

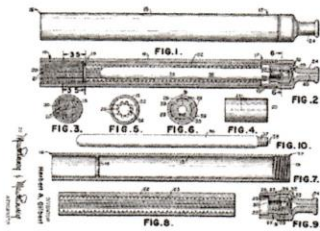
Emerging Issues of Electronic Nicotine Delivery Devices (ENDS) (aka Electronic Cigarettes or E-Cigarettes)

Barry Hummel, Jr., MD, FAAP
Quit Doc Research and Education Foundation

History of E-Cigarettes

- 1963: Herbert A. Gilbert files a US Patent as the first person to conceive of a smokeless cigarette.
- His concept? Create "an object to provide a safe and harmless means for and method of smoking by replacing burning tobacco with heated, moist flavored air; or by inhaling warm medication into the lungs in case of a respiratory ailment under the direction of a physician."

History of E-Cigarettes

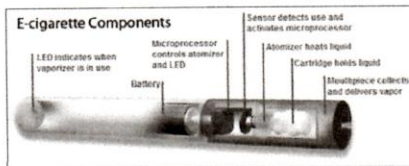


History of E-Cigarettes

- 2003: The electronic cigarette is first developed in Beijing, China by Hon Lik, a 52 year old pharmacist, inventor and smoker.
- April 2006: Electronic cigarettes, imported from China, introduced to Europe
- 2006-2007: Electronic cigarettes, imported from China, introduced to the U.S.

History of E-Cigarettes

- Modern E-Cigarette designs are similar to the original Gilbert patent with one key change: the devices are designed to simulate cigarette smoking and deliver heated nicotine to the user, not "moist flavored air".



History of E-Cigarettes

- Initial models were fairly expensive (\$150-\$250), and were mostly sold online and in mall kiosks.



History of E-Cigarettes

- They were marketed as safe, creating "harmless water vapor".



History of E-Cigarettes

- Smoking Everywhere, one of the early product leaders, even used celebrity endorsements.



History of E-Cigarettes



WFAA TV, Dallas, Texas, November 2008

History of E-Cigarettes

- March 2008: Turkey's Health Ministry bans the sale and importation of e-cigarettes.
- September 2008: The World Health Organization (WHO) proclaims that it does not consider the electronic cigarette to be a legitimate smoking cessation aid and demands that marketers immediately remove from their materials any suggestions that the WHO considers electronic cigarettes safe and effective.

History of E-Cigarettes

- January 2009: Australia bans the possession and sale of electronic cigarettes which contain nicotine, citing that "every form of nicotine except for replacement therapies and cigarettes are classified as a form of poison."
- March 2009: Canada bans the sale, advertising and import of electronic cigarettes. Health Canada advises Canadians not to purchase or use them, claiming they contain a "known irritant" (propylene glycol.)

History of E-Cigarettes

- March 2009: FDA adds electronic cigarettes to Import Alert 66-41 and directs the U.S. Customs and Border Protection to reject the entry of electronic cigarettes into the United States.
- March 2009: FDA notifies electronic cigarette company "Smoking Everywhere" that its shipments have been refused entry into the U.S. The FDA maintains that electronic cigarettes "appears to be a combination drug-device product" that requires preapproval, registration and listing with the FDA.

History of E-Cigarettes

- April 2009: *Smoking Everywhere* files a federal complaint seeking an injunction against the FDA with respect to the FDA's attempts to ban the import of Electronic Cigarettes. *Smoking Everywhere* contends that the FDA has no authority over electronic cigarettes, as they are a "tobacco product" and the FDA's attempt to regulate them infringes on Congress's intent to withhold FDA jurisdiction over tobacco products. They contend that electronic cigarettes are not "drugs" or "drug delivery systems," under 21 U.S.C 321(g).
- May 2009: NJOY (Sottera) joins *Smoking Everywhere* lawsuit against FDA.

History of E-Cigarettes

- June 2009: President Obama signs into law the Family Smoking Prevention and Tobacco Control Act, giving the FDA the power to regulate the tobacco industry. Although nicotine and cigarettes as a whole cannot be banned outright, flavoring such as fruit or mint can. Additionally, new tobacco products seeking to enter the market will be required to meet FDA pre-market standards, which could affect electronic cigarette regulation.
- June 2010: American Medical Association (AMA) House of Delegates (HOD) passes a policy urging the FDA to regulate e-cigarettes as drug delivery devices.

History of E-Cigarettes

- December 2010: U.S. Court of Appeals in Washington rules the FDA can only regulate e-cigarettes as a tobacco product, unless therapeutic claims are made by a company.
- April 2011: FDA announces it will regulate e-cigarettes as it currently regulates traditional cigarettes and other tobacco products under the Tobacco Control Act. However, any e-cigarette products advertising claims of helping the user to stop smoking or providing any other health benefit will be more strictly regulated as a drug or medical device.

The "Science" of E-Cigarettes

- Virtually every study published on e-cigarettes, regardless of the outcome, has been a small pilot study with inadequate control groups.
- As a result, virtually every study suggests more comprehensive research on larger groups of patients.
- This is what the FDA hoped to accomplish by classifying e-cigarettes as a medical device; this is what the industry fought in court to avoid.

The "Science" of E-Cigarettes

- Initial FDA Study (May 2009)
 - Tested cartridges from 2 leading brands of e-cigarettes for nicotine levels and other chemicals.
 - Division of Pharmaceutical Analysis (DPA) showed that the product contained detectable levels of known carcinogens and toxic chemicals to which users could potentially be exposed, including diethylene glycol (antifreeze), tobacco-specific nitrosamines (carcinogens), and several tobacco-specific impurities (anabasine, myosmine, and B-nicotyrine) suspected of being harmful to humans.
 - DPA also found large variations in nicotine delivery per puff.

The "Science" of E-Cigarettes

- "Effect of an electronic nicotine delivery device (e-cigarette) on desire to smoke and withdrawal, user preferences and nicotine delivery: randomised cross-over trial" University of Auckland, NZ (*Tobacco Control* 2010;19:98-103).
 - Methods:
 - Single-blind, randomized repeated measures using 16 mg ENDS, 0 mg ENDS, Nicorette Inhalator, and regular cigarettes.
 - 40 participants surveyed on desire to smoke after overnight abstinence using an 11-point scale.

The "Science" of E-Cigarettes

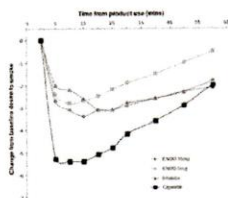


Figure 2 Change in desire to smoke from baseline over the first hour after each product use.

The "Science" of E-Cigarettes

- "Effect of an electronic nicotine delivery device (e-cigarette) on desire to smoke and withdrawal, user preferences and nicotine delivery: randomised cross-over trial" University of Auckland, NZ (*Tobacco Control* 2010;19:98-103).
 - Results:
 - 16 mg ENDS reduced desire to smoke similar to Nicorette inhalator.
 - Blood nicotine levels were also similar, and much less than patients using regular cigarettes.
 - Conclusion: **Further research is needed!**

The "Science" of E-Cigarettes

- "Effect of an Electronic Nicotine Delivery Device (e-Cigarette) on Smoking Reduction and Cessation" (*BMC Public Health*. 2011;11, p. 786).
 - Methods:
 - Prospective proof of concept study.
 - 40 smokers unwilling to quit tobacco use were enrolled in a 24-week study
 - Only 27 participants completed the study.

The "Science" of E-Cigarettes

- "Effect of an Electronic Nicotine Delivery Device (e-Cigarette) on Smoking Reduction and Cessation" (*BMC Public Health*. 2011;11, p. 786).
 - Results:
 - Sustained 50% reduction in per day cigarette use in 32.5% of participants.
 - Sustained 80% reduction in cigarette use in 12.5% of participants.
 - Sustained abstinence in 22.5% of participants.
 - Conclusions: E-cigs decrease consumption in smokers NOT intending to quit.

The "Science" of E-Cigarettes

- "Electronic Cigarettes As a Smoking-Cessation Tool: Results from an Online Survey". Boston University School of Public Health. (*Am J Prev Med* 2011;40(4):472-475).
 - Methods
 - Anonymous, cross-sectional online survey of 222 first-time purchasers of Blu E-cigarettes.
 - Primary outcome was smoking abstinence at 6 months.

The "Science" of E-Cigarettes

- "Electronic Cigarettes As a Smoking-Cessation Tool: Results from an Online Survey". Boston University School of Public Health. (*Am J Prev Med* 2011;40(4):472-475).
 - Results
 - 6-Month point prevalence of smoking abstinence among e-cigarette users in the sample was 31%; almost half reported some period of abstinence during the study
 - 34% of the non-smokers (10.7% of all participants) were using no nicotine-containing products.
 - 66.9% reported a reduction in cigarettes use.

The "Science" of E-Cigarettes

- "Electronic Cigarettes As a Smoking-Cessation Tool: Results from an Online Survey". Boston University School of Public Health. (Am J Prev Med 2011;40(4):472-475).
- Conclusions: E-cigarettes may hold promise as a smoking-cessation method and **they are worthy of further study.**

The "Science" of E-Cigarettes

- "Electronic Cigarettes (E-Cigs): Views of Aficionados and Clinical/Public Health Perspectives". (Int J Clin Pract. 2011;65(10): 1037-1042)
- Methods
 - Face-to-face interviews with 104 experienced e-cig users at a National Vapers Club Convention.
 - Poorly designed study with obvious bias throughout the article
 - Main problem: interviews conducted among committed users with no intention of overcoming nicotine addiction.

The "Science" of E-Cigarettes

- "Electronic Cigarettes (E-Cigs): Views of Aficionados and Clinical/Public Health Perspectives". (Int J Clin Pract. 2011;65(10): 1037-1042)
- Results
 - 78% of interviewees had not used tobacco in the prior 30 days.
 - On average, respondents had tried to quit using tobacco nine times before using e-cigs
 - 75% started using e-cigs with the intention of quitting smoking and **almost all felt that they had succeeded.**

The "Science" of E-Cigarettes

- "Electronic Cigarettes (E-Cigs): Views of Aficionados and Clinical/Public Health Perspectives". (Int J Clin Pract. 2011;65(10): 1037-1042)
- Conclusions
 - "Until we have more evidence on the safety and efficacy of e-cigs for smoking cessation, smokers should be advised to use proven treatments (e.g. counseling and FDA-approved medicines). However, for those who have successfully switched to e-cigs, the priority should be **staying off cigarettes, rather than quitting e-cigs.**"

The "Science" of E-Cigarettes

- "Conventional and electronic cigarettes (e-cigarettes) have different smoking characteristics." University of California - Riverside. (Nicotine Tob Res. 2010; 12(9):905-12.)
- Methods
 - Vacuum was measured using manometers coupled with smoking machines.
 - Density of aerosol was measured spectrophotometrically
 - Data compared to traditional cigarettes.

The "Science" of E-Cigarettes

- "Conventional and electronic cigarettes (e-cigarettes) have different smoking characteristics." University of California - Riverside. (Nicotine Tob Res. 2010; 12(9):905-12.)
- Results
 - Vacuum required to smoke e-cigarettes was higher than conventional cigarettes.
 - Density of aerosol among e-cigarettes dropped after the first ten puffs, and higher vacuums were needed to generate aerosol as the puff number increased.

The "Science" of E-Cigarettes

- "Conventional and electronic cigarettes (e-cigarettes) have different smoking characteristics." University of California – Riverside. (Nicotine Tob Res. 2010; 12(9):905-12.)
 - Discussion
 - "Generally, e-cigarettes required stronger vacuums (suction) to smoke than conventional brands, and the effects of this on human health could be adverse."
 - "(This) makes dosing non-uniform over time and calls into question their usefulness as nicotine delivery devices."

The "Science" of E-Cigarettes

- "Electronic nicotine delivery systems: is there a need for regulation?". University of California – Riverside. (Tobacco Control 2011;20:47-52.)
 - Methods
 - Six brands of ENDS were evaluated, including NJOY and Smoking Everywhere.
 - Researchers looked at design, nicotine content, labeling, leakiness, defective parts, disposal, errors in filling orders, instructional manuals, and advertising.

The "Science" of E-Cigarettes

- "Electronic nicotine delivery systems: is there a need for regulation?". University of California – Riverside. (Tobacco Control 2011;20:47-52.)
 - Results
 - While basic design among ENDS is similar across brands, specific design features varied significantly.
 - Fluid contained in cartridge reservoirs leaked out of most brands.
 - Labeling of cartridges was very poor.

The "Science" of E-Cigarettes

- "Electronic nicotine delivery systems: is there a need for regulation?". University of California – Riverside. (Tobacco Control 2011;20:47-52.)
 - Results
 - Print an internet materials often contained information or made claims for which there is currently no scientific proof.
 - None gave instructions for disposal of spent cartridges, which generally contain leftover liquid.
 - Conclusions: Data indicates that regulation of manufacturing, quality control, sales, and advertising of ENDS is needed.

The "Science" of E-Cigarettes

- "Short-term Pulmonary Effects of Using an Electronic Cigarette." (CHEST.2012;141(6): 1400-1406.)
 - Methods
 - 30 healthy smokers received pulmonary standard function tests after five-minutes of e-cigarette use.

The "Science" of E-Cigarettes

- "Short-term Pulmonary Effects of Using an Electronic Cigarette." (CHEST.2012;141(6): 1400-1406.)
 - Results
 - Immediate significant decrease in fraction of exhaled nitric oxide (reflective of an increase in airway inflammation).
 - Immediate significant increase in airway resistance.

The "Science" of E-Cigarettes

- "Short-term Pulmonary Effects of Using an Electronic Cigarette." (CHEST.2012;141(6): 1400-1406.)
 - Conclusions:
 - "e-Cigarettes assessed in the context of this study were found to have immediate adverse physiologic effects after short-term use that are similar to some of the effects seen with tobacco smoking; however, the long-term health effects of e-cigarette use are unknown but potentially adverse and worthy of further investigation."

The "Science" of E-Cigarettes

- "Levels of selected carcinogens and toxicants in vapour from electronic cigarettes." Medical University of Silesia, Sosnowiec, Poland. (*Tob Control* 2013;0:1-7.)
 - Methods
 - Vapors were generated from 12 brands of e-cigarettes and a reference product (Nicorette inhalator) using a modified smoking machine.
 - Selected toxic compounds were extracted from vapors in a solid or liquid phase for analysis.

The "Science" of E-Cigarettes

- "Levels of selected carcinogens and toxicants in vapour from electronic cigarettes." Medical University of Silesia, Sosnowiec, Poland. (*Tob Control* 2013;0:1-7.)
 - Results
 - Some toxic substances were identified in e-cigarette vapors (formaldehyde, acetaldehyde, acrolein, toluene, and two nicotine-specific nitrosamines).
 - Levels ranged from 9-450 times slower than the levels of the same chemicals in cigarette smoke.
 - Levels were similar to the reference product.

The "Science" of E-Cigarettes

- "Levels of selected carcinogens and toxicants in vapour from electronic cigarettes." Medical University of Silesia, Sosnowiec, Poland. (*Tob Control* 2013;0:1-7.)
 - Conclusions
 - "Findings are consistent with the idea that substituting tobacco cigarettes with e-cigarettes may substantially reduce exposure to selected tobacco specific toxicants."
 - "E-cigarettes as a harm reduction strategy among smokers unwilling to quit warrants further study."

The "Science" of E-Cigarettes

- "Variable and potentially fatal amounts of nicotine in e-cigarette nicotine solutions." Washington State University/University of Utah. (*Tob Control* 2013;0:1-2.)
 - Methods
 - Samples from seven different e-cigarette nicotine solutions were analyzed by liquid chromatography and mass spectrometry.

The "Science" of E-Cigarettes

- "Variable and potentially fatal amounts of nicotine in e-cigarette nicotine solutions." Washington State University/University of Utah. (*Tob Control* 2013;0:1-2.)
 - Results
 - All solutions contained nicotine at levels less than or equal to what was marked or expected given the manufacturer concentration ranges provided.
 - All samples provided could be toxic or lethal if taken other than directed.

The "Science" of E-Cigarettes

- "Variable and potentially fatal amounts of nicotine in e-cigarette nicotine solutions." Washington State University/University of Utah. (Tob Control 2013;0:1-2.)
 - Conclusions
 - Nicotine concentration range of e-cigarette solutions varies by manufacturer, and there is no standard dose for each strength category.
 - Fatal dose of nicotine is 30-60 mg for adults, and 10 mg in children; results confirm that e-cigarette cartridges contain potentially lethal doses of nicotine.

The "Science" of E-Cigarettes

- "Variable and potentially fatal amounts of nicotine in e-cigarette nicotine solutions." Washington State University/University of Utah. (Tob Control 2013;0:1-2.)
 - Conclusions
 - "We believe nicotine solutions should be regulated and accurately labeled with appropriate warnings and recommend healthcare providers screen for use of e-cigarettes and warn of potential dangers of toxicity risk in children."

The "Science" of E-Cigarettes

- "Electronic nicotine delivery systems: adult use and awareness of the 'e-cigarette' in the USA." Office on Smoking and Health, CDC. (Tobacco Control 2013;22:19-23.)
 - Methods
 - Consumer-based mail-in survey of 10,587 adults in 2009 and 10,328 adults in 2010.
 - Surveys were used to monitor awareness, ever use of ENDS, past month use of ENDS, and assess demographics.

The "Science" of E-Cigarettes

- "Electronic nicotine delivery systems: adult use and awareness of the 'e-cigarette' in the USA." Office on Smoking and Health, CDC. (Tobacco Control 2013;22:19-23.)
 - Results
 - In US, awareness of ENDS doubled from 2009 to 2010 (16.4% to 32.2%)
 - In US, ever use quadrupled from 2009 to 2010 (0.6% to 2.7%)
 - Ever use of ENDS was most common among women and those with lower education.

The "Science" of E-Cigarettes

- "Electronic nicotine delivery systems: adult use and awareness of the 'e-cigarette' in the USA." Office on Smoking and Health, CDC. (Tobacco Control 2013;22:19-23.)
 - Results
 - Current smokers and tobacco users were most likely to try ENDS.
 - Current smokers who tried ENDS did NOT say that they planned to quit smoking more often than smokers who had never tried them.

The "Science" of E-Cigarettes

- "Electronic nicotine delivery systems: adult use and awareness of the 'e-cigarette' in the USA." Office on Smoking and Health, CDC. (Tobacco Control 2013;22:19-23.)
 - Conclusions
 - "Given the large increase in awareness and ever use of ENDS during this 1-year period and the unknown impact of ENDS use on cigarette smoking behaviours and long term health, continued monitoring of these products is needed."

The "Science" of E-Cigarettes

- There is currently no peer-reviewed evidence that ENDS promote long-term tobacco cessation or long-term abstinence from nicotine.
- Most studies demonstrate that ENDS are being used for smoking cessation, **not nicotine cessation.**
- There are numerous peer-reviewed studies demonstrating that NRT in its various forms, bupropion (Zyban), and varenicline (Chantix) promote long-term cessation.

Marketing of E-Cigarettes

- Problems with initial pricey models (atomizers that needed frequent replacement, product-specific nicotine cartridges), and the rise of cheaper products have forced most of the early companies out of business.
- The next wave included moderately-priced products that were mostly marketed by direct mail...

Marketing of E-Cigarettes



Marketing of E-Cigarettes



Marketing of E-Cigarettes



Marketing of E-Cigarettes

- Remember: No one that sells an addictive substance for profit has any interest in seeing their customers quit.
- Manufacturers and distributors of e-cigarettes are not interested in eliminating Big Tobacco, they are interested in becoming Big Tobacco.
- E-Cig industry is currently using Big Tobacco's playbook of harm reduction to sell another generation on a supposedly "safe alternative" until the long-term data proves otherwise...

The "Science" of E-Cigarettes

- There is currently no peer-reviewed evidence that ENDS promote long-term tobacco cessation or long-term abstinence from nicotine.
- Most studies demonstrate that ENDS are being used for smoking cessation, **not nicotine cessation.**
- There are numerous peer-reviewed studies demonstrating that NRT in its various forms, bupropion (Zyban), and varenicline (Chantix) promote long-term cessation.

Marketing of E-Cigarettes

- Problems with initial pricey models (atomizers that needed frequent replacement, product-specific nicotine cartridges), and the rise of cheaper products have forced most of the early companies out of business.
- The next wave included moderately-priced products that were mostly marketed by direct mail...

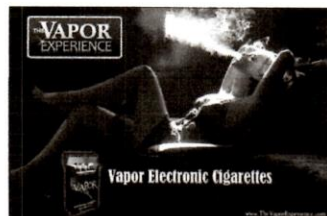
Marketing of E-Cigarettes



Marketing of E-Cigarettes



Marketing of E-Cigarettes



Marketing of E-Cigarettes

- Remember: No one that sells an addictive substance for profit has any interest in seeing their customers quit.
- Manufacturers and distributors of e-cigarettes are not interested in eliminating Big Tobacco, they are interested in becoming Big Tobacco.
- E-Cig industry is currently using Big Tobacco's playbook of harm reduction to sell another generation on a supposedly "safe alternative" until the long-term data proves otherwise...

Harm Reduction's Greatest Hits



Harm Reduction's Greatest Hits



Harm Reduction's Greatest Hits



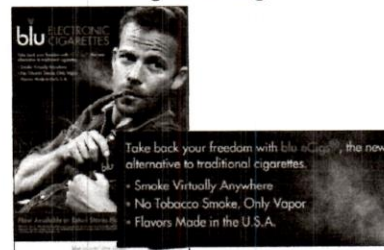
Marketing of E-Cigarettes

- Instead of being relegated to expensive products in mall kiosks and direct mail marketing, modern e-cigarettes have discovered the distribution pipeline long exploited by Big Tobacco: Convenience Store.
- Using this strategy to sell inexpensive disposable products, NJOY captured roughly 33% of the e-cigarette market, and Blu E-Cigarettes captured another 25% of the e-cigarette market, making them the industry leaders.

Marketing of E-Cigarettes

- Big market share means big target: In April 2012, Lorillard (Newport, True), the nation's oldest tobacco company, acquired Blu E-Cigarettes for \$135 Million **in cash**.
- Remember: No one that sells an addictive substance for profit has any interest in seeing their customers quit.
- Remember: Manufacturers and distributors of e-cigarettes are not interested in eliminating Big Tobacco, they are interested in becoming Big Tobacco.

Marketing of E-Cigarettes

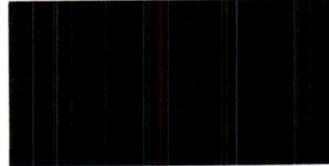


Marketing of E-Cigarettes



Marketing of E-Cigarettes

- Big market share creates a big target! Analysts believe that Altria/Philip Morris will ultimately acquire the industry leader, NJOY.



Marketing of E-Cigarettes

- Big market share creates a big target! Analysts believe that Altria/Philip Morris will ultimately acquire the industry leader, NJOY.
- Meanwhile, rumors are circulating that Camel is developing their own e-cigarette; given their aggressive youth marketing strategies, don't be surprised to see products similar in design to those marketed to youth as "e-hookah"

Regulation of E-Cigarettes

- 2010 Court Case made it very clear that the FDA has the authority to regulate e-cigarettes as a tobacco product unless companies made claims that devices could be beneficial in tobacco cessation.
 - Remember: That designation was made at the request of the e-cigarette industry
 - If that's what the industry requested, let's get started!
 - The Tobacco Control Legal Consortium has published a fact sheet with some regulatory options for electronic cigarettes...

Regulation of E-Cigarettes

- Option 1: E-cigarettes should be included in existing clean air laws.
 - Many smoke-free laws define the act of "smoking" as inhaling or carrying a lighted tobacco product intended for inhalation. E-cigarettes, which are not burned, but "vaped," are generally not covered under these laws. Using e-cigarettes in public may lead conventional smokers to assume that smoking.
 - Local and state governments should include e-cigarettes in their smoke- and tobacco-free restrictions by revising definitions of "smoking" or "tobacco products" to expressly cover e-cigarettes and other electronic nicotine delivery systems.

Regulation of E-Cigarettes

- Option 2: E-cigarettes should not be available to minors.
 - Under federal law, retailers cannot "sell cigarettes or smokeless tobacco to any person younger than eighteen years of age." The FDA has yet to assert jurisdiction over electronic cigarettes and extend restrictions like this to e-cigarettes.
 - State and local governments could consider passing stronger, more comprehensive youth access laws to prohibit the sale of e-cigarettes to minors, require these products to be kept behind the counter, allow them to be sold only in places adults are permitted to enter, or raise the minimum legal age to purchase them.

Regulation of E-Cigarettes

- Option 3: E-cigarettes should be taxed as tobacco products.
 - The Tobacco Control Act expressly preserves the authority of state and local governments to levy taxes on tobacco products.
 - Some states have addressed this issue by clarifying the definition of "tobacco products" in their tax codes so e-cigarettes are considered tobacco products for taxation purposes.

Regulation of E-Cigarettes

- Option 4: Free samples of E-cigarettes should NOT be available.
 - Under the Tobacco Control Act, tobacco manufacturers are restricted from distributing free samples of "cigarettes, smokeless tobacco or other tobacco products."
 - At present, this restriction does not apply to e-cigarettes.
 - State and local governments could prohibit the distribution of all free samples of tobacco products, including e-cigarettes and other nicotine delivery systems.

Regulation of E-Cigarettes

- If, on the other hand, the industry wants to be treated like every other approved smoking cessation product, they must undergo the same rigorous, double-blind, placebo controlled studies that other Nicotine Replacement Products were subject to; those studies should be conducted by independent scientists, and published in peer reviewed medical journals.
- You can bet that e-cigarette companies won't submit to such scrutiny, because no company that sells an addictive substance for profit wants its "loyal" (i.e. addicted) consumers to quit.