Submission from Ron Borland PhD FASSA,

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This submission is made in a personal capacity. It does not represent the position of my employer.

I write as a scientist who has worked on issues of tobacco control for more than 30 years. My research focus has been, and continues to be, on mass-disseminable strategies to facilitate smoking cessation. These range from country-wide policies to services such as Quitlines and automated programs delivered via computers and/or smart phones. This work includes a recent study of an Internet delivered intervention I developed which shows clear relapse prevention effects (1). My work on the quantitative evaluation of the impact of tobacco control policies and widely disseminated anti-smoking campaigns has contributed considerably to our understanding of what policies work, and importantly, increased insights as to how they work. I draw on that work directly in my suggestions as to a more effective set of policy responses to the epidemic of smoking-related mortality and morbidity. I have published around 300 peer-reviewed papers on aspects of tobacco control. I have had a long-term interest in harm reduction strategies as they might apply to tobacco control, and have published a number of papers on comprehensive approaches to tobacco control (2-7).

Summary of my submission

In my considered opinion, the use of non-combusted nicotine-containing products (including vapourised nicotine) is the only strategy with any realistic chance of eliminating smoking as a mass consumer activity in the foreseeable future. I acknowledge that it is uncertain as to whether these products have the consumer acceptability to achieve this goal, but all the evidence available suggests that an appreciable proportion of existing smokers will, and with appropriate policies, many more than at present can be motivated to shift. Further, with the products that may appear in the next few years, it is likely that the vast majority will be enticed to shift away from smoking if the policy settings help facilitate the move.

This submission makes the case for more liberal regulation of ANDS as an important way of reducing smoking and thus the death and disease it produces. It outlines a framework for an extension of the current tobacco control agenda to incorporate efforts to regulate tobacco products and to maximise the transition to the least harmful, consumer-acceptable forms of nicotine. In this submission I go beyond the specific terms of reference on vapourised nicotine, to consider the broader range of products that are both potentially consumer-acceptable and deliver a fraction of the toxicants in tobacco smoke. They are collectively called Alternative Nicotine Delivery Systems (ANDS).

While the vaping products tested have not been shown to be superior to conventional nicotine replacement products as cessation aids, more modern systems have not been tested in RCTs and survey research suggests they are more effective than the early generation products. Furthermore, vaping products are vastly more consumer acceptable, and at least theoretically have greater relapse prevention potential. In my opinion the evidence is sufficient to act now to free up access to these products, but should be done in ways that are designed to maximise their potential, while minimising the harms. I do not

believe that it is necessary to wait for more evidence. On human rights grounds, smokers have a right to seek less harmful options for obtaining nicotine, and are doing so, often in spite of the laws. This is not going to change.

Types of nicotine containing products

The range of current and potential ANDS that will be on the market in some countries, or are already being marketed, includes:

- Vaporised Nicotine (VN). These deliver nicotine by generating an aerosol, colloquially referred to as vapour (a term used throughout). These began with e-cigarettes, but there is now a burgeoning range of products, from ones that are designed to look like cigarettes (reasonably called e-cigarettes), to ones that look distinctly different (better described as Personal Vaporisers, PVs). Levels of toxicants in these products can be extremely low. A major form of toxicant creation is due to overheating. This is self-limiting as the resultant vapour is aversive, so the person stops using. The consumable liquids and the PVs (the delivery devices) are increasingly differentiating into separate markets. The open systems whereby the liquid containing nicotine is placed in to the tank of the device by the user are dominated by non-tobacco interests. The tobacco companies seem more interested in developing and marketing closed systems where the cartridge of liquid can be designed in ways to make proprietary control easier and presumably profit margins higher.
- Heat not burn (HnB) tobacco. A technology invested in heavily by large tobacco companies. Philip Morris International (PMI) report great success with their iQos product using Heets tobacco sticks the only product that has gone beyond the test market stage and is now available in several countries. PMI report very high consumer acceptance and problems keeping up with demand. Other big tobacco companies have related products: BAT, with a similar product called Glo, and Japan Tobacco with a hybrid device called Ploom that passes nicotine–free vapour (generated by the same mechanism as personal vapourisers) through a wad of specially prepared tobacco, where it picks up nicotine and tobacco flavours. Both companies report high levels of consumer interest, but only in limited test markets, leading to plans to go into general production. Such products are higher in toxicants than most ANDS, but may deliver more of the ‘smoking experience’. These may have high consumer appeal than PVs, but at a potential health cost, albeit still likely a fraction of that attributable to smoking.
- Clean oral smokeless tobacco, while it is the most important product in Scandinavia, but it is unlikely to be sufficiently attractive to smokers in Australia to play any more than a minor role, at least unless there were concerted efforts to promote it supported (or not actively opposed) by relevant health authorities. Its main advantage is that there is overwhelming scientific evidence that it is low in harm. Given the evidence from Sweden, there is a strong case for the current ban on the sale of these products to be removed. If this were done, strict upper limits on the levels of toxicants in smokeless tobacco would be needed, as some other forms of smokeless are high in toxicants and established carcinogens.
- New, more efficient delivery, oral forms of nicotine. Similar to smokeless tobacco, they may not have the appeal to be long-term alternatives, but potential as more potent cessation aids. Oral products have one advantage in that they are less

socially obvious and thus there is less likely to be social contagion effects around the use.

- PMI also has in test a product that creates a vapour by means of a chemical reaction between nicotine and a weak acid, resulting in respirable nicotine salts being formed. They claim similar uptake of nicotine to cigarettes. They claim they will be test marketing this product this year. Prototypes are reported to have high consumer appeal.

In this paper we will refer to ANDS where we want to be comprehensive, but at other times we will focus on VN/PVs (vaping) or HnB products.

The Changing nature of the vapourised nicotine market

The early development of vaporised nicotine products, beginning with the cigalike products produced by the Chinese company Ruyan, we all outside the sphere of the big tobacco companies. However, as these products became more successful and threatened their markets, the big tobacco companies rapidly bought up most of the larger e-cigarette companies. Their focus then and now seems to be primarily on promoting systems with closed, proprietary cartridges for the liquids, rather than open tank systems. However the market for vaping products is moving away from these products to what are called tank systems. These products are typically larger, don't look like cigarettes (indeed they come in an increasing range of shapes and sizes), and have a reservoir which can be refilled from a bottle of the liquid. Some are now available with sophisticated technologies to prevent the e-liquid overheating and/or to increase ease of use (ie to get satisfying doses of the nicotine-containing vapour). As a result of these innovations the market appears to be dividing in two. One for the nicotine containing liquids, which are now available in a wide range of strengths and flavours. Second, the market for the PV devices is proliferating, with products available from a few dollars to hundreds (I suspect thousands). The nicotine liquids are cheap and easy to produce without compromising quality, so they are likely to operate more like commodities than value added consumer products, greatly restricting the capacity of companies to make the kinds of profits they make from selling cigarettes. This is likely to mean that the concentration of high profits and the resultant power that provides, is unlikely to remain in such a few hands with VN, and with the lower likely profit margins, the capacity of cartels of big companies to unduly influence governments will be somewhat diminished. It will also likely limit the budgets available for advertising and other forms of promotion. That said, those interested in public health will need to keep their eyes open and be ready to challenge any pressures to move public policy away from that best serving community interests.

Comparative health effects

Cigarette smoking is the most harmful way to ingest nicotine (8), but it is (or at least has been) the most psychologically attractive form. It is estimated to cause premature death in between half and two thirds of regular users (9), with smokers losing an average of around 10 years of their lives. They also suffer at least as many years of disability (QALYS). Indeed, the average smoker loses more time off the end of their lives than they spend smoking during it.

Cigarettes deliver nicotine to the brain in a particularly attractive way (10). So much so, that many people continue to use even in the face of knowledge that it is causing high levels of harm. Peak prevalence of smoking in Australia at present is among 25-29 year olds at 20% (National Drug Strategy Household Survey, 2016). All this use occurs in the face of the most comprehensive tobacco control programs in the world. There is clearly some intrinsic interest in using nicotine in its psychoactive forms. This is the core of the tobacco problem. By contrast, it is possible to have non-combusted forms of tobacco, or distilled nicotine, that have few of the toxicants and most of the remaining ones at levels well below that from smoking, in some cases no more than background levels.

The evidence suggests that for the oral forms that have been used for decades, there are few, if any, long term adverse health consequences ((11, 12). In other words, it is technically possible to have low toxin varieties of non-combusted tobacco products (not the high-toxin smokeless prevalent in South Asia), but while toxicants can be reduced somewhat, combustion creates so many that there will never be an acceptably low toxin combusted product (13). It is likely that vapourisers where nicotine is inhaled will have similar low long-term harm profiles. The main unknown is the effect of prolonged lung exposure to the carriers as well as the nicotine.

The weight of evidence is that use of ANDS, including VN, is likely to be far less harmful than smoking. However, the committee is also likely to be presented with studies purporting to show large adverse effects of vaping or of nicotine more generally. These latter studies need to be evaluated carefully as those using in vitro preparations or animals often use doses well above what any human would voluntarily ingest. Studies of vaping equipment also often use the product in ways that would never be used by real users. This includes using when the flow of liquid is inadequate, a phenomenon known as dry puffing (when it happens to a user). The first signs of dry puffing motivates users to stop vaping as the taste is quite aversive. Thus exposures are only acute and infrequent.

When reviewed critically, the evidence shows that while there are some exposures to toxicants, these only constitute a minority of those in smoked tobacco and of those present most are at levels orders of magnitude less, and, as I understand it, there are no toxicants which are clearly higher. As a result, it is reasonable to assume that the risk of long term use will be markedly less than for smoking. The best estimate is around 95% less, originally arrived at by a group of experts led by David Nutt (a former Chief Medical Advisor to the British Government)(14), and subsequent assessments by among other groups, the expert group behind the Royal College of Physicians report, concluded this was a reasonable estimate (15).

Modelling of the potential effects of varying levels of uptake of vaporised nicotine and its role in smoking cessation suggest that unless the reduction in risk is less than 70% there is virtually no conceivable scenario in which there would not be clear net health benefits (16, 17). If the likely risks of long-term vaping are indeed around 95%, it is arguably a level where it should be acceptable to allow adults a choice as to whether to use these products. One argument against this is that nicotine is dependence forming. This is not entirely correct, nicotine can cause dependence when delivered in some forms, most notably in the form of cigarette smoking, but does not appear to have any significant dependence potential when delivered in the form of nicotine patches. It is not clear how dependence forming vaporised nicotine will be. To the extent that it is less immediately psychologically attractive than

smoking, it is likely to be less dependence forming, and there is some emerging evidence that the delivery mechanism may generally result in lower levels of dependence than for smoking even when the level of reported satisfaction is comparable.

The challenges of quitting smoking

The main means by which a smoker can increase their chances of quitting successfully are: by enhancing executive capacity to resist use (ie, exercising self-control), by seeking suitable alternatives, by changing their beliefs about the value and importance of smoking in their lives, by focussing on the benefits of incompatible alternative behaviours, by changing their personal environments to reduce cues to smoke, by retraining their bodies to no-longer desire the experiences of smoking (difficult), or by use of pharmacotherapies to replace or mask the desired effects of smoking. Most of these can be influenced by broadly based social actions, except the effects of pharmacotherapies and retraining reactions.

If the goal of eliminating smoking as a mass behaviour is to be achieved, new strategies are likely to be required over and above those currently endorsed (e.g., through the FCTC), particularly those that reduce relapse rates beyond periods of active intervention. Currently there are few if any such strategies (18), albeit some with promise, including one I developed (1). It is likely that strategies requiring restraint, including sacrifice of short term benefits for longer term gains, are likely to be impractical for many, especially more disadvantaged smokers. The most effective strategy, for some at least, is likely to be the use of maintenance or substitute products that people use long term. Unfortunately, approved NRT products are not consumer acceptable for long-term use, levels of uptake, even when encouraged have been low.

Put simply, for those who value smoking or otherwise find it difficult to quit, the switch to a viable substitute is a far easier option than quitting all nicotine, something requiring sustained self-control. However, for most, even a product that eventually will be come to preferred over smoking, will take some getting used to; ie, adjusting to the differences in rituals, cues, and altered timing of the experienced effects. Thus some may need help, and others encouragement to make such a switch. In the context where most smokers believe there is little or no health gain, and have distorted views of the role of nicotine, it is not surprising that at present the move towards alternatives is slower than it could be if it was encouraged.

Use as cessation aids

The first term of reference for this committee is of the role of vaporised nicotine as a smoking cessation aid. The notion of smoking cessation, and its treatment as a medical issue arose in a period when the only solution considered viable was complete abstinence from nicotine. A range of pharmaceutical products have emerged including short-term use of nicotine replacement products that were designed to assist a smoker in quitting all forms of nicotine. Similarly, a range of cognitive behavioural interventions have also had some positive effects. The nature of the challenge changes if long-term use of consumer acceptable, low-toxicant nicotine is seen as an acceptable alternative to smoking. In this case, it would seem more appropriate to apply a consumer choice model, such that smokers can be encouraged to choose a less harmful alternative, perhaps even though it is not quite as immediately satisfying. If the alternative is a sufficiently attractive, this is not going to require any kind of

therapeutic intervention. That said, there may still be a need for therapeutic interventions for people who want to stop using all forms of nicotine.

There is a need for positive action

There is a strong human rights argument supporting the availability of these products. In the past, when any interest in use of nicotine was restricted to its use in tobacco products, primarily smoked tobacco, it was sensible to have a public policy directed at eliminating use. However, with the emergence of low-toxicant products and the evidence that at least some of them result in very low levels of harm, the whole issue changes. People who choose to use nicotine have a right to access to the least harmful (safest) possible forms. In my opinion, the identified or likely level of harm from ANDS is sufficiently low as to make decisions about use an individual choice for adults, given that adequate information on their health effects is available to them. While use of nicotine may not be desirable (at least for many), it does remarkably little harm of itself. It does not cause intoxication with the resultant increased risks of incidental harms, and there are no confirmed adverse effects of long term use in adults, although it is plausible that it increases risks in those with active heart disease, and may increase risk of diabetes. There is evidence that it has some adverse effects in pregnancy on the foetus, and may have adverse effects on development, especially neuro-development, although these are not certain. Thus there is a case for discouraging use during pregnancy and use by children and adolescents.

I argue that even for those not convinced of the potential huge benefits, that these products will almost inevitably have to be accepted at some time, and that the costs of making Australia a laggard in this area is too high. The US and UK and the rest of Europe all allow these products at least in part as consumer products (not medicines) and the Canadian and New Zealand governments have announced an intention to legalise some forms of use. In addition, in countries where these products are widely used, both smoking rates and rates of uptake of smoking are declining demonstrating that there is no meaningful gateway effect (ie, these products are not leading to more smoking). At the very least we need to adopt an approach that maximises whatever benefits there may be and minimises the potential downsides.

The status quo

Tobacco control efforts have made great progress by focussing on a range of psycho-social measures that are largely encapsulated in the WHO Framework Convention on Tobacco Control. Public education and acceptance that smoking is unacceptably harmful has been the foundation on which other tobacco control efforts have built, both in terms of the effects they have had on smoking rates and on the political climate to enact increasingly strong tobacco control efforts. In this context, there is compelling evidence that increases in price reduces use, probably more for youth uptake than for reduced use by existing smokers (including cessation). Strong graphic public education campaigns also drive attempts to quit smoking and inhibit uptake, and may have some small effect on reducing relapse, especially when they are present and actively used by the quitting smoker to help resist cravings (19, 20). Graphic imagery works by generating concern (i.e., negative affect) and appears to work in much the same way when presented in public educations as when mandated on tobacco packaging. The benefit of the latter is that it is available virtually every time the person goes to light up, while the benefit of the public education campaigns is that they can

provide more extensive and nuanced messages. Smoke-free public places have led to reductions in average consumption, but appear to have had little direct effects on cessation rates, and it is uncertain how much impact they have on uptake, although it is likely that there is some (21). They have certainly contributed greatly to the denormalization of smoking, and thus reduce some of the pressure that young people used to feel to take up or try smoking. We know compelling marketing messages can have marked effects on use. Advertising and marketing restrictions have almost certainly contributing to the denormalization, although as the effects of removal of something tend to be delayed, the evidence for this is more indirect. One area where there are been more immediate effects has been the mandating of plain packaging. It is had modest immediate effects and plausibly longer term effects at least on uptake. There is a consensus that school-based education is generally ineffective in preventing youth uptake, however, according to psychological theory, to put in the effort to resist engaging in an attractive activity, a person requires good reasons. Thus having young people well informed is a precondition for resisting pressures to smoke. It is likely a necessary but not sufficient condition, and when other conditions are controlled for, it is not surprising that it has little independent effect, or at least little sustained effect.

The availability of various forms of cessation help, from pharmaceuticals and/or cognitive behavioural interventions, is making a small contribution to reduction in population smoking rates, allowing some to quit who would have been unable to without the assistance. There is evidence that promoting cessation help also leads to more quitting than can be accounted for by use of the source of help. It helps communicate about the importance of taking action.

There is only one major strategy that does not appear to have helped much if at all. That is bans on terms like Light and Mild (22). This is likely because the underlying sensory differences, largely created by filter venting have been allowed to remain and consumers have simply come to use whatever terms or colours are allowed to choose the products they want.

In countries which have been pursuing this agenda for a generation or more, rates of smoking have declined markedly, in some cases to around 15% (less for daily use), with greatly reduced uptake of smoking and a majority of ever smokers having quit. However, there remain large inequalities as a function of SES with smoking rates above 50% among some highly disadvantaged groups. This continues even in countries like Australia that have done virtually everything on the tobacco control agenda that targets smokers and the social conditions influencing use. It is now becoming clear that most of the effects on smokers have been by encouraging more quit attempts, but they have relatively little effect on success rates. There is a broad consensus that the achievements to data have come from taking a comprehensive approach to the problem, at least with respect to psycho-social determinants, although it needs to be made more comprehensive by taking bio-behavioural factors into account. It is not clear how much further progress can be made without large new initiatives designed to make it easier to give up smoking.

Is a harm reduction approach feasible

Tobacco use is maintained by a complex mix of biopsychosocial forces[i] (10, 23). There is a tendency by some, especially clinicians, to ignore the psychosocial aspects and some, especially those working in population health, to ignore the biobehavioral aspects of smoking. For example, the mode of promoting tobacco products influences use in

interaction with characteristics of the product. People differ in their capacity to live without nicotine, and similarly there are differences in interest in use among the nicotine naïve. Our understanding of the variation in use is limited. There appear to be two major sets of factors that are primary determinants of persistent use of psychoactive forms of nicotine in a context where use is not socially encouraged: varying biological sensitivity to the effects of nicotine (10), and having a life that is diminished in the normal rewards of living such that whatever benefits nicotine may bring are effectively amplified, because they contrast with the low level of rewards from other sources. The latter is inferred from the higher rates of smoking in disadvantaged groups and that there is apparently a stronger relationship with measures of psycho-social disadvantage, rather than with measures of material disadvantage (24-26). The differential is primarily due to the greater difficulty such groups have in sustaining quit attempts as they appear to attempt to quit at comparable rates, and in some cases, even try more often. The psychologically disadvantaged are over-represented among those of low SES and among oppressed (or disenfranchised) minority groups (27) and obviously include those with diagnosed mental health problems (28), with biological factors also more likely to contribute to the high levels of use among the latter group.

The capacity of VN products (individually or collectively) to displace smoking is currently uncertain, but there are extremely promising signs, including the spontaneous movement of some smokers to them and the emergence of a vibrant Vaper community and the emerging success of heat not burn products. We know the better VN products are for replicating the experiences of smoking, or of providing different but desirable experiences, the better they will be as alternatives. Unfortunately it is also likely that they will be more attractive to non-smokers. More attractive products are likely to result in less dual use (with smoking) as they are more likely to be complete substitutes (ie, acceptably good enough given the reduced risk of harm).

The empirical case for a positive role for alternative nicotine products comes from the epidemiology of smokeless tobacco, mainly from Scandinavia, which has shown that relatively low-toxin smokeless tobacco is much less harmful than smoking. Indeed, there are no certain adverse life-threatening effects in otherwise healthy users, although some remain plausible, and there is evidence that they can exacerbate risks for those with existing heart disease (ref Snus quitting and heart disease paper). In Scandinavia, use of snus (the low toxin smokeless tobacco) has risen, to be the dominant form of tobacco use in men. Sweden, the country with the longest tradition of snus use and where use is by far the highest, has the lowest rates of tobacco-related diseases in Europe (at least for men), consistent with the smoking rates, even though total nicotine use is about average. This has occurred largely in the absence of information about the relative harmfulness of the two kinds of tobacco, relying largely on price differentials which the Swedish government kept to discourage cigarette use. Notably, there has been no concerted effort by health authorities to encourage snus use as an alternative, perhaps due to strong opposition to it from some elements of the public health community.

Complementing this evidence is the likelihood that pharmaceutical grade nicotine is at least as low in harm, potentially lower as it contains even less toxicants. Recent research, of which I was part (29) demonstrates at a population level that taking up daily snus use protects against the likelihood of subsequently being a smoker, and that any daily snus use among smokers is associated with significantly higher rates of smoking cessation than those who have just smoked on a daily basis. Thus, not only is snus a relatively harmless product

it would appear to be paying a major role both in preventing the uptake of smoking and in helping those who become smokers to quit.

One concern that could undermine health gains would be if vaping resulted in a lot of dual daily use rather than complete substitution. Experience with Swedish Snus suggests that dual daily use of snus and smoking is rare, except in transitional periods, although occasional use of the non-preferred form of nicotine is much more common. Whether this can be generalised to dual use of VNPs and cigarettes, is unclear, but it is clear than there is a lot of dual use at least in the transition stage and that can last for years. As most dual users don't know about the relative harms, it is plausible that public education could be used to reduce the extent and duration of dual use. In assessing dual use, we should restrict that term to daily use, or exclusive use on days that the person does not smoke, not occasional use. Some ex-smokers may smoke again from time to time if VN is unavailable, or to re-experience cigarettes. Unlike the situation with quitting nicotine completely, they can revert to their PV rather than relapsing to smoking, so rates of relapse from occasional smoking should be far lower.

Why not regulate ANDS as therapeutic goods

A position taken by many who are cautious about the benefits of ANDS is to have them regulated as therapeutic goods. On the surface, this looks like a good idea, but there are a number of good reasons to resist it. First of all, many of the people using these products are not using them in a therapeutic way but rather as an alternative consumer product and are likely to use them long-term. There are real disadvantages of having therapeutic goods effectively used as consumer products as it blurs the distinction between what is a medicine and what is a consumer product.

Second, is the great diversity of ANDS that are appearing, and the rapidity of innovation and improvement. There are a large number of products, and only the most well-resourced companies would have the capacity to submit their products for any kind of therapeutic goods regulatory assessment, these being most likely to be the big tobacco companies. The rapidity of technological change means that it is unlikely that products that pass through this channel will be as effective as less regulated alternatives for the foreseeable future. In the UK, where a dual approach has been taken, none of the few products approved for therapeutic use have made it onto the market, at least in part because by the time they were approved the technology was out of date, and thus they were unlikely to be competitive with the new consumer products which either deliver nicotine in more effective ways, and/or have increased safety features.

Further, the separation of the devices from the nicotine containing liquid creates a range of additional regulatory problems. It would be eminently reasonable to require the nicotine in e-liquids meet pharmaceutical grade standards. Indeed, many already do and this is seen as a selling point. Having such standards is quite different to full regulation as therapeutic goods. This channel should be kept open, and may be used in future for products that are designed to stop all nicotine use, or by products that require higher levels of nicotine than are allowed for consumer products. In the UK, where there is a dual route, none of the small number of vaping products approved by the TGA have made it onto the market, as by the time they were approved, the market had moved and they were no-longer likely to be competitive (including potentially on safety features).

Finally, ceding regulatory authority to an agency whose core business is regulating medicines, runs the risk of over medicalising decision making. This could involve decisions to maintain comparability with rules on medicines, rather than rules to maximise public health outcomes. For example, abuse potential is a major issue for medicines, but translates to consumer appeal, and is a major factor in influencing both uptake and potential to substitute completely.

This is an important enough public health issue to deserve dedicated regulation.

What do we need to do?

The first priority for tobacco control should be to eliminate as far as possible cigarette smoking, and then secondarily to manage any continuing use of lower toxin nicotine (including those containing tobacco) to maximize the societal benefit and minimize the social costs (i.e., the effects among those who are unable or unwilling to cease all nicotine use).

It has been generally accepted that it is impractical to move towards the prohibition of cigarettes (and perhaps other forms of smoked tobacco), because if they were prohibited it is likely a substantial black market would emerge, and the social costs of this would be considerable. However, to the extent that there are viable alternatives to smoking, increased restrictions on availability becomes feasible to the extent that users can either quit or use the alternatives rather than seeking the "real thing" on the black market. If sufficiently consumer-acceptable alternatives are available, use should decline to levels where prohibition would be unnecessary. Indeed, if it does not get to such levels, then prohibition is likely to be problematic.

So what can governments do, and what should they do. In looking to government action, it is important to realise that governments cannot directly influence the characteristics of the products. They can and should regulate as to what products are allowed, but cannot require new products that industry has not developed. Thus if there is to be innovation it requires industry to innovate, and the nature of the regulations controlling the products can facilitate or inhibit that innovation. Society rightly places a high bar on the introduction of new pharmaceuticals as even ones theoretically safe have sometimes been shown to have adverse effects on people. However, this level of requirement is not appropriate for nicotine products that are widely used with little or no immediate negative consequences. Governments also have a major role, both direct and indirect, in regulating the environment in which smoking takes place, and to ensure the public are adequately informed, so they can at least try to make the appropriate choices.

As a civilised society we should be creating the conditions that make it as easy as possible to do what is socially and personally desirable, and/or not encouraging or facilitating competing undesirable alternatives. Such an approach provides space for personal choices or personal habits that are contrary to what the society is encouraging, but at a small cost of some additional inconvenience, or with reduced opportunity to organise environments to systematically support these behaviours. This is the basis of a range of strategies recently popularised through Thaler and Sunstein's (30) book Nudge, although they have been integral to health promotion practice for much longer (23, 31, 32).

Finding the right balance of nudging is not easy and what is acceptable at any one time can change with changing social norms and expectations. The main things for governments to

focus any regulation on are to place constraints on the systematic actions of organised groups (in this case, the tobacco industry and more broadly other parts of the nicotine industry) to pursue agendas that are in their interests rather than the long-term interests of their customers and for the society as a whole.

As a consequence, I argue that faster progress can be made, and the continuing harms to disadvantaged groups reduced most quickly, if two additional sets of strategies are integrated into the existing mix: namely, regulating smoked tobacco more stringently, and differentially regulating (including pricing) lower harm smokeless nicotine and tobacco products to make switching to these products a more viable option for those unwilling or unable to quit nicotine use completely.

Product regulation is a poorly implemented element of the FCTC, while the use of nicotine substitutes was not considered as a viable alternative at the time the FCTC was being negotiated. The addition of these strategies are only likely to provide maximal net benefit if they are integrated with existing strategies as part of a comprehensive and integrated approach.

The rational for this extension of the current approach is based on three sets of facts: 1) the evidence that a subset of smokers are either unable or unwilling to quit tobacco use, at least given the current mix of strategies to support them to do so (Many smokers continue to smoke until they die from smoking related causes); 2) that there are unacceptable engineering additions to smoked products that make these inherently harmful products more attractive to people than they need be (33-35); and 3) the recent emergence of ANDS which are consumer-acceptable to at least some. The emerging evidence shows that these products are more attractive to smokers where they are not actively discouraged (eg, England), and are at least as effective at helping smokers quit (probably more so, if we consider the newer more sophisticated products) and are also more likely to be used longer-term, potentially reducing the otherwise high risks of relapse back to smoking, and that their use appears to undermine the positive experiences of smoking for some, further reducing the probability of relapse.

A comprehensive approach to tobacco control including ANDS

My aim is to spell out a set of policy settings and organised activities fir governments and health agencies that if applied, are likely to lead to the most rapid possible decline in smoking, but in ways that minimise associated costs; ie maximize the reduction in nicotine-related harms. The overall strategy considers overall community well-being, so effects on poverty, quality of life, and the risks of a black market are considered as well as health-related issues. The degree of regulation should be the least necessary to achieve the policy objective.

The strategies recommended involve both acting to reduce the harmfulness and appeal of the most harmful products while encouraging the development and uptake by smokers of ANDS. The basis of the argument is the well-known adage first coined by Michael Russell that “People smoke for the nicotine but die from the tar.”(36)p1431) highlighting the low level of harm that comes from the nicotine compared to other sources in tobacco smoke, particularly carbon monoxide and tar, all made worse by delivering the toxic mix to the lungs. I argue that VNs may be transformational technology that could potentially be the tool that

we require to eliminate smoking in our lifetimes (37-44)The aim is to outline an agenda as to how to maximize the likelihood of using ANDS being used to help eliminate smoked tobacco as a mass consumer activity, by which I mean getting the prevalence of daily use below 1%.

Regulating ANDS quality. There should be standards for manufacture of the delivery devices and quality standards for e-liquid or other consumables. For devices, the product standards should cover such features as the safety features of the battery for electronic nicotine delivery systems, some mechanisms to prevent overheating, limits on shedding of metals, as part of general quality standards.

The regulations for liquids should allow for setting maximum levels of toxicants. The toxicants assessed should include thermal degradation products of nicotine and the carrier chemicals (PG and/or VG). There is no doubt that the nicotine used in non-tobacco products can meet the quality standards currently required for therapeutic nicotine, which requires keeping levels of impurities low (ie, virtually eliminated).

Levels of nicotine in the products should be provided on all containers it is sold in, as should the make-up of the carrier fluid (eg, propylene glycol, vegetable glycerine). Consideration should be given to adopting a threshold nicotine level, but this should be higher than the EU level. The EU directive sets the threshold at 20 mg/ml but there should be consultation as to the optimal cut-off, which is likely somewhat higher. Any product, with the nicotine containing medium above the threshold should have to pass through therapeutic goods evaluation, at least for safety and plausible benefit. There may also be a need to regulate the relationship between voltage and wattage of electronic delivery systems and or to have other mechanisms to prevent them overheating the liquid thus producing toxicants from thermal degradation of the base products. However, this may not be essential, given the low risks of short-term use and the self-regulating nature of much of the risk of exposure to toxicants such as formaldehyde due to overheating, because users typically cease use when this happens as it makes the taste unacceptable.

There is a case for restricting flavours with known adverse effects or which can be shown to be differentially attractive to adolescents, either completely or by setting upper limits. There is some evidence that flavours help with quitting smoking, most plausibly in reducing relapse as the user comes to enjoy the distinctively different and pleasant flavour, the less pleasant taste of a cigarette may become mildly aversive. Thus caution is required regarding possible over-regulation as any blanket bans may prove counterproductive. It is also likely to result in many end users adding their own flavourings. I recommend that the enabling legislation allow for restrictions on flavours under certain conditions, but that at this point, it may not be necessary to proscribe any.

For open delivery devices, refill containers should have childproof lids and be fitted with devices to allow the tanks to be filled with the minimum chance of spillage. The EU has developed some standards

There is no justification for limiting the size of the container of e-liquid either in the device or in refill containers. Consideration should also be given to changing the current rules to allow low-toxicant smokeless tobacco products, but as these are likely of only minor importance in the Australian context, for practical purposes this is not an essential part of what is required.

The effects of the delivery system also need to be considered. The existing evidence is that most PVs can generate vapour without detectable levels of toxicants when used under normal conditions, so it should be possible to regulate to remove those that do not. Taken together devices could be regulated to ensure that did not exceed maximum yields of toxicants of concern when used under standard (plausible) testing conditions. Given the knowledge that nicotine users titrate their dose, a usage pattern consistent with the ingestion of around 1 mg of nicotine over a period of minutes. Such standards are needed to define a reduced toxicant product, and to ensure that the class of such products is as low in potential harm as practical. I refer to these products below as harm-reduced products although at this point, this is not demonstrated, abut is highly plausible given the known science of toxicology.

Sales to minors. Sales to minors should be prohibited, but the minimum age of sale should be lower than that for cigarettes. This may be an opportunity to raise the age for purchase of cigarettes to 21, while having the level for ANDS at 18. Penalties for selling alternative products to minors should also be lower than those for selling smoked tobacco products. Some consideration might be useful to deal with supply to young people who have already become nicotine users to minimise the risks that they will turn to smoking.

Public Education. Public education will continue to be central to optimising outcomes. Knowledge is the driving force for both developing goals and for providing evidence to generate affective force behind those goals. Government agencies have an important obligation to support public education to support informed choice. This involves both providing information on the consequences of smoking that are not immediately salient, and for providing it in ways that make that information meaningful to the target populations. This should facilitate people setting appropriate goals for themselves, and for giving the goals the affective force required for their pursuit. The main change from the current situation will be that some of the communication will need to focus on the huge gap in toxin exposure and large difference in harms between combusted and non-combusted tobacco/nicotine products. Education should continue to encourage complete cessation of nicotine use as the most desirable strategy, while accepting a role for low harm alternatives such as VN as much preferable to continuing to smoke.

People in general appreciate health authorities graphically depicting the harms, not just talking about them. Qualitative work with smokers around messages, repeated shows that they want these hard hitting graphic messages as this is what motivates them towards action. For non-smokers it makes the idea of smoking disgusting, and thus something to avoid. Even occasional avoidance of these messages is not a problem, as smokers who avoid them sometimes are also more likely to try to quit over the next year (45).

Price. Price is perhaps the most important determinant of use after extent of satisfaction. It will remain imperative to keep the price of smoked tobacco as high as possible. This is best done by increasing taxes and by other means of minimising tobacco companies capacity to generate very high levels of profits (as they have from smoking). The capacity of governments to increase taxes and thus to raise prices of smoked tobacco is likely greater in the presence of VNs, but only if these products are taxed at lower levels (Chaloupka et al). If the substitute products are good enough, disadvantaged smokers, particularly those on low or irregular incomes, will be more likely to switch the larger the price differential, as the economic benefits are relatively greater than for the more affluent. NB: Savings are an

incentive when thought about, which only naturally occurs at purchase points, so may have less of a role in sustaining change, although the price needed to be paid is a direct disincentive for buying cigarettes. Having viable substitutes also minimizes the risk of a black market developing. In short, switching to VNPs provides a credible strategy for those who are unable to quit which does not involve forcing them into increased deprivation or to seek illicit tobacco. The base price of the low harm alternatives can be kept at levels which do not unduly encourage youth uptake, while acting as an incentive for smokers to save money by trading down, The consumable parts of devices should be taxed at a rate that is meaningfully lower than that for smoked tobacco products. I suggest one rate for products using pharmaceutical grade nicotine, and another for those using tobacco. A useful starting point would be to tax at a rate such that 1 mg of nicotine was taxed at around 5% of the level for one cigarette, and heated tobacco was taxed at double this rate. Once smoking has virtually disappeared, there is likely to be potential for increasing taxes on these substitute products to maintain government revenues and/or signal disapproval of persistent nicotine use, the magnitude of which could be commensurate with the established level of harms.

Advertising and promotion. The almost complete restrictions on the advertising and marketing of smoked tobacco must continue, but if the level of substitution is to be maximised, there is a need to allow some limited forms of promotion of VNs. This should be directed primarily at smokers encouraging switching or short-term use to facilitate complete cessation of nicotine. This can be done in ways that do not unduly increase the appeal of the products to non-users, but ensures those otherwise drawn to nicotine, seek these less harmful products instead. This may be achieved by restricting active promotion of ANDS to points of sale (of any tobacco or nicotine products), Any advertising should be restricted in the imagery that can be used (prohibiting use of attractive role models and or implications of glamour) and there should be specified forms of wording prescribed to indicate the toxicant reduction and/or likely harm reduction potential of the product. Rules should prohibit push advertising in all other communication channels (ie promotions that target those not actively seeking the product). Websites with factual information about products that are available on the market could be allowed. Such advertising could be subject to the same kinds of regulatory controls that are imposed on the marketing of scheduled pharmaceuticals.

There could also be consideration of what kinds of organisations can market VN and other ANDS, including restricting this to non-for-profit entities (4, 5). This should minimise the risk of whatever promotional activities are allowed being used to grow the overall market beyond what is societally desirable. It is likely that leakage of whatever promotion is allowed into youth markets would be greater under a for-profit marketing framework, than one controlled by agencies without a profit-related motive for selling more.

Smokefree policies. The expansion of Smokefree places may be facilitated if the existence of alternatives reduces the challenges associated with complete prohibition of places to smoke for addicted users. This could require that vaping be allowed in some places where smoking is banned (eg, multi-unit residences, institutional accommodation, crowded city areas). There is no reasonable justification for banning vaping on health grounds, but it can be justified on amenity grounds, so it would seem sensible to have decisions over where to vape left up to the controllers of the space. Many places where smoking is currently banned might like to also prohibit vaping; e.g., workplaces, especially in shared spaces, and crowded indoor locations. In this regard we point out that PVs don't create as much vapor as cigarettes do smoke, it has far few toxicants per unit volume, and it dissipates faster (ie

falls out of the atmosphere). There are no grounds for discouraging vaping in private homes, even in multi-unit accommodation, and if this facilitates encouraging home smoking bans, it is likely to result in a net benefit to health. Thus allowing VN may actually facilitate increases in smoke-free areas.

Product Accessibility. ANDS should be available in all places where smoked tobacco is sold, and also should be able to be sold in some outlets where smoked tobacco was not sold. All outlets selling smoked tobacco should be licensed, with the licence fee being used to monitor compliance with sales to minors laws and to check for illicit, including excise-not-paid products. This could facilitate long overdue moves to reduce legal outlets for cigarettes by reducing the risk of unintended effects; ie, development of a black market. As VNs became more prevalent and smoking less so, the number and kind of outlets selling smoked tobacco could be increasingly restricted. The economic costs to small business would be partly (at least) offset from sales of VNs. Rules about not selling cigarettes in outlets close to schools could continue to apply to all nicotine products. If smoking is effectively eliminated, then access to VNs could be reduced if the level of harm turns out to be greater than current estimates. Nothing should be done to discourage the kinds of vape shops where staff are actively helping smokers switch.

Support for transitions away from smoking. Smoking cessation services should be redesigned to support people who want to shift from smoking to alternative products as well as continuing to help those who want to quit all forms of nicotine. This ideally should be framed around a quit or substitute model, with complete cessation of nicotine the preferred option. Services also need to have the capacity to help people using alternative products who wish to quit them but are unable to do so unassisted. As noted elsewhere in this submission, the addictiveness of currently available alternative products appears to be lower than for smoking, but it is prudent to assume that some will have difficulty stopping if and when they decide that this is in their best interests.

Cessation services are unlikely to be the main means of helping people to transition from smoking to vaping. There is a role for retailers. Vape shop staff are often mentioned as an important source of advice, and as vaping becomes more common, peer to peer transmission of information is also likely to become more important.

Product innovation. If it is true that current VNs are not suitable substitutes for many smokers, then there is a need to facilitate continued product innovation. Excessive regulation, particularly expensive requirements that need to be met to get products on the market can act to reduce innovation. There is unlikely to be a lot that is patentable about PVs that cannot be achieved in other ways, so the potential to dominate the market with new innovations is less, making it uneconomical to invest heavily in product innovation unless there is a rapid translation onto the market. We should be seeking the minimum possible level of product regulation to protect consumers, but with rules that allow products to be temporarily or permanently removed from the market if sufficient problems are identified.

Stronger regulation of tobacco products commensurate with harmfulness.

At the same time that alternative products are made more available there should be increased efforts at the control of tobacco products. For products like cigarettes which are unacceptably harmful, product regulation should be directed at reducing their attractiveness,

including both addictive potential and those elements of attractiveness that are (largely) independent of addictiveness. Restrictions on attractiveness are justified where the unavoidable harms of use are deemed unacceptably high.

There are two sets of product rules for which we believe there is sufficient evidence to act immediately with regard to smoked products, particularly cigarettes; banning filter venting and removal of many of the additives, particularly characterising flavours that artificially improve the taste of some cigarettes. This would include the prohibiting the inclusion of flavour capsules in the filters or elsewhere. Restrictions on additives are likely to have their greatest potency in places where cigarettes are blended mixes of tobacco types rather than being 100% flue-cured Virginia tobacco as is the case in Australia, and some other countries. Thus here the focus should be on characterising flavours, as that is relatively easy to do, and likely to generate the greatest benefit.

The most important strategy, we believe, is the prohibition of filter venting, which is likely the major cause of cigarettes possibly becoming more harmful (US Surgeon general), is the basis of the “lights” fraud and the main mechanism by which tobacco companies have been able to create an extended range of variants. Removing filter venting would result in nearly all cigarettes tasting stronger, and probably more difficult for novice smokers to inhale. It would also likely result in a marked reduction in the number of brand variants available as some are differentiated on levels of filter venting.

Collectively bans on filter venting and on characterising flavours would have a positive effect on driving down consumption. They will make smoking a bit less attractive and in the presence of acceptable alternatives (eg, ANDS), they should increase substitution rates (ie smoking cessation). On top of its effects on existing smokers, it is likely to have a large effect on uptake by reducing rates of experimenting and transitions from experimenting to regular smoking. Again such effects are likely greater in the presence of acceptable ANDS.

The other major change suggested is to make smoked products less addictive by reducing the nicotine level in cigarettes (Benowitz and Henningfield). This could not only make cigarettes less addictive, it would concurrently also make them far less attractive to use (the two being strongly associated). However, if nicotine levels were reduced to non-satisfying levels, it could be seen as a form of prohibition, as smokers are smoking for the nicotine. There is a large amount of research going on focussing on nicotine reduction, largely in the US, where it is a strategy that appears feasible within the framework of their tobacco control legislation which gives control for regulating tobacco products to the FDA. In my opinion, this strategy will only work if there are sufficiently attractive ANDS around to act as substitutes, and if these substitutes are satisfying enough, then the nicotine reduction strategy would not be necessary (46).

Monitoring and evaluation In any area where there is uncertainty there is a need to carefully monitor the impacts of new products on the market. This is particularly the case here. Use patterns should be monitored in regular surveys, at least annual is to be preferred, at least until the patterns of use stabilise. There is also a need to establish a long term study to explore the consequences of use, both to those who have smoked for many years, and those who have not (they could be quite different). Ideally such a cohort study would be international in scope and have repeated observations (surveys) in the early years to help us better understand how transitions in and out of VN use occur.

Summary. The adoption of the above set of strategies is likely to lead to a fairly rapid decline in the rate of smoking, but at this point, it is uncertain as to whether it will be sufficient to rapidly transition to a situation where smoking is no-longer a mass, long-term, consumer behaviour. Even if current technology is inadequate, technologies in the pipeline are likely to be more effective substitutes. People who are drawn to use nicotine, are overwhelmingly sensible people who, given adequate acceptability of alternatives, will move to those alternatives if they believe it is in their best interests. That is, there may be no need to eventually prohibit the sale and/or use of smoked tobacco products, if the alternative is a good enough consumers will naturally move away from them.

This ambitious agenda will be best achieved by a single piece of coordinating and enabling legislation. If that this not practical care will be needed to ensure the elements of Commonwealth and state laws are congruent.

Possible downsides.

It is becoming very clear that the main motive for resistance to the use of ANDS is concern about the risk of this leading to increased uptake of smoking, or even just nicotine, by youth. To the extent that vaping comes to be seen as socially desirable, there is a risk that people who would otherwise not take up smoking will take up vaping. Take up of ANDS is predicted by expectancy-value and other rational balancing theories, but so far this appears to be limited, likely due to the generalised negative affect associated with smoking that most have. Strong barriers on promotion of ANDS can limit their uptake by non-smokers. Although, it will never be perfect, strategies that have been developed to reduce smoking can be applied, at least in part to reducing undesirable levels of vaping. At present in countries where vaping is allowed, there is only a very small amount of uptake by never smokers, and a percentage of those are young people who may otherwise become smokers.

Prohibition of these products is not a solution, it will not end use and can create additional problems. The paradigm case here is marijuana where use in some places is higher than smoking, even though it is illegal. From all we know of human behaviour, prohibition usually reduces prevalence and /or frequency of the target behaviour, but sometimes at unacceptable social costs where there is sufficient interest in engaging in the behaviour, and it is reasonable to expect it here.

The main concern is the gateway hypothesis; that these products will act as conduits to smoking, rather than exclusively a means of helping people quit. First of all, if the ANDS are good enough, there will be little motivation to use the much more harmful cigarettes, given that most people choose not to smoke with no alternative (ie, a greater sacrifice). I accept that there may be some occasional use, but it is extremely unlikely that this would lead to people taking up regular smoking who would not otherwise have done so. The problem with the gateway hypothesis is that there is no direct way to test it at the individual level. However, it can be tested at a population level. It predicts that increased ANDS use will result in increases in smoking. All the evidence is to the contrary. In the US up until 2106 vaping was increasing in youth while smoking was declining. In 2016 rates of vaping declined and smoking continued to decline. This suggests a faddish initial interest in vaping, and which had dissipated in part. Although it does not prove it, this evidence is more supportive of vaping inhibiting the uptake of smoking. It totally disproves gateway as a significant influence on smoking in the US at least. In Australia youth smoking declined from

2011 to 2104, while there was some small amount of vaping, again inconsistent with gateway. I acknowledge that there are a number of longitudinal studies that show that vaping is associated with increased rates of future smoking. These studies have usually tried to control for susceptibility to smoking, but the best measure of this, and those used in most studies (if not all), are only weakly predictive, so propensity to smoke cannot be fully controlled. There is a need to explore transitions to and from daily use to see if the positive effects found for smokeless tobacco in Sweden are replicated for vaping.

The other main concern relates to the renormalization of smoking. Renormalization of smoking is most unlikely. People are very good at making distinctions, even between products that look similar, even though they have quite different properties (eg vodka and water), so as long as there are noticeable differences, people will see the two behaviours (vaping and smoking) as distinctly different. To the extent they see vaping as a substitute for smoking, then it might act to further denormalize smoking as there are now even fewer reasons to tolerate it. The main risk of renormalizing smoking would come if these new vaping behaviours were equated with smoking and seen to be equally inappropriate (which would only occur if they were seen to be equivalently harmful). Ironically, the main risk of this comes from those most concerned about their use who have often exaggerated the possible risks (typically by promoting studies which appear to show some risk, rather than making explicit clams). This has led to reductions in beliefs that VNs are far less harmful than smoking in some countries. That said, it is notable that vapers are increasingly trying to differentiate themselves from smokers, including by eschewing cigalikes, so even with the misinformation, renormalization of smoking is extremely unlikely, just an unfortunate slowing of the transitions away from smoking.

The challenge of managing these products is to find the right balance between maximising their use by smokers, while minimising use by those who would not otherwise have used nicotine (or at least those for whom it is not beneficial). Logically, if the goal is to minimise uptake of nicotine by non-smokers, the optimum strategy should be to seek the least attractive ANDS that can replace most smoking when the regulatory “playing field” is tilted as far as possible in their favour. The risk of high levels of uptake by youth is also likely to be exacerbated if the products can be mass marketed by large corporations, most likely dominated by big tobacco companies, however, as argued above, this may be more limited for VNs.

Because smokers are motivated to reduce their health risks, it is probable that there will be little movement from VNs to smoked tobacco, especially among those who had not previously smoked, and even among past smokers. It is only likely to occur when the experience of ANDS is insufficient to sustain their use longer term and thus smoking is positively missed. Indeed, there is likely to be less relapse than among ex-smokers who stop all nicotine, as vaping can provide the nicotine and this acts as an alternative to full relapse.

If there continues to be a group for whom movement to VNs is not sufficiently acceptable, some care will be required to ensure that they are not turned into social outcasts as it is likely that they will be largely the more disadvantaged and dispossessed elements of society as they are in many societies already.

Implications for the disadvantaged.

Equity issues are extremely important. It is becoming increasingly clear that a major factor in the increasing divergence in smoking rates between those living relatively privileged lives and those whose lives are psychologically or socially impoverished, is almost entirely due to greater difficulty in staying quit. The most likely explanation for this is that the rewarding aspects of smoking are relatively more important to these people than others, perhaps because of the lower levels of alternative rewards. Alternatively, at least some of these groups might have a greater than normal response to nicotine. In either case, the use of a nicotine substitute that provides much of the psychological effects obtained from smoking, is more likely to result in increased quit success. We can see no major downsides for such groups, but note that the potential upsides remain theoretical at this point. That said, if a proportion of disadvantaged smokers are unable to switch, then care would need to be taken not to socially ostracise these unfortunates.

The cost of ANDS may act as a disincentive to use among the very poorest, but the cost of use beyond an initial purchase of the PV device, should be less, there are likely to be ways of overcoming this. Further, with mass production, the cost of basic vaping devices is likely to be able to be within the reach of anyone who can afford to smoke. In the medium term, the potential is for anyone to be able to afford at least some forms of ANDS. That said, effort should be made to tax the products if the costs looked like being too much cheaper than smoking, such that it might encourage new use.

Conclusions

Making current smoked products overall less attractive and tilting the regulatory and public discourse in support of abandoning smoked tobacco could lead to smoking disappearing as a mass behaviour relatively rapidly. We do not know if the current ANDS are good enough to make smoking effectively disappear, if we were to adopt the full range of strategies outlined here. However, if current products are not effective enough, it is unlikely that they will prove attractive to many non-users. They are clearly helping some smokers to quit, so are making a contribution to tobacco control efforts. Further, having them available is likely to provide a more stimulatory environment to the innovation that will still be needed to allow them to eventually replace smoking completely as a mass consumer behaviour, by which we mean daily smoking rates below 1%.

This represents a two stage approach to tobacco control. First using VNs (and perhaps other ANDS) to eliminate smoking as a mass consumer product as quickly as possible, Second, once this is achieved, using many of the same strategies to manage the remaining problem, with the ultimate aim dependent on what we find out about long term effects of use of clean nicotine and if that differs by mode of administration, given all are as low in toxicants as possible.

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