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Dear Legislator Dixon,

Please find enclosed some literature, including current study results with regard to electronic cigarettes and vaping. This research paper was published in 2013 by The American Council on Science and Health. We feel that it scientifically contradicts some of the opinions expressed at your last legislative meeting regarding electronic cigarettes.

Also included is AEMSA information. This includes the E-liquid Manufacturing Standards required in order to be an AEMSA member.

Thank you for your time and attention. We look forward to the prospect of being able to provide you with any other information that you might require.

Warmest Regards,

Leigh Smith
Operations Manager

NICOTINE and HEALTH

A publication of the

American Council on Science and Health
Science. Not Hype.

WRITTEN BY
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The Lung Study in the USA followed thousands of ex-smokers for a total of 12.5 years. As these people had smoked for many years in the past, they were already prone to cancer. Yet, compared to those who quit smoking entirely, risk of cancer of the lung was increased only in those who continued to smoke, but not in those using nicotine gum.[53]

NICOTINE DELIVERY FROM ELECTRONIC CIGARETTES

In 2012, some European brands delivered up to 50 micrograms of nicotine per puff, in the lower tobacco cigarette range, but most fell far short.[54] Some products are inconsistent in nicotine delivery across the same brand, the same variant, and by cartridge or label.

IN CARTRIDGE LIQUID

The nicotine content may range from zero through low, medium, and strong. The nicotine in the cartridge liquid in many brands was less than the label claimed. The usual strength was 18 mg or 1.8 percent of a 1 ml solution.[54]

IN VAPOR

A study of 16 European brands has shown that nicotine content of the cartridge and vaporization efficiency can vary greatly by brand. On average 50 percent to 60 percent of the nicotine in the liquid was vaporized, and in many brands much less.[54] Brands tested delivered anything from 2.5 percent to 77 percent as much as the nicotine delivered by a regular cigarette.[54]

DELIVERY OF NICOTINE

FDA scientists found that 33 puffs of 100 ml each from an electronic cigarette without pause delivered 1 mg of nicotine[55] (the same as one tobacco cigarette). Many experienced vapers achieve this sort of absorption.

NICOTINE IN ROOM AIR

One e-cigarette releases 3 millionths of a gram of nicotine per cubic meter of room air.[56] Modern laboratories can detect such traces.

ABSORPTION OF NICOTINE

E-cigarette vaping and smoking both result in similar levels of nicotine absorption as judged by serum levels of the nicotine-derivative cotinine. Fifteen smokers increased their cotinine levels by 61 ng/ml after actively smoking or

vaping. Similarly, passive smoking or vaping resulted in similar amounts of nicotine inhaled. Fifteen never-smokers increased their cotinine levels by 2.4 to 2.6 ng/ml after passive smoking or passive vaping.[57] (Toxic gases behave quite differently; for example, e-cigarettes do not emit carbon monoxide, whereas smoke does.)

Nicotine from electronic cigarettes used in planes or crowded situations is clearly not a health risk to those in close proximity. Measuring trace toxicants is difficult and no-one has so far succeeded in measuring toxicants in the blood of passive vapers. Airlines have understandably banned e-cigarette use, as security is their priority, and trains may ban them for passenger comfort, but restrictions on e-cigarette use indoors would be hard to justify on medical grounds, as e-cigarettes (no ash, no smoke, no second hand smoke) do not emit sidestream smoke. Propylene glycol, water vapor, and a trace of nicotine on the exhaled breath of e-cigarette users are not harmful for vapers or bystanders. Legislation could deter smokers from switching to less harmful vaping. In countries now enjoying smokefree laws and spaces, however, once the social norm is not to smoke, then by implication, the norm would be not to vape either.

We will take a more detailed look at e-cigarettes in Part 3 (and prior to that we will examine "smokeless tobacco" in Part 2).

CONCLUDING THOUGHTS ON PART 1

Cigarettes are deadly, and far safer alternative products are now available. The availability of lower-priced alternatives can be expected to greatly aid a switch away from cigarette smoking.

Quitting cold turkey is the commonest way to quit, but quitting by switching to using an electronic cigarette may be a more pleasant way to reach the same goal.

- Cigarette smoking should be much more highly taxed now that a safer and satisfying alternative product is now available. This is the tipping point principle.
- Electronic cigarettes should be made as accessible as cigarettes. Electronic cigarettes should be sold widely and lightly regulated to ensure product safety (whether by regulation as a medicine as in the UK, or under consumer law).
- Smokeless tobacco is of much lower risk than cigarettes, and health warnings and taxes should to reflect this.

PART THREE

Electronic Cigarettes

Electronic cigarettes are nicotine inhalers designed to deliver nicotine without the toxicants in cigarette smoke. Manufacturing quality varies but is improving, and sales are rapidly increasing.

Mostly smokers want a safer way to smoke, or want e-cigarettes to help them quit.

Electronic cigarette vapor appears chemically incapable of causing cancer as cigarette smoke has done. E-cigarette vapor contains toxicants concentrations averaging less than one percent of the concentrations in tobacco cigarette smoke.

E-cigarettes consist of a mouthpiece, a cartridge containing nicotine in a liquid, atomizer and battery. They were invented in China, where most are still made—hand-made, under variable quality control—and exported all over the world. The liquid is equally important—nicotine in propylene glycol or glycerol, water, and flavors. Brands vary as to the proportions of PG and VG (vegetable glycerol) in the liquid. Many e-cigarette users tend to take one or two puffs quite frequently, as the e-cigarette generates no flame and can be kept in the pocket.

Electronic cigarettes make it possible to enjoy inhaled nicotine without health concerns, while enjoying flavors such as tobacco, menthol, coffee, or chocolate as desired, without even lighting up.

Most smokers will see electronic cigarettes simply as vastly safer cigarettes.

THE ELECTRONIC CIGARETTE MARKET

GROWTH OF ELECTRONIC CIGARETTE SALES

Electronic cigarettes were first sold outside of China in 2007, and global sales of electronic cigarettes reached an estimated two billion dollars in 2012, and are expected to eclipse the 2.4 billion dollar global sales of nicotine medications in 2013. The three leading electronic cigarette markets by value are the United States, Russia, and Germany.[1]

In the United Kingdom electronic cigarette users are expected to number one million by 2013. In 27 European Union (EU) countries in 2012, one percent of adults used e-cigarettes regularly—about four percent of smokers,[1] a remarkable achievement within only five years. In the EU consumers spent an estimated €400-€500 million on electronic cigarettes in 2011.

In the United States annual sales have risen to between 250 and 500 million dollars[2] where six percent of smokers were using e-cigarettes in early 2012.[3]

First time nicotine vapers buy cigarette look-alike (analogue-equivalent) e-cigarettes with tobacco extract flavor, and in some countries these are sold under cigarette-similar brand names. This is sufficient to wean themselves off tobacco. Created to miniaturize the e-cigarette, small batteries require a personal battery-charging case to last through the day.

The next generation of e-cigarettes, designed for connoisseurs, are bulkier, look nothing like cigarettes, can cost $100 to $200, are often of stainless steel, and provide larger batteries. Running costs are minimized by using nicotine liquid from child-proofed 5 ml dropper bottles.

COMPETITORS, RIVALS, REGULATORS, AND HEALTH AGENCIES

The fledgling nicotine electronic cigarette industry as of 2013, faced opposition from many quarters:

- The cigarette industry's profits are now under threat as smokers switch from combustible tobacco to flameless electronic cigarettes. However, five major tobacco companies or their subsidiaries are now selling or plan to sell electronic cigarettes, including Altria.[4]
- The pharmaceutical industry's medicinal nicotine sales and profits will diminish as smokers use electronic cigarettes as another kind of NRT.
- Medical practitioners, quit-line advisors, and smoking cessation workers are required by law to use licensed medicines from the pharmaceutical industry. They will learn about e-cigarettes informally from patients.
- Major anti-smoking groups in the United States currently oppose the sale of e-cigarettes. They are funded by the pharmaceutical industry. They deeply distrust the tobacco industry.
- Governments looking to recoup future excise losses on declining tobacco sales could be tempted to tax e-cigarettes. This would make electronic cigarettes less price-competitive and would have the unwanted side effect of protecting tobacco sales.
- The World Health Organization's Conference of the Parties to the WHO FCTC (Framework Convention on Tobacco Control) as of 2012 encouraged Parties (nations) to ban e-cigarettes, even including non-nicotine e-cigarettes, because they could "undermine the de-normalization of tobacco use upheld by WHO FCTC" and because their use "could be considered a direct or indirect promotion of tobacco use" and "could hamper implementation of Article 8 (protection from

exposure to tobacco smoke)."[5] As of 2013, almost no country has legislation in place to allow sale of nicotine products as a medicine or a tobacco product. Many countries have responded with reflexive bans rather than creative, flexible regulation. Bans of e-cigarettes, based on harms that are minor compared to smoking, are likely to perversely protect tobacco sales from competition.

- Regulators have problems with electronic cigarettes, as they are neither combustible tobacco products nor medicines. E-cigarettes neither pay tax like tobacco products nor conform to medicinal and pharmaceutical standards. UK law requires medicine regulators to promote public health, but in other countries medicine safety policy may not consider the reduction of tobacco sales as part of their brief.

- Smokers too, have had problems with the first generation electronic cigarettes; they want legal access to purchase better quality, longer lasting batteries, nicotine to match the label, efficient vaporization of nicotine, adequate puff generation, and at a lower price.

PUFFING PATTERNS

Vapers tend to take larger and stronger puffs, and pause less between puffs compared with smoking tobacco cigarettes, to maximize nicotine from each puff of e-cigarette vapor.[98]

Two separate small studies measured puffs with the Cress Micro device (*Chart 6*) show that whereas the average smoke flow or puff velocity of tobacco cigarette smokers was 34 ml per second[6a] a faster flow of 52 ml per second was required to activate the atomizer of common brands of electronic cigarettes in FDA's laboratories.

Goniewicz and other Polish scientists studied ten experienced vapers and recorded an average 70 ml per puff, greater than the 59 ml per puff noted for 22 tobacco cigarette smokers. Duration of puff noted with tobacco cigarettes[6a] and e-cigarettes[99] was 1.8 seconds, but some brands have atomizers that take longer to heat.

METHODS FOR BENCH-TOP COMPARISONS OF E-CIGARETTE BRANDS

E-cigarettes glow only when puffed and require more draw: tobacco cigarettes smolder between puffs. The puffing regimes used to machine test tobacco cigarettes had to be adjusted for the shorter interval between electronic cigarette puffs.

Until puffing parameters standards for testing electronic cigarettes are standardized internationally, Goniewicz's observations in *Table 3* are the de-facto standard except that 3 seconds should be allowed as duration of puff, to prevent under-reporting of toxicants from some brands.

CHART 6. CLINICALLY OBSERVED PUFF PATTERNS OF TOBACCO AND ELECTRONIC CIGARETTES

Using Cress Micro flow meters.	Factory-made tobacco cigarettes[5a] n=22	Nicotine electronic cigarettes[7] n=10
Puffs per cigarette or session	14	15
Volume per puff, ml	59	70
Duration of puff, seconds	1.8	1.8
Inter-puff interval, seconds	19	10
Smoke flow, ml per second	34	52 to activate[6]

CLINICAL HARM AND SAFETY REPORTS

We know of no deaths due to use of these devices despite open sale of these devices since 2007 in the United States and the United Kingdom and in other countries, even though sales have greatly increased. Two cases of exploding lithium batteries have been reported globally.

ADVERSE EVENTS REPORTED TO FDA

From 2008 to 2012, eight out of 47 reports of adverse events on electronic cigarettes received by the FDA were serious. These included pneumonia, heart failure, and burns to the face from a battery explosion, and possibly an infant choking fatally on a cartridge refill, chest pain and rapid heart beat.[8]

MAJOR RESPIRATORY EFFECTS

Most vapers are former smokers, many with chronic lung disease. One death in a UK user due to interstitial pneumonia was reported in 2010, but the coroner returned an open verdict as to whether this was due to e-cigarettes. One case of lipoid pneumonia was reported, suspected to be due to glycerin-based fluids in the electronic cigarette vapor.[9]

MINOR RESPIRATORY EFFECTS

Mild mouth and throat irritation and weak dry cough may occur after inhalation, but as in the Sicilian clinical trials described below, respiratory symptoms waned over time. These randomized controlled trials followed participants for six and 12 months, and found no serious adverse events attributable to electronic cigarettes.

LUNG FUNCTION

In 2012 a detailed study of thirty Greek smokers vaping an electronic cigarette for five minutes found an increase of airway resistance and a decrease in the fraction of expired nitric oxide (FENO) that was greater than for sham use. The effects were about half that measured by the same authors in smokers exposed to second-hand cigarette smoke in a car.[10 11]

The reduction in FENO was not confirmed by a further study in Greece in 2013 using a robust repeated measures design. Lung function was measured by spirometry before and after 30 minutes of active smoking or vaping, and after one hour of passive smoking or passive vaping. Lung function was not significantly decreased in 15 smokers using e-cigarettes, or in 15 never-smokers inhaling the vapor of e-cigarettes or inhaling smoke; lung function was, however, significantly decreased seven percent by active tobacco smoking.[12]

MINOR SYMPTOMS

One study examined 543 posts (mostly symptoms) from 481 users of an electronic cigarette forum in 2011. The comments were 80 percent negative, and 20 percent positive—as might be expected, as these sections are designed to deal with complaints. The authors found that the generally negative short-term effects reported by e-cigarette users "appear relatively minor compared to more serious long-term conditions (e.g., cancer and stroke) that occur in conventional smokers."[13]

GENERAL HEALTH EFFECT

Most vapers responding to an online survey recruiting in 2013 mainly from the same e-cigarette forum, as above, believed their health has been improved by switching. Of over 1,044 vapers (38 percent vaping for more than one year), and despite eight percent still smoking tobacco cigarettes, and 15 percent an occasional cigarette: 73 percent reported improved ability to exercise, and 66 percent improved in their ability to do strenuous jobs after switching to e-cigarettes. Smoker's cough afflicted 67 percent but on e-cigarettes, only afflicted three percent.[14]

CARDIOVASCULAR EFFECTS

- Arterial stiffness is not increased from vaping, as it is from smoking a cigarette.[15]
- Red and white blood cells are not increased in the peripheral blood in the first hour after an e-cigarette either actively or passively inhaled, as they were after smoking a cigarette or passively inhaling cigarette smoke.[16]
- Nicotine administered by electronic cigarette can relieve chronic idiopathic neutrophilia (high white cell count, often due to smoking) by inducing successful smoking cessation.[17]

EFFECTS ON THE BRAIN

Nicotine in e-cigarettes reduces the urge to smoke and improves mood, working memory,[18] and prospective memory (remembering to execute a delayed intention at a given time),[19] consistent with previous research on nicotine.[31 in Part One]

TOXICOLOGICAL PROFILE OF E-CIGARETTE LIQUID AND VAPOR

ACUTE POISONING RISK FROM E-CIGARETTE LIQUID

As little as 10 mg of nicotine is a fatal dose for a child and 40 to 60 mg for an adult. Small 10 ml bottles of liquid for electronic cigarettes routinely contain 180 mg and skin absorption can be rapid. Child-proof caps are becoming routine, but regulators should insist on fully child-proof designs.

Even 10 mg of nicotine—the amount found in 0.5 ml to 2 ml of bottled liquid nicotine used for filling electronic cigarettes—is enough to kill a child. Since the taste is bitter swallowing is less likely, and skin absorption is the main risk for adults and children. In 2012 bottled nicotine was sold on the Internet in concentrated solutions containing up

to 8 g of nicotine, and 10 ml bottles of nicotine of 18 mg per ml were widely sold. These bottles are sold with child-proof caps, but the device itself needs to be fully child-proof.

In the future, regulators are likely to only approve product designs that eliminate any possibility of child access to nicotine liquid.

TOXICOLOGICAL PROFILE OF E-CIGARETTE LIQUID

The chemistry of the liquid can change as it is vaporized, so tests of the liquid are not adequate for a full safety report.

> **The most complete review of toxicology of e-cigarette liquid and vapour to date is that of Burstyn. Over 9000 observations of highly variable quality were extracted from peer reviewed and gray literature. He estimates actual exposures of vapers to possible contaminants in vapour, using the formula mg per puff x 150 puffs per day. For the few carcinogens detectable and measurable in the vapour, such as acetaldehyde and formaldehyde, exposure was estimated in micrograms per day, and for tobacco specific nitrosamines as a few nanograms per day.[20]**

E-CIGARETTE VAPOR

E-cigarette fluid or "juice" is liquid over a wide range of temperatures, but when small quantities are vaporized by the e-cigarettes atomizer (heater), the puff of aerosol or mist comprises particles containing water and propylene glycol.

a) The particle size of the e-cigarette aerosol. Measurements of particle size and number are comparable with tobacco smoke. An aerosol is a suspension of liquid or solid particles in a gas. The undiluted particles of average mass in the e-cigarette aerosol have particle diameters in the range 0.25-0.45 microns, and particle numbers are in the 10^9 per cm^3 range.[21] With dilution in room air the particles evaporate and the mist becomes an invisible vapor.

A further study argues that similar particle size should result in similar deposition patterns, and based on the International Commission of Radiological Protection respiratory tract model, estimate seven to eighteen percent alveolar particles depositing in the alveoli, with 73-80 percent lost by exhalation. These particles would be propylene glycol.[22]

b) Intense testing of the Ruyan e-cigarette aerosol. Although the Ruyan classic brand is sold in few countries today, it remains the brand most intensively tested. In 2008-9 Health New Zealand arranged for 62 toxicants to be tested, courtesy of British American Tobacco UK, with laboratory assistance from Labstat International ULC, Canada.

- Of 62 toxicants, 51 were non-detectable. The rest were found in negligible amount.

- No carbon monoxide (CO) was found in the vapor (nor increased in exhaled breath).
- 1,3 butadiene, the leading carcinogen in cigarette smoke was not detected.
- Hydrogen cyanide, the leading cardiovascular toxicant was not detected.
- Tobacco-specific nitrosamines (NNN, NNK) were detected, but at low levels—equivalent to the daily dose from using the nicotine patch and gum and over 300 times less than in Marlboro full flavor cigarette smoke.[23]

Toxicants in electronic cigarette vapor vary from negligible to non-detectable.

c) Volatiles and nitrosamines in 12 European e-cigarette brands. In 2013, Goniewicz and other Polish researchers reported tests on 12 brands of e-cigarette for presence of three aldehydes, toluene, xylene, two tobacco specific nitrosamines, and three heavy metals. Goniewicz tested 10.5 liters of vapor per toxicant.

The vapors contained toxicants at levels nine to 450 times lower than in cigarette smoke, and concentrations were in many cases comparable with trace amounts found in a medicinal inhalator. There was 30- to 40-fold variation in the range of toxicant yields across the 12 brands.[24]

Electronic cigarette brands high in nicotine yield were not the highest in toxicant yields, thus judicious choice of brands could select the most effective and safest brand.

Regulation can encourage manufacturers to manufacture only the most satisfying and the safest e-cigarettes, by excluding all others from the market.

Further study of six brands showed that acetaldehyde was present in the vapor of all six, but at a thousand-fold less than in cigarette smoke. Those e-cigarette brands with glycerol in the liquid all generated acrolein and formaldhyde in the vapor. Brands containing propylene glycol but not glycerol did not generate acrolein or formaldehyde,[25] but this requires confirmation. Increasing the voltage, taking longer puffs, or dripping liquid onto a hot heating coil (atomizer) greatly increased formaldehyde in the vapor.[26] New style e-cigarettes with higher or adjustable voltage may produce more toxicants, and test results on these second generation e-cigarettes are not yet available.

d) Analysis of the vapor for metals and nanoparticles.

Carcinogens: Cadmium, nickel and hexavalent chromium are grade 1 human carcinogens that are found in e-cigarettes. Cadmium levels are low. Nickel and chromium are widely used as the alloy for the heating element. Heavy metal

concentrations in e-cigarette vapor are low (*Chart 7*), 25-84 times lower than in Marlboro full flavor cigarette smoke,[27] and one to three times greater than in medicinal Nicorette inhalator vapor.

Tin: Talbot's group purchased and examined a popular unnamed U.S. brand minutely and found tin particles in the aerosol, attributed to the solder.[28] High use (880 puffs daily) exposure per day was equivalent to only four percent of the upper limit for occupational eight hours continuous exposure.[29]

Nickel: Values for this brand and the other e-cigarette brands were mostly lower and not, as claimed, higher[28] than for cigarette smoke (*Chart 7*).

Nanoparticles: This group at the University of California used electron microscopy to study the heating coil (atomizer) of this unnamed leading U.S. e-cigarette brand in detail, and found the aerosol contained tin and other metals as particles (*Chart 7*), some present as very small nanoparticles (< 100 nM diameter, which can penetrate cell membranes). The e-cigarette studied produced 4 billion nanoparticles per litre of vapor as opposed to 36 billion per litre of cigarette smoke.[28] Some nanoparticles contained heavy metals.

CHART 7. HEAVY METALS IN SMOKE AND NICOTINE VAPORS, MEAN CONCENTRATIONS, AND ESTIMATED DAILY EXPOSURE.

	Cigarette [27, 30, 31]	Nicorette nicotine medicinal Inhalator[24]	European (12 e-cigarette brands) [24]	Unnamed US electronic cigarette brand[25]	Daily dose estimate At 880 e-puffs/ day	Permitted Daily Exposure[30]
	Ng / litre	Ng/litre	Ng/litre	Ng/litre	Ng/day	Ng/day
Cd	160	3	8	NR	400	1500
Chr	0.2-500	NR	NR	14	620	25000
Ni	0, 136, 151	18	18	10	440	1500
Pb	105	4	9	34	1500	5000
Sn	NR	NR	NR	39	1720	NR

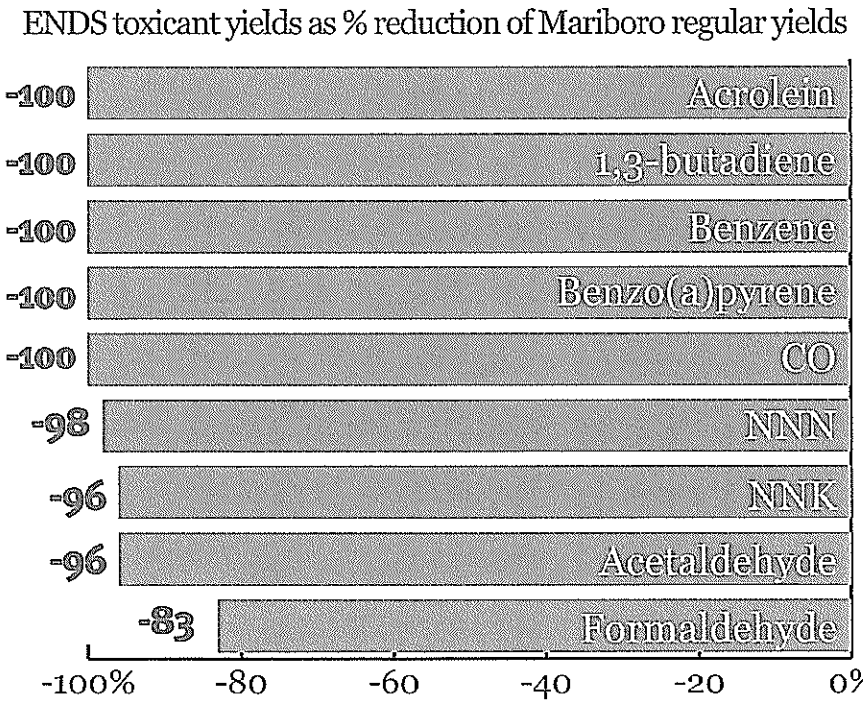
NR = not reported. E-cigarette puffs calculated at 50 ml / puff. Sn = tin.
Nanogram (ng) =one billionth of a gram.

Metallic concentrations and metallic fine particulate in e-cigarette aerosols even at high e-cigarette use were below the permitted maximum for daily exposure, and in the much the same range as for the medicinal inhalator. The great variation in metal values across brands, suggests that regulation of e-cigarettes would minimize vapers' toxicant exposures.

Relative harm reduction: Switching from inhaling cigarettes smoke to inhaling e-cigarette vapor would greatly reduce toxicant exposure. The World Health Organization prioritized nine leading chemicals for "modest reduction" in cigarette smoke over the coming years.[32] By contrast, *Chart 8* shows the percentage by which these cigarette gas emissions would be reduced by use of the Ruyan classic e-cigarette brand, based on that brand's emissions. The electronic cigarette on this basis is capable of achieving complete or near complete reductions in all nine toxicants, rather than the modest reductions proposed for cigarette smoke.

CHART 8. EXPECTED REDUCTION IN LEADING TOXICANTS INHALED IF THE SMOKER SWITCHED FROM SMOKING TO VAPING

(for nine toxicants prioritised by World Health Organization's TobReg Committee for reduction;[32] nicotine adjusted, comparing the Ruyan Classic e-cigarette with Marlboro king size regular[23, 27])



RISKS OF LONG-TERM USE OF NICOTINE E-CIGARETTES

- Assessment of mortality from smoking required 50 years of follow-up. With e-cigarettes, although e-cigarette vapor contains negligible cigarette-type toxicants, regulation is needed to minimize human exposure.

- The question arises as to whether e-cigarettes if used by millions over their lifetimes, could cause serious diseases not yet known. But diseases have causes, and the priority is to eliminate or reduce vapers' exposure to toxicants already known.

- ***Cigarette type toxicant gases.*** The aldehydes acrolein, acetaldehyde and formaldehyde though in negligible quantity in e-cigarette vapor, remain the main concern. If improved atomizers cannot greatly reduce these toxicants, charcoal filters could do so.

- ***Risk of cancer from heavy metals.*** The known carcinogenic heavy metals, cadmium, nickel, and chromium, are measurable in aerosol *(Chart 7)* and comparisons are needed to compare the levels of metals in smokers' and vapers' body fluids, for the levels of carcinogen-derivatives known as DNA adducts.

- ***The active ingredient,*** pharmaceutical grade nicotine, has been used safely for over 25 years in nicotine gum.

- ***The main carrier, propylene glycol (PG),*** has very low toxicity. Maximum advisable dose of PG as a solvent for intravenous drugs has been estimated to be 69 g per 24 hours,[33] which is equivalent to the PG in 100 e-cigarette cartridges, whereas vapers mostly report consumption in the range of 0.5 to 5 cartridges per day. PG is metabolized to lactate and up to half is excreted unchanged in the urine. PG has been used in asthma inhalers, in foods and in skin products. Glycerol also has a good safety profile and is an excipient for at least one therapeutic inhalational product. Neither PG nor glycerol cause cancer.

- ***What can be done?*** Regulation is needed to ensure 1) high purity for liquid ingredients, 2) minimal inhalation of toxicants, and 3) child-proofing to prevent acute poisoning.

NICOTINE DELIVERY FROM ELECTRONIC CIGARETTES

In 2012, some European brands delivered up to 50 micrograms of nicotine per puff, in the lower tobacco cigarette range, but most fall far short.[24] Some products are inconsistent in nicotine delivery across the same brand, the same variant, and by cartridge or label.

In cartridge liquid. The nicotine content may range from zero through low, medium, and strong. The nicotine in the cartridge liquid in many brands was less than the label claimed.[24] The usual strength was 18 mg or 1.8 percent of a 1 ml solution.

In vapor. E-cigarettes generate similar absorption of nicotine as tobacco smoke whether smoked actively or passively, as measured by serum levels of the nicotine-derivative cotinine (61ng/ml for active smoking, 2.4 to 2.6 ng/ml for passive smoking, using 15 smokers for active smoking/vaping, and 15 never-smokers for passive smoking/vaping).[12]

A study of 16 European brands has shown that nicotine content of the cartridge and vaporization efficiency can vary greatly by brand. On average 50 percent to 60 percent of the nicotine in the liquid was vaporized, and in many brands much less.[24] In bench-top testing a day's nicotine delivery from electronic cigarettes was compared with a tobacco cigarette brand. From 300 puffs of one e-cigarette cartridge (20 episodes of 15 puffs) nicotine delivery varied from 0.5 mg to 15.4 mg, as against 20 mg from 20 Marlboro king size full flavor tobacco cigarettes. The brands tested thus delivered anything from 2.5 percent to 77 percent as much as the nicotine delivered by a regular cigarette.[24]

Delivery and absorption of nicotine. Our first clinical testing of the Ruyan e-cigarette brand in 2008-9 showed low plasma absorption of nicotine. Later brands tested on experienced users have shown absorption equaling tobacco cigarettes. FDA scientists found that 33 puffs of 100 ml each from an electronic cigarette without pause delivered 1 mg of nicotine[6] (the same as one tobacco cigarette).

When e-cigarette users take more frequent puffs the atomizer stays hot and adequate nicotine is absorbed.

In an Internet survey in 2011, 31 subjects (16 percent) returned a vial of saliva for analysis. These experienced vapers used five nicotine refills per day, taking a median 200 puffs a day. Median cotinine level in these vials was 322 ng per ml, which equates to 26 mg of nicotine per 24 hours,[34] comparable to cigarette smoking.

PASSIVE INHALATION OF ELECTRONIC CIGARETTE VAPOR IN ROOM AIR

Electronic cigarettes used in planes or crowded situations are clearly not a health risk. Their use may annoy those close by. Once people enjoy the benefits of smokefree laws, the social norm is not to smoke, and by implication, not to vape either. Airlines have banned them, as security is their priority. E-cigarettes do not produce sidestream smoke.

One e-cigarette releases 3 millionths of a gram of nicotine per cubic meter of room air. Modern laboratories can detect such traces, but it is of no clinical consequence.

Similarly, the chemistry of fine particulates in e-cigarette vapor argues against it being harmful to health.

A cigarette smolders to produce sidestream smoke when not puffed, but the heating element of an e-cigarette is only red-hot during each puff, and there is no sidestream smoke emitted. Any "second-hand" vapor is exhaled propylene glycol with a trace of nicotine.

In a recent study, smokers accustomed to using both types smoked first an e-cigarette then a tobacco cigarette. Nicotine in the room air was three micrograms/m^3 after the electronic cigarette, and 32 mcg/m^3 after the tobacco cigarette. For carbon monoxide and volatile gases, the exposure levels for e-cigarettes were in the same range as for not smoking.[35]

Nicotine in room air after vaping an e-cigarette is only 3 millionths of a gram per cubic meter of air.

In another study, the toxicants profile of four brands of electronic cigarette when applied to a poorly ventilated room of 40 m^3 showed no significant risk against hazard and cancer risk indices, whereas the tobacco cigarette tested showed significant risk.[36]

Fine particulates. Visible electronic cigarette vapor, a white aerosol or mist, is exhaled from the mouth, disperses and vanishes within seconds to become an invisible vapor. The visible e-cigarette vapor consists of droplets (< 1 micrometer diameter) of propylene glycol (PG) and glycerol in the same proportions as in the liquid.[37] Fine particulate is able to penetrate into the gas-exchange areas of the lung, but size is not the only factor, and the nature of the particulate is important. No harm has been reported due from water-soluble e-cigarette vapor or from the

salt and water content of sea spray aerosol[38] —or from PG mist, which was found safe for inhalation by hospitalized children over months, and was highly effective in killing respiratory bacteria and the influenza virus.[39] Unlike diesel, coal, and cigarette smoke, electronic cigarette vapor on the evidence is not harmful to health because of its particulates.

FREQUENTLY ASKED QUESTIONS

The answers to these questions will influence policy makers as to whether they want:

- *e-cigarettes banned or not* (prohibition of e-cigarettes only leads to a grey market, and to a policy at odds with the government's tobacco control aims)
- *e-cigarettes sold as recreational products and medicines*, or only as medicines.

QUESTION 1. DO E-CIGARETTES LEAD CHILDREN INTO SMOKING?

On the evidence to date, the answer is no. The percentage risk of never smokers using e-cigarettes (whether adolescents or adults) is near zero (*Chart 9*). However, *Chart 9* surveys were carried out before mass media advertising of e-cigarettes had become established in early 2013.

In 2013, never smokers in Britain reported 0 percent (<0.5 percent) use of e-cigarettes, whether adolescents or adults. Thus the chances of a never smoker becoming addicted to e-cigarettes at any age in 2013 were virtually zero. This is confirmed by surveys in other countries. (*Chart 9*)

Any e-cigarette use was confined mainly to smokers. Two percent of adolescent smokers used e-cigarettes more frequently than weekly and half used them less frequently.

QUESTION 2. DOES VAPING ACT AS A GATEWAY TO CIGARETTES?

- Less than 0.5 percent of never smokers have taken up e-cigarettes and fewer still have moved from e-cigarettes to smoking. (*Chart 12*)
- Although an important theoretical possibility, the risks so far are close to zero.
- Adolescents face real and greater risks from continuing to start smoking tobacco.

CHART 9. PREVALENCE OF E-CIGARETTE USE IN NEVER SMOKERS

Year	Ages surveyed	Survey	Number surveyed	Prevalence % use in past month
2010	18 and over	US National Online survey	2,649	0.3
2010	18-49	US Legacy Longitudinal smoker cohort study, phone survey[40]	3,658	0.0
2010-11	15-24	Poland, national sample, school surveys[41]	13,250	1.4
2013	Adults	Great Britain, national survey[42]	12,701	0
2013	11-18	Great Britain national survey[135]	1,428	0

- Fortunately never-smoking adolescents have shown no interest so far in vaping.
- Gateways allow two-way traffic; many smokers are increasingly using e-cigarettes to exit smoking.

What can be done?

Various policies can be employed to protect adolescent never smokers from e-cigarettes:

- Prevention of glamorized e-cigarette advertising would discourage never-smokers from trying e-cigarettes (even though a ban might discourage smokers from switching to e-cigarettes).
- Cigarette taxes could encourage smokers to switch to vaping, as could graphic health warnings on tobacco packaging.
- Prohibit retailers from selling e-cigarettes—as is the law for tobacco sales.
- Require manufacturers to warn consumers with package warnings that say, for example, "This product contains nicotine and is addictive. Nicotine is not known to cause cancer."

QUESTION 3. DO ELECTRONIC CIGARETTES NORMALIZE OR DENORMALIZE SMOKING?

CHART 10. DIFFERENT VIEWPOINTS ON WHETHER E-CIGARETTES DENORMALIZE SMOKING

A health promotion view	Vaping mimics and role-models smoking, and should be discouraged.
A child	There is no cigarette smoke odor, no lighting up, no use of a cigarette lighter, and, as is especially likely to be remembered, no ash dropped.
A smoker	The e-cigarette is a cigarette look-alike, and he or she is likely to try it—and may like it, possibly leading to quitting by switching.
Family view	A successful switch to e-cigarettes will denormalize smoking for that smoker and for family, home, friends, and children.
Market view	By reducing cigarette sales in the U.S. in 2013, e-cigarettes are beginning to seriously denormalize the sale of cigarettes.[43]
Research view	Now that research shows that e-cigarettes increase smoking cessation,[44] it proves also that e-cigarettes denormalize being a smoker.

QUESTION 4. IS VAPING LESS ADDICTIVE THAN SMOKING?

4.1 Addiction to e-cigarettes in never smokers: development of addiction may be no less rapid than with first cigarettes.

A person who has not previously inhaled nicotine and who starts using e-cigarettes might expect to become addicted as rapidly as adolescents smoking their first cigarettes (*Chart 3*). In fact as e-cigarettes are less harsh, it is possible that e-cigarette nicotine could be inhaled more easily and more rapidly, making for a more rapid onset of addiction.

As *Chart 10* shows, zero percent of never-smoking adolescents are using e-cigarettes but more may do so if e-cigarette companies continue to glamourize e-cigarettes in the mass media.

4.2 Electronic cigarettes decrease addiction to tobacco.

For ex- or current smokers, vaping is less addictive than smoking; e-cigarette use reduces cravings for, and consumption of, tobacco.

In 2009 a randomized controlled trial at the University of Auckland showed that a nicotine electronic cigarette reduced the urge to smoke for up to an hour, more than a zero-nicotine electronic cigarette, and more than a nicotine inhalator, but not nearly as much as a tobacco cigarette.[45]

In 2013 an online survey of 1,027 e-cigarette users, 95 percent of those who were now ex-smokers reported craving for tobacco cigarettes had decreased since they switched. Cravings for tobacco decreased 70 percent in the 14 percent still smoking tobacco. In over half of those still smoking tobacco, tobacco consumption "decreased dramatically."[46]

Vapers who had quit smoking altogether by using e-cigarettes, however, had started to smoke at an earlier age, which may explain their higher addiction scores than vapers who also smoked.)[46]

On interviewing vapers as to current and past experiences, a hundred experienced vapers gave their average time from waking to first vape as 38 minutes, as against 24 minutes average from waking to the first cigarette when they used to smoke.[47]

4.3 Most e-cigarette users quit e-cigarettes without becoming permanent vapers.

Of those using e-cigarettes for quitting tobacco, only a minority become long term vapers. In its 2013 population survey in 2013, Action on Smoking and Health London found that while eight percent of ex-smokers had quit smoking using e-cigarettes, five percent used them temporarily, and only three percent still used e-cigarettes.[42]

Product improvements and promotions could increase the proportion of vapers who take up vaping long term.

QUESTION 5. DO E-CIGARETTES RESULT IN DUAL USE?

Is dual use a problem? Dual use of cigarettes is harmful, as even a few cigarettes a day increase mortality risk (*Chart 4*), and so to obtain the full health benefit from using e-cigarettes, the switch needs to be complete. On the other hand, dual use may be the norm at the start of the switching period.

What can be done? Taxation on tobacco and graphic health warnings encourage people to fully quit smoking. Regulation of e-cigarette packaging and health warnings on e-cigarette packaging could warn vapers of the dangers of an incomplete switch.

What not to do. Restricting access to e-cigarettes would favor reversion to smoking.

CHART 11. PERCENTAGE OF E-CIGARETTE USERS WHO CURRENTLY SMOKE: DUAL USE

Year	Ages surveyed	Survey	Number surveyed	Prevalence: % smoking
2010	18 and over	US National Online survey[40]	2,649	4.1 (past 30 days)
2010	18-49	US Legacy Longitudinal smoker cohort study, phone survey[40]	3,658	6.1 (ever use)
2010	Adults	US Consumer Styles. Past month users of e-cigarettes[48]	115	6.3
2010-11	15-24	Poland, national sample, school surveys[41]	13,250	15.3
2011	Adults	Experienced vapers, face to face interviews, some cigarette use in past 30 days[47]	104	22
2013	Adults	Online survey of vapers[14]	1044	8.0
2013	Adults	Great Britain, national population-based survey[42]	12,701	11.0
2013	Adults	On-line survey of e-cigarette users.[18]	1338	14

ELECTRONIC CIGARETTES FOR SMOKING CESSATION

Electronic cigarettes fit where cigarettes once did, with much less harm.

Many may vape for life, just as many smoke for life.

E-CIGARETTES AS QUITTING AIDS IN BRITISH ADULTS IN 2013

Approximately 20 percent of British adults in 2011 smoked cigarettes.[50] *Chart 12* shows that 7 percent of adults (35 percent of smokers) still smoked after trying vaping, while approximately 1 percent (100,000) of adults (3 to 8 percent of smokers) had used vaping to successfully quit smoking.

For British smokers from 2012 to 2013, the percentage of smokers who had ever vaped increased from 22 percent to 42 percent and the number vaping and quit increased from one percent to three percent approximately of the smoking population. Thus for the extra 16 percent of smokers taking up vaping, an extra two percent quit and were still vaping, which would tend to lock in the decision to quit. A decline in national smoking prevalence in 2013 would be expected if the survey results are correct.

ELECTRONIC CIGARETTES AS QUITTING AIDS IN EUROPE

In 2012, a survey of 4470 smokers across the 27-member European Union who had tried to stop smoking in the previous 12 months showed that 66 percent had tried to stop unaided, 22 percent had used NRT, 7 percent had used health services, 7 percent had used electronic cigarettes.[50] Data was not available on the success rate for these recent quit attempts.

In Europe during 2011-12 electronic cigarettes as an aid for quitting attempts, became as popular as health services.

ELECTRONIC CIGARETTES AS QUITTING AIDS IN THE UNITED STATES

In a nationally representative survey in 2011 of 1,836 smokers and recent ex-smokers, 8 percent had used e-cigarettes in the past month, but there was no association of use with increased quitting of tobacco. However, unsuccessful quitters were more open to using e-cigarettes in future, and those intending to quit in future had a higher interest in e-cigarettes than those not planning to quit.[51]

Of 2,476 ever users of e-cigarettes using tobacco cessation quit lines in various states in 2011-12, 31 percent of callers had used e-cigarettes. Most callers were mailed NRT, but e-cigarettes were not FDA approved and not part of the treatment protocol. Of those using e-cigarettes for a month or more, 22 percent quit for the past 30 days; for never users of e-cigarettes, 31 percent quit, but due to confounding factors the authors did not draw firm conclusions about the effectiveness of e-cigarettes for quitting.[52]

In a focus group, 11 e-cigarette users, asked open-ended questions about e-cigarettes, said e-cigarettes helped quit smoking by providing bio-behavioural feedback, social benefits, hobby elements, personal identity, and distinction between smoking cessation and nicotine cessation.[53]

ELECTRONIC CIGARETTES IN PATIENTS WITH SCHIZOPHRENIA

Bupropion or varenicline may not be suitable to prescribe for mentally ill patients for smoking cessation, and some form of nicotine is required. In Sicily, e-cigarette use over 52 weeks decreased average cigarette consumption from 30 to 15 per day, without significant side effects and without increase in symptoms for 14 patients with

CHART 12. EVER USERS OF ELECTRONIC CIGARETTES, BRITISH ADULTS, 2013*[42]

Smoking and vaping status	Percentage of smokers or of ex-smokers*	Estimated % of adult population*
Has not tried vaping	65 percent of smokers	13.0
Remained a smoker after trying vaping	24 percent of smokers	4.8
Smoker and vaper	11 percent of smokers	2.2
Ex-smoker, ex-vaper	5 percent of ex-smokers	1.2
Ex-smoker and vaper	3 percent of ex-smokers	0.7
Ever –vapers	45 percent of smokers	8.9
Current vapers		2.9
Exclusively vapers		0.7

*Based on the 91 percent of smokers who were aware of e-cigarettes

chronic schizophrenia patients who smoked not intending to quit. Two quit smoking and were still quit when surveyed.[54] This is a small non-randomized study without controls, and the first of its kind.

RANDOMIZED CONTROLLED TRIALS (RCTS)

Trials up to 2013 have been encouraging though not proof that electronic cigarettes help smokers quit. Additional, larger studies are presently planned, recruiting or underway.

Against the conventional wisdom, these or similar devices are reported to succeed with and without nicotine, despite low levels of plasma nicotine initially reported, and with and without a desire to quit, though the numbers are small. A problem for clinical trials is selecting a product that guarantees to delivers sufficient nicotine.

Randomized controlled trials are considered the gold standard.

1) In 2009, a cross-over RCT trial at the University of Auckland evaluated the electronic cigarette's ability to reduce the urge to smoke in overnight tobacco-deprived smokers and found that the nicotine electronic cigarette had a similar effect to a medicinal nicotine inhaler, despite low plasma nicotine levels attained. The zero nicotine e-cigarette also reduced the urge to smoke.[45]

2) In 2011, a RCT with six months follow-up at the University of Catania, Sicily on 40 smokers who had failed to quit smoking in a hospital programme showed that the e-cigarette substantially halved cigarette consumption for the total cohort, and 22.5 percent quit smoking altogether, without causing significant side-effects.[55]

3) A further RCT with 12 months follow-up of 300 smokers in Sicily who were *unwilling* to quit showed that 13 percent quit on high nicotine cartridges as against four percent who quit on zero nicotine at 12 months, and all groups reduced cigarette consumption.[56]

4) The Auckland New Zealand trial, the first to compare e-cigarettes with nicotine patches, shows comparable success in helping smokers to quit and no serious reactions due to e-cigarettes.[44]

Of 657 smokers randomly allocated to e-cigarettes or nicotine patch use for 13 weeks, and after three months further follow-up, 7.3 percent quit smoking using nicotine e-cigarettes, 5.8 percent using nicotine patches, and 4.1 percent using placebo e-cigarettes (The differences were not significant). More than half the nicotine e-cigarette users reduced cigarette consumption by half, significantly more than for patch users. Nine in ten users of e-cigarettes said they would recommend it to friends wishing to quit smoking.

Adverse reactions were no different for e-cigarettes and nicotine patch, and no major reactions were attributable to either product. Of smokers allocated to use e-cigarettes, 40 percent liked their cigarette-like qualities, sensory familiarity and perceived health benefits, taste, absence of cigarette odor, and ease of use.

The e-cigarette used in this trial provided only 20 micrograms of nicotine per standard puff vs. up to 50 micrograms from cigarette look-alike brands currently sold internationally. Moreover, users consumed an average one e-cigarette refill daily, around 20 percent of the nicotine from cigarette smoking.

STAGES OF SWITCHING TO QUIT

Some smokers wanting to quit smoking may buy electronic cigarettes as cessation aids and use them to Quit and Switch. Success is aided by making an executive decision to stop smoking.

Stage 1. Switching and stopping smoking. Cigarette consumption is reduced, e-cigarette consumption increases.

Stage 2. Fully smoke-free, and reducing nicotine. Free of the risks of smoking, the ex-smoker now decides at leisure what nicotine strength of e-cigarette is most satisfying, and continues for three to six months to ensure no relapse.

Stage 3. Nicotine and tobacco-free. Uses a zero nicotine e-cigarette, and not smoking any tobacco, the ex-smoker may now choose to continue with nicotine free e-cigarettes or to dispense with them. A nicotine-free substitute can assist quitting.[57]

REGULATION OF ELECTRONIC CIGARETTES

Among countries where e-cigarettes are sold there is widespread agreement on the need for some regulation, and widespread disagreement as to the whether they should be sold for pleasure or medications or both, and whether the regulation should be light or heavy.

Countries with bans in place may eventually permit sales once they see e-cigarette sales reducing tobacco cigarette sales in Europe and the U.S.

Under the 2009 U.S. Family Smoking Prevention and Tobacco Control Act, nicotine, even when sold on its own is considered a tobacco product because it was made from tobacco. U.S. courts have held that nicotine electronic cigarettes come under that same Act, rather than under the Food, Drug, and Cosmetic Act[58]; however, the Food and Drug Administration regulates all tobacco, nicotine, and nicotine replacement therapy (NRT) products and has also asserted its intention to regulate electronic cigarettes.

Important questions remain.

1) Whether nicotine electronic cigarettes should be banned from sale in the meantime - and how long the ban should continue: Canada, Australia and New Zealand have banned sales of nicotine electronic cigarettes but permit import for personal use. In Canada despite the sales ban in 2009, by 2013 at age 16-30 years 33 percent of smokers had tried electronic cigarettes; 14 percent of smokers had used them in the past 30 days, as had one percent of non-smokers.[59] In New Zealand, the legal sale of non-nicotine electronic cigarettes means wasteful purchases by desperate smokers, with no provable public health benefit because the active ingredient is banned. Prohibition as a practical policy for e-cigarettes is discussed extensively but found untenable by Etter, a political scientist and professor of public health (see Bibliography).

2) Whether e-cigarettes should be sold to deliver nicotine for recreation and pleasure, and sold as freely as cigarettes; or sold only as medicines.

3) Whether regulation can be light-touch so as to raise standards and not so onerous that improved products cannot reach the smoker:

- *General sale provisions* under consumer protection laws usually require the product to be reasonably safe, to be fit for purpose, and to be true to label. In Sweden the industry has adopted a voluntary standard for snus, the

Gothiatek standard. The standard has been raised over time. Such a standard could be useful for e-cigarettes. Some electronic cigarette brands could progress to regulation.

Tobacco firms already control 99 percent of the nicotine supply, and the firms could soon dominate the growing e-cigarette market. Unless constrained by the laws of the country concerned, tobacco firms could raise electronic cigarettes prices and their profit, decreasing the incentive for smokers to switch to safer products, and protecting firms' tobacco cigarette sales revenue from competition.

- *Medicinal regulatory standards* require medicines to be free of toxicants, and for the manufacturer to certify that the medicine is produced under license at a site operating under good manufacturing practices. With current designs and materials it may be difficult to completely eliminate all toxicants from e-cigarette vapor, but the door should be left open should any manufacturer be able to afford to take safety and manufacturing responsibility to a higher level.
- *Light-touch* regulation is likely to require some proof of drug efficacy, and the standard (pharmacokinetic) method is to measure plasma nicotine during and after use of the drug. This is costly, and few brands have been tested.

In Sweden, tobacco cigarettes, cans of snus, nicotine patches, and gum can all be sold across the counter in the same shop. Electronic cigarettes could be sold the same way.

MANUFACTURING STANDARDS

Several refills may be required daily but the content per refill is not standardized. One cartridge may produce 150 to 300 puffs or more of vapor, but there is no standard or regulation to enforce this, or to ensure adequate nicotine delivery.

Electronic cigarettes vary in quality, and the product is still evolving. A switch from selling cartridges to selling disposable cartomizers (cartridge-atomizers) has ensured atomizers no longer need replacement. Reducing e-cigarette length and weight to mimic a tobacco cigarette has resulted in smaller batteries with lower capacity, but which often do not last a full day's vaping. Vaporization efficiency of popular electronic cigarette brands, if improved to match the best now available, would further increase the readiness of smokers to switch.

THE TIPPING POINT: NICOTINE E-CIGARETTES VERSUS TOBACCO

Cigarette volumes sold in the United States are now decreasing more rapidly than before, partly due to electronic cigarette sales, which are credited with an additional one percentage point decrease below the usual trend over recent years. As sales of electronic cigarettes continue to increase, cigarette volumes sold are likely to decrease slightly more steeply. Four major tobacco companies will be selling electronic cigarettes by the end of 2013; they will soon dominate that market and ensure increased quality of product, wide distribution, and further increases in electronic cigarette sales.

What is not clear is the proportion of current smokers who eventually become vapers and how long will they vape before losing interest and becoming ex-vapers.

Will the new vapers simply use electronic cigarettes to quit smoking, or will they go on to enjoy vaping as a safe way to continue to enjoy inhaling nicotine?

In either case, there are public health benefits, because fewer cigarettes are smoked. Cigarette makers will aim to make e-cigarette nicotine refills attractive enough to generate repeat sales.

The recent move of five major tobacco manufacturers (Altria, British American Tobacco, Imperial Tobacco, Lorillard, and Reynolds American) into the electronic cigarette market means electronic cigarettes are here to stay, as these firms have the capacity to rapidly fund, develop, and market improved products that can overcome current regulatory barriers. These firms also have the networks to sell nicotine refills daily, possibly jostling for display space alongside cigarettes at the nearest corner shop.

The tipping point may have been reached in the United States in the first quarter of 2013, when increasing electronic cigarette sales accounted for an estimated one percent decrease (out of a six percent decline) in national industry-wide cigarette sales (equal to 600 million cigarettes not sold).[60]

By showing they can reduce cigarette consumption, e-cigarettes will gain public support and public health credibility. E-cigarettes will still need much further research and regulations to guarantee safety of the product.

The achievement of the public health community has been to make cigarette smoking less popular and less desirable, so that cigarette sales have declined, so that the manufacturers are seeking alternatives to replace the revenues lost. As virtually any alternative is safer than cigarettes, their moves into less harmful

products such as electronic cigarettes and smokeless tobacco are difficult to criticize. Their motive is still profit, but the move would be good for public health. The public health community may regard it as galling and an affront to natural justice that its bête noire, the tobacco industry, whose products have killed 100 million people last century, will now be applauded for selling harm reduction electronic cigarettes.

Public health people are now well positioned to propose tougher than ever policies to reduce the continued sale of deadly cigarettes and encourage research and sale of less harmful substitutes. By advocating an approach based on "out with the bad, in with the good" they can expect increasing public support.

BRIEF BIBLIOGRAPHY ON ELECTRONIC CIGARETTES AND THEIR REGULATION

Library Briefing. Electronic cigarettes, 27 March 2013. Library of the European Parliament. http://www.europarl.europa.eu/eplibrary/Electronic-cigarettes.pdf

Action on Smoking and Health, London. Electronic cigarettes. Briefing. January 2013.
www.ash.org.uk/files/documents/ASH_715.pdf

J-F Etter. The electronic cigarette: an alternative to tobacco. Geneva, Switzerland, 2012. As e-book: Jean-François Etter, *The Electronic Cigarette: an Alternative to Tobacco?* CreateSpace Independent Publishing Platform, February 2013.

Key messages for policy makers

The current confusion around nicotine and misinformation around the risks of smokeless would be greatly improved by wide publicity for statements such as these:

MORTALITY RISKS AND CANCER RISKS VARY GREATLY BY PRODUCT

- Cigarettes and smoking tobacco are the most deadly recreation products on shop shelves.
- Two thirds of persistent smokers die from their smoking, losing on average, over 10 years of lifespan.[12, 37 in Part One]
- Nicotine has been widely used as a medicine since 1984 and is safe at the doses used in medicines.
- Nicotine products do not cause cancer or lung cancer, lung or heart disease.
- By contrast, tobacco smoking is the main cause of lung cancer, the leading cause of cancer deaths.

ADDICTION SCIENCE

- Virtually all tobacco smokers are addicted.
- Cigarette smoking is highly addictive, and more than nicotine by itself (the spectrum of addiction, *Chart 2*).
- Nicotine is the main cause of addiction to tobacco, but it does not act alone, aided by rituals and behavioral habits and possibly by other substances in tobacco and smoke.

INFORMATION FOR SMOKERS

Smokers switching to electronic cigarettes can reduce inhaled toxicants by approximately 99 percent. Smokers switching to smokeless can reduce their risk of dying sooner than non-smokers by about 95 percent.

Endnotes to Part 3

1 *Euromonitor International.* E-cigarettes: a US$2 billion global industry- who should be worried? Nov 23 2012. http://blog.euromonitor.com/2012/11/e-cigarettes-a-us2-billion-global-industry-who-should-be-worried.html

2 Esterl M. E-cigarettes draw fire from legislatures. *Wall Street J* 12 March 2012. www.online.wsj.com

3 Zhu Shu-Hong, Gamat A, Lee M, Cummins S, Yin L, Zoref L. The use and perception of electronic cigarettes and snus among the US population. PA 10-3. *Society Research Nicotine Tobacco Conference,* Boston March 2013.

4 Kell J. Altria to launch e-cigarette a cigarette demand softens. 25 April 2013. *Dow Jones Newswire.*

5 WHO FCTC Conference of the Parties. Electronic nicotine delivery systems, including electronic cigarettes. Report by the Convention Secretariat. Provisional agenda item 6.5 for the Fifth Session, Seoul November 2012. *Electronic nicotine delivery systems, including electronic cigarettes.* FCTC/COP/5/13. 18 June 2012. http://apps.who.int/gb/fctc/PDF/cop5/FCTC_COP5_13-en.pdf

6 Trehy M, Wei Ye, Hadwiger ME, Moore TW, Allgire JF, Woodruff JT, et al. Analysis of electronic cigarette cartridges, refill solutions, and smoke for nicotine and nicotine related impurities. *J Liquid Chromatography and Related Technologies* 2011;34:1442-58.

6a Laugesen M. Epton M, Frampton C, Glover M. Lea RA. Hand-rolled cigarette smoking patterns, compared with factory-made cigarette smoking in New Zealand men. *BMC Public Health* 2009, 9:194. http://www.biomedcentral.com/1471-2458/9/194

7 Goniewicz ML, Kuma T, Gawron M, Kuysak J, Kosminder L. Nicotine levels in electronic cigarettes. *Nicotine and Tob Res* 2013;15:158-166.doi:10.1093/ntr/nts103.

8 Chen Li-Lun. FDA summary of adverse reports on electronic cigarettes. (2013) 15 (2): 615-616 *Nicotine Tob Res* 2013;15:615-6.

9 McCauley L. An unexpected consequence of electronic cigarette use. *Chest* 2012;141:1110-1113.

10 Vardavas CI, Anagnostopoulos N, Kougias M, Evangelopoulou V, Connolly GN, Behrakis PH. Short term effects of using an electronic cigarette: impact on respiratory flow resistance impedance and exhaled nitric oxide. *Chest* 2012;141:1400-6.

11 Vardavas CI, Anagnostopoulos N, Kougias M, Evangelopoulou V, Connolly GN, Behrakis PH. Acute pulmonary effects of sidestream secondhand smoke at simulated car concentrations. *Xenobiotica* 2012; Dec 4. Epub ahead of print. doi:10.3109/00498254.2012.741272

12 Flouris AD, Chorti MS, Poulianiti KP, Jamurtas AZ, Kostikas K, Tzatzarakis MN et al. Acute impact of active and passive electronic cigarette smoking on serum cotinine and lung function. *Inhal Toxicol* 2013;25:91-101.

13 Hua M, Alfi K, Talbot P. Health-related effects reported by electronic cigarette users on on-line forums. *J Med Internet Res* 2013;15(4):e59.

14 Farsalinos K. How electronic cigarettes affect your lungs: results of an on-line survey of users. *Ashtray Blog: an electronic cigarette blog.* 2013 April.

15 Goniewicz ML, Zielinska-Danch W, Szoltysek-Boldys I, Jeliczek M, Sobczak A. Acute effects of electronic cigarette delivery systems (ENDS) on arterial stiffness in healthy cigarette smokers. POS3-11, Soc *Res Nicotine Tobacco,* Toronto 2011.

16 Flouris AD, Poulianiti KP, Chorti MS, Jamurtas AZ, Kouretas D, Owolabi EO, et al. Acute effects of electronic and tobacco cigarette smoking on complete blood count. *Food Chem Toxicol* 2012;50: 3600-3.

17 Farsalinos KE, Romagna G. Chronic idiopathic neutrophilia in a smoker, relieved after smoking cessation with the use of electronic cigarette: a case report. Clin Med Insights Case Rep 2013;6:15-21. Free PMC article.

18 Dawkins L, Turner J, Hasna S, Soar K. The electronic-cigarette: effects on desire to smoke, withdrawal symptoms and cognition. *Addict Behav* 2012 37;970-3.

19 Dawkins L, Turner J, Crowe E. Nicotine derived from the electronic cigarette improves time-based prospective memory in abstinent smokers. *Psychopharmacology*(Berl) 2013; Jan 24 (Epub ahead of print).

20 Burstyn I. *Peering through the mist: What does the chemistry of contaminants in electronic cigarettes tell us about health risks.* Technical report. July August 2013. Philadelphia PA: Drexel University. http://publichealth.drexel.edu/SiteData/docs/ms08/f90349264250e603/ms08.pdf

21 Ingebrethsen BJ, Cole SK, Alderman SL. Electronic aerosol particle size distribution measurements. *Inhal Toxicol* 2012;24:976-84.

22 Zhang Y, Sumner W, Chen DR. In vitro particle size distributions in electronic and conventional cigarette aerosols suggest comparable deposition patterns. *Nicotine Tob Res* 2013;15:501-8.

23 Laugesen, M. (2008) Safety Report on the Ruyan e-Cigarette Cartridge and Inhaled Aerosol. Christchurch, New Zealand: *Health New Zealand website.* http://www.healthnz.co.nz/RuyanCartridgeReport30-Oct-08.pdf, accessed 16 March 2012.

24 Goniewicz ML, Knysak J, Gawron M, Kosmider L, Sobsczak, Kurek J, Prokopowicz A, Jablonska-Czapla M, Rosk-Dulewska C, Havel C, Jacob P III J, Benowitz N. Levels of selected carcinogens and toxicants in vapor from electronic cigarettes. *Tob Control* March 6, 2013. 10.1136/tobaccocontrol-2012-050859.

25 Sobczak A, Kosmider L, Goniewicz M, Knysak J, Zaciera K, Kurek J. Substantial reduction in emission of selected carbonyls and volatile organic compounds from electronic cigarettes compared to tobacco cigarettes. POS 4-49. Soc. *Res Nicotine Tobacco Conference*, Boston March 2013.

26 Shihadah AL, Eissenberg T. Factors influencing the toxicant content of electronic cigarette vapor: device characteristics and puff topography. POS 4-42. Soc. *Research Nicotine and Tobacco Conference*, Boston March 2013.

27 Counts ME, Morton MJ, Laffoon SW, Cox RH, Lipowicz PJ. Smoke composition and predicting relationships for international commercial cigarettes smoked with three machine-smoking conditions. *Regul Toxicol Pharmacol* 2005;41:185-227. Appendix A, Canadian intensive smoke machine method: 10 puffs per cigarette, each puff 35 ml.

28 Williams M, Villarreal A, Bozhilov K, Lin S, Talbot P. Metal and silicate particles including nanoparticles are present in electronic cigarette cartomiser fluid and aerosol. PloS ONE 2013;8:e579987.

29 *US Pharmacopeia Convention* on Inhalation exposure, 2013. http://www.usp.org/sites/default/files/usp_pdf/EN/USPNF/key-issues/c232_final.pdf

30 Smith CJ, Livingston SD, Doolittle DJ. An international literature survey of 'IARC Group 1 carcinogens' reported in mainstream cigarette smoke. *Food Chem Toxicol* 1997;35:1107-30.

31 Chiba M. Masironi R. Toxic and trace elements in tobacco and tobacco smoke. *Bull World Health Organ* 1992;70:269-275.

32 Burns DM, Dybing E, Gray N, Hecht S, Anderson C, Sanner T. et al. (2008). Mandated lowering of toxicants in cigarette smoke: a description of the World Health Organization TobReg Proposal. *Tob Control.* 2008;17:132-41

33 Zar T, Graeber C, Perazella MA. Recognition, treatment, and prevention of propylene glycol toxicity. Semin Dial 2007;20:217-9.

34 Etter JF, Bullen C. Saliva cotinine levels in users of electronic cigarettes. *Eur Resp J.* 2011 (5): 1219-20.

35 Czogala J, Goniewicz M, Fidelus B, Zielinska-Danch W, Sobczak A. Assessment of passive exposure to aerosol from electronic cigarettes. PA 9-2. *Soc. Res Nicotine Tob Conference*, Boston March 2013.

36 McAuley TR, Hopke PK, Zhao, J. Babaian S. Comparison of the effects of e-cigarette vapor and cigarette smoke on indoor air quality. *Inhal Toxicol* October 2012; 24:850-857.

37 Pellegrino RM, Tinghino B, Mangiaracina G, Marani A, Vitali M, Protano C, et al. Electronic cigarettes: an evaluation of exposure to chemicals and fine particulate matter (PM). Ann Ig. 2012 Jul-Aug;24(4):279-88.

38 de Leeuw, G., Andreas EL, Anguelova MD, Fairall CW, Lewis ER, O'Dowd C, et al. Production flux of sea spray aerosol, Rev. *Geophys.* 2011; 49, RG2001, doi:10.1029/2010RG000349. ftp://ftp.etl.noaa.gov/users/cfairall/oceanobs/pubs/fy11/DELEEUW_SeaSrayFlux_REVGEO_2010RG000349.pdf

39 Harris TN, Stokes J Jnr, Summary of 3-year study of the clinical application of the disinfection of air by glycol vapor. *Am J Med Sci* 1945;209:152-156.

40 Pearson JL, Richardson A, Niaura RS, Vallone DM, Abrams DB. e-Cigarette Awareness, Use, and Harm Perceptions in US Adults. *Am J Public Health.* 2012; 102:1758-66.

41 Goniewicz KL, Zielinska-Danch W. Electronic cigarette use among teenagers and young adults in Poland. *Pediatrics.* 2012;130:879-885 http://pediatrics.aappublications.org/content/early/2012/09/12/peds.2011-3448

42 Use of e-cigarettes in Great Britain among adults and young people (2013). Fact sheet 33. London: Action on Smoking and Health. http://www.ash.org.uk/files/documents/ASH_891.pdf

43 Felberbaum M. Cigarette maker Lorillard's 1Q profit up 47 pct on higher pricing, e-cig sales lower costs. *Daily Journal* April 24, 2013. Comment from Murray Kessler, CEO of Lorillard. http://www.daily-journal.net/view/story/0355746fce8b42f4aa7d5e69cb849a2e/US--Earns-Lorillard/

44 Bullen, C, Howe C, Laugesen M, McRobbie H, Parag V, Williman J, Walker N. Electronic cigarettes for smoking cessation: a randomised controlled trial. Published Online September 8, 2013 http://dx.doi.org/10.1016/S0140-6736(13)61842-5 http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(13)61686-4/abstract

45 Bullen C, McRobbie H, Thornley S, Glover M, Lin R, Laugesen M. Effect of an electronic nicotine delivery device (e cigarette) on desire to smoke and withdrawal, user preferences and nicotine delivery: randomized cross-over trial. *Tob Control* 2010 April;19: 98-103. doi:10.1136/tc.2009.031567.

46 Dawkins L, Turner J, Roberts A, Soar K. 'Vaping' profiles and preferences: an online survey of electronic cigarette users. *Addiction* 2013;Mar 28, doi:10.1111/add.12150.{Epub ahead of print].

47 Foulds J, Veldheer S, Berg A. Electronic cigarettes (e-cigs): views of aficionados and clinical/public health perspectives. *Int J Clin Pract* 2011;65: 1037-42.

48 Regan AK, Promoff G, Dube SR, Arrazola R. Electronic delivery systems: adult use and awareness of the 'e-cigarette' in the USA. *Tob Control* 2013;22:19-23.

49 Smoking statistics, who smokes and how much. *ASH fact sheet 1.* London: Action on Smoking and Health. http://www.ash.org.uk/files/documents/ASH_106.pdf

50 50. TNS Opinion and Social. Special Eurobarometer 385. Attitudes of Europeans towards tobacco. Report to the European Commission. May 2012. http://ec.europa.eu/health/tobacco/docs/eurobaro_attitudes_towards_tobacco_2012_en.pdf

51 Lucy Popova and Pamela M. Ling. Alternative Tobacco Product Use and Smoking Cessation: A National Study. *Am J Public Health.* May 2013, Vol. 103, No. 5, pp. 923-930.

52 Vickerman KA, Carpenter KM, Altman T, Nash CM, Zbikowski SM. Use of electronic cigarettes among state tobacco cessation quitline callers. *Nicotine Tob Res* 2013; May 8 (Epub ahead of print).

53 Barbeau AM, Burda J, Siegel M. Perceived efficacy of e-cigarettes versus nicotine replacement therapy among successful e-cigarette users: a qualitative approach. *Addict Sci Clin Pract* 2013; 8 (1):5.

54 Caponnetto P, Auditore R, Russo C, Cappe GC, Polosa R. Impact of an electronic cigarette on smoking reduction and cessation in schizophrenic smokers: a prospective 12-month pilot study. *Int J Environ Res Public Health* 2013;10:446-61.

55 Polosa R, Caponnetto P, Morjaria JB, Papale G, Campagna D, Russo C. Effect of an electronic nicotine delivery device (e-Cigarette) on smoking reduction and cessation: a prospective 6-month pilot study. *BMC Public Health* 2011, 11:786 doi:10.1186/1471-2458-11-786. http://www.biomedcentral.com/1471-2458/11/786

56 Caponnetto P, Campagna D, Cibella F, Morgaria JB, Russo C, Polosa R. The efficacy and safety of an electronic cigarette (Eclat) study: a prospective 12-month randomized control design study. P54. *Soc. Res Nicotine and Tob.* (Europe) Abstracts. Helsinki 2012. www.srnt.org

57 Caponnetto P, Cibella F, Mancuso S, Campagna D, Arcidiacono G, Polosa R. Effect of a nicotine-free inhalator as part of a smoking cessation program. *Eur Respir J.* 2011 November 1, 2011;38 (5): 1005-1011,

58 US Court of Appeals. *Sottera Inc (NJoy) v Food and Drug Administration.* Appeal from the US District Court, District of Columbia. Decided Dec 7, 2010, no. 105032.

59 Czoli CD, Hammond D, White CM. Electronic cigarettes in Canada: prevalence of use and perceptions among young adults. POS-3-121. *Soc Research on. Nicotine and Tobacco Conference,* Boston; March 2013. www.srnt.org

60 Felberbaum M. Cigarette maker Lorillard's 1Q profit up 47 pct on higher pricing, e-cig sales lower costs. Comment from Murray Kessler, CEO of Lorillard. *Daily Journal* April 24, 2013. http://www.dailyjournal.net/view/story/0355746fce8b42f4aa7d5e69cb849a2e/US--Earns-Lorillard/

AMERICAN E-LIQUID
MANUFACTURING STANDARDS ASSOCIATION

Creating responsible and sustainable practices and process for the safe manufacturing of "e-liquids" used in electronic cigarettes.

Version 2.0 | 2.14.2014

E-LIQUID MANUFACTURING STANDARDS

RESPONSIBILITY • STANDARDS • TRANSPARENCY

877.68.AEMSA (23672) INFO@AEMSA.org www.AEMSA.org

Purpose

The purpose of these Standards is to create a responsible and sustainable practices and process for the safe manufacturing of "e-liquids" used in electronic cigarettes. Our members believe we have a responsibility to self-regulate the e-liquid manufacturing process based on professional criteria. AEMSA aims to accomplish this by creating, implementing and upholding standards for the manufacture of e-liquids. One of AEMSA's primary goals is to provide consumers with higher degrees of confidence our members' products are manufactured with professionalism, accuracy and safety

AEMSA standards are established based on the following Core Beliefs:

- We have a responsibility to verify the accuracy of any nicotine content in the products we distribute.
- We have a responsibility to ensure the quality and safety of all ingredients in our e-liquids.
- We have a responsibility to prepare our products in a clean, sanitary and safe environment.
- We have a responsibility to ensure our products are packaged and delivered in a safe manner.
- We have a responsibility to provide a level of transparency into the monitoring and verification process.

The 2012 AEMSA Standards are living documents and subject to changes according to the AEMSA corporate structure and procedures.

Scope

These standards apply to all AEMSA general members that engage in the manufacturing or processing of E-liquids. 2012 E-Liquid Manufacturing Standard will be used as a basis for:

- Evaluating compliance for membership acceptance
- Confirming compliance of existing membership

Definitions

Term	Definition
Active Age Verification	Taking active measures to ensure that all customers are of legal age. Can be accomplished in many ways including Photo Identification and 3rd party verification systems. Note: Having pop up box asking the person to indicate they are over a specified age is not Active Age Verification
ASTM - American Society for Testing and Materials	An international standards organization that develops and publishes voluntary consensus technical standards for a wide range of materials, products, systems, and services
Chain of custody	The chronological documentation or, showing the custody, control, transfer, analysis, and disposition of physical component; tracking a product along the supply chain to the point of sale
Components	A part or element of a larger whole; a substance that forms part of a mixture. Any substance, material or the tangible substance that goes into the manufacturing of e-liquid
Contaminants	An impurity or foreign substance present in a material or environment that affects one or more properties of the material
Custard Notes	Flavor compounds that impart a buttery, creamy, or custard taste or sensation. Most commonly used are acetoin, acetyl propionate and diacetyl
Dedicated Manufacturing Space	A clean safe environment that is used exclusively for the manufacturing of e-liquid
Diacetyl	A natural byproduct of fermentation. It is a vicinal diketone (two C=O groups, side-by-side) with the molecular formula C4H6O2. Diacetyl occurs naturally in alcoholic beverages and is added to some foods to impart a buttery flavor. It has been eliminated from many commercial flavorings due to risk of lung damage
Direct Operation	A facility or process where Full time employees for an organization directly supervise and oversee production and process
DIY	Do it Yourself
Electronic cigarette	Also known as an e-cigarette (e-cig) is an electrical inhaler that vaporizes a propylene glycol and/or glycerin-based liquid solution into an aerosol mist simulating the act of tobacco smoking
E-liquid	Liquid for producing vapor in electronic cigarettes, known as e-juice or e-liquid
E-liquid manufacturing	Fabrication: the act of making something (a product) from raw materials; to include all processes from supply acceptance to the point of customer delivery
Free-base	An amine or nitrogen-containing organic compound, such as nicotine, in its basic (high pH) form, in contrast to its acidic (low pH) form, which is often called the "salt" form. Unless an acid has been added to nicotine, or it is purchased as the salt, it is in the free-base form. Free-base describes the form of the compound, not its purity
Generally Recognized as Safe (GRaS)	Generally recognized as safe (GRAS) is an American Food and Drug Administration (FDA) designation that a chemical or substance added to food is considered safe by experts, and so is exempted from the usual Federal Food, Drug, and Cosmetic Act (FFDCA) food additive tolerance requirements
Indirect Operation	A facility or process where supervision and/or oversight of production and/or process for an organization is conducted by a 3rd party or contractor (subcontractor)

Mg / ml	Milligrams per Milliliter – a scale (or ratio) for measuring an ingredient component, in liquid form, where accuracy is measured in mg per ml - or a percentage equivalent
Nicotine	Nicotine is an alkaloid found in the nightshade family of plants (Solanaceae) that acts as a nicotinic acetylcholine agonist. The biosynthesis takes place in the roots and accumulation occurs in the leaves of the Solanaceae. It constitutes approximately 0.6–3.0% of the dry weight of tobacco and is present in the range of 2–7 µg/kg of various edible plants
NIST -The National Institute of Standards and Technology	A non-regulatory agency of the United States Department of Commerce. The institute's official mission is to: Promote U.S. innovation and industrial competitiveness by advancing measurement science, standards, and technology in ways that enhance economic security and improve our quality of life
OSHA	The United States Occupational Safety and Health Administration (OSHA) is an agency of the United States Department of Labor. Congress established the agency under the Occupational Safety and Health Act, was signed into law on December 29, 1970. OSHA's mission is to "assure safe and healthful working conditions for working men and women by setting and enforcing standards and by providing training, outreach, education and assistance"[2]. The agency is also charged with enforcing a variety of whistleblower statutes and regulations
PPM	Parts Per Million
SINGLE-USE ARTICLES	Utensils, containers and tools designed and constructed to be used once and discarded
Tamper Evident	Tamper-evident describes a device or process that makes unauthorized access to the protected object easily detected. Seals, markings or other techniques may be tamper indicating
Titration	Also known as titrimetry, is a common laboratory method of quantitative chemical analysis that is used to determine the concentration of an identified component; the determination of rank or concentration of a solution with respect to water with a pH of 7 (the pH of pure H2O under standard conditions)
USP (US Pharmacopoeia)	The United States Pharmacopeia (USP) is the official pharmacopeia of the United States, published dually with the National Formulary as the USP-NF. The United States Pharmacopeial Convention (usually also called the USP) is the nonprofit organization that owns the trademark and copyright to the USP-NF and publishes it every year. Prescription and over–the–counter medicines and other health care products sold in the United States are required to follow the standards in the USP-NF. USP also sets standards for food ingredients and dietary supplements
WTA (whole tobacco alkaloids)	A full-spectrum mixture of all alkaloids extracted from whole tobacco. WTA can contain, in addition to nicotine, anabasine, cotinine, myosmine, anatabine, and/or nornicotine, in varying compositions, largely dependent on the tobacco species

E-Liquid Manufacturing Standard

Article I. Verifying the accuracy of the nicotine content in products

Section 1.01 ..... Accuracy of nicotine

(a) All manufactures must confirm the accuracy of nicotine content upon delivery from supplier

Section 1.02 ..... Titrated/verified after dilution

(a) All nicotine must be titrated/verified for content accuracy after dilution to working level

Section 1.03 ..... Measuring nicotine equipment

(a) All equipment used in measuring nicotine from working level to final product must be either
  (i) NIST (calibrated)
  (ii) ASTM compliant (calibrated)

Section 1.04 ..... Tolerance level

(a) All products produced will be within the tolerance level of +/-10% nicotine content in final product

Section 1.05 ..... Maximum allowable nicotine content

(a) The maximum allowable nicotine content in final flavored product will be no greater than 36 mg / ml

Section 1.06 ..... Retail nicotine sold for unflavored/DIY nicotine

(a) Will follow the same criteria for verifying the nicotine content and quality on all batches when received and titrated after dilution at various sales levels

(b) Is not subject to maximum allowable nicotine content in final flavored product

Article II. Ensure the quality and safety of the all ingredients of in e-liquid

Section 2.01 ..... Nicotine Sources

(a) All manufacturers must purchase and comply with at least one of the following:
  (i) USP CERTIFIED nicotine (with evidentiary documentation from a certified lab)
  (ii) Free-base nicotine from suppliers who can provide source evidentiary documentation from a certified lab confirming (batched) nicotine conforms to the Nicotine Quality Standard (see Section 2.02)
  (iii) Purchase from nicotine suppliers who can provide evidentiary documentation from a certified lab confirming the incoming (batched) free-base nicotine conforms to the Nicotine Quality Standard (see Section 2.02)

Section 2.02 ..... Nicotine Quality Standard

(a) All nicotine used in manufacturing must meet the following nicotine quality standards:
  (i) Nicotine purity greater than or equal to 99.0% *
  (ii) Total combined of all other possible contaminants less than or equal to 1.0%
  (iii) Per existence of any solvent must not exceed 0.06%
  (iv) Per existence nicotine oxide less than or equal to 1%
  (v) Per existence nicotine-N-oxides less than or equal to 1%
  (vi) Cumulative heavy metals *content* cannot exceed 10ppm
  (vii) Cumulative Arsenic *content* cannot exceed 1ppm
  (viii) All diluents after source pure must be USP certified thru chain of custody

Section 2.03 ..... Base liquid ingredients

(a) Base liquid diluent ingredients such as Propylene Glycol, Vegetable Glycerin, Glycerol, or any other e-liquid bases (either regularly or exclusively) will be at a minimum level of USP (US Pharmacopoeia) grade certified

(i) Material must maintain full certification throughout chain of custody on raw materials used in manufacturing process
(ii) Manufacturer must exclusively use certified base products throughout the manufacturing process

Section 2.04 ..... Ingredients/ Components other than base liquids

(a) Ingredients/ Components other than base liquids will contain only safe or highest grade base materials
  (i) Flavorings (including menthol) used will be at a minimum of food grade and/or Generally Recognized as Safe (GRAS) standard certifications whenever the ingredient is produced at those standards
  (ii) Flavorings containing artificial food coloring will identify food coloring information to include coloring number in advertising and product descriptions
  (iii) Flavorings containing Custard Notes will identify advertising and product descriptions
  (iv) Water used (if any) will be either deionized or distilled
  (v) Alcohol and additional additives (if any) will be:
    1) Used in the purest form commercially available and safe for human consumption
    2) Minimum of US Food grade standards

Section 2.05 The following will not be added or used in the creation of e-liquids

(a) Including but not limited to:
  (i) Diacetyl
  (ii) WTA (whole tobacco alkaloids)
  (iii) Medicinal - or prescription medicinal
  (iv) Illegal or controlled substances
  (v) Caffeine
  (vi) Vitamins or Dietary supplements (other than for preservative purposes)
  (vii) Acetyl Propionyl (2,3--Pentanedione)
  (viii) Artifical Food Coloring
    1) AEMSA members will not add any artificial coloring or dyes during the e-liquid manufacturing process. Non vendor manufactured flavorings containing artificial food coloring will identify food coloring information to include coloring number in advertising and product descriptions
  (iv) AEMSA reserves the right to review, evaluate and deny/approve any potential substance used in the creation of e-liquids at any given time

Section 2.06 ..... Process/Records/Traceability

(a) Manufactures will maintain sufficient process and records to enable the manufacturer to trace any individual product distributed to the test results for nicotine content to include source nicotine (see section 2.02)

Article III. Clean, Sanitary and Safe Preparation of Products

Section 3.01 ..... General

(a) All Lab/Mixing employees are required to be fully familiar with all AEMSA standards
  (i) There will be a special emphasis placed on nicotine handling, storage and clean-up
(b) Each member will create and maintain written lab/mixing protocol and make accessible to all lab/mixing employees
(c) All Persons allowed in process area must comply with applicable protection/ safety and standards
(d) All products will be created and/or bottled in dedicated manufacturing space reserved exclusively for e-liquid

Section 3.02 ..... Manufacturing Environment

(a) Manufacturing processes will meet food preparation standards to include

(i) Non-porous sanitized preparation work surface

(b) All surfaces in lab/mixing area (floors, counters, etc.) shall be cleaned with anti-bacterial agents at least once each day and after any spill of any mixing ingredient or any possible-contaminants

(c) Equipment will be cleaned by FDA Approved Chemical Sanitation or autoclave

(d) All supplies and material will be disposed of in a manner that is appropriate to component disposal - proper disposal of production material

(e) There shall be no open fans, dusty boxes and/or other potential sources of airborne contaminants etc. in dedicated space

(f) All bottles and materials unpacked outside of dedicated lab/mixing space

Section 3.03 ..... Hand washing / sanitation

(a) Not in sink used for cleaning mixing utensils, and/or other e-liquid materials

(b) Minimum 20 seconds with commercial (food handler's grade) antibacterial hand washing agent and warm water

(c) Hands washed each and every time entering mixing room

(d) After bathroom use, coughing, sneezing, eating and/or drinking, engaging in any other activities which potentially expose hands to any form of potential contaminants

(e) During mixing as often as necessary to remove any mixing products on hands

(f) Before proceeding to a subsequent mixing session -> to prevent any cross contamination from one batch to the next

Section 3.04 ..... Health / illness

(a) All open wounds or abrasion will be properly covered

(b) Any/All mixing employees report any illness/abrasion(s)/lesions to person in charge before entering the process

(c) Employees must report to person in charge if exposed to any contagion or infection - viral or bacterial - from anywhere (including others in their homes, other work environments, other domiciles, etc.) before entering lab/mixing area

(i) Such exposure/conditions excludes said individual from entering mixing room for a period of three (3) asymptomatic days have passed and/or cleared with medical documentation (equivalent to commercial food handling)

(ii) Discharge from eyes, nose and/or mouth:

(iii) Report to business any persistent discharge from eyes, nose, and/or mouth. Any employee exhibiting such symptoms shall not enter the mixing room until such symptoms cease

Section 3.05 ..... Eating/Drinking

(a) No eating, drinking, vaping and/or smoking in the lab/mixing area at any time

Section 3.06 ..... Hair Restraints

(a) Each member must establish written hair and beard standards

Section 3.07 ..... Animals

(a) No animals shall be permitted in the mixing room at any time for any reason

Section 3.08 ..... POISONOUS OR TOXIC MATERIALS

(a) POISONOUS OR TOXIC MATERIALS shall be stored so they cannot contaminate PRODUCT COMPONENT, FOOD, EQUIPMENT, UTENSILS, and SINGLE-USE ARTICLES by:

(i) Separating the POISONOUS OR TOXIC MATERIALS by spacing or partitioning

(ii) Locating the POISONOUS OR TOXIC MATERIALS in an area that is not above PRODUCT COMPONENTS, FOOD, EQUIPMENT, UTENSILS, or SINGLE-USE ARTICLES

(iii) This does not apply to EQUIPMENT and UTENSIL cleaners and SANITIZERS that are stored in WAREWASHING areas for

availability and convenience if the materials are stored to prevent contamination of PRODUCT COMPONENT, FOOD, EQUIPMENT, UTENSILS, LINENS, and SINGLE-SERVICE and SINGLE-USE ARTICLES

(iv) All POISONOUS OR TOXIC MATERIALS will be disposed of in a safe manner

(v) Only those POISONOUS OR TOXIC MATERIALS that are required for the operation and maintenance of a lab/mixing area, such as for the cleaning and SANITIZING of EQUIPMENT and UTENSILS and the control of insects and rodents, shall be allowed in a lab/mixing area (kept sealed and separate - never above - from any/all mixing supplies)

(vi) A container previously used to store POISONOUS OR TOXIC MATERIALS may not be used to store, transport, or dispense any other substance

Section 3.09 ..... Employee Safety

(a) Employers MUST provide their employees with a workplace that does not have serious hazards and follow all relevant OSHA safety and health standards including - but not limited to - the following mandatory personal protective equipment (P.P.E.):

(i) Eye protection

(ii) Lab Coat / Apron

(iii) Fully covered footwear

(iv) All manufacturing spaces must have easily accessible

1) First aid kit

2) Emergency eye wash kit

Article IV. Safe Packaging and delivery of products

Section 4.01 ..... Child proof caps

(a) Child proof caps required for all consumer level e-liquid products

(b) Zero Nicotine Products do not require child proof caps

Section 4.02 ..... Tamper evident packaging

(a) All Products require tamper evident packaging once leaving vendor chain of custody

Section 4.03 ..... Labeling

(a) Smear Resistant Labeling is required on all e-liquid products

(i) Must pass "30 second submerged" test for all required elements

(b) Nicotine content must be clearly displayed

(c) Safety and health Warning must be clearly displayed

(i) Contains Nicotine

(ii) Keep away from Children and Pets

(d) Nicotine Traceability elements (i.e. Batch ID or nicotine batch ID or production date)

Section 4.04 ..... Delivery

(a) All shipped liquid must be bagged or wrapped to provide waterproof barrier between packaging and product for spill protection

(b) Safe handling information must be included in all packaging

Section 4.05 ..... Active age verification

(a) All Vendors must use Active age verification for all sales (retail and/or online) (

b) AMESA Members will not knowingly sell products to any persons under the legal smoking age

Article V. Transparency into the monitoring and verification process

Section 5.01 ..... Within the organization

(a) Members must provide information to applications and compliance committees required to establish compliance including:
  (i) Documented evidence of compliance
    1) Photographic and Video evidence
    2) Unfettered access to facilities for inspection (scheduled and/or unscheduled)
    3) Process and records
(b) Member to member profiles will contain only minimal information for the identification and communication amongst and between members
  (i) Current status of compliance - by facility
  (ii) Contact Information
    1) Name
    2) DBA
    3) Email
    4) Phone
    5) Location(s)/ Facilities of production

Section 5.02 ..... To the consumer

Note: Subsections (a) and (b) are already posted on AEMSA website. **Subsections (c) and (d) are intended for specific information warranted situations ONLY; these may include - but not limited to - allergy sensitivities, other specific medical conditions/sensitivities, etc.** Subsection (e) shall be available on member's web site

(a) A substantive version of the AEMSA Standards be published on Website
(b) AEMSA Membership Status
(c) **Members will provide consumers tracking nicotine test results as far back as the source nicotine**
  (i) Information on the supplier may be redacted to protect intellectual property and trade secrets
  (ii) The member may charge a reasonable and fair fee for said tracing requests
(d) Members will provide answers to consumers on ingredients of products
  (i) Yes/No answers to specific questions as pertains to specific customer sensitivity questions
  (ii) No intellectual property or trade secrets of the e-liquid ingredient has to be revealed
    1) This includes revealing the source supplier and trademarked/brand name ingredient
(e) Clearly identified products that are not manufactured by AEMSA Members
    1) If the member sells liquid that is manufactured in a non AEMSA compliant facility it must:
    2) Clearly identify/ differentiate products that are AEMSA compliant and those that are not AEMSA compliant on a product by product basis

Section 5.03 ..... To potential regulators

(a) To be decided on case by case basis

AEMSA

An all volunteer nonprofit 501(c)(6) Professional Trade Association - is the first, and only, Manufacturers' Trade Association completely dedicated to creating Reasonable, Realistic and Sustainable Standards for the manufacture of American made e-liquids. AEMSA is consumer founded, formation facilitated and led by consumer volunteers who have no financial involvement in the industry.

AEMSA Standards are one delineation of Good Manufacturing Practices (cGMPs) representing responsible and professional Self-Regulation and Product Stewardship. AEMSA, with help from highly credentialed scientific and medical Subject Matter Experts (SMEs), has established verifiable manufacturing Standards demanding the highest obtainable quality ingredients, accuracy in content, professional manufacturing environments, professional packaging and transparency.

Our Members all agree to scheduled and unscheduled (unannounced) inspections.

AEMSA advocates Tobacco Harm Reduction. Our Standards (cGMPs) enhance Consumer Confidence in the Quality and content Accuracy of the products our Members sell. Consumer Protections are enhanced through multiple verifications.

Subject Matter Experts (SMEs)

ALL VOLUNTEERS

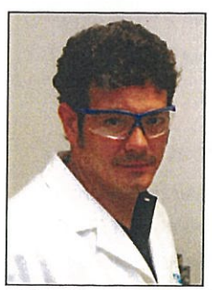
ADVOCATING AND SUPPORTING MEDICAL AND SCIENTIFIC RESEARCH

Dr. Kistler is a Chemistry Instructor and Researcher at Penn State University. He has a Ph.D. in Physical Chemistry (Temple University) and an MS in organic chemistry (University of Illinois).

KURT KISTLER, Ph.D.
Chemistry Consultant

Dr. Konstantinos Farsalinos is a Cardiologist and Researcher at the Onassis Cardiac Surgery Center and at Medical Imaging Research Center in Leuven-Belgium. He has been dedicated to research on e-cigarettes since 2011.

KONSTANTINOS FARSALINOS, MD
Medical Consultant



Dr. Melvin serves as the Group Leader of Enthalpy Analytical's Liquid Chromatography Laboratory. He has a Ph.D. in Organic Chemistry from Wake Forest University.

MATT MELVIN, Ph.D.
Chemistry Consultant

AEMSA Verifications:

- Multi-Stage product testing and analysis
- Evidentiary Documentation • Traceability
- On-Site Inspections (scheduled and unscheduled)
- Random product testing

On our website "Members" page, this logo is displayed next to members logos who have earned certification.

Advocating Good Manufacturing Practices (cGMPs) for Rigorous Manufacturing Standards, Re-fillable e-liquids and Tobacco Harm Reduction.

Advocacy and Presentations

- FDA Public hearing presentation Dec. 17, 2012
- FDA "Listening Session" March 21, 2013
- FDA "Listening Session" July 12, 2013

Tobacco Merchants Association Annual Meeting and Industry Conference May 15-17, 2013
Keynote speaker: Mitch Zeller, CTP/FDA

- AEMSA presented on Self-Regulation

More Advocacy and Industry presentations scheduled, watch our website and Facebook page (group/aemsapublic) for announcements

Adoption rates are more than nicotine replacement and physical emulations – the many combinations of gear and refillable e-liquids allows user customizations to subjective preferences. This all contributes to efficacy.

AEMSA General Members

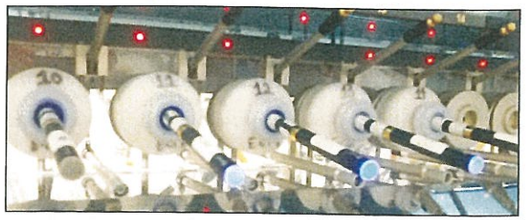
AEMSA Standards,
and ALL of AEMSA, grew from the
FIVE CORE BELIEF STATEMENTS

We have a responsibility to:

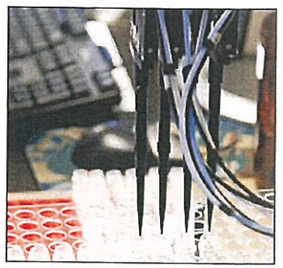
- Verify the accuracy of any nicotine content in the products we distribute.
- Ensure the quality of all ingredients in our e-liquids.
- Prepare our products in a clean, sanitary and safe environment.
- Ensure our products are packaged and delivered in a safe manner.
- Provide a level of transparency into the monitoring and verification process.

AEMSA advocates Tobacco Harm Reduction and supports informative/factual ongoing Scientific and Medical Research/testing to effectively and accurately analyze any and all potential health implications of this newer Harm Reduction alternative.

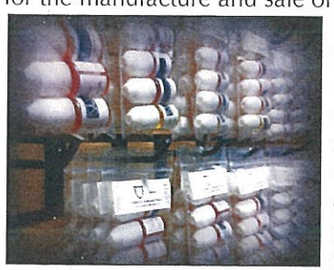
AEMSA Member Benefits
include, but are not limited to:



- Members and their customers know products are made in compliance with professional Science based Manufacturing Standards (cGMPs).
- Access to, and **input from, AEMSA's highly credentialed Subject Matter Experts (SMEs)**
- Only General (manufacturing) Members have final vote on ALL Standards, By-Laws and Dues. One Member = One Vote.
- **Product Liability** Insurance discounts.
- Access to our (free) Production Tracking Database software.
- **FDA and industry advocacy representation by a Registered Nonprofit 501(c)(6) Professional Trade Association - AEMSA represents its Membership.**



AEMSA has been created, in both form and function, to accommodate any and all American e-liquid manufacturers who choose to participate. Our structure is designed to facilitate collaboration, growth, creativity and to influence reasonable, realistic and sustainable regulation for the manufacture and sale of electronic cigarette e-liquids. We have established processes along with a full structure for various committees, evaluations, reviews, amendments, and more.



Active in the Community:
Receiving, Evaluating and Including Community Input/Feedback

- AEMSA attends Industry and Related Events
- AEMSA follows ECF: www.e-cigarette-forum.com and other industry forums and publications
  - See ECF Forum "INFO ZONE"/News for AEMSA interview 8/15/13
- AEMSA follows Industry Studies and Research
- AEMSA follows The Vape Team: www.VapeTeam.com and other industry broadcasts

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AEMSA encourages (more-so we implore) any and all **regulators** to learn about these products and read Published and Peer reviewed studies **BEFORE PROPOSING** and/or **ENACTING ANY REGULATION.**

Notable research sources available:

Dr. Konstantinos Farsalinos, Dr. Michael Seigel, Dr. Riccardo Polosa, Dr. Joel Nitzkin, Dr. Brad Radu, Professor Etter, Dr. Chris Bullen, Dr. Murray Laugesen, Professor Igor Burstyn, ClearStream LIFE, ClearStream Air and others.

Research Links: www.AEMSA.org/Links

Ecigarette Research Advocates Group

www.ecigarette-research.com

AMERICAN E-LIQUID MANUFACTURING STANDARDS ASSOCIATION

AEMSA

A Nonprofit 501(c)(6)
Professional Trade Association
Launched October 8, 2012

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AEMSA Advocates Electronic Cigarette products for adult use only. AEMSA supports banning sales to minors

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