing and prevalence of use of ENDS;
- ENDS containing nicotine are available and may be mislabelled as nicotine-free at some Australian retail outlets;
- People under age 18 can legally purchase ENDS in all states except WA, Queensland and NSW, and given the practices of some ENDS suppliers, it seems likely they are purchasing products containing nicotine;
- ENDS containing fruit or confectionery flavours may have added appeal to young people and further be encouraging purchase and use;
- There may be harms from active and passive exposure to the use of ENDS that contain flavourings, nicotine or other chemicals in ENDS;
- Although requiring a medical prescription to import ENDS containing nicotine for therapeutic use may minimise any harmful effects from the use of ENDS, it may be a barrier for those wishing to use ENDS as an aid in quitting smoking;
- ENDS with or without nicotine are not held to any manufacturing standard and may be mislabelled;
- Some manufacturers and retailers may use general health claims to undermine prohibitions on making false or misleading statements;
- Lack of product labelling standards, no requirements for child resistant packaging, no standards to minimise risk of explosions and fires caused by poor quality products, and no mandated health warnings may risk exposing consumers to harm;
- Allowing ENDS to be advertised may act as another enticement for people, particularly youth, to purchase ENDS;
- It is unclear if smokefree environment laws that do not include ENDS are offering adequate protection to employees and the public from the potentially harmful particulates and constituents in ENDS vapour, or protect against renormalisation of smoking behaviours.

4.3 Possible policy approaches to minimise the risks associated with the marketing and use of ENDS

Seven possible, high-level, policy approaches are proposed for consultation. It is **HIGHLY** recommended that respondents read all options prior to forming opinions on which policy approach is most suitable. The preceding document and appendix is also highly recommended as essential reading prior to assessing the policy options.

In brief, the seven policy approaches are as follows:

Policy approach 1: Maintain the status quo
Policy Approach 2: Increase awareness and enforcement of and compliance with existing legislation
Policy approach 3: Regulate ENDS as consumer products
Policy approach 4: Regulate ENDS as tobacco products

Policy approach 5: Regulate ENDS as medicines
Policy approach 6: Develop an ENDS regulatory framework
Policy approach 7: Adopt measures to ban ENDS

The policy options are fully outlined in table 2 below. These policy approaches are not meant to be mutually exclusive. For example, consultation respondents may suggest they prefer ENDS to be regulated as medicines, but also to include ENDs in tobacco control regulations that prohibit use in smokefree areas.

For the purposes of clarity **only brief points are made in table 2**, it is essential to review the text in the policy situation analysis and the preceding section on the policy discussion for full details on the context and possible impacts. Additionally, it is fully expected that consultation respondents will raise additional issues and/or considerations not fully addressed.

Analysis of ENDS policy concerns

Below is a high-level summary of some of the priority concerns when considering ENDS policy approaches.

Nicotine regulation

Article 5.2(b) of the WHO Framework Convention commits Parties not only to preventing and reducing tobacco consumption and exposure to tobacco smoke but also to preventing and reducing nicotine addiction independently from its source. Therefore, while medicinal use of nicotine is a public health option under the treaty, recreational use is not. WHO has also recommended that ENDS only be made available to existing smokers.(1)

In Australia, no ENDS products have been subject to a transparent regulatory process or safety standard. Additionally, importing products from overseas and online outlets compromises the accuracy of product labelling and what can be known about the actual ingredients contained within the products.

There are strict controls regarding the supply (including sale) of nicotine. However, it may be unclear for consumers whether state and territory poisons legislation precludes the lawful possession of liquid nicotine (i.e as a Schedule 4 poison) for therapeutic use in ENDS when imported via the TGA's personal importation scheme. The avenue for obtaining liquid nicotine under this specific circumstance may warrant further clarification/agreement by the states and territories.

Overall, Canada's and Australia's existing regulatory framework appears to have helped to limit the marketing and prevalence of use of ENDS compared to countries with more liberal regulatory frameworks such as the USA and the UK.

There is not currently a consistent approach to ENDS regulation across Australia, which may be serving as a source of confusion to users, retailers, employers and the general public.

Significant risks associated with liberalising the supply of nicotine include that:

- Prevalence of the use of ENDS containing nicotine is likely to increase at a point in time when the overall benefits/harms of market proliferation are not known.

- If governments are required to provide resources to implement and support options to allow ENDS containing nicotine on the market while regulating to minimise their risks, it weakens arguments that ENDS are solely a market-based solution to reducing the harms from smoking related disease. These concerns are especially important given that the benefits of ENDS are not agreed and there are concerns they may be harmful.

Sales to young people

Our literature review suggests there is little debate or controversy in banning the sale of ENDS to young people and such a policy would be consistent with norms in other jurisdictions. Evidence regarding the prevalence of ENDS use amongst young people aged 14 – 17 years is of concern (4.3% having used ENDS in the last 12 months) and provides support for the need to ensure that young people do not have access to such products. There are concerns about the potential influence of ENDS use on tobacco use. Maintaining the low rates of smoking amongst young people is paramount.

Equally, this policy measure should not be considered a comprehensive approach to ENDS, but just one possible measure within a suite of measures. Similar laws have long been in place for the sale of tobacco products and it is well recognised that they form only a part of a comprehensive approach to tobacco control regulation. Tobacco retailers are already well versed in and equipped for restrictions of sales to minors and including ENDS in such laws is unlikely to incur additional costs on tobacco retailers.

Smoking cessation and health claims

The review of the evidence has shown that, while the short-term health effects of ENDS use appear to be minimal, there is insufficient evidence available to determine the long-term health effects of ENDS. Additionally, available evidence is equivocal as to the usefulness and effectiveness of ENDS as a smoking cessation aid. Therefore, there is sufficient cause for concern that allowing manufacturers to make therapeutic claims without TGA approval would be inappropriate at this time. Current regulations allow general health related claims, such as claiming ENDS are a “less harmful alternative” and allow users to “regulate your nicotine intake.” Such claims have been widely documented in Australian ENDS promotions. ENDS making specific therapeutic claims are not permitted for sale under existing Australian regulations and any ENDS that do make such claims are to be referred to the TGA.

ENDS use in smoke-free areas

There is limited evidence available to determine whether exposure to second-hand vapour has meaningful health effects, in either the short- or long-term. However, the WHO report on ENDS states that “smoke free policies are designed not only to protect non-smokers from second hand smoke, but also to provide incentives to quit smoking and to denormalize smoking as adolescents are particularly vulnerable to visual cues and social norms.”(1) Smoke-free laws as applied to conventional tobacco products are well received, readily enforced, and common in Australia. These laws are primarily the responsibility of individual states and territories.

Advertising of ENDS

The evidence that advertising increases ENDS use, particularly among young people, is cause for concern. Given the propensity for nicotine addiction and other possible health harms, advertising such products may be counter to public health goals. Tobacco retailers are already well versed in and equipped for point-of-sale display restrictions and including ENDS in such laws is unlikely to incur additional costs on businesses.

Any ENDS advertising must however comply with the Commonwealth *Tobacco Advertising Prohibition Act (1992)* and not be deemed to promote smoking or tobacco products in any way. Additionally, advertisements for ENDS must not make, or imply, therapeutic claims unless the product has been approved by the Therapeutic Goods Administration (TGA) as a therapeutic good for supply in Australia.

Personal importation of ENDS

The personal importation of ENDS is an aspect of the status quo. None of the policy options address the quality, safety, and efficacy of products imported directly by the consumer.

Additional and emerging products

It is important to note that the priority concerns noted above focus on ENDS (with or without nicotine). However, when considering these concerns, Australian governments may also wish to assess their relevance to a broader range of products available which deliver an aerosol and/or vapour via inhalation. The *Tobacco and Other Smoking Products Act 1998* (Qld) was recently updated to include the term 'personal vapouriser'. Examples of these products have been provided in sections 1.2 and 2.3 in the Appendix, respectively.

Table 2 Policy options to minimise the risks associated with the marketing and use of ENDS in Australia

Policy Approach and Description	How the approach addresses the problem	Potential positives of the approach	Potential drawbacks of the approach
1. Maintain the status quo • Refer to section 3.1 for a description of the status quo.	• Affirms and assures that should an ENDS product be developed that has provable therapeutic benefits there is a regulatory mechanism to bring such a product to the Australian market	• Requires no additional government action or investment	• There is a risk that consumers will be misled as to the benefits and risks of ENDS use by the generalised health- or cessation-related claims that are currently permitted under existing regulations • Does not provide for consistent protection across Australia, as there are some differences in regulations across states/territories
2. Increase awareness and enforcement of and compliance with existing regulations • Improve compliance with existing regulations by implementing retailer education, compliance and enforcement strategies	• Educating retailers about, and increasing enforcement of and compliance with, existing regulations pertaining to the sale of ENDS could reduce the sale of mislabelled products and the sale of illegal products containing nicotine	• Does not require the development of additional regulations and so can be implemented relatively quickly	• Reaching all ENDS vendors is likely to be difficult given they are not required to be registered or licensed • Funding for education, enforcement and compliance activities would be necessary • There are ambiguities in the existing regulatory framework that may impede the effectiveness of education, compliance and enforcement activities

Policy Approach and Description	How the approach addresses the problem	Potential positives of the approach	Potential drawbacks of the approach
3. Regulate ENDS as medicines • Declare **all** ENDS (with or without nicotine) as therapeutic goods under the Therapeutic Goods Act • In effect this would require all ENDS suppliers meet safety, quality and efficacy standards in order to supply and market products	• Ensures each product is assessed by the TGA and only supplied if approved by TGA • Ensures that ENDS or refillable liquids do not contain dangerous chemicals • Products have adequate premarket research demonstrating their safety and quality – specifically, adequate provision of pharmacological and toxicological data, and clinical efficacy • Level of access and advertising restrictions are proportionate to the level of risk and benefits to individual products For example, any products demonstrated to be low risk could be sold at retail outlets, high-risk products would require a prescription and be subject to more stringent advertising restrictions	• Minimises population health impacts, such as increases in ENDS use by non-smokers, when population health outcomes are unclear • No new legislative mechanism required and expertise already in place which will minimise government investment • Responsibility and cost is largely on suppliers • Consumer access to and marketing of ENDS remains flexible and readily changed in light of new evidence • ENDS are only available to existing smokers	• Does not address all the risks, additional measures may be required from tobacco control laws, such as prohibiting use of ENDS in smokefree areas, • Reduces access to products that some consumers may be using in place of cigarettes • No ENDS are available on the market until such time a product is approved by the TGA, which may be a lengthy process
4. Regulate ENDS as tobacco products	• Tobacco control regulations have been highly successful, especially in preventing young people from taking up smoking,	• The general public is highly supportive of tobacco control • Some of these measures may reduce the risk of ENDS serving	• ENDS would remain on the market, and their contents/composition would be largely unregulated

Policy Approach and Description	How the approach addresses the problem	Potential positives of the approach	Potential drawbacks of the approach
• Apply selective/appropriate tobacco control legislation to all ENDS, such as bans on sales to minors and smokefree environment laws	applying the same approaches is likely to result in avoiding increased ENDS uptake among non-smokers	as a gateway to tobacco use	• Tobacco control legislation is guided exclusively by decreasing product use. Assessing if ENDS should be regulated as a tobacco product then depends on whether the regulation of ENDS should also be exclusively guided by minimising use. • Little evidence as yet available on whether applying tobacco control policies to ENDS would encourage or discourage smokers who would have otherwise not quit smoking to switch to exclusive ENDS use
5. Regulate ENDS as consumer products • Implement standards for ENDS and/or their components under the Commonwealth *Competition and Consumer Act 2010*. This could include but may not be limited to: emissions,	• Potentially reduces the risks associated with the use and/or mishandling of individual products.	• Potentially minimises some of the known risks of ENDS, such as: exposure to toxic flavourings and other harmful contents such as heavy metals, spontaneous fires and explosions and accidental poisonings • Follows other jurisdictions that have developed product	• Compared to therapeutic goods and tobacco control approaches, standards implemented through consumer legislation in isolation may create an unwarranted perception of safety.

Policy Approach and Description	How the approach addresses the problem	Potential positives of the approach	Potential drawbacks of the approach
ingredients, packaging, marketing etc. • The intention of this option is to implement standards on any ENDS device and/or component(s) on the market. • Standards implemented under this approach would build on the existing framework that applies to ENDS and nicotine. For instance, they could also apply to any ENDS product (containing nicotine) that had received approval for marketing from the TGA (in addition to therapeutic standards).		standards for ENDS, such as the revised EU Tobacco Products Directive which covers all consumer ENDS sold in the EU	
6. Develop an ENDS regulatory framework • Develop a comprehensive ENDS regulatory framework. • This option could include but would not be limited to product standards.	• Developing a comprehensive and well-designed regulatory framework that ensures the domestic market is well controlled and continuously monitored could assist in avoiding any unwanted outcomes such as increased uptake among non-smokers/youth and dual use	• An ENDS framework could allow users highly controlled, local access to a product that does contain nicotine, but is likely less dangerous than conventional tobacco products • An ENDS framework could be structured to capture future development and innovations in tobacco and tobacco-like	• Developing an exclusive ENDS framework could be costly and will likely take time to create and implement. • Developing the standards, including but not limited to: emissions, ingredients, nicotine strength and packaging will require more widespread consultation and

Policy Approach and Description	How the approach addresses the problem	Potential positives of the approach	Potential drawbacks of the approach
	of ENDS and traditional cigarettes among smokers	products	additional resources. • Current evidence is not definitive that standards will prevent potential long-term harms associated with the use of ENDS nor guarantee products will not appeal to youth and/or non-smokers.
7. Adopt measures to ban ENDS • Prohibit the commercial importation or commercial supply of **all** ENDS (with or without nicotine).	• Reinforces and clarifies for consumers that ENDS have not been demonstrated to be a safe product (with or without nicotine) and that ENDS containing nicotine are likely to be addictive and as such should not be available for domestic supply.	• Relatively straightforward to legislate and likely requires limited government resources.	• Severely limiting the supply of ENDS may be seen as a contradiction when more harmful conventional cigarettes are still widely available in Australia • Enforcement may be difficult and effectively monitoring use of an illegal product is more challenging • Reduces access to products that some consumers may be using in place of cigarettes

AUTHOR DISCLOSURE STATEMENT

None of the authors have engaged in work including but not exclusive to government relations work or regulatory affairs work for, or associated with, the tobacco industry or the ENDS industry, or intends to do so in the future.

In 2000-1 Chapman was a member of a group of researchers that received research funding from GlaxoSmithKline for researching beliefs about smoking cessation. Australian Smoking Cessation Research Consortium (R Borland, S Chapman, K Jamrozik, L Roberts, C Silagy) 2000-2001. Funding received for: Oakes W, Chapman S, Balmford J, Borland R, Trotter L. "Bulletproof skeptics in life's jungle": which self-exempting beliefs about smoking most predict lack of intention to quit? Prev Med 2004;39:776-82.

None of the other authors have undertaken work for, or has had an association with, pharmaceutical companies that market smoking cessation therapies.

Authors Freeman, Chapman, Bellew and Walsberger have publicly advocated for increased ENDS regulation. Freeman and Chapman have published research and opinion pieces on ENDS and tobacco harm reduction.

REFERENCES

1. Conference of the Parties to the WHO Framework Convention on Tobacco Control. Electronic nicotine delivery systems. Report by WHO. (2014). Accessed on 11 May 2015. Available from: http://apps.who.int/gb/fctc/PDF/cop6/FCTC_COP6_10-en.pdf?ua=1.
2. Conference of the Parties to the WHO Framework Convention on Tobacco Control. DECISION FCTC/COP6(9) Electronic nicotine delivery systems and electronic non-nicotine delivery systems. (2014). Accessed on 14 May 2015. Available from: http://apps.who.int/gb/fctc/PDF/cop6/FCTC_COP6%289%29-en.pdf.
3. Cahn Z, Siegel M. Electronic cigarettes as a harm reduction strategy for tobacco control: A step forward or a repeat of past mistakes? Journal of Public Health Policy. 2011;32(1):16-31.
4. Farsalinos KE, Polosa R. Safety evaluation and risk assessment of electronic cigarettes as tobacco cigarette substitutes: a systematic review. Therapeutic Advances in Drug Safety. 2014;5(2):67-86.
5. Hajek P, Etter J-F, Benowitz N, Eissenberg T, McRobbie H. Electronic cigarettes: Review of use, content, safety, effects on smokers and potential for harm and benefit. Addiction. 2014;109(11):1801-10.
6. McNeill A, Etter J-F, Farsalinos K, Hajek P, le Houezec J, McRobbie H. A critique of a World Health Organization-commissioned report and associated paper on electronic cigarettes. Addiction. 2014;109(12):2128-34.
7. Farsalinos KE, Stimson GV. Is there any legal and scientific basis for classifying electronic cigarettes as medications? The International journal on drug policy. 2014;25(3):340-5.
8. Pepper JK, Brewer NT. Electronic nicotine delivery system (electronic cigarette) awareness, use, reactions and beliefs: a systematic review. Tobacco Control. 2013.

9. Zhu SH, Gamst A, Lee M, Cummins S, Yin L, Zoref L. The use and perception of electronic cigarettes and snus among the U.S. population. PloS one. 2013;8(10):e79332.
10. Drummond MB, Upson D. Electronic cigarettes. Potential harms and benefits. Ann Am Thorac Soc. 2014;11(2):236-42.
11. Dutra LM, Glantz SA. High International Electronic Cigarette Use Among Never Smoker Adolescents. Journal of Adolescent Health.55(5):595-7.
12. Grana RA. Electronic Cigarettes: A New Nicotine Gateway? Journal of Adolescent Health.52(2):135-6.
13. Callahan-Lyon P. Electronic cigarettes: human health effects. Tobacco Control. 2014;23(suppl 2):ii36-ii40.
14. Australian Institute of Health and Welfare. 2013 National Drug Strategy Household Survey. Tobacco smoking in the general population. Product types. (2014). Accessed on 07 May 2015. Available from: http://www.aihw.gov.au/alcohol-and-other-drugs/ndshs-2013/ch3/.
15. Dunlop S, Lyons C, Currow D. E-cigarettes: Patterns of use, places of purchase, and reasons for using among adult smokers and recent quitters in New South Wales [Abstract]. Australia Population Health Congress 2015.
16. Australian Institute of Health and Welfare. Table 3.4: Tobacco smoking status, people aged 12 years or older, by age, 2001 to 2013 (per cent) National Drug Strategy Household Survey. (2014). Accessed on 18 May 2015. Available from: http://www.aihw.gov.au/WorkArea/DownloadAsset.aspx?id=60129549644.
17. Goniewicz ML, Gawron M, Nadolska J, Balwicki L, Sobczak A. Rise in Electronic Cigarette Use Among Adolescents in Poland. Journal of Adolescent Health.55(5):713-5.
18. Euromonitor International. Cigarettes in termonal decline? The future of cigarettes. (2014). Accessed on Available from: http://www.euromonitor.com/medialibrary/PDF/pdf_cigaretteDecline-v1.0.pdf.
19. Milenkovic Z. Euromonitor International. New Tobacco Data - What is it Telling Us? (2014). Accessed on 10 May 2015. Available from: http://blog.euromonitor.com/2014/05/new-tobacco-data-what-is-it-telling-us.html - more.
20. Robinson D. Japan Tobacco joins rivals in e-cigarette market with E-Lites buy. Financial Times, June 11 online edition 2014 24 June 2015. Available from: http://www.ft.com/cms/s/28e13462-f179-11e3-9161-00144feabdc0,Authorised=false.html?_i_location=http%3A%2F%2Fwww.ft.com%2Fcms%2Fs%2F0%2F28e13462-f179-11e3-9161-00144feabdc0.html%3Fsiteedition%3Duk&siteedition=uk&_i_referer= - axzz3deGyu5Rb.
21. Pokhrel P, Fagan P, Kehl L, Herzog TA. Receptivity to e-cigarette marketing, harm perceptions, and e-cigarette use. American Journal of Health Behavior. 2015;39(1):121-31.
22. Bertholon JF, Becquemin MH, Annesi-Maesano I, Dautzenberg B. Electronic cigarettes: a short review. Respiration. 2013;86(5):433-8.
23. Harrell PT, Simmons VN, Correa JB, Padhya TA, Brandon TH. Electronic nicotine delivery systems ("e-cigarettes"): review of safety and smoking cessation efficacy. Otolaryngol Head Neck Surg. 2014;151(3):381-93.
24. Oh AY, Kacker A. Do electronic cigarettes impart a lower potential disease burden than conventional tobacco cigarettes? Review on E-cigarette vapor versus tobacco smoke. Laryngoscope. 2014;124(12):2702-6.
25. Durmowicz EL. The impact of electronic cigarettes on the paediatric population. Tobacco Control. 2014;23(suppl 2):ii41-ii6.
26. Grana R, Benowitz N, Glantz SA. E-Cigarettes: A Scientific Review. Circulation. 2014;129(19):1972-86.

27. Pisinger C, Døssing M. A systematic review of health effects of electronic cigarettes. Preventive Medicine. 2014;69(0):248-60.
28. Brown CJ, Cheng JM. Electronic cigarettes: product characterisation and design considerations. Tobacco Control. 2014;23 Suppl 2:ii4-10.
29. Daniel IS, Brett DN, James MW, Blalock JE, William CB, Patricia LJ. Mechanical and Chemical Components of Electronic Cigarettes Affect Combustion Product Formation and Biological Pathways of Inflammation. B31 INFLAMMATION AND COPD. American Thoracic Society International Conference Abstracts: American Thoracic Society; 2015. p. A2712-A.
30. Franck C, Budlovsky T, Windle SB, Filion KB, Eisenberg MJ. Electronic cigarettes in North America: history, use, and implications for smoking cessation. Circulation. 2014;129(19):1945-52.
31. Matthew DF, Raju SV, Vivian YL, Li Ping T, Courtney MF, Marina M, et al. Effect of E-Cigarettes on Airway Epithelial Ion Transport and Implications for Mucociliary Clearance Defense. B110 COPD GALORE: NEW INSIGHTS INTO BRONCHITIS AND EMPHYSEMA DEVELOPMENT AND TREATMENT. American Thoracic Society International Conference Abstracts: American Thoracic Society; 2015. p. A3868-A.
32. Matthew DF RS, Vivian YL, Li Ping T, Courtney MF, Marina M, et al. Effect of E-Cigarettes on Airway Epithelial Ion Transport and Implications for Mucociliary Clearance Defense. B110 COPD galore: new insights into bronchitis and emphysema development and treatment: American Thoracic Society; 2015. p. a3868-a. 2015.
33. Andrew JH, Nicholas R, Jennifer AD, Roy G, Dave S. The Effect of Electronic Cigarette Exposure on Innate Immune Cells. B31 INFLAMMATION AND COPD. American Thoracic Society International Conference Abstracts: American Thoracic Society; 2015. p. A2716-A.
34. Cobb NK, Byron, M. J., Abrams, D. B., Shields, P. G. Novel nicotine delivery systems and public health: the rise of the "e-cigarette". American journal of public health. 2010;100(12):2340-2.
35. Chatham-Stephens K, Law R, Taylor E, Melstrom P, Bunnell R, Wang B, et al. Notes from the field: calls to poison centers for exposures to electronic cigarettes--United States, September 2010-February 2014. MMWR Morbidity and mortality weekly report. 2014;63(13):292-3.
36. The Lancet. E-cigarettes: Public Health England's evidence-based confusion. The Lancet.386(9996):829.
37. Combes RD, Balls M. On the safety of e-cigarettes: "I can resist anything except temptation". ATLA. 2015;43:417-25.
38. Vansickel AR, Eissenberg T. Electronic Cigarettes: Effective Nicotine Delivery After Acute Administration. Nicotine & Tobacco Research. 2013;15(1):267-70.
39. Dawkins L, Corcoran O. Acute electronic cigarette use: nicotine delivery and subjective effects in regular users. Psychopharmacology (Berl). 2014;231(2):401-7.
40. Herzig Z. Letter by Herzig regarding article, "Electronic cigarettes: a scientific review". Circulation. 2015;131(6):e341.
41. Grana R, Benowitz N, Glantz S. Response to letter regarding article, "Electronic cigarettes: a scientific review". Circulation. 2015;131(6):e342.
42. McRobbie H, Bullen C, HartmannBoyce J, Hajek P. Electronic cigarettes for smoking cessation and reduction. Cochrane Database of Systematic Reviews. 2014(12).
43. Rahman MA, Hann N, Wilson A, Mnatzaganian G, Worrall-Carter L. E-Cigarettes and Smoking Cessation: Evidence from a Systematic Review and Meta-Analysis. PloS one. 2015;10(3):e0122544.
44. Kalkhoran S, Glantz SA. E-cigarettes and smoking cessation in real-world and clinical settings: a systematic review and meta-analysis. The Lancet Respiratory medicine. 2016;4(2):116-28.

45. Bullen C, Howe C, Laugesen M, McRobbie H, Parag V, Williman J, et al. Electronic cigarettes for smoking cessation: a randomised controlled trial. Lancet. 2013;382(9905):1629-37.
46. Adkison SE, O'Connor RJ, Bansal-Travers M, Hyland A, Borland R, Yong HH, et al. Electronic nicotine delivery systems: international tobacco control four-country survey. American journal of preventive medicine. 2013;44(3):207-15.
47. Pisinger C, Godtfredsen NS. Is there a health benefit of reduced tobacco consumption? A systematic review. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2007;9(6):631-46.
48. Tverdal A, Bjartveit K. Health consequences of reduced daily cigarette consumption. Tob Control. 2006;15(6):472-80.
49. 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.
50. 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.
51. Walsberger S, Havill M, Burton S, S. E. Baseline Report on Retail Availability and Promotions of Electronic Cigarettes in Registered Tobacco Retail Outlets in NSW - 2014/15. Sydney: Cancer Council NSW. (2015). Accessed on.
52. Grana RA, Ling PM. "Smoking revolution": a content analysis of electronic cigarette retail websites. American journal of preventive medicine. 2014;46(4):395-403.
53. Maloney E, Capella J. Does Vaping in E-Cigarette Advertisements Affect Tobacco Smoking Urge, Intentions, and Perceptions in Daily, Intermittent, and Former Smokers? Health Communication,. 2015;online(11 Mar 2015).
54. Durkin S, Bayly M, Murphy M, Wakefield M. Non-smokers, Smokers and Former Smokers responses to Electronic Cigarette advertisements: preliminary findings. Cancer Councl Victoria. (2015). Accessed on.
55. Quit Victoria. Legal status of electronic cigarettes in Australia. (2015). Accessed on 06 May 2015. Available from: http://www.quit.org.au/downloads/resource/policy-advocacy/policy/legal-status-electronic-cigarettes-australia.pdf.
56. Therapeutic Goods Administration. Posions standard 2015. Canberra: Department of Health, 2015.
57. Gartner C, Douglas H, Hall W. E-cigarettes and the law in Australia. Australian Family Physician. 2015;in press.
58. NSW Ministry of Health. Are electronic cigarettes and e-liquids safe? Factsheet. (2014). Accessed on 07 May 2015. Available from: http://www.health.nsw.gov.au/tobacco/Factsheets/e-cigarettes-safe.pdf.
59. Tasmanian Government. Department of Health and Human Services. Warning on e-cigarettes. (2014). Accessed on 03 August 2015. Available from: https://www.dhhs.tas.gov.au/news/2014/warning_on_e-cigarettes.
60. Qantas. Dangerous Goods. What you can carry and where. e-cigarettes. (2015). Accessed on 22 May 2015. Available from: http://www.qantas.com.au/travel/airlines/dangerous-goods/global/en - e-cigarettes.
61. Institute for Global Tobacco Control. Country Laws Regulating E-cigarettes: A Policy Scan. Baltimore, MD: Johns Hopkins Bloomberg School of Public Health;. (2015). Accessed on 16 February 16. Available from: http://globaltobaccocontrol.org/node/14052.
62. Ministerial Council on Drug Strategy. National Drug Strategy 2010–2015 (2010). Accessed on 01 June 2015. Available from: http://www.nationaldrugstrategy.gov.au/internet/drugstrategy/publishing.nsf/Content/DB4076D49F13309FCA257854007BAF30/$File/nds2015.pdf.

APPENDIX

SECTION 1 INTRODUCTION....36
1.2 What are ENDS?....36
SECTION 2 LITERATURE REVIEW....38
2.1 Methods....38
2.2 Prevalence of ENDS use....38
Australia - vulnerable populations....43
United Kingdom [UK]....44
United States [US]....45
US: Youth Prevalence Data....45
Canada....46
New Zealand....46
2.3 International ENDS market....47
2.4 Health effects of use and second-hand exposure to ENDS....48
Propylene glycol or glycerol and their by-products....48
Nicotine....49
Flavourings....51
Particulate matter....51
Other chemicals....51
2.5 Cessation and reducing consumption of conventional tobacco products....52
Risk of dependence for inhaled nicotine aerosols....52
Smoking cessation....52
2.6 Marketing....54
SECTION 3 SITUATION ANALYSIS....56
3.3 ENDS policy - situation analysis for other jurisdictions - country case studies....57
Canada....57
European Union....58
United Kingdom....59

United States 61

New Zealand 62

Brazil 63

SECTION 1 INTRODUCTION

1.2 What are ENDS?

Not all of these products look like conventional cigarettes. All ENDS have three basic components: a battery; an atomiser; and a fluid cartridge (Figure 1). The fluid used in ENDS usually contains propylene glycol and/or glycerol, nicotine, and flavourings (e.g. tobacco, menthol, fruit).

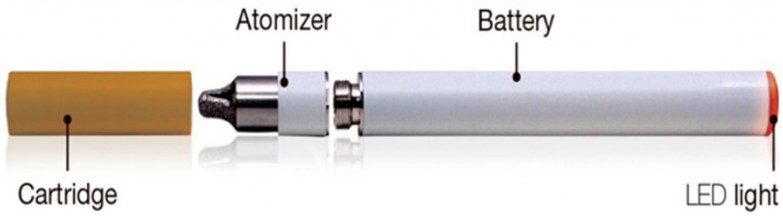

Figure 1 - The basic components of a first generation ENDS

Source: http://vaping360.com/archives/what-is-an-electronic-cigarette-the-beginners-guide/

The first generation ENDS (commonly called 'cigalikes') were invented in China in the early 2000s and were intended as a less harmful substitute for smoking conventional tobacco products.(1) Indeed, these ENDS were intended not only to simulate the feeling and action of smoking but also to physically resemble cigarettes. More recently, second and third generation ENDS have come onto the market (see examples in Figure 2). These generally do not resemble conventional cigarettes and the user can replace the fluid cartridge when it runs out, due to the open tank system, allowing them to vary the flavour of the vapour. In the case of third generation ENDS, users can also modify their device in order to customise its performance (so-called "mods" or "tanks").

Figure 2 - Second and third generation ENDS

Source: http://vaping.com/science/ENDS-summit-dr-lynne-dawkins

Other devices that are currently available in some test markets, such as the Marlboro iQOS (Figure 3) are a hybrid of ENDS and traditional tobacco products. Like ENDS, it has a battery and heating system, but instead of filling with a liquid, users plug in a modified cigarette that contains tobacco.

Figure 3 – Marlboro iQOS system.

Source: http://media.corporate-ir.net/media_files/IROL/14/146476/PM_AR_2014/images/iqos-sidebar-brands.png

Three central health benefits claimed for ENDS are that:

1. they are far less hazardous to health than combustible tobacco products;(2-8)
2. they are an effective means of stopping smoking, comparable to or more effective than other smoking cessation strategies;(2, 7, 8) and
3. smokers who also use ENDS ("dual users") reduce the number of cigarettes they smoke and that this is likely to be harm reducing.(7, 8)

Four central health concerns expressed for ENDS are that:

1. smokers who might otherwise have quit smoking, may continue smoking and vaping (dual-using) in the belief that their reduced smoking is significantly harm reducing;(9)
2. non-smokers (especially youth) who may have never used any nicotine product, may take up vaping in the belief that ENDS are risk-free;(10)

3. a proportion of non-smokers may commence smoking in addition to vaping (the so-called gateway effect)(11); and
4. The longer term health effects of use are unknown(12)

SECTION 2 LITERATURE REVIEW

2.1 Methods

We initially conducted a search of the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects, Medline, and PsycINFO for systematic and narrative reviews. Search terms were restricted to title and abstract only and included: [electronic cigarette? OR electronic ?nicotine delivery system? OR ENDS? OR vap*] AND [review OR meta?analy*]. Search results were limited to articles published from 2010 onwards. Articles published in a language other than English were excluded.

We then searched Medline and PsycINFO for any significant primary studies published in 2014 and 2015 that therefore would have not been included in any of the included reviews. Search terms were restricted to title and abstract only and included: [electronic cigarette? OR electronic ?nicotine delivery system? OR ENDS? OR vap*] AND [ban? or smokefree or smoke?free or cessation or harm reduction or policy or regulation or legislation or benefits or risks or youth or prevention or prevalence or cost? or health or tax?] NOT [ventilat*]. Articles published in a language other than English were excluded.

We also searched for relevant grey literature files, with particular emphasis on leading cancer control agencies and public health organizations including: the World Health Organization, the International Agency for Research on Cancer, the Union for International Cancer Control, the Framework Convention Alliance, and the World Lung Foundation.

2.2 Prevalence of ENDS use

Table 1 Recent[a] use of ENDS, among smokers[b] aged 14 years or older, by age and sex, 2013 (per cent)

Source: 2013 National Drug Strategy Household Survey

Sex	18–24	25–29	30–39	40–49	50–59	60–69	70+	14+	18+
Male	31.6	18.5	14.8	11.0	6.7	*7.2	*4.3	15.4	14.5
Female	21.6	17.7	13.6	10.2	13.5	7.2	*6.5	13.9	13.6
Persons	27.2	18.1	14.4	10.6	9.8	7.2	*5.3	14.8	14.1

* Estimate has a relative standard error of 25% to 50% and should be used with caution.

(a) Used in the previous 12 months.

(b) Smoked daily, weekly or less than weekly.

Table 2 Prevalence of ENDS ((both nicotine and non nicotine) stratified by demographics, Australia 2013

Source: Unpublished data from the Australian Institute of Health and Welfare. National Drug Strategy Household Survey, 2013 [computer file]. Canberra: Australian Data Archive, The Australian National University, 2015, cited in Greenhalgh, E Ch 18, Potential for harm reduction in tobacco control, in Scollo, MM and Winstanley, MH [editors]. Tobacco in Australia: Facts and issues. Melbourne: Cancer Council Victoria; 2015. To be available from http://www.tobaccoinaustralia.org.au/

Demographic variable		Used ENDS in last 12 months	Have used ENDS, but not in last 12 months
		% within each demo category	
All (14+ years)		3.2%	1.2%
Gender	Male	4.0%	1.5%
	Female	2.5%	1.0%
Age group	14-17 years	4.3%	1.7%
	18-24 years	7.3%	2.2%
	25-29 years	5.4%	2.5%
	30-39 years	3.8%	1.3%
	40-59 years	2.3%	0.8%
	60+ years	0.9%	0.6%
SEIFA	Low SES	3.9%	1.2%
	Mid SES	3.0%	1.2%
	High SES	2.6%	1.3%
State	NSW	2.8%	1.2%
	Victoria	2.9%	1.2%
	Queensland	3.7%	1.3%

Demographic variable		Used ENDS in last 12 months	Have used ENDS, but not in last 12 months
		% within each demo category	
	Western Australia	4.0%	1.4%
	South Australia	3.4%	1.0%
	Tasmania	3.5%	0.9%
	ACT	3.0%	0.5%
	Northern Territory	6.0%	2.8%
Smoking status	Daily smoker	15.3%	4.0%
	Weekly smoker	14.5%	4.2%
	Less than weekly smoker	10.7%	4.0%
	Ex-smoker	1.8%	1.3%
	Non-smoker (<100 cigs)	0.8%	0.5%
Current smoker (smoked in the past 12 months)	Yes	15.0%	4.0%
	No	1.0%	0.7%

*N = weighted by absolute person weights, so 'n' represents number within Australian population (of those who answered relevant questions)

SEIFA – Socio-Economic Indexes for Areas

SES – Socio-Economic Status

Correlation with smoking variables: Smoking tobacco is strongly correlated with ENDS use. Daily smokers, smokers who smoke more than 20 cigarettes per day, users of both factory-made cigarettes and roll-your-own tobacco, those who unsuccessfully attempted to reduce their consumption in the past 12 months, and those who unsuccessfully tried to quit in the last 12 months are most likely to be users of ENDS (see Tables 2 and 3)

With regard to quit smoking intentions, smokers who intend to quit in the next 30 days report the highest level of use at 21.7% (see Table 3), followed by those who plan to quit in the next 1 to 2 months (16.6%) and those who plan to quit in 3 months plus (14.4%). 12% of smokers not planning to quit have used ENDS in the past 12 months and 10.8% of smokers who already quit have used an ENDS in the past 12 months.

Data from the Cancer Institute NSW's Tobacco Tracking Survey of adult smokers and recent quitters, show that 9% of survey participants (total *n*=1951) reported current use of ENDS, with 6% using them at least monthly.(13) ENDS users were more likely to be males, younger, and lighter smokers. Common reasons for using ENDS were 'to help me quit smoking' (34%), 'to cut down on the number of cigarettes I smoke' (26%), 'they are not as bad for your health as cigarettes' (17%), and 'so I can smoke in places where smoking cigarettes is not allowed' (13%). Of those who had quit or tried to quit in the past 12 months, 12% used ENDS to help them quit (vs. 26% for NRT, 15% for prescription medications).

Table 3 Prevalence of ENDS use (both nicotine and non nicotine) among current smokers age 18+ stratified by demographics and smoking variables, Australia 2013

Source: Unpublished data from the Australian Institute of Health and Welfare. National Drug Strategy Household Survey, 2013 [computer file]. Canberra: Australian Data Archive, The Australian National University, 2015, cited in Greenhalgh, E Ch 18, Potential for harm reduction in tobacco control, in Scollo, MM and Winstanley, MH [editors]. Tobacco in Australia: Facts and issues. Melbourne: Cancer Council Victoria; 2015. To be available from http://www.tobaccoinaustralia.org.au/

		Used ENDS in last 12 months	Have used ENDS but not in last 12 months
All current smokers aged 18+ years (includes those who smoked in the past 12 months)		% within each demo category	
		14.2%	3.9%
SEIFA	Low SES	15.0%	3.3%
	Mid SES	13.0%	4.1%
	High SES	15.2%	5.5%
State	NSW	13.6%	4.6%
	Victoria	12.4%	4.1%
	Queensland	15.8%	3.4%
	Western Australia	14.5%	4.2%
	South Australia	16.7%	1.6%
	Tasmania	14.6%	3.0%

	ACT	16.6%	3.4%
	Northern Territory	17.4%	5.7%
Type of tobacco smoked	FMC only	13.4%	3.6%
	RYO only	15.1%	2.9%
	FMC and RYO	18.7%	5.8%
	Neither FMC or RYO	10.3%	3.2%
Cigarettes per day	Less than 10	14.2%	3.8%
	10-20	13.7%	4.0%
	More than 20	16.3%	4.2%
Quit intentions	Have already given up	10.8%	3.1%
	Within 30 days	21.7%	3.6%
	Within 1-2 months	16.6%	3.9%
	Yes, but not within 3mths	14.4%	3.9%
	Not planning to quit	12.0%	4.1%
Attempted to quit in past 12 months	Did not attempt to quit	11.9%	4.4%
	Quit for 1+mnth	12.4%	2.5%
	Unsuccessfully tried to quit	20.9%	3.6%
Attempted to reduce consumption in past 12mths	Did not reduce consumption	13.2%	3.6%
	Reduced consumption	14.6%	4.3%
	Unsuccessfully reduced	21.0%	3.8%
Attempted to switch to lower tar/nicotine brand	Did not switch brands	13.9%	3.8%
	Successfully switched	20.2%	4.5%

	Unsuccessfully switched	21.9%	4.4%

*N = weighted by absolute person weights, n represents number within Australian population (of those who answered relevant questions)
FMC – Factory-Made Cigarettes
RYO – Roll-Your-Own

Data from the International Tobacco Control survey (ITC), a survey of a cohort of 1500 Australian adult smokers and former smokers, suggest that ENDS use prevalence increased between 2010 and 2013.(14) Among current and former smokers:

- levels of awareness of ENDS increased from 20.0% in 2010 to 64.8% in 2013;
- 19.7% had tried ENDS in 2013, compared to 2.2% in 2010;
- 6.6% were current users, this included any use of ENDS in 2013 ranging from daily use to less than monthly use, compared to 0.6% in 2010; and
- among the current users in 2013, 42.5% reported that their ENDS brand contained nicotine and 21.1.% reported not knowing if their brand contained nicotine.

Australia - vulnerable populations

According to Australian Institute of Health and Welfare data, smokers from more disadvantaged socioeconomic communities were slightly more likely to have ever used an ENDS in the last 12 months (3.9% compared to mid SES, 3.0%, and high SES, 2.6%). Differences in ENDS use are not as marked across SES groups as for smoking tobacco, and ever use outside of the last 12 months was consistent across all three SES groups.

Among current smokers, analysis by SES groups shows similar proportions of people from low and high SES having used ENDS within the past 12 months (15% and 15.2% respectively); mid SES current smokers had marginally lower use at 13%. ENDS use outside of the past 12 months was highest among high SES (5.5%) and lowest among low SES groups (3.3%). Given the low numbers and with data being available for one time point only, it is difficult to interpret this data, but it does not yet appear that there are major differences in the proportion of ENDS use across SES groups. However, as smoking prevalence is higher in low SES groups, the total number of people using ENDS is also likely to be higher in low SES groups.

Data on ENDS use among other vulnerable populations in Australia including mental health consumers, culturally and linguistically diverse communities, pregnant women, and Aboriginal and Torres Strait Islander people could not be located.

Data from surveys of Australian psycho-stimulant users and people who inject drugs suggest substantially higher prevalence of ENDS use among these populations.(15) (See Table 4) Frequency of use is low with a median of only 3 days use in the past 6 months among recent users. Given that recent ENDS users (in these two populations) were not less likely to have used tobacco compared to non-users, it appears that ENDS are being used primarily for recreational or experimental purposes, rather than as an alternative to tobacco or as a smoking cessation tool.(15)

Table 4 Prevalence of ENDS use among regular psycho-stimulant users and people who inject drugs, Australia 2014

ENDS	Ecstasy and Related Drugs Reporting System[1] (n=800)	Illicit Drug Reporting System[2] (n=898)
% ever used	51	25
% recent use	34	17
Median days recent use (previous 6 months)	3	3
Range of days used	1-180	n.a.

[1]Sindicich, N. & Burns, L. (2015). Australian Trends in Ecstasy and related Drug Markets 2014. Findings from the Ecstasy and Related Drugs Reporting System (EDRS). Australian Drug Trends Series No. 136. Sydney, National Drug and Alcohol Research Centre, UNSW Australia.

[2]Stafford, J. and Burns, L. (2015). Australian Drug Trends 2014. Findings from the Illicit Drug Reporting System (IDRS). Australian Drug Trend Series. No. 127. Sydney, National Drug and Alcohol Research Centre, UNSW Australia.

United Kingdom [UK]

According to the 2010 and 2013 ITC survey, ENDS awareness, trial and current use has also increased among current and former smokers in the UK:

- awareness of ENDS rose from 54.4% (2010) to 90.5% (2013) in the UK;
- 39.9% had tried ENDS in 2013, up from 9.6% in 2010;
- current ENDS use (ranging from daily to less than monthly) increased from 4.5% in 2010 to 18.8% in 2013; and
- 73.1% reported that their current brand contained nicotine and 9.0% reported not knowing if their current brand contained nicotine.

A 2012 study based on survey samples of an online panel, found that ENDS trial among non-smokers in the UK was low, at around 0.5%.(16)

Comparison with Australia: Overall, awareness, trial and current use of ENDS is higher in the UK among current and former smokers than in Australia. In both countries, younger people were more likely to have tried ENDS, but fewer of the younger people who had trialled ENDS were current users. Interest in quitting was a strong predictor of greater awareness, trial, and use of ENDS in the UK but only predicted greater trial in Australia. Between 2010 and 2013, awareness, trial, and current use of ENDS increased markedly among adult current and former smokers in both Australia and the United Kingdom,

albeit reaching much higher absolute levels in the United Kingdom by 2013. Despite the differences in ENDS regulatory environments between the UK and Australia, there was no evidence of a difference in trend in the rate of increase in awareness, trial or current use of ENDS by current and former smokers between the two countries across the 3-year study.(14)

United States [US]

A cross-sectional survey representing a national probability sample of US adults was administered in 2010, 2011, 2012, and 2013 and found that there has been rapid growth in ever and current ENDS use over the 4-year period.(17) Use is highest among young adults and current cigarette smokers. The survey included both smokers and non-smokers and shows that:

- ever use of ENDS increased from 1.8% (2010) to 13.0% (2013), current use increased from 0.3% (2010) to 6.8% (2013) (current use included those who stated that they now use ENDS every day or some days)
- current use among young adults age 18–24 (14.2%) was higher than older adults age 25–44 (8.6%), 45–64 (5.5%), and 65+ (1.2%);
- daily smokers (30.3%) and non-daily smokers (34.1%) were the most likely to currently use ENDS, compared to former smokers (5.4%) and never smokers (1.4%); and
- 12.8% of current ENDS users are never smokers, 5.8% are long term (more than five years) former smokers, 67.4% are current smokers, and 14.1% are recent quitters (less than five years).

US: Youth Prevalence Data

The 2014 National Youth Tobacco Survey, published by the Centers for Disease Control and Prevention and the U.S. Food and Drug Administration's Center for Tobacco Products, shows that:

- current ENDS use (use on at least 1 day in the past 30 days) among high school students increased from 4.5% in 2013 to 13.4% in 2014(18);
- among middle school students, current ENDS use more than tripled from 1.1% in 2013 to 3.9% in 2014; and
- current ENDS use among high- and middle-school students has surpassed current use of every other tobacco product overall, including conventional cigarettes (9.2% of all high-school students and 2.5% of middle-school students).

Comparison with Australia: Trialling and current use of ENDS appears to be higher in the US than in Australia. This may be due to the different regulatory environment in the US for ENDS (See the country regulation review section of this paper). As prevalence is measured quite differently, direct comparisons are somewhat problematic. However, in

the US current ENDS use (defined as use on at least some days) among daily smokers is reported as 30.3%, whereas in Australia only 15.3% of daily smokers reporting having used an ENDS in the last 12 months (2013 data). Dual use of both ENDS and cigarettes is then common in the US. ENDS use among US youth also appears to be much higher than in Australia. But again, as prevalence is measured and reported differently direct comparisons are challenging.

Canada

According to data from the 2013 Canadian Tobacco, Alcohol and Drugs Survey (CTADS), which includes non-smokers as well as current and former smokers:

- 9% of all Canadians age 15 and older reported having ever tried an ENDS;(19)
- 2% of all Canadians age 15 and older reported having used an ENDS in the past 30 days;
- ever-use of ENDS was 37.3% among current smokers, compared to 3.6% among non-smokers;
- past 30-day use was 9.6% among current smokers and 0.5% among non-smokers;
- prevalence of ENDS use is highest among young people with one in five youth (aged 15-19) and young adults (aged 20-24) ever having tried an ENDS; and
- 25% of ENDS users reported that the last ENDS they had used contained nicotine, and nearly 20% of users did not know if there was nicotine in their last ENDS.

Comparison with Australia: Data on trialling and current use of ENDS among smokers appear to be comparable to Australia. Again, similar to Australia, young people were more likely to have trialled ENDS. ENDS containing nicotine cannot be legally sold at retail in Canada, as is the case in Australia (See section 3 for more details).Trial and current use among Canadian non-smokers is low, just as it is in the UK.

New Zealand

Data from a biennial face-to-face in-house survey of New Zealand adults aged 15 years or over, show that in 2014:

- ever-use and current use (defined as at least once a month) of ENDS were 13.1% and 0.8% (there were only 31 current users of cigarettes among the 2594 survey participants);
- ever-use was very common among current smokers at 49.9% compared with an ever-use rate of 8.4% among ex-smokers and 3.4% among never smokers;
- a higher rate of current ENDS use was reported by current tobacco smokers (dual use of ENDS and cigarettes) at 4% with only 0.1% of ex-smokers and non-smokers reporting current use;
- the most common reason reported for trying ENDS was curiosity at 57.1%, followed by quit smoking completely at 31.3%; and

- 17.8% of current ENDS users could not name the brand they used.

Comparison with Australia: Compared with US, UK, Australia and Canada, New Zealand has a high rate of ever use (or trialling) of ENDS, but this has not resulted in high levels of current use. As has been reported in the other countries, young adults were more likely to have trialled ENDS. ENDS are regulated similarly in New Zealand as in Australia, but New Zealand has not yet adopted some tobacco control policies, such as plain packaging. New Zealand has also had other polices such as tobacco retail display bans and on-pack graphic health warnings in place for less time than Australia.

2.3 International ENDS market

BAT (the tobacco company with the largest market share in Australia) was the first international tobacco company to launch a cigalike disposable tobacco product, Vype. (See Figure 4 for a summary of BAT ENDS product development in the UK.)

Figure 4 BAT UK ENDS development

Source: Euromonitor International

The best available data on the ENDS retail market come from the US. One such study examined Nielsen national market scanner data to assess sales volume, market share and growth in 2012 and 2013 at convenience stores, drug stores, grocery stores, and mass merchandisers.(20) The researchers found:

- ENDS sales more than doubled between 2012 and 2013, from $273.6 million to $636.2 million
- Growth was strongest in convenience stores
- Blu eCigs quickly became the best-selling brand and in 2013 constituted nearly half (44.1%) of overall sales
- Unflavoured and menthol ENDS dominated the market

- Disposable ENDS sales increased by 216.4%, a much faster rate than multi-unit packs and cartridge refills

The study did not include online retailer data or data from specialised "vaping" shops, so therefore underestimates total sales volume.

As of April 2015, the top four mainstream ENDS brands in the U.S. are owned by tobacco companies following JTI's agreement to purchase the Florida-based ENDS firm, Logic.

The popularity of open "tank" systems appears to be overtaking the cigalike ENDS. According to Wells Fargo Securities, open system vaporizers now contribute more than $1.5 billion to the overall electronic vaporizer market in the U.S., with cigalike electronic cigarettes accounting for $1 billion. In the US, the combined electronic vaporizer market is estimated at $2.5 billion. Open system vaporizers are suggested to be a lower-cost vaping option, with the weekly spend for an open system user estimated to be 30% less than that of a cigalike user.(21) The tobacco industry stake in the open tank system ENDS market is currently small.

A significant portion of ENDS business appears to be conducted on the internet, although it is difficult to ascertain the exact volume, but is estimated to be as much as 30–50% of total ENDS sold.(22) A study examining the availability and type of ENDS online found that(22):

- there are more than 460 brands and 7700 flavours of ENDS available online for purchase;
- a comparison of two online searches for these brands in August 2012 and January 2014 found the number of brands increased by 10.5 per month and 242 new flavours emerged;
- older brands were more likely than newer brands to anchor themselves to conventional cigarettes; and
- newer websites were more likely to offer eGos and mods (tank style ENDS), which allow users to manipulate nicotine content or add other ingredients.

2.4 Health effects of use and second-hand exposure to ENDS

Propylene glycol or glycerol and their by-products

Propylene glycol (PG) or glycerol, commonly used in ENDS as stabilising compounds, are known to irritate the upper airway and to dry out mucous membranes and eyes but have not been shown to have cytotoxic effects.(12) PG can form propylene oxide, classed as a Group 2B carcinogen (*possibly carcinogenic to humans*) by the International Agency for Research on Cancer (IARC), when heated and vaporised.(23) There is also a growing body of evidence that formaldehyde, a Group 1 carcinogen (*carcinogenic to humans*), (24) can be formed in the vaporisation process.(23, 25-27)There is, however, some debate as to whether ENDS have the potential to generate significant formaldehyde exposure under normal user puffing conditions. (28-31)

Burstyn, in a comparison of the exposure to aerosols and liquids through ENDS use and occupational safety standards funded by the Consumer Advocates for Smoke-free Alternatives Association, concludes that of all known contaminants found in ENDS aerosols and liquids, only PG and glycerol specifically deserve attention, and even then only on a precautionary basis.(32) However, Grana et al note that such comparisons may be unwarranted because threshold limit values used in occupational settings are not suitable for assessing health effects for population-level exposures.(23) Moreover, it is noteworthy that there were less than ten studies contributing the data summarised in the Burstyn review and that a few results of potential concern (e.g. high formaldehyde, ethylene glycol, acrolein) were ruled out on the basis that they were not representative, or were not found in other studies, or that there appeared to have been some misuse of the product.

PG has been classified by the USA Food and Drug Administration (FDA) as safe for use in mist generators, commonly used for theatrical effect.(33) There is evidence, however, that acute exposure to such mists may reduce lung function, although this evidence comes from just one study in a small sample of healthy adults.(9) Indeed, Dow Chemicals, a major manufacturer of PG, advises that inhalation of PG should be avoided.(34) While it must be acknowledged that the comparison between PG in mist generators and ENDS is somewhat irrelevant due to the very different patterns of exposure, it nonetheless highlights the potential long-term effects of inhalation of PG.(9, 33) Daily vapers take some 200 inhalations per day (equivalent to 73,000 inhalations per year).(35) Few people would be exposed to such levels of PG through other means. Currently available data are not sufficient to determine the safety of these compounds for long-term, regular users of ENDS.(12)

Nicotine

Nicotine is included in most ENDS, including some marketed as not containing nicotine.(36) The amount of nicotine has been shown to vary considerably, both across different ENDS products and in the same product.(9, 12) Further, the amount declared on product labelling has been found to differ from the measured amount by up to 50%.(9) While data from smoking machines suggest that ENDS deliver less nicotine per puff than conventional cigarettes, studies with ENDS users suggest that experience plays a significant role in the amount of nicotine absorbed.(37) More experienced users can achieve similar nicotine and/or cotinine concentrations as those found after use of conventional cigarettes.

Nicotine is rated as a schedule 7 poison in Australia except when in tobacco products or in approved therapeutic products.(38) To put this into perspective, this is the same classification as strychnine, cyanide, and arsenical pesticides. These classifications are based largely around the low estimates of the acute dose causing lethal toxicity in mammals. Nicotine is poisonous if ingested, inhaled, or absorbed through the skin or eyes at high levels in its pure form.(39) That said, the risks of acute life threatening nicotine toxicity are low except if there is deliberate or accidental oral ingestion of the ENDS fluid. However, it should be noted that small children are at particular risk of

accidental exposure due to the lack of child-resistant containers and the often bright and attractive packaging that could appeal to children.

Nicotine specifically for smoking cessation purposes, when prepared as required by Australian law, must be approved by the TGA for sale in Australia. Notably, products approved by the TGA for sale in Australia for this purpose are slow release preparations absorbed through the user's skin or lining of the mouth, and also have other risk mitigations, e.g. consumer medical information and appropriate packaging. The risk profile of these products has been shown to be low.

The specific health effects of nicotine have been difficult to ascertain due to the many other harmful chemicals found in conventional cigarettes.(39) There are a great many potentially serious risks from long-term nicotine exposure raised by animal and mechanistic studies but human data that are not confounded by a smoking history are largely lacking. Nonetheless, nicotine is known to affect heart rate and blood flow and may be a risk factor for diabetes.(4, 39)

The 2014 US Surgeon General's report concluded that:(40)

1. The evidence is sufficient to infer that at high-enough doses nicotine has acute toxicity.
2. The evidence is sufficient to infer that nicotine activates multiple biological pathways through which smoking increases risk for disease.
3. The evidence is sufficient to infer that nicotine exposure during fetal development, a critical window for brain development, has lasting adverse consequences for brain development.
4. The evidence is sufficient to infer that nicotine adversely affects maternal and fetal health during pregnancy, contributing to multiple adverse outcomes such as preterm delivery and stillbirth.
5. The evidence is suggestive that nicotine exposure during adolescence, a critical window for brain development, may have lasting adverse consequences for brain development.
6. The evidence is inadequate to infer the presence or absence of a causal relationship between exposure to nicotine and risk for cancer.

Nicotine is not currently considered to be a direct carcinogen by leading cancer agencies, although it is thought to be a tumour promoter.(41) Recent laboratory research results indicate that nicotine induces genomic variations, promotes instability potentially mediated by oxidative stress, implicating nicotine in carcinogenesis, and establishes MUC genes as potential targets (MUC genes provide instructions for making proteins called mucins which make up mucus in the body).(42) That said, a large longitudinal study of Swedish male construction workers found that exclusive users of snus (smokeless tobacco) had similar increased risks of cancer-specific death (from all cancers combined) to exclusive smokers, suggesting that nicotine may play a role in cancer causation; potential confounding variables in the study render this evidence equivocal however.(43) As a result of studies such as this there have been recent calls for further investigation of the role of nicotine in cancer causation(41) and the IARC has identified nicotine as a high priority for review.(44)

Any potential health effects are made more salient due to nicotine being highly addictive.(45) A review by Evans and Hoffman identified two studies that examined the potential addictiveness of ENDS compared to conventional cigarettes.(46) Both studies concluded that ENDS may have a lower addiction potential than conventional cigarettes, although there were significant selection biases evident in the design of the studies. On the other hand, a review by Palazzolo found that it was unclear whether ENDS decrease or increase addiction.(47)

Flavourings

Flavourings are often added to ENDS cartridges but they are often not listed on packaging other than in general terms like "artificial flavours".(33) The US Flavor and Extract Manufacturers Association (FEMA) has advised that none of the major safety assessment programs for flavourings evaluate the use of such flavourings as inhalants and has advised ENDS manufacturers and marketers that marketing the flavourings used in their products as approved by FEMA is misleading.(48) Moreover, a study by Tierney et al notes that many of the flavour chemicals are aldehydes, which have been associated with respiratory irritation.(49) They conclude that regulatory limits should be considered, as should ingredient labelling. Current evidence suggests that some flavourings may be cytotoxic but that they appear to have no effect on particle number of size distribution, which is important when considering the potential health effects of the particulate matter generated by ENDS (discussed further below).(23) Based on the findings of the literature review, no data were available on the short- or long-term health effects of inhalation of these flavourings.

Particulate matter

Nicotine in ENDS is delivered by creating an aerosol of ultrafine particles, with the number of and size distribution of particles similar to that in conventional tobacco products. (23) Particle delivery appears dependent on the level of nicotine in the e-liquid. While it is unclear what effect ultrafine particles in ENDS aerosols have on health, frequent, low-level exposure to fine and ultrafine particles from tobacco smoke or air pollution has been shown to contribute to inflammation and increased risk of cardiovascular and respiratory morbidity and mortality.

Other chemicals

Other harmful chemicals have been detected in ENDS, although mostly at trace levels.(4, 50) Of particular concern are tobacco-specific nitrosamines (TSNAs) and diethylene glycol (DEG).(2, 9) TSNAs have long been known to be carcinogenic,(51) while DEG is toxic and has been responsible for numerous mass poisonings around the world.(52) Cahn et al contend that neither chemical has been detected at large enough levels or consistently enough to warrant significant concern regarding ENDS.(2) They conclude that the amount of TSNAs detected in ENDS is comparable to that found in conventional nicotine replacement therapies (and between 500 to 1400 times less than that found in conventional cigarettes). Similarly, DEG was detected in only one cartridge out of 18

tested, with no other study detecting it. Drummond and Upson, on the other hand, point out that the levels of carcinogens and toxins, including TSNAs, typically exceeded the amount measured in FDA-approved nicotine inhalers.(9)

2.5 Cessation and reducing consumption of conventional tobacco products

Risk of dependence for inhaled nicotine aerosols

The high potential dependence risk associated with the inhalation of nicotine aerosols compared with NRT products is an important issue. Some ENDS have been shown to have a similar nicotine absorption profile to conventional cigarettes (i.e. very rapid absorption and a subsequent rapid fall) in experienced users.(53, 54) The rapid onset and offset of nicotine is key to the development of dependence.(55) This is very different to the profile of NRT products, which are generally absorbed slowly,(56) meaning that they have low potential for long-term dependence and therefore can assist with a move to a non-dependent non-smoking state.(57)

Smoking cessation

In addition to the systematic reviews highlighted in the discussion paper, we identified four significant primary studies published in five papers not included in the reviews.

Biener and Hargraves conducted a longitudinal study of a sample of US smokers in 2011-2012.(39) They found that daily users of ENDS were six times as likely as non-users to report that they quit smoking, with no such relationship evident for intermittent users. Indeed, intermittent users significantly decreased their belief that they would have quit smoking in one year.

The authors concluded that daily use of ENDS was associated with smoking cessation but noted that only 51% of those contacted at baseline completed the follow-up survey, creating the possibility of important attribution biases. Further, we note that intensive users represented the highest proportion (63%) whose readiness to quit *decreased* between baseline and follow-up. In the light of these features of the study, the results may be regarded as equivocal regarding the possibility that ENDS use may lead to reduced motivation to quit smoking.

The English Smokers Toolkit Study is a continuing study of English smokers that commenced gathering data from July 2009. Three reports have been published from the study on the associations between smoking cessation and ENDS use, the first of which reported on pooled cross-sectional self-reported data obtained from adult smokers between July 2009 and February 2014.(40) This study found that ENDS users were more likely to be abstinent from smoking than either those using NRT bought over-the-counter or those who used no aid on their last quit attempt. However, as this study was cross-sectional it cannot be used to infer causality between method of cessation used and outcome. The authors emphasise this stating that it "was not possible to assess all factors that may have been associated with the self-selection of treatment and we

cannot rule out the possibility that an unmeasured confounding factor is responsible for the finding". This study was excluded from the Cochrane review as it was a cross sectional study.

Two later papers from the same study provide stronger evidence about longer term use of ENDS and cessation.(41, 42) Both papers report on the same study that followed up smokers for 12 months who made a quit attempt. These two papers were able to differentiate between casual, occasional, and very light ENDS users and intensive (daily) users.

The first paper found that there was no evidence that daily ENDS use per se is superior in cessation to either non-daily use or to non-ENDS use.(41) Moreover, the study demonstrated that by far the most common outcome for daily ENDS users after one year of follow-up was continuing dual use (cigarettes and vaping): 91.9% of daily vapers at baseline were either dual using at follow-up or had gone back to smoking. Several limitations of the study should be noted. The follow up rate was 43%, resulting in small sample sizes for some analyses. Respondents who were followed-up differed from those not followed-up on some demographic variables, specifically age and gender, potentially reducing the generalizability to younger and female smokers (however, key smoking characteristics and ENDS use were not associated with follow-up). Also, those initiating ENDS use during the follow-up period were included with baseline non-users. Any short-term use of ENDS around baseline and uptake during follow-up will therefore have led to an underestimation of their effects on quit attempts and cessation. Additionally, the baseline sample by including only smokers would have excluded any recent ex-smokers who had used ENDS and successfully quit, thus potentially biasing the sample in favour of 'treatment failures'.

The second paper (42) reported on differences in cessation outcomes between users of different types of ENDS: "cigalikes" (first generation ENDS) and "tank" systems (second and third generation ENDS). The study found that daily and non-daily cigalike users and non-daily tank users were less likely to have quit smoking since baseline but that daily tank users were more likely to have quit, compared to no ENDS use at follow-up. This suggests that the type and frequency of use of ENDS may impact on quitting. However, the authors note that the study may have significantly over-sampled vapers (36% had used ENDS on a daily or less than daily basis in the last 12 months compared to 18% of the general smoking population). This brings the population generalisability of the study's results into question.

Borderud et al conducted a longitudinal study of cancer patients who smoke and were enrolled in an organised smoking cessation program.(43) Controlling for level of addiction, the study found that ENDS users were no more likely to have quit smoking than non-users. Further, using an intention-to-treat analysis, ENDS users were twice as likely to be smoking at the time of follow-up as non-users. Although the generalisability of these findings is limited, the study suggests that ENDS may not be useful for facilitating smoking cessation in cancer patients.

2.6 Marketing

In November 2013, Cancer Research UK published a comprehensive report and research study on the breadth and diversity of ENDS advertising in the UK.(58) ENDS ads are permitted in all forms of media in the UK including: on television, in print media, at point of sale, and online. An analysis of the advertising content and positioning found distinct marketing strategies for two consumer groups emerged: 1) the committed smoker who may be thinking about quitting and 2) the younger social smoker/ non-smoker (Figure 5) In addition the study found that there was extensive evidence of marketing aimed at stakeholders.

Marketing challenge	Alternate strategies		
Who	**Smokers**	**Non- smokers**	**Stakeholders**
Objective	Long-term sales through 'next generation' product, profit-maximisation	Long-term growth through 'next generation' product, profit maximisation	Respectability, distance from tobacco, part of the solution
What	Nicotine, dependence and loyalty, potential cessation aid, dual use (with cigarettes), cutting down	Lifestyle, 'must have' accessory	A lifeline for hardened smokers, harm reduction, public health gain
How	**Product:** safe nicotine, used anywhere **Price:** financial – cheaper than tobacco, psychological – no risk **Promotion:** press, trade press, TV, magazines, social media, sponsorships **Place:** everywhere tobacco is available, company websites, point of sale displays **Positioning:** socially acceptable smoking alternative, necessity	**Product:** innovations like shisha, flavours, lifestyle accessories **Price:** financial –'reassuringly expensive', psychological – cool as can be **Promotion:** lifestyle and celebrity **Positioning:** socially acceptable luxury	**Product**: harm reduction **Price:** financial – priceless, saving lives, psychological – it would be negligent to ignore this offering **Promotion:** health bodies/ experts, charities, politicians **Place:** regulated or unregulated/self-regulated space **Positioning:** reframe perceptions of nicotine use, alternative for those who can't or won't quit

Figure 5 Summary of ENDS marketing strategies

Source: Andrade, Hastings et al. (2013)(58)

Additional research that has examined the amount and nature of ENDS advertising in print, on television and online is primarily focused on the US market. Overall, these studies have found that ENDS marketing has increased in amount and total expenditure over time,(59) is more prevalent than for traditional tobacco products, is included in media channels accessible to youth,(60, 61) and includes content that positions ENDS as a safe or safer alternative to smoking.(62) In terms of the effect these ads may have on smokers, daily smokers had an increased urge to smoke cigarettes after viewing ENDS ads that included images of vaping when compared to smokers who viewed ENDS ads that did not contain vaping images. Former smokers who watched ENDS advertisements with vaping had less confidence that they could refrain from smoking tobacco cigarettes.(63) One systematic content analysis of ENDS website marketing found misleading information - ninety-five percent of the websites made explicit or implicit

health-related claims, 64% had a smoking cessation–related claim. Comparisons to cigarettes included claims that ENDS were cleaner (95%) and cheaper (93%). Eighty-eight percent stated that the product could be smoked anywhere and 71% mentioned using the product to circumvent clean air policies.(64) Several recent studies provide evidence that some ENDS companies are marketing ENDS as smoking cessation aids.(64-67)

Promotions for ENDS are not exclusively a recent phenomenon. A promotional story for Zero Style ENDS appeared in a free entertainment newspaper in Sydney when the product was launched in 2010 (Figure 6).

Figure 6 Promotional story in a Sydney free entertainment newspaper on the launch of Zero Style (2010)

Research from the Cancer Council Victoria assessing non-smokers, smokers, and former smokers' responses to ENDS television and online video advertisements (sourced from the UK and US) found that ENDS ads focusing on personal attributes of users were thought to be more glamorous and had increased appeal than ads focusing purely on product attributes.(68) Ads that included images of vaping reminded people of smoking more than ads that did not include such images. Smokers were most interested in trying the products after viewing the ads, while comparatively fewer former smokers and non-smokers were interested in trying products. However, the researchers concluded that there may be some danger in widespread promotion of ENDS given there was a small number of smokers reporting an urge to smoke after viewing the ads and some young non-smokers reported interest in trying the products after exposure to the ads. Examples of a personal attribute ad and a product attribute ad can be viewed here and here.

No comprehensive or published study has been undertaken of the extent or nature of online ENDS advertising aimed at the Australian market. However, as purchasing of

ENDS online appears to be common,(13) an example of an ENDS website, The Vaper Empire, that prices products for, and ships products to Australia is shown below (Figure 7). The Vaper Empire website suggests that a 25 cigarettes per-day smoker will need to spend $75.00 per month on e-liquids in comparison to $570 per month on cigarettes.

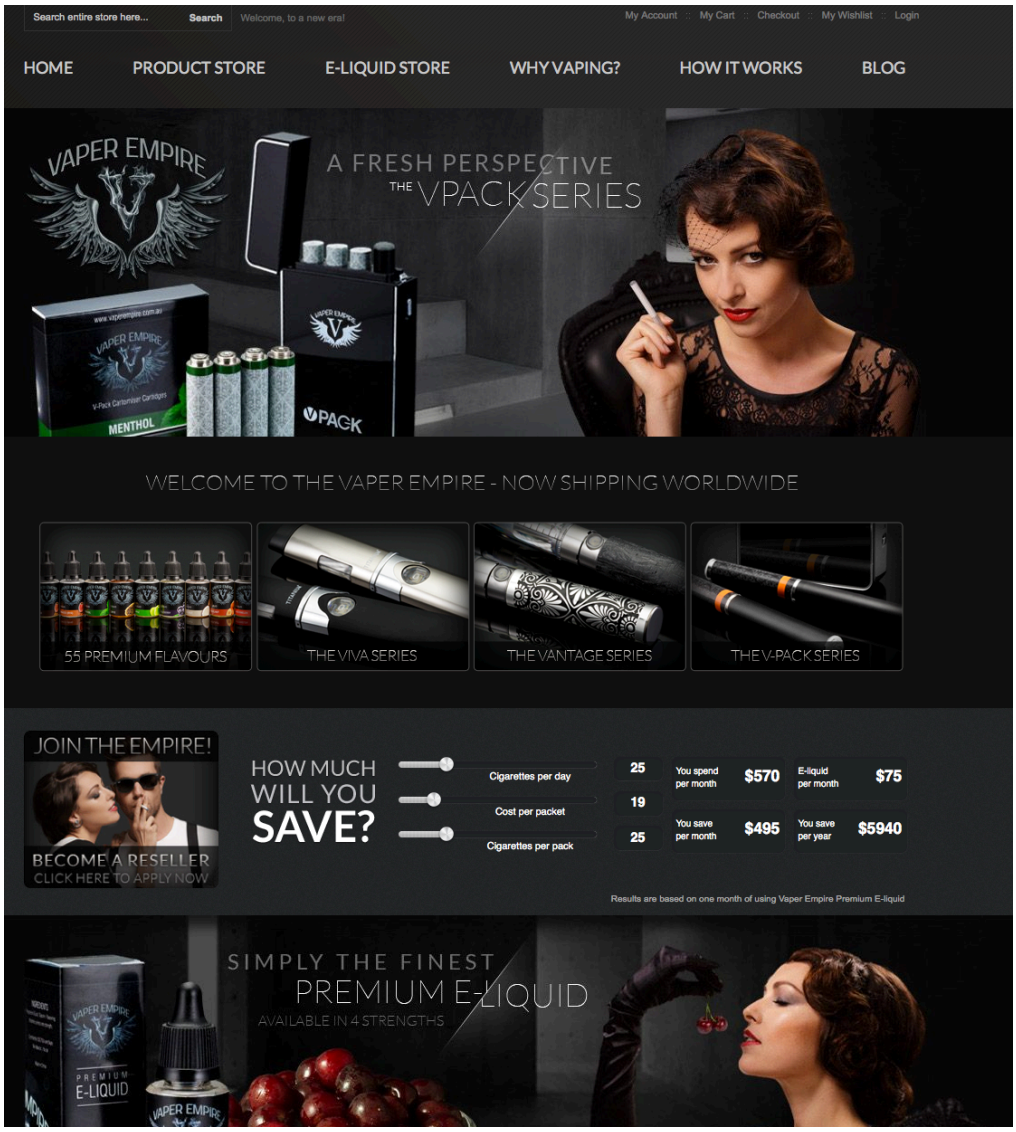

Figure 7 Vaper Empire online ENDS retailer

Source: http://www.vaperempire.com.au/

The online Australian vaping community, aussievapers.com, includes forums discussing and promoting a number of ENDS vendors, including those based in Australia and overseas. Vendors also post online shopping discount codes, special promotions, ads for new products and flavours, and giveaways.(69)

SECTION 3 SITUATION ANALYSIS

3.3 ENDS policy - situation analysis for other jurisdictions - country case studies

Canada

The current ENDS regulatory situation in Canada is very similar to Australia in that ENDS containing nicotine have not been approved for sale. In Canada, ENDS containing nicotine are regulated as drugs and drug delivery devices under the *Food and Drugs Act.* As is the case in Australia, non- nicotine ENDS that do not make health claims are legal for sale with certain exceptions (e.g. Nova Scotia has banned the sale of ENDS to minors [youth under 19]). Despite ENDS containing nicotine not being approved for sale, ENDS are widely available for sale in Canada, including both nicotine and non-nicotine containing ENDS.(53)

In March 2015, a Parliamentary report on ENDS was released by the House of Commons Standing Committee on Health. (54) The Committee heard from a panel of expert witnesses ranging from health organisations, medical professionals, academics, lawyers, ENDS manufacturers and retailers and government agencies. While all witnesses agreed that better regulation of ENDS is needed, how best to regulate these products was contested. Frameworks suggested include regulating ENDS as:

1) tobacco products, under the federal *Tobacco Act;*

2) therapeutic products;

3) consumer products; or

4) a new legislative framework created specifically for ENDS.

- The majority of witnesses who spoke about how electronic cigarettes should be regulated expressed the opinion that none of the existing frameworks (tobacco products, therapeutic products, or consumer products) were suitable;
- nicotine in ENDS is neither a medicine nor a tobacco products and therefore requires its own regulatory framework;
- tobacco regulation was designed to only discourage use, this is not the case with ENDS; and
- ENDS should not require a prescription as this is disproportionate to the product risk profile and will be detrimental to innovation.

The report identifies 14 recommendations, including changes with respect to how ENDS are regulated relative to other tobacco and nicotine products, a series of potential measures with respect to product standards, market and sale, as well as the need for increased research in Canada. The government of Canada has not yet responded to this report but is expected to table a comprehensive response to the report.

Several Canadian provinces, namely Ontario, British Columbia, Nova Scotia and Quebec, have already begun to develop policies for the sale, marketing and use of both nicotine and non-nicotine- ENDS. As of 31 May 2015, the Canadian province of Nova Scotia prohibited the sale of ENDS to persons under 19 years of age, restricted promotions and marketing, and banned using ENDS in workplaces and public places where smoking is

also banned by provincial legislation. Some Canadian municipalities, including Vancouver, have also enacted their own bylaws and prohibit ENDS use in public places including restaurants and bars.

European Union

In February 2014, the European Parliament approved a revised EU Tobacco Products Directive (TPD).(55) The new Directive entered into force in May 2014, with a transition period of two years to allow the 28 Member States to bring national legislation into line with the revised Directive.(56) This means that most of the new regulations will come into effect in the first half of 2016. The focus of the TPD is on standardising ENDS across the EU and improving consumer information and enhancing monitoring of the market.

The revised Directive included a number of regulations that were designed to ensure equal treatment across the EU for ENDS containing nicotine; products that do not contain nicotine are **not** covered by the Directive. The stated primary goal of the regulations is to improve product safety and monitoring of the burgeoning ENDS market. Additionally, the regulations will not apply to medicinal ENDS or medical devices, but will cover all consumer ENDS sold on the EU market. Regulations on flavours, age limits for purchase and advertising that does not have cross border effects are left to individual member states. Monitoring and reporting on all developments relating to ENDS – including market and health-related developments – has been built into the Directive.

Specifically the TPD requires:

- mandatory text health warnings on ENDS packs:
    - "This product contains nicotine which is a highly addictive substance. It is not recommended for use by non- smokers." or
    - "This product contains nicotine which is a highly addictive substance."
- no promotional elements on ENDS packs;
- inclusion of instructions on their use, information on addictiveness and toxicity, a list of all substances contained in the product and information on nicotine content;
- child and tamper-proof containers, cartridges and tanks and protection against leakage;
- with the exception of nicotine, only ingredients that do not pose a risk to human health in heated or unheated form are permitted;
- a maximum nicotine concentration level for ENDS of 20 mg/ml; and maximum volume of liquid containing nicotine in refill containers not exceeding 10 ml and of 2 ml in cartridges or tanks and disposable electronic cigarettes or in single use cartridges; and
- delivery of nicotine dose at consistent levels under normal conditions of use.

Additionally, ENDS manufacturers will be required to:

- notify Member States before placing new products on the market. This includes information on the manufacturer, the ingredients used and emissions, nicotine dose and uptake, product and production process, and a declaration that the

manufacturer takes full responsibility for the quality and safety of the product under normal use;
- report annually to Member States on the sales volumes of the products, types of users, and their preferences and trends; and
- comply with specific rules on advertising, including existing rules that apply to conventional tobacco products on cross-border advertising and promotion.

United Kingdom

Currently in the UK ENDS are regulated as general consumer products, which mean they are generally readily available for sale and there are no restrictions on their nicotine content.(57) Once the EU TPD comes into effect in May 2016, ENDS containing up to 20mg/ml of nicotine will come under the TPD. Above that level, or if manufacturers and importers decide to opt into medicines regulation, such products will require authorisation by the Medicines and Healthcare Products Regulatory Agency (MHRA) as over the counter medicines in the same way as nicotine replacement therapy. Currently in the UK, any nicotine product that claims or implies that it can treat nicotine addiction is considered to be a medicinal product and is therefore subject to regulation by the MHRA. Products, including those with and without nicotine, which do not make these claims, can be freely sold.

On 12 September 2014, Kind Consumer, a healthcare research and development company, announced that it had been granted marketing authorisation from the MHRA for a novel nicotine inhaler. The product called Voke, was developed with the company's partner, Nicoventures, a wholly-owned subsidiary of British American Tobacco [BAT]. It is not yet available for sale but according to February 2015 media reports, "BAT has reached the second stage of its bid to bring the device to market, after being awarded a variation to its license from the UK Medicines and Healthcare products regulatory agency." (58)

The company website states that: "Unlike traditional ENDS, Voke does not require elevation in temperature to heat a nicotine formulation to vapour. Voke works on a pressurised system that atomises a nicotine formulation into fine droplets, capable of lung absorption. It comes in a refill pack containing one stick. Each stick provides a dose of approximately 0.43mg, and is able to be refilled 20 times." The product is shaped and coloured like a typical, traditional cigarette. (See figure 8 and 9.)

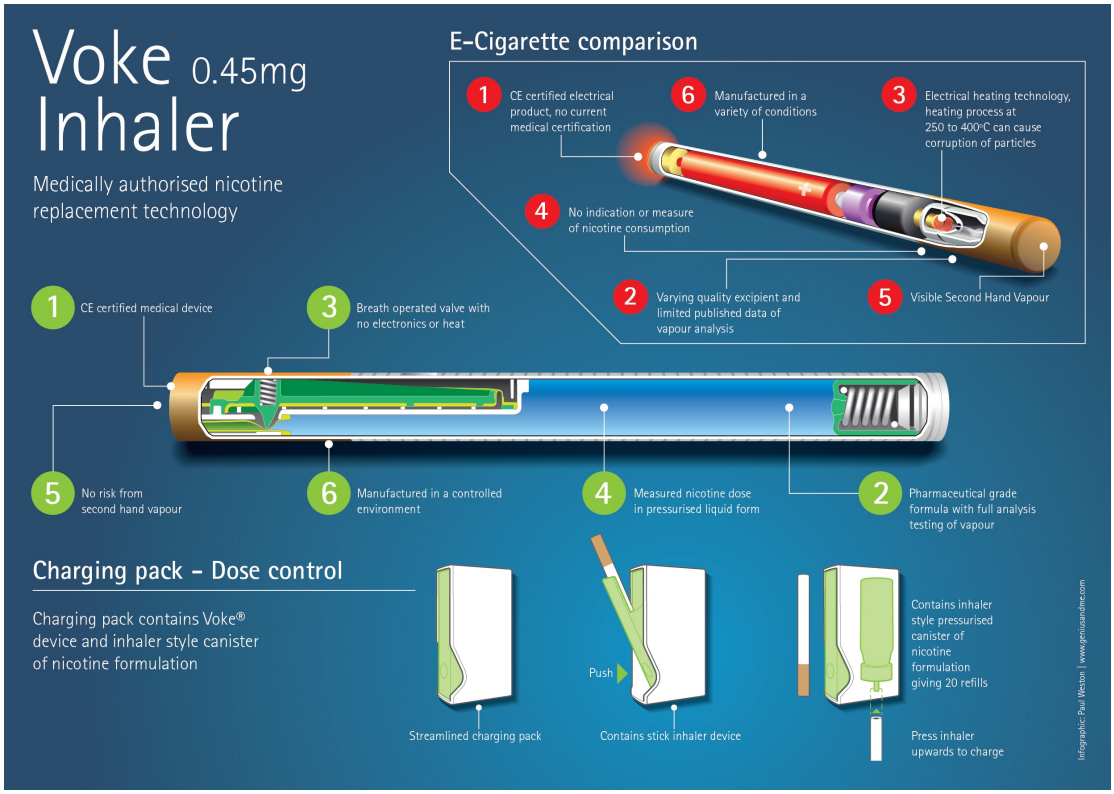

Figure 8 . The Voke inhaler, developed by the British American subsidiary, Nicoventures

Source: http://www.kindconsumer.com/products/voke-inhaler-technology

Figure 9 The Voke inhaler, developed by the British American subsidiary, Nicoventures

Source: http://www.kindconsumer.com/products/voke-inhaler-technology

Advertising

ENDS advertising is permitted in the UK, including on television.(59) The Committee on Advertising Practice (CAP) has published rules on the advertising of electronic cigarettes to cover the interim period until the TPD comes into effect:

- Ads must not be likely to appeal to people under 18;
- People shown using ENDS must not be nor seem to be under 25;
- Ads must not be directed at people under 18 through the selection of media or the context in which they appear;
- Ads must not encourage non-smokers or non-nicotine users to use ENDS; and
- Ads must make clear that the product is an ENDS and not a tobacco product.

At least four ENDS television ads and an ENDS poster have been banned for violating these rules by appearing to glamorise smoking and encouraging use among former smokers.(60-62)

Sales to minors

In England and Wales, it is no longer legal to sell ENDS to people under age 18 as of 1 October 2015.(63)

Smoke-free laws

ENDS are not included in smoke-free laws. However, several national coffee shop, restaurant, and pub chains have banned indoor ENDS use. Museums and public transport have also banned indoor ENDS use.(64)

United States

Compared to Australia, there is currently very little regulation of ENDS in the US. The Food and Drug Agency (FDA) Center for Drug Evaluation and Research (CDER) only has the authority to regulate the sale or use of ENDS that are marketed for therapeutic purposes. The FDA has issued a proposed rule that would extend the agency's tobacco authority to cover additional products that meet the legal definition of a tobacco product, such as ENDS. All public comments regarding the proposed rule were to be submitted to the FDA by 8 August 2014. A final decision on this proposed rule has not yet been announced.

Should ENDS be deemed to fall under FDA tobacco regulatory authority then the following regulations will apply to manufacturers and retailers of ENDS:

- register with FDA and report product and ingredient listings;
- only market new tobacco products after FDA review;

- only make claims of reduced risk if FDA confirms that scientific evidence supports the claim and that marketing the product will benefit public health as a whole;
- not distribute free samples;
- minimum age and identification restrictions to prevent sales to underage youth (although several states already ban the sale of ENDS to minors);
- requirements to include health warnings; and
- prohibition of vending machine sales, unless in a facility that never admits youth.

In a completely separate process to this proposed rule change, the FDA has held three public workshops and a written consultation process to gather scientific information and stimulate discussion among scientists about ENDS.(65) The final of these workshops was held in June 2015 and to date no report has been issued.

Smoke-free laws

A number of US states and local-level jurisdictions include ENDS in smoke-free laws.(66) At the federal level, the U.S. Department of Transportation has stated that it interprets the federal regulations that prohibit smoking on airplanes to apply to ENDS.

Sales to minors

A number of US states (e.g. California) ban the sale of ENDS to minors under age 18.(67)

Taxation

In the United States, only Minnesota imposes an excise tax on ENDS.(68) In October 2012, the US state of Minnesota, Department of Revenue clarified its position that the state's tobacco products tax applies to electronic smoking devices. Electronic smoking devices that contain nicotine constitute tobacco products under the assumption that all nicotine is derived from tobacco. Products containing nicotine that are not derived from tobacco are exempt from the tax. However, the burden is on the taxpayer to prove this to the Department.(67)

New Zealand

In New Zealand, Nicotine free ENDS may be sold and advertised provided they do not make any therapeutic claims. (69) Medsafe, the national medicines authority, must approve any ENDS making health claims. It is illegal to sell an ENDS in New Zealand that contains nicotine. It is also illegal to sell an ENDS (with or without nicotine) that claims to help smokers quit.

ENDS are categorised depending on how they are presented for sale, including the intended use claimed for the product by the supplier and whether this use has a therapeutic purpose as defined in the *Medicines Act 1981*.(70)

- ENDS are **medicine**s when they are supplied for use as an aid to smoking cessation and with one or more cartridges;
- ENDS are **medicines** when supplied with one or more cartridges containing nicotine even if they are not represented as aids to smoking cessation;

- ENDS are **medical devices** when they are supplied for use as an aid to smoking cessation and without cartridges; and
- ENDS are **not** therapeutic products when they are supplied as a 'gadget' that consumers may choose to use as a social prop or as an item that is to be used interchangeably with cigarettes.(71)

Therapeutic purposes include(70):

- Supports or aids smoking cessation;
- Remedy against/ helps alleviate nicotine addiction or the symptoms of nicotine addiction;
- Helps you quit smoking/ smoke less; and
- Reduce your nicotine intake.

Sales to minors

ENDS that look like a tobacco product (or a smoker's pipe) cannot be sold to a person under 18 years old.

Brazil

In 2009, Brazil, through the National Health Surveillance Agency, ANVISA, prohibited the sale, import, and advertising of all electronic smoking devices.(72) Primary reasons given for banning ENDS included a lack of evidence they assist people in quitting smoking and that they mimic tobacco products. Survey data of smokers from 2012/13 shows that awareness of ENDS in Brazil is relatively low, in comparison to Australia, at 37%, and only 8% of smokers have ever trialled an ENDS.(73)

1. Grana R, Benowitz N, Glantz S. Background paper on E-cigarettes (electronic nicotine delivery systems). Prepared for World Health Organization Tobacco Free Initiative. Center for Tobacco Control Research and Education, University of California, San Francisco, a WHO Collaborating Center on Tobacco Control, 2013.
2. Cahn Z, Siegel M. Electronic cigarettes as a harm reduction strategy for tobacco control: A step forward or a repeat of past mistakes? Journal of Public Health Policy. 2011;32(1):16-31.
3. Farsalinos KE, Polosa R. Safety evaluation and risk assessment of electronic cigarettes as tobacco cigarette substitutes: a systematic review. Therapeutic Advances in Drug Safety. 2014;5(2):67-86.
4. Hajek P, Etter J-F, Benowitz N, Eissenberg T, McRobbie H. Electronic cigarettes: Review of use, content, safety, effects on smokers and potential for harm and benefit. Addiction. 2014;109(11):1801-10.
5. McNeill A, Etter J-F, Farsalinos K, Hajek P, le Houezec J, McRobbie H. A critique of a World Health Organization-commissioned report and associated paper on electronic cigarettes. Addiction. 2014;109(12):2128-34.
6. Farsalinos KE, Stimson GV. Is there any legal and scientific basis for classifying electronic cigarettes as medications? The International journal on drug policy. 2014;25(3):340-5.
7. Pepper JK, Brewer NT. Electronic nicotine delivery system (electronic cigarette) awareness, use, reactions and beliefs: a systematic review. Tobacco Control. 2013.
8. Zhu SH, Gamst A, Lee M, Cummins S, Yin L, Zoref L. The use and perception of electronic cigarettes and snus among the U.S. population. PloS one. 2013;8(10):e79332.

9. Drummond MB, Upson D. Electronic cigarettes. Potential harms and benefits. Ann Am Thorac Soc. 2014;11(2):236-42.
10. Dutra LM, Glantz SA. High International Electronic Cigarette Use Among Never Smoker Adolescents. Journal of Adolescent Health.55(5):595-7.
11. Grana RA. Electronic Cigarettes: A New Nicotine Gateway? Journal of Adolescent Health.52(2):135-6.
12. Callahan-Lyon P. Electronic cigarettes: human health effects. Tobacco Control. 2014;23(suppl 2):ii36-ii40.
13. Dunlop S, Lyons C, Currow D. E-cigarettes: Patterns of use, places of purchase, and reasons for using among adult smokers and recent quitters in New South Wales [Abstract]. Australia Population Health Congress 2015.
14. Yong H-H, Borland R, Balmford J, McNeill A, Hitchman S, Driezen P, et al. Trends in e-cigarette awareness, trial, and use under the different regulatory environments of Australia and the UK. Nicotine & Tobacco Research. 2014.
15. Sutherland R, Burns L. E-cigarettes: Holy smoke! [poster] National drug trends conference 2014 [cited 07 May 2105]. Available from: https://ndarc.med.unsw.edu.au/sites/default/files/newsevents/events/Poster%28SA%29 - E-cigarettes.pdf.
16. Dockrell M, Morison R, Bauld L, McNeill A. E-Cigarettes: Prevalence and Attitudes in Great Britain. Nicotine & Tobacco Research. 2013;15(10):1737-44.
17. McMillen RC, Gottlieb MA, Shaefer RMW, Winickoff JP, Klein JD. Trends in Electronic Cigarette Use Among U.S. Adults: Use is Increasing in Both Smokers and Nonsmokers. Nicotine & Tobacco Research. 2014.
18. Centers for Disease Control and Prevention. E-cigarette use triples among middle and high school students in just one year 2015 [cited 10 May 2015]. Available from: http://www.cdc.gov/media/releases/2015/p0416-e-cigarette-use.html.
19. Czoli C, Reid J, Rynard V, Hammond D. E-cigarettes in Canada - Tobacco Use in Canada: Patterns and Trends, 2015 Edition, Special Supplement. 2015 [cited 05 May 2015]. Available from: http://www.tobaccoreport.ca/2015/TobaccoUseinCanada_2015_EcigaretteSupplement.pdf.
20. Giovenco DP, Hammond D, Corey CG, Ambrose BK, Delnevo CD. E-Cigarette Market Trends in Traditional U.S. Retail Channels, 2012–2013. Nicotine & Tobacco Research. 2014.
21. MarketWatch. Press Release. Open System Vaporizers Officially Overtake E-Cigs, Top $1 Billion in Sales for the First-Time Ever 2014 [cited 18 May 2015]. Available from: http://www.marketwatch.com/story/open-system-vaporizers-officially-overtake-e-cigs-top-1-billion-in-sales-for-the-first-time-ever-2014-09-25.
22. 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.
23. Grana R, Benowitz N, Glantz SA. E-Cigarettes: A Scientific Review. Circulation. 2014;129(19):1972-86.
24. Humans IWGotEoCRt. Chemical agents and related occupations. IARC monographs on the evaluation of carcinogenic risks to humans / World Health Organization, International Agency for Research on Cancer. 2012;100(Pt F):9-562.
25. Jensen RP, Luo W, Pankow JF, Strongin RM, Peyton DH. Hidden Formaldehyde in E-Cigarette Aerosols. New England Journal of Medicine. 2015;372(4):392-4.
26. Kosmider L, Sobczak A, Fik M, Knysak J, Zaciera M, Kurek J, et al. Carbonyl Compounds in Electronic Cigarette Vapors—Effects of Nicotine Solvent and Battery Output Voltage. Nicotine & Tobacco Research. 2014.
27. Hutzler C, Paschke M, Kruschinski S, Henkler F, Hahn J, Luch A. Chemical hazards present in liquids and vapors of electronic cigarettes. Arch Toxicol. 2014;88(7):1295-308.

28. Sodhi SK, Khanna A. More on hidden formaldehyde in e-cigarette aerosols. The New England journal of medicine. 2015;372(16):1576.
29. Thomson RH, Lewis PM. More on hidden formaldehyde in e-cigarette aerosols. The New England journal of medicine. 2015;372(16):1575-6.
30. Nitzkin JL, Farsalinos K, Siegel M. More on hidden formaldehyde in e-cigarette aerosols. The New England journal of medicine. 2015;372(16):1575.
31. Pankow JF, Strongin RM, Peyton DH. More on hidden formaldehyde in e-cigarette aerosols. The New England journal of medicine. 2015;372(16):1576-7.
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;14(1):18.
33. Bertholon JF, Becquemin MH, Annesi-Maesano I, Dautzenberg B. Electronic cigarettes: a short review. Respiration. 2013;86(5):433-8.
34. The Dow Chemical Company. Product safety assessment: Propylene Glycol-based low temperature thermal fluids. The Dow Chemcial Company, 2014.
35. Etter JF, Bullen C. A longitudinal study of electronic cigarette users. Addictive behaviors. 2014;39(2):491-4.
36. NSW Ministry of Health. Are electronic cigarettes and e-liquids safe? Factsheet. 2014 [cited 07 May 2015]. Available from: http://www.health.nsw.gov.au/tobacco/Factsheets/e-cigarettes-safe.pdf.
37. Schroeder MJ, Hoffman AC. Electronic cigarettes and nicotine clinical pharmacology. Tobacco Control. 2014;23(suppl 2):ii30-ii5.
38. Therapeutic Goods Administration. Posions standard 2015. Canberra: Department of Health, 2015.
39. Drug and Therapeutics Bulletin. Republished: Nicotine and health2014 2014-11-26 15:17:28.
40. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health. The health consequences of smoking – 50 years of progress: a report of the Surgeon General. Chpater 5 Nicotine. 2014 [cited 16 February 2016]. Available from: http://www.surgeongeneral.gov/library/reports/50-years-of-progress/sgr50-chap-5.pdf.
41. Grando SA. Connections of nicotine to cancer. Nat Rev Cancer. 2014;14(6):419-29.
42. Bavarva JH, Tae H, McIver L, Garner HR. Nicotine and oxidative stress induced exomic variations are concordant and overrepresented in cancer-associated genes. Oncotarget. 2014;5(13):4788-98.
43. Nordenvall C, Nilsson PJ, Ye W, Andersson TM, Nyren O. Tobacco use and cancer survival: a cohort study of 40,230 Swedish male construction workers with incident cancer. International journal of cancer Journal international du cancer. 2013;132(1):155-61.
44. 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.
45. Stolerman IP, Jarvis MJ. The scientific case that nicotine is addictive. Psychopharmacology. 1995;117(1):2-10.
46. Evans SE, Hoffman AC. Electronic cigarettes: abuse liability, topography and subjective effects. Tobacco Control. 2014;23(suppl 2):ii23-ii9.
47. Palazzolo DL. Electronic Cigarettes and Vaping: A New Challenge in Clinical Medicine and Public Health. A Literature Review. Frontiers in Public Health. 2013;1:56.
48. 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.
49. Tierney PA, Karpinski CD, Brown JE, Luo W, Pankow JF. Flavour chemicals in electronic cigarette fluids. Tobacco control. 2015.

50. Franck C, Budlovsky T, Windle SB, Filion KB, Eisenberg MJ. Electronic cigarettes in North America: history, use, and implications for smoking cessation. Circulation. 2014;129(19):1945-52.
51. Hecht SS, Hoffmann D. Tobacco-specific nitrosamines, an important group of carcinogens in tobacco and tobacco smoke. Carcinogenesis. 1988;9(6):875-84.
52. Schep LJ, Slaughter RJ, Temple WA, Beasley DMG. Diethylene glycol poisoning. Clinical Toxicology. 2009;47(6):525-35.
53. Vansickel AR, Eissenberg T. Electronic Cigarettes: Effective Nicotine Delivery After Acute Administration. Nicotine & Tobacco Research. 2013;15(1):267-70.
54. Dawkins L, Corcoran O. Acute electronic cigarette use: nicotine delivery and subjective effects in regular users. Psychopharmacology (Berl). 2014;231(2):401-7.
55. Henningfield JE, Keenan RM. Nicotine delivery kinetics and abuse liability. Journal of Consulting and Clinical Psychology. 1993;61(5):743-50.
56. Benowitz N, Hukkanen J, Jacob P, III. Nicotine Chemistry, Metabolism, Kinetics and Biomarkers. In: Henningfield J, London E, Pogun S, editors. Nicotine Psychopharmacology. Handbook of Experimental Pharmacology. 192: Springer Berlin Heidelberg; 2009. p. 29-60.
57. Moore D, Aveyard P, Connock M, Wang D, Fry-Smith A, Barton P. Effectiveness and safety of nicotine replacement therapy assisted reduction to stop smoking: systematic review and meta-analysis2009 2009-04-02 23:06:14.
58. Andrade M, Hastings G, Angus K, Dixon D, Purves R. The marketing of electronic cigarettes in the UK. Cancer Research UK. 2013 [22 May 2015]. Available from: http://www.cancerresearchuk.org/prod_consump/groups/cr_common/@nre/@pol/documents/generalcontent/cr_115991.pdf.
59. Kim AE, Arnold KY, Makarenko O. E-cigarette Advertising Expenditures in the U.S., 2011–2012. American journal of preventive medicine. 2014;46(4):409-12.
60. Richardson A, Ganz O, Vallone D. Tobacco on the web: surveillance and characterisation of online tobacco and e-cigarette advertising. Tobacco Control. 2014.
61. Wagoner KG, Song EY, Egan KL, Sutfin EL, Reboussin BA, Spangler J, et al. E-cigarette Availability and Promotion Among Retail Outlets Near College Campuses in Two Southeastern States. Nicotine & Tobacco Research. 2014;16(8):1150-5.
62. Paek H-J, Kim S, Hove T, Huh JY. Reduced harm or another gateway to smoking? Source, message, and information characteristics of e-cigarette videos on YouTube. Journal of health communication. 2014;19(5):545-60.
63. Maloney E, Capella J. Does Vaping in E-Cigarette Advertisements Affect Tobacco Smoking Urge, Intentions, and Perceptions in Daily, Intermittent, and Former Smokers? Health Communication,. 2015;online(11 Mar 2015).
64. Grana RA, Ling PM. "Smoking revolution": a content analysis of electronic cigarette retail websites. American journal of preventive medicine. 2014;46(4):395-403.
65. Lee S, Kimm, H., Yun, J. E., Jee, S. H. Public health challenges of electronic cigarettes in South Korea. Journal of preventive medicine and public health = Yebang Uihakhoe chi. 2011;44(6):235-41.
66. de Andrade M, Hastings, G. The Marketing of E-Cigarettes: A UK Snapshot BMJ Group Blogs2013. Available from: http://blogs.bmj.com/tc/2013/04/06/the-marketing-of-e-cigarettes-a-uk-snapshot/.
67. Yamin CK, Bitton A, Bates DW. E-cigarettes: a rapidly growing Internet phenomenon. Annals of internal medicine. 2010;153(9):607-9.
68. Durkin S, Bayly M, Murphy M, Wakefield M. Non-smokers, Smokers and Former Smokers responses to Electronic Cigarette advertisements: preliminary findings. Cancer Councl Victoria 2015.
69. AussieVapers. Forum. Vendors. 2015 [22 May 2015]. Available from: http://forums.aussievapers.com/forum.php.