Honorable Chair and members of the Senate committee,

I am very gratified that you have taken the time and effort to better understand the emerging role of electronic vaporizers in the fight against tobacco related illness and harm. As a practicing, cardiothoracic surgeon for over 20 years, I have witnessed first-hand the ravages of tobacco smoking. It is responsible for over 95% of all primary lung cancers, and is a major player in causing cardiovascular disease, the leading cause of death in our society\(^1\). Since a peak of 50%, education and regulation has reduced the smoking rates in our society to approximately 16%. While this is encouraging, between 15% and 20% of Canadians continue to be victims of first hand tobacco smoke, even more the unwilling victims of second hand smoke\(^2\).

While medical interventions including behavioral therapy, prescription pharmaceuticals, and nicotine replacement therapy have been available for years, smoking cessation rates remain frustratingly low. The Annual Tobacco Report sponsored by the Cancer Care Society in Canada reported a 13% smoking cessation rate per year among motivated smoker seeking to quit\(^3\). The causes of failure are multifactorial, but recurrent themes do emerge, relapse is due to nicotine dependence and loss of the oral tactile habit of having a cigarette. Stress, which was dealt with previously by smoking, is often cited in a relapse to that habit. Electronic vaporizers like e-cigarettes are a unique modality that has the potential to add to the armamentarium of smoking cessation and tobacco harm reduction therapies, allowing us to reduce human suffering and save valuable health care dollar.

Two terms that require significant clarification are smoking cessation and tobacco harm reduction. Smoking cessation is the complete abstinence from smoking and is generally considered the desired outcome. Tobacco harm reduction is the philosophy that by reducing the deleterious effects of tobacco consumption we can improve the health and welfare of users even if complete cessation is not achieved. The health consequences of tobacco are dose dependent and reducing the exposure of a smoker to the combustible products of tobacco will have a significant impact on health.

Parallel examples of harm reduction strategies are currently in available. Safe site drug use facilities have been established in Vancouver where drug addicts can avail themselves of clean injecting paraphernalia. Although opponents have argued this is promoting the use of illicit drugs, it is a pragmatic acceptance of the harm that needle sharing and contaminated paraphernalia is doing. While this government sponsored enterprise is not lowering addiction rates and it has been shown not to increase them either. This undertaking was based in evidence and did not succumb to misinformed opinion about drug addiction resulting in less risk of blood borne infections amongst drug addicts.

It is only prudent to examine the technology behind e-cigarettes, potential threats they may pose and advantages they offer, but it must be done with evidence, logic and science rather than by anonymous innuendo, fear mongering and narrow-minded ideology. I have had the opportunity to
review the available literature and did so over a period of 6 months prior to supporting e-cigarettes as a tobacco harm reduction tool in the fall of 2012. It is my aim in this document and subsequently in person presentation to alleviate concerns that members of this committee may have regarding the safety and efficacy of e-cigarettes and electronic vaporizers. In respect of the member’s time, I have attempted to minimize technical jargon but included the reference material in the appendices.

1. Safety of e-cigarettes

The continued exhortations that there is not enough information regarding the safety of e-cigarettes have become a mantra of many opponents of the device. One may ask what is the burden of evidence that they would require? In the scientific community, this occurs when results reproduced at multiple labs over a period of time generate a volume of credible information that at some point in time reaches a level so that consensus is achieved that the hypothesis is proven. While I support this academic ideal one must be pragmatic in clinical scenarios where health is at risk. A recent example is the early release of unproven therapies for the Ebola epidemic. A decision was made that based on available evidence that the benefit outweighed the risk of the treatments. There is evidence that e-cigarettes pose no short or intermediate danger to the user or to bystanders.

In a comprehensive peer reviewed paper evaluating over 9000 scientific papers looking at the chemical composition of vapor from e-cigarettes, Burstyn showed that the concentrations of heavy metals, polyaromatic hydrocarbons, tobacco specific nitrosamines, and Volatile organic compounds were less than 1% of occupational safety standard Threshold limits. This is specifically relevant to the safety argument, as these chemicals among others are the cancer causing agents present in tobacco smoke in high concentrations. The bystanders would experience even less than this, as they are not exposed to inhaled vapor, unlike with tobacco cigarettes in which burning combustible smoke is directly emitted into the environment. The lone FDA analysis document has been often referenced in relation to the presence of formaldehyde in nicotine containing e-cigarette vapor. The original work was done using first generation e-cigarettes and showed an unquantifiable trace amount of formaldehyde when the liquid was combusted at over 200°C. When the liquid was vaporized at the common temperature associated with e-cigarettes, 60°C (99% of e-vaporizes limit this temperature by design), there were not even trace amounts of formaldehyde found. Despite this, only a portion of the FDA document is quoted by e-
cigarettes opponents which is academically disingenuous. The largest percentage of e-cigarette vapor is produced from the polyglycol vaporization. In a study in which primates were exposed to continuous high concentration of polyglycol vapor nearly continuously for a period of 12 to 18 months no adverse health outcomes were seen\(^7\). In a very nice study, cell cultures were exposed to tobacco vapor and to e-cigarette vapor, which demonstrated that tobacco smoke caused mutagenic effects while e-cigarette vapor did not\(^7\). **There is no cancer causing agents of practical concern in e-cigarette vapor regardless of whether an e-cigarette contains nicotine or not.**

The effect of smoking and e-cigarette use on human heart function has been recently carried out. After using a tobacco cigarette users experience a measure decline in function of the heart muscle as determined by echocardiography, no decline in function was seen in users of nicotine containing e-cigarettes\(^8\).

Current assertions that the safety of e-cigarettes has not been established are not true. **Even if one is to ignore the anecdotal evidence of millions of users who have not had any negative health outcomes attributable to e-cigarette use, the available scientific evidence demonstrates nothing in the vapor that is of long term cytotoxic concern.** E-cigarette users do so voluntarily to reduce their exposure to tobacco smoke that is orders of magnitude more harmful. This is demonstrated in a survey of German e-cigarette users, which showed that the overwhelming majority of users are either current smokers or ex-smokers. Recent study has shown that intensive e-cigarette users are 6 times as likely as non-users to report they quit smoking\(^9\). Providing smokers less harmful alternative can have immediate beneficial effects in reducing pulmonary inflammatory diseases and have a long-term benefit in reducing their exposure to cancer causing agents.

## 2. Nicotine

Nicotine is of the same chemical class as Caffeine. It is a naturally occurring alkaloid and found in many plants and vegetable including eggplants, tomatoes, peppers, black/regular and decaffeinated teas\(^10\). Produced in the roots of the tobacco plant it is found in high concretions in the tobacco leaf and sap of the tobacco plant. Nicotine exerts its effect in the human body by a series of mechanisms, the most important of which are releasing dopamine in the brain and epinephrine in the adrenal glands. The intake of nicotine is self-regulating in that the user will take in enough nicotine to release the dopamine in the brain to the level that satisfies the craving after which time the use ceases. **Nicotine itself does not cause cancer, and despite it being potentially addictive, no serious adverse health outcomes are related directly to nicotine use**\(^11\). Physical addiction wanes after approximately 14 days of abstinence. Tobacco smoking addiction is more complex since MAO (monoamine oxidase inhibitors) is also released making tobacco smoking much more than just about nicotine addiction.

The presence of nicotine in e-cigarettes has been a matter of controversy. Research has shown that e-cigarettes deliver approximately 20% of the nicotine that a conventional tobacco cigarette does\(^12\) and
thus **assertion that e-cigarettes can deliver a toxic dose of nicotine are implausible.** The only conceivable way one would become toxic would be to ingest the nicotine containing solution undiluted. This could of course occur with a multitude of everyday household items, such as detergents, Draino, Lysol, and caustic soda none of which are regulated. Toxic doses of nicotine could more easily be consumed from misuse of nicotine gums or patches as chewing gum left in reach of children may well be attractive to them as a candy look alike. Misuse of a product cannot be used to implicate a substance that is safe when used in a rational fashion. In the 2014 annual report of the American association of Poison control centers, nicotine liquids accounted for an annualized 651 calls; in 2012 there were over 300,000 calls for analgesic poisoning, over 200,000 for cosmetic related ingestions and almost 200,000 from inadvertent ingestion of cleaning liquids\(^1\)\(^3\). Nicotine toxicity is hardly an epidemic. Nicotine toxicity has been evaluated, and recent review showed that the LD50 (lethal dose to 50 percent of the exposed population) is 500 to 1000 mg\(^1\)\(^4\). Given the typical concentration of e-juice is 24 mg/ml an individual would have to purposely ingest 20 to 50 ml of e-juice in one attempt to achieve a near lethal dose. This knowledge should be incorporated into retail e-juice concentrations and bottling standards.

The committee is of course aware that physicians routinely support the use of nicotine replacement therapy in the form of gum, patches and sprays. Nicotine replacement therapy is a cornerstone of smoking cessation therapy so that the administration of nicotine itself cannot be considered a negative component of e-cigarettes. The supposition that nicotine-containing e-cigarettes will encourage nicotine addiction is not supported by any evidence; nicotine is already available to any smoker or non-smoker, as no prescription is required for the NRT products. They are easily obtainable for anyone wishing to obtain the physiologic effect of nicotine.

### 3. It’s a Gateway

This statement has gained deep traction in the anti e-cigarette lobby, and it origin is not certain. However, the earliest references to it are attributable to Tom Friedan the director of the CDC, Dr Tim Mcfee of the CDC, and Mitch Zeller of the FDA. **It did not originate from research work nor is it supported by research work.**

The Gateway phenomenon is presently regarded as an effect where using one substance leads to the increased risk of using another presumable more harmful substance. The actually hypothesis is claimed have been described by Dr. Kendall who studied addiction behavior with an emphasis on
Dr. Kendall found that cocaine users typically were smokers before and passed through a sequence of tobacco use, marijuana use then ultimately cocaine\textsuperscript{15}. They conducted rather elegant experiments in mice showing nicotine exposure increase the mice’s cocaine seeking behaviour. Extrapolating this research to support a gateway hypothesis for e-cigarettes is dubious. Experimentally mice had a forced exposure to cocaine, nicotine did not increase spontaneous cocaine seeking behaviour, thus all that can be concluded is that if mice are given nicotine then forced to take cocaine then they subsequently seek cocaine more often if pretreated with nicotine\textsuperscript{15}. They do not spontaneously display cocaine-seeking behaviour just because they were force fed nicotine. This article was published in the New England Journal of Medicine as a special lecture article and then implicated e-cigarettes in their conclusion. The article had nothing to do with e-cigarettes but the authors used the controversy to increase the fashionability of their article, in short they used e-cigarettes to make their article appear clinically relevant. The original description of the “gateway hypothesis” examined the behaviour of cocaine users, so it was a retrospective analysis of behaviour. It simply pointed out that many cocaine users began as tobacco users. This may be multifactorial; tobacco is a legal, cheaper and more easily available for a person with a predisposition to addictive substances. Cocaine users are a very tiny subset of the tobacco smoking population and extrapolating causality is not logical. Smoking does not cause cocaine use, rather those persons that have an addictive predisposition simply start with the most easily available addictive substance to modify mood, namely tobacco. It is interesting to note that studies in East Asia show that most cocaine users do not use tobacco first thus the gateway myth is not even at play.

**E-cigarette use by non-smokers is negligible and similar to NRT use**

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Smoking Toolkit Study in 2014 found that in UK, e-cigarette use amongst non-smokers is negligible and similar to NRT use, which is below 0.5% of the total e-cigarette users. This recent evidence clearly debunks the gateway theory that many opponents of e-cigarette are clinging to smear electronic vaporizer like e-cigarettes.
There is no credible evidence of e-cigarettes acting as a gateway to tobacco use among children or adults. In persons predisposed to nicotine addiction they may even provide an alternative to tobacco use and reduce harm. In a national survey of German e-cigarette users less than 0.13% of users were under the age of 19. In the CDC national youth tobacco survey of 2013, participants were asked if they had ever used an e-cigarette. The respondents who answered yes increased from 0.3% in 2011 to 0.6% in 2012. This was presented as a doubling of e-cigarette use and shocking news. What is lost is that smoking rates actually went down, and the use of tobacco cigarettes decreased from 14.6% to 11.8% due to an increased use of e-cigarettes. Amongst smoking youth, those in middle school, 61% were dual users and this rose to 80% in high school\textsuperscript{16}. While it is certainly preferable that youth use no nicotine containing products pragmatically using a less harmful product reduces exposure of the developing body to the toxic effects of tobacco. The issue of harm is the fact that 14% youths use of tobacco products, not the 0.6% that use of e-cigarettes. The most recent survey in New York City showed that smoking rates went up from 16 to 18% after an “e-cigarette ban” was put in place\textsuperscript{17}.

A great deal has been made of flavoured e-juice potentially attracting youth, although a similar concern has not been expressed regarding fruit flavored alcoholic beverages or caffeinated flavors like...
pumpkin spiced latte. It has been demonstrated that anecdotally as well as in objectively conducted surveys that ex-smokers prefer the use of flavored products so that they are not drawn back to the use of combustible products by mental recall of the tobacco flavor. **While it may be fashionable to believe flavored e-cigarettes are attractive to youth, no evidence in any jurisdiction supports this.**

### 4. Smoking cessation

This is of course the central argument of proponents of e-cigarettes, that they are a tobacco harm reduction tool that are better or equivalent of approved NRTs. It must be understood that the harmful effects of combustible tobacco including emphysema, COPD, cancer and heart disease are dose dependent\(^\text{18}\) and while total cessation is the most desirable state, significant reduction in exposure to the toxic products of combustion leads to a reduction of harmful effects. **This means that reduction in smoking is helpful in reducing the incidence of disease even if total cessation is not achieved.** It is almost important to note that current standard medically approved smoking cessation therapy has a success rate of less than 25% within motivated quitters; this is an unacceptable state of affairs. Current pharmaceutical therapy includes Varenicline, which the FDA warns has neuropsychiatric dangers, and Bupropion, which also carries warnings of depression, hostility and suicidal ideations\(^\text{19}\). Clearly these therapies have harm but the harm is considered less than that of ongoing tobacco use.

The ITC study, which included smokers in Canada, USA, AUSTRALIA and the UK, showed that compared to baseline e-cigarette users significantly reduced their exposure to tobacco cigarettes from **20.1 per day to 16.3**\(^\text{20}\). While total cessation was not statistically significant the study did not control for the degree of tobacco addiction at baseline. Polosa, in a clinical study showed that e-cigarette use led to greater than 50 % reduction in the use of tobacco cigarettes, compared NRT with e-cigarettes\(^\text{21}\). **The use of e-cigarettes containing nicotine lead to a 57% reduction in the use of tobacco cigarettes over the course of the study.** This cessation rate surpassed the numbers seen with standard NRT (41%). There was a 45% reduction in cigarette use in users of e-cigarettes, which contained no nicotine\(^\text{21}\).

The UK smoker’s toolkit study showed that 30% of quit attempts involved the use of e-cigarettes and the growth in e-cigarette use has been accompanied by an increase in the incidence of quit attempts and quit success in the UK. The availability of e-cigarettes actually motivates smokers who had no intention of even trying to become motivated towards quitting \(^\text{5,22}\).
While the definitive study has not yet been performed, the anecdotal evidence from millions of users coupled with well-done, smaller studies show e-cigarettes to be as effective or better compared to current day NRTs therapy in reducing cigarette consumption. They carry no danger of the neuropsychiatric effect associated with prescription smoking cessation drugs. Thus if the same parameter regarding safety and efficacy are applied to e-cigarettes as to accepted smoking cessation therapies in Canada, e-cigarettes are as effective as approved NRTs and safer than prescription drugs.

5. Positions of the Medical Health Officers and Health Organizations

It remains somewhat of an enigma to me why Medical Officers of Health and Healthcare organizations charged with recommending and enacting health policy remain focused on denying the health benefits of e-cigarettes. Primary due diligence is a time consuming endeavor, in which conflicting scientific data must be analyzed by content experts, interpreted and then weighted as to the quality of each piece of information. Heart and Stroke Societies, Cancer Care Organizations and Local Health officials have the mandate to do this but have not devoted the resources to do so. The same misinformation and standard positions statements are simply reiterated by each organization assuming another has done the diligence. Comments made in the lay press are taken up by these organizations and research simply becomes reading each other’s position papers. It becomes a static cycle that does not allow for incorporation of new scientific or epidemiological information. This committee is breaking that cycle and once again should be congratulated. Federal oversight to ensure leadership and not just bureaucratic management over the emerging e-cigarette technology is welcome. The health and welfare of Canadians cannot be left solely to the unsupported opinion of a few non-stakeholders.
6. Conclusions

1. Significant research has been and continues to be done establishing that e-cigarettes pose neither short term nor intermediate term health risk to the users. While long-term risk remains to be established all available cytotoxic and chemical analysis research shows that e-cigarettes have a risk profile that is orders of magnitudes less than that of traditional combustible tobacco products.

2. Nicotine does not cause cancer.

3. Tobacco smoking causes cancer, heart disease and chronic lung disease.

4. There is no evidence at the molecular level or from epidemiological studies that supports that e-cigarettes are a gateway to the use of tobacco products.

5. Ongoing tobacco use in youth remains a concern and the presence of e-cigarette availability may be reducing youth use of combustible tobacco products.

6. Flavored e-cigarettes products are not being produced to target a youth market but are the preferred choice of adult (ex-smokers.

7. Second hand vaping falls within the acceptable air quality standards.


**Suggestion for the committee's consideration**

1. Treat e-cigarettes in a new category of tobacco harm reduction products and not as a tobacco product or a drug.

2. Establish manufacturing standards for e-cigarette hardware, such as battery composition, duration and materials.

3. Establish manufacturing standards for e-juice, including but not limited to,
   
   a. Physical requirements of the manufacturing facility,
   
   b. Accurate labeling following best practices
   
   c. Maximum concentrations of nicotine to 24mg/ml
   
   d. Maximum single bottle sizes of 10 ml
   
   e. Lot tracking mechanisms.
   
   f. Ingredient quality

4. Mandate the bottling of juices in childproof, tamper proof containers and labeling.

5. Restrict sale of products and devices to individuals aged 18 and older.

6. Place a cautionary warning on use by women who are or maybe pregnant.

7. In principle provide for an incentive to use e-cigarettes over combustible tobacco products, by such mechanisms as
   
   a. Less taxation than tobacco products
   
   b. Wider latitude for public use indoors
   
   c. Not restricting sales of e-cigarettes to tobacco retailers

8. Restrict and or ban lifestyle advertising of e-cigarettes.

9. Allow for e-cigarettes to be represented, promoted and freely advertised in all forms of media as a “tobacco harm reduction strategy” and possibly smoking cessation aid.

10. Allow the development and sale of flavours based on consumer demand.

11. Increase taxation on tobacco products to compensate for loss of taxation income from increased e-cigarette use.
12. Direct Health Care organizations to fund unbiased, brand neutral research by academically based scientists for effectiveness of vapor products like e-cigarettes.

13. Establish a standing committee on tobacco harm reduction as part of the Health Protection Board composed of content experts, public policy experts, community representatives and legislative representatives. This committee will evaluate evolving evidence and provide recommendations on e-cigarettes as well as any future technologies or products claiming tobacco harm reduction.

**Declaration of Interest:** Dr. Gopal Bhatnagar is a practicing cardiothoracic surgeon. After witnessing the effects of tobacco smoking first hand in patients, and after thorough review of medical literature on vaping, Dr. Bhatnagar agreed to be the Chief Medical and Scientific advisor for a Canadian vape provider.

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