



American Association of Public Health Physicians  
*The voice of public health physicians, guardians of the public's health*  
Tobacco Control Task Force  
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## **Tobacco Control Task Force**

February 7, 2010

Division of Dockets Management  
Food and Drug Administration  
Department of Health and Human Services  
5630 Fishers Lane, rm. 1061  
Rockville, MD 20852

Re: Citizen Petition to reclassify E-cigarettes from “drug-device combination” to “tobacco product”

Dear FDA:

The undersigned submits this petition under the provisions of the new Tobacco Center legislation for which authority has been delegated to the Commissioner of Food and Drugs under 21 CFR 5.10 to request the Commissioner of Food and drugs to reclassify nicotine vaporizers, also known as “E-cigarettes” or “electronic cigarettes” from “drug-device combinations under 201(g) and 201(h) of the Federal Food, Drug and Cosmetic Act, to “tobacco product” under the new FDA/Tobacco legislation.

This is one of two petitions I am submitting today on behalf of the Tobacco Control Task Force of the American Association of Public Health Physicians. The other petition is a request to FDA to follow-up on its July 22, 2009 press release with another press release to amend certain statements on the basis of new information provided as attachments to both of these petitions.

We have generated these petitions because reclassification of E-cigarettes to tobacco products could open the door to a new harm reduction component to current tobacco control programming. That new component, in turn, could rapidly and substantially reduce tobacco-related illness and death without increasing the numbers of teens initiating nicotine use.

Neither I nor AAPH have received or anticipate receipt of any financial support from any electronic cigarette enterprise, any other tobacco-related enterprise, or any pharmaceutical enterprise.

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## A. Action requested

**AAPHP urges the Food and Drug Administration (FDA) to reclassify nicotine vaporizers (E-cigarettes) from “drug-device combination” to “tobacco product.”** This reclassification would be limited to E-cigarettes marketed as an alternative to conventional cigarettes for smokers wishing to avoid the toxic substances (other than nicotine) in cigarette smoke.

Since E-cigarettes meet the definition of “tobacco product” under the new FDA/Tobacco law, but do not meet the definition of either cigarette or smokeless tobacco product, **it is our request that they be in a new category of “nicotine vaporizer” with strict FDA regulation of quality of manufacture and marketing, but with warning labels limited to the issue of nicotine addiction.**

## B. Statement of grounds

### **Summary:**

This request for reclassification of E-cigarettes from “drug-device combination” to “tobacco product” is based on the following:

**Legal:** In the mid-1990’s, the Supreme Court blocked FDA’s attempt to regulate tobacco products as drugs and ruled that separate legislative authority would be required for FDA to oversee tobacco products. This was reaffirmed by an opinion expressed by Judge Leon in January of this year, when he excoriated FDA for attempting to regulate E-cigarettes as drugs.

**Ethical:** FDA priorities are expected to be the protection of the public’s health. Agency decisions are expected to be based on the best available science. FDA should not mislead health-related organizations or the general public as to the health hazard posed by any product. FDA’s current stance relative to E-cigarettes, as presented at the July 22, 2009 FDA press conference, fails on all three of these considerations.

**Medical Science and Epidemiology:** Even FDA’s own analysis shows E-cigarettes to have the same nicotine with about the same levels of trace contamination found in pharmaceutical products already approved by FDA. Propylene glycol, the other major ingredient is generally recognized as safe. The risk of death attributable to tobacco use from smokeless tobacco products is less than 5%, and, for some products, less than 0.1% the risk of death from conventional cigarettes. The risk of death from E-cigarettes, as best we can estimate from available data, should be about the same as for long term use of pharmaceutical nicotine replacement therapy (NRT) products, at the lower end of this range.

**Public Health Impact:** Tobacco harm reduction is already well recognized as legitimate in the medical community in terms of long term use of NRT products. Tobacco harm reduction is endorsed by and the new FDA tobacco law in terms of reduced exposure conventional cigarettes. The new harm reduction component recommended in this petition would consist of honest communication to smokers as to the relative risk profiles presented by tobacco and tobacco-related products. On the basis of its review of the medical literature and the unpublished analyses of E-cigarettes presented in this petition, AAPHP has reached three conclusions: 1) reclassification of E-cigarettes as a tobacco product could open the door to a new harm-reduction component to current tobacco control policy; 2) this new harm reduction component presents the only feasible approach to rapidly and substantially reduce tobacco-related illness and death in the United States; and 3) with appropriate regulation of marketing now possible through the new FDA/Tobacco law, the public health benefits of this new harm reduction component could be secured without increasing the numbers of teens initiating nicotine use.

**Objections** to FDA approval of E-cigarettes as tobacco products are **speculative and largely based on misinformation.**

## **Legal**

E-cigarettes and all other tobacco and tobacco-related nicotine delivery products meet the FDA definitions of both “drug,” and “tobacco product.” In the mid 1990’s the Supreme Court blocked then-Commissioner Kessler’s assertion of FDA oversight over tobacco products. This was reaffirmed by Judge Leon’s January 2010 opinion regarding electronic cigarettes (Attachment B3). It therefore seems incumbent upon FDA to regulate all tobacco and tobacco-related products as tobacco products rather than drugs, unless they are clearly intended for medical treatment.

E-cigarettes closely resemble Nicotine Replacement Therapy (NRT) products approved by FDA as drugs prior to the passage of the new FDA/Tobacco law. FDA approval was based on requests for such approval by the manufacturers who desired to market these items as drugs. E-cigarettes deliver the same nicotine extract to the user. The difference is the intent of the manufacturer. E-cigarettes are intended for long term use as a recreational substitute for conventional cigarettes. They should be classified as tobacco products. Manufacturers intending their products for short term use for nicotine cessation could still be regulated as drugs. The best way to manage this situation would be for FDA to advise E-cigarette manufacturers as to the claims they could or could not make for classification as tobacco products. Whether tobacco product or drug, all would be regulated by FDA.

Most E-cigarette products are marketed as a substitute for conventional cigarettes for smokers who would like to continue nicotine use in a satisfying way, while virtually eliminating their exposure to products of combustion and other toxic substances (other than nicotine) in cigarette smoke. Given this purpose, the standard for comparison should be the health hazard posed by conventional cigarettes. The standard should not be a drug safety standard not imposed on other tobacco products.

Under the new FDA/Tobacco law, FDA could require that only pharmaceutical grade ingredients be used in E-cigarettes. FDA could also impose the same age-related marketing restrictions imposed on other tobacco products.

## **Ethical**

### ***Ethical Dilemma Posed by New FDA/Tobacco Law***

The dictionary definition of “ethical” (Webster’s New World College, 4<sup>th</sup> Ed, 2000) is “1 having to do with ethics or morality; or of conforming to moral standards. 2 conforming to the standards of conduct of a given profession or group.” The new FDA/Tobacco law presents a number of ethical issues never before faced by FDA. It forces FDA to grandfather-in currently marketed conventional cigarettes – the most hazardous of tobacco products, while placing formidable barriers to lower risk products. The new law encourages creation and marketing of lower exposure conventional cigarettes without the need for scientific proof that such lower exposure will result in lower risk of illness Section 911(g)(2)(A)(iii), while placing much stiffer requirements on lower risk non-cigarette products. These provisions in the law directly conflict with the ethical responsibility of FDA to protect the health of the American public and FDA commitment to base their decisions on the best available scientific data.

The question then becomes how the FDA should proceed in a manner consistent with both the new law and FDA’s traditional ethical responsibilities. This question is front and center when considering the issue of the classification of E-cigarette products.

## ***Drug vs. Tobacco Product Standards***

The first major difference between the drug and the tobacco-product standards has to do with the requirement for controlled clinical trials for drug products. There is no such requirement for tobacco products. The second difference between the drug and the tobacco-product standards has to do with safety standard to be met – an absolute standard for drugs, as opposed to a relative standard for tobacco products.

### ***AAPHP Analysis, Findings and Recommendations***

Analysis of these issues by the Tobacco Control Task Force (TCTF) of the American Association of Public Health Physicians (AAPHP) has led us to the conclusion that reclassification of E-cigarettes from drug-device combinations to tobacco products is legally and ethically justified, and scientifically sound. Such FDA action could open the door to a new harm reduction component to current tobacco control programming. This, in turn, could substantially reduce tobacco-related illness and death without increasing the numbers of teens initiating cigarette or other nicotine use.

The AAPHP Task Force, on the basis of extensive literature review and analysis (Attachment A1), has concluded that a national harm reduction initiative, based partly on the potential attractiveness of E-cigarettes to current smokers, could save the lives of 4 million of the 8 million current adult American smokers who will otherwise die of a tobacco-related illness over the next 20 years (Attachment A1). This could result in a situation in which, 20 years from now, there would be less than 10,000 tobacco-related deaths per year in the United States instead of the current 400,000+ per year.

E-cigarettes would be a major part of the proposed harm reduction initiative, because they appear to satisfy the nicotine addiction and the habituation to the cigarette-handling ritual more effectively than any other product now on the market. For many current smokers, E-cigarettes may be the only low risk nicotine delivery product acceptable as a substitute for conventional cigarettes (Attachment B2). Cost and other considerations will limit the attractiveness of E-cigarettes to teens. Enforcement of FDA restrictions on marketing to minors and health education programming should enable us to secure the public health benefits E-cigarettes can offer without increasing initiation of nicotine use by teens.

As envisioned, this new harm reduction initiative would include all tobacco-related products with the potential to substantially reduce the risk of illness among smokers. “Substantial reduction” in this context is taken to mean a 50% reduction in tobacco-related illness and death within a decade of policy implementation, with eventual reduction of 99% or better for those smokers switching to very low risk tobacco-related products (Attachment A1). This difference in short-term vs. long term reduction in illness and death rates is due to the fact that elevated rates of illness and death continue for about fifteen years after discontinuation of cigarette use.

### ***Harm Reduction***

Harm reduction is already a well established principle in tobacco control. It currently takes the form of physicians recommending long term use of NRT products. Long term use of NRT products has not been approved by FDA.

Harm reduction is written into the new FDA/Tobacco law in the form of reduced exposure conventional cigarettes. Manufacturers are encouraged to develop such products and market them as reduced exposure products with no scientific evidence required to show that such reduction in exposure will result in a reduction in risk (Section 911(g)(2)(A)(iii)). This is in the face of a recent review by Pankow et al (Attachment C1) that shows that such reduction in exposure in conventional cigarettes would not result in a measurable reduction in risk. By contrast, E-cigarettes, basically providing the

same nicotine found in NRT products already approved by FDA, promise better than a 99% eventual reduction in tobacco-related illness and death (Attachments A1-3).

The harm reduction initiative envisioned by AAPHP would consist of honestly and directly communicating to smokers the relative risks of tobacco-related illness and death posed by different types of tobacco products (Reference A1,A9). The word “honest” in this context is taken to mean either abandonment of the current warning that smokeless tobacco products are not a safe substitute for cigarettes, or other communication intended to overcome the misimpression that smokeless products carry the same risk as conventional cigarettes. The word “direct” in this context means direct communication from the FDA to actual and potential users of tobacco-related products to overcome limitations imposed on tobacco product manufacturers by the new FDA/Tobacco law.

To effectively reach current smokers the lower risk tobacco related products should be attractive to smokers, are competitively priced, and are available where cigarettes are sold (Attachment A1). In contrast, currently available NRT products tend to be unattractive, unsatisfying to smokers, unduly expensive (Attachment A10), and, as specified by FDA regulation, only for temporary use.

American smokers are very health conscious, as evidenced by the popularity of light” and filter cigarettes. They have not, however, switched in very large numbers to smokeless products and other nicotine delivery products because of a federally mandated warning label that such products are not safe substitutes for cigarettes. A 2003 survey found that while 80% of American smokers were aware of smokeless products, only 11% correctly believe that they are less hazardous than cigarettes (Attachment A11). Another survey found that 82% of American smokers incorrectly believe that chewing tobacco is just as likely to cause cancer as is smoking cigarettes (Attachment A12). A 2007 study of adult smokers in Australia, Canada, UK and US found that only 13% correctly believed that smokeless products are less hazardous than cigarettes (Attachment A13).

Reclassification of E-cigarettes to tobacco products could open the door to a new harm reduction component to current tobacco control programming. This new component, in turn, could enable FDA, in collaboration with others, to take the action needed to substantially reduce illness and death among current smokers without increasing initiation of nicotine use by teens.

## ***Medical Science and Epidemiology***

### ***Tobacco Related Illness and Death***

Cigarette smoking directly or indirectly kills about 440,000 Americans each year (Attachment A17). This death rate has been stubbornly persistent for a number of years despite our best efforts. Also, despite our best efforts to date, reductions in the percentage of teens initiating cigarette use has slowed in recent years (Attachment A18). Our best current estimate is that all other tobacco products, combined, result in less than 10,000 deaths per year in the US (Attachment A1).

### ***Tobacco Unique among Addictive Substances***

Tobacco is unique among addictive substances in that it is the carrier, not the active drug that causes almost all the illness and death. All tobacco products are nicotine delivery devices. The nicotine causes the addiction. Almost all the illness and death is due to toxic products of combustion of the combustible products, with about four percent due to other toxic substances found in almost all whole-tobacco tobacco products (Attachments A1 and A20).

## ***Cigarettes Unique among Tobacco Products***

Cigarettes carry a risk of illness and death two to three orders of magnitude greater than any other tobacco product. This excess risk is due to products of combustion inhaled deep into the lungs and momentarily held there, resulting in the deposit of tar that remains in the lungs, prolonging tissue contact with trace radioactive elements and the multiple other toxic substances in the tobacco smoke.

Another element to be considered with cigarettes and other combustible tobacco products is the the habituation to the cigarette ritual of handling the tobacco product. This, for many, represents a second addiction, in addition to the nicotine addiction.

The importance of this habituation has been dramatically shown in two ways. One is the remarkable ineffectiveness of the pharmaceutical nicotine replacement products as a means of achieving long-term abstinence from cigarette use (Attachment C1). The other is the experience of significant numbers of E-cigarette users who have transitioned to no-nicotine E-cigarettes, while maintaining the habituation to the cigarette behavioral rituals (Attachment B2).

E-cigarettes, more than any other tobacco or tobacco-related product, satisfies both the habituation and nicotine addiction.

## ***Toxicity of Cigarettes as Baseline***

Given the strength of the addiction and habituation to conventional cigarettes and the fact that conventional cigarettes pose a risk of serious illness and death two to three orders of magnitude greater than any other tobacco or tobacco-related product – the baseline for comparison for all tobacco and nicotine delivery products should be the health hazard posed by conventional cigarettes.

The worst of smokeless tobacco products (powdered dry snuff) carries a risk of cancer 95% less than conventional cigarettes, and an overall risk of death better than 98% less than conventional cigarettes (Attachment A1). The best of smokeless products, a form of moist snuff, known as “snus” has been in widespread use in Sweden for over 100 years, and well studied since the 1980’s. These studies show a very small increase in heart disease morbidity (likely due to the nicotine) but no increase in any cause of death due to snus use (Attachments A1-4, A7-9, A16). Unfortunately, the new law specifically prohibits marketing of smokeless tobacco products as lower risk than cigarettes by virtue of their being smokeless.

As best we can determine from available information – use of nicotine extracts such as those found in E-cigarettes and NRT products should enable smokers to eventually achieve a reduction in risk of future tobacco related illness of 99% or better (Attachments A1, B6a-j). The term “eventually” is used in this context because elevated risks of illness and death persist for up to fifteen years after quitting cigarettes, thus limiting the initial benefit to no more than a 50% reduction during the first decade following quitting or transitioning to an alternate nicotine delivery product.

All of the above points to the feasibility of a harm reduction strategy by which informing current smokers about the difference in risk posed by different tobacco products could rapidly and dramatically reduce tobacco-related illness and death among smokers who cannot or will not discontinue their nicotine addiction (Attachments A1-4, A7,A8).

## ***Historical Record***

The historical record shows that lung cancer was an exceedingly rare disease prior to the widespread use of machine made and mass marketed cigarettes. While tobacco use has been considered a health problem since introduction of tobacco use into Western society in the 16<sup>th</sup> century, we could find no

attribution of increased death rates to tobacco use prior to the mid 20<sup>th</sup> century. This lack of data is consistent with our current understanding that modern conventional cigarettes stand alone as a product with risk of death one or more orders of magnitude higher than any other commonly used tobacco product.

### ***80% of Nicotine Intake, 98% of Mortality***

Based upon published calculations by Karl Fagerstrom, Smokefree Pennsylvania has estimated that the percentage of nicotine consumed in the US from smokefree tobacco/nicotine products has increased from about 10% a decade ago to about 20% in 2009, while the percentage of nicotine consumed from cigarettes has declined from about 90% a decade ago to about 80% in 2009 (Attachment A5,A6).

Furthermore, about 90% of the nicotine consumed from smokefree tobacco/nicotine products in the US is now obtained from smokeless tobacco products, while about 10% is now obtained from nicotine gums, lozenges, patches, and electronic cigarettes (Attachment A6).

About 98% of tobacco related illness and death in the US is attributable to conventional cigarettes (Attachment A1).

### ***Quit Rates and Progress Toward Tobacco Free Society***

Promoting Snus, [Response to Zhu](#) et al, February 6, 2009 "The Zhu paper summarizes the most recent survey data strongly suggesting that encouraging smokers to switch to lower risk smokeless products is likely to result in substantial public health benefits. His summary, however, concludes that such benefits might not occur -- apparently because there are no case-control studies to back up these impressions. His conclusions have been taken out of context by anti-harm-reduction activists as "proof" that harm reduction will not result in public health benefits in the United States" (Attachment A4). In other words, the data within the Zhu study shows that encouraging smokers to switch to lower risk smokeless products could accelerate our progress in the direction of a smoke-free society. Unfortunately, this is not reflected in the study abstract.

Pharmaceutical smoking-cessation products, even with the best of counseling and health education are remarkably ineffective. On a short-term basis they only double quit rates from about 3% to about 5%. When measured at 20 months, only about 2% remain cigarette free (Attachments C1,C7).

### ***Environmental Tobacco Smoke and Fire Damage***

Environmental tobacco smoke kills an estimated 40,000 non-smokers each year (Attachment A17). This is a hazard limited to combustible tobacco products. Almost all of this smoke is sidestream smoke – the smoke that curls off the end of the cigarette or cigar when no one is puffing on it. E-cigarettes have no sidestream smoke. The only possible air pollution would be from exhaled vapor – and this is likely to be minimal. While at least one small study will be needed to confirm or deny the impression that E-cigarettes are harmless to bystanders – clearly the elimination of almost all of the environmental contamination is an additional public health benefit of getting smokers to switch to E-cigarettes.

By the same token – no combustion – no property damage due to fire – yet another significant benefit.



## ***Relative Safety of E-Cigarettes and July 22 FDA Press Conference***

The relative safety of E-cigarettes compared to other tobacco products and compared to FDA approved pharmaceutical smoking cessation products currently on the market should not be an issue for the following reasons:

1. If regulated by FDA as tobacco products, FDA could require standards for chemical composition and quality of manufacture similar to those imposed on pharmaceutical products.
2. The limited studies done to date by FDA on E-cigarette liquid, and publicly announced July 22, 2009 (Attachments B5a-c) prove that the products tested have levels of carcinogenic contaminants similar to the concentrations of these same contaminants in nicotine replacement products already approved by FDA (Attachments B5d-i). These levels are several orders of magnitude less than conventional cigarette smoke. Both within this petition, and as a separate petition to FDA, AAPHP is requesting a follow-up to the July 22, 2009 press release to address the following:
  - a. How the risk posed by E-cigarettes, based on chemical composition, compares to the risk posed by pharmaceutical nicotine replacement products and conventional cigarettes,
  - b. The issue of “drug-device combination” vs. “tobacco product.”
  - c. The possible role E-cigarettes and other low-risk tobacco products might play relative to reducing future tobacco-related illness and death among current smokers.
  - d. What is currently known about the attractiveness of E-cigarettes, compared to low-exposure conventional cigarettes and NRT products to teens and whether there is evidence that such products play a significant role in attracting teens to nicotine use.
3. With over three years of experience with E-cigarettes in the United States, we are not aware of any reports of illness directly attributable to their use. It is important to note that there were E-cigarette products on the American market prior to the February, 2007 date specified in the new FDA/Tobacco law relative to introduction of new products to the marketplace.
4. E-cigarettes use the same nicotine, with about the same level of trace contaminants as FDA approved NRT products. There are a large number of studies and reviews that demonstrate the safety of E-cigarettes in comparison with pharmaceutical NRT products and conventional cigarettes (Attachments B6a-j).
5. Propylene glycol and the other major ingredients in E-cigarettes are generally recognized as safe (Attachment B6i).
6. Judge Leon, in his January 14, 2010 opinion, stated the following: “Together, both Smoking Everywhere and NJOY have already sold hundreds of thousands of electronic cigarettes, yet FDA cites no evidence that those electronic cigarettes are any more an immediate threat to public health and safety than traditional cigarettes, which are readily available to the public” (Attachment B3).

Please note that a more detailed discussion of the major problems with the FDA July 22, 2009 press conference, and the urgent need for FDA to address these issues was the subject of correspondence forwarded to FDA by AAPHP August 29 (Attachment B5f) and will be the subject of a second petition to FDA being submitted by AAPHP today.

## *Levels of Evidence*

**50% plus one:** In common legal, administrative and policy-related parlance, the level of evidence needed to justify a policy decision is “more likely than not.” This is “50% plus one” level of evidence is readily secured by anecdotal reports and non-research-related experience.

**95%:** In the medical world, our custom is to require proof of a hypothesis with 95% assurance that this result could not have occurred by chance. This level of evidence cannot be secured without research (most commonly controlled clinical trials) designed and scaled to achieve this level of statistical significance. This policy has served us well in the development of modern medical care. This same policy, however, has caused problems in areas where clinical trials may be impossible to conduct or where prevailing thought patterns strongly bias federal and other agencies against any consideration of funding such trials. This appears to be the case with regard to E-cigarettes and tobacco harm reduction.

**Conventional Thinking in the Total Absence of Evidence:** Herein lays a curious paradox. While opposing tobacco harm reduction because clinical trials have not been done, there has been no objection to long term use of NRT products in a harm reduction mode. Nor has there been vocal opposition to the provision in the new FDA/Tobacco law that encourages development and marketing of reduced exposure conventional cigarettes as a means of harm reduction (Section 911(g)(2)(A)(iii)). For this last item, the weight of scientific evidence is against such reductions in exposure having any measurable impact on tobacco related illness and death (Attachment A20).

### *Evidence, Proof and the Ultimate Clinical Trial*

In its July 22, 2009 press conference, FDA adopted the position, that since the safety of E-cigarettes has not been proven in a clinical trial, FDA will presume that E-cigarettes are as hazardous than conventional cigarettes, and possibly even more hazardous. FDA cited results of its own laboratory studies which showed trace contamination with carcinogenic substances as evidence in favor of this view, without mentioning that the contaminants and levels of contamination are similar to those of FDA approved NRT products, and orders of magnitude less than conventional cigarettes. In that same press conference, FDA asserted the presumption that E-cigarettes are being aggressively marketed toward teens and are likely inducing large numbers of teens who otherwise not initiate nicotine use to become nicotine addicts (Attachment B5b). All this, in turn, has been interpreted by a number of national organizations and political jurisdictions as FDA having proven that E-cigarettes represent a public health hazard so severe that they should be banned (Attachment B4).

All this raises the question as to what kind of study would be required to confirm or deny both the relative safety of E-cigarettes (compared to conventional cigarettes and NRT products) and the degree to which E-cigarette marketing is attracting large numbers of teens to nicotine use who otherwise would have abstained.

The body of this petition document and its multiple attachments demonstrate the relative safety of E-cigarettes compared to other tobacco products in terms of chemical analyses, anecdotal reports, and estimation of health impacts based on studies of other products. The missing level of evidence is data from clinical trials of sufficient duration and power to address these issues at a 95% level of confidence.

The best estimate of our AAPHP Tobacco Control Task Force is that a controlled trial to conclusively demonstrate that E-cigarettes pose a miniscule risk of tobacco-related death compared to conventional cigarettes would be impossible to conduct for both ethical and logistical reasons. The investigator would have to recruit 2,000 to 5,000 young adult non-smokers. They would then

have to be randomized into a “control” group assigned to smoke two packs a day of a specified conventional cigarette, and a “case” group assigned to vape (use an E-cigarette product) to secure an equivalent dose of nicotine. Both groups would then have to be followed for about fifteen years to document differences in multiple causes of illness and death. In addition, family members and occupational contacts would have to be followed for evidence of illness related to environmental tobacco smoke vs. environmental E-cigarette vapor.

In an article published in December of 2009, Murrelle, et al, considered this issue from the perspective of continuing to smoke conventional cigarettes vs. switching to a lower risk product vs. quitting altogether (Attachment A19). Without addressing whether such a study would be an observational or experimental study, they reached similar conclusions as to sample sizes and duration of study. Limiting their end point to incidence of lung cancer as the outcome variable, they estimated that a study to document the efficacy of a modified risk tobacco product expected to reduce lung cancer risk to a level equal to quitting smoking altogether (as would be the case with E-cigarettes) would require observation of 8,000 subjects for five years, with 2,000 subjects in each of four groups: continuing smokers, quitters, switchers to the modified risk product, and non-smokers. If testing a modified risk product expected to only reduce lung cancer risk by only a few percentage points (as would be the case with reduced exposure conventional cigarettes) the sample sizes would have to be about ten times larger, and the duration fifteen years or more.

Separate studies of similar magnitude would be required to document whether such marketing of E-cigarettes or any other presumably modified risk tobacco product would attract large numbers of teens to tobacco use, reduce long-term quitting of nicotine use, or serve as a gateway to use of conventional cigarettes.

All of the questions noted above could be easily and inexpensively addressed by implementation of the proposed harm reduction initiative, then implementing research and surveillance to track the issues noted above. Since participation would be huge, the time required to gather the needed data would be minimized. If results did not meet initial expectations, mid-course policy changes could be made.

### ***Toxicity of E-cigarette fluid***

Bulk E-cigarette fluid presents a theoretical hazard due to the concentration of nicotine. If ingested by children or applied to the skin in large amounts, it could cause adverse reactions. It would be prudent to take the same precautions as with other potentially hazardous household products by providing warning labels and child-proof caps (Attachment B6b). Bulk E-cigarette liquid is commonly used by vapers (E-cigarette users) to refill the cigarette cartridges. This is easily done and is considerably less expensive than buying more cartridges.

## **Objections to FDA Approval of E-Cigarettes as Tobacco Products**

### ***Recruitment of Teens to Nicotine Use***

Concern expressed by certain opponents to E-cigarettes that they should not be classified as tobacco products because such classification will recruit large numbers of teens to nicotine addiction or otherwise serve as a gateway to use of conventional cigarettes should not be an issue for the following reasons:

- a. FDA, when regulating E-cigarettes, could impose the same age-related restrictions on marketing imposed on other tobacco products.

- b. The newly adopted FDA/Tobacco law encourages makers of conventional cigarettes to develop reduced –exposure products and market them as such with no requirement for scientific evidence that such reductions in exposure will translate to reduced risk. Opponents to E-cigarettes have not expressed any concern that such marketing will attract large numbers of teens to conventional cigarettes.
- c. There is no evidence that E-cigarettes as marketed to date have been marketed to teens or are popular among teens. This is likely due to the high initial cost of E-cigarette kits (\$80 to \$125).
- d. There is no evidence that E-cigarettes have resulted in either initiation of nicotine use or transition to conventional cigarettes. All of the (limited) available evidence points in the opposite direction (Attachments B2, B5e).

### ***Objections to Harm Reduction***

Two tobacco harm reduction initiatives are already in place and well accepted within FDA and the medical and public health communities. The first is long term use of NRT products in a harm reduction mode. The second is the provision in the FDA/Tobacco law encouraging makers of conventional cigarettes to manufacture lower exposure conventional cigarettes and market them as such, with no requirement for scientific proof that such lower exposure will reduce risk.

The only approach to harm reduction not currently endorsed by the medical and public health communities, and the new FDA/tobacco law is harm reduction based on use of non-pharmaceutical smokeless tobacco and other commercially available tobacco-related products. In our judgment, this is the only approach that has the potential to rapidly and substantially reduce tobacco related illness and death among current cigarette smokers. Advantages include cost, convenience and respect for the independence and intelligence of smokers.

Objections to this proposed harm reduction approach (reduction of tobacco-related illness and death by encouraging inveterate smokers to switch to lower risk tobacco products) are not based on any challenge to the findings that non-combustible products are far less hazardous than conventional cigarettes. Prior to posting our Resolution and White Paper on our AAPHP Web Site (Attachment A1), we shared our then proposed White Paper with persons and agencies we deemed to be both knowledgeable in this area and opposed to any consideration of such a harm reduction approach. None offered any criticism of the key findings or offered any bibliographic references with contradictory findings. The objections we did get were along the lines noted below. (All of these communications were verbal between the author of this petition and others. Some refused to respond. Others responded verbally. None offered written response that could be included as attachments.)

### ***Goal of Tobacco Free Society***

The vision of a world free of tobacco use and related illness is a commonly stated goal of tobacco control (Attachment A21). This aspect of harm reduction is **opposed by NIH and CDC**, apparently on the basis of their presumption that adding this type of a harm reduction component to current tobacco control programming would divert attention from their goal of a tobacco free society. In making this presumption, they are ignoring the published data that strongly suggest that spontaneous quit rates from smokeless tobacco are triple the spontaneous quit rates from cigarettes (about 10% per year as opposed to about 3% per year (Attachment A4).

### ***E-cigarettes could Reduce Quit Rates***

Some have speculated that E-cigarettes would reduce quit rates among smokers who would have quit nicotine use altogether. Given the dismal record of NRT products in achieving long term abstinence from smoking, this result seems unlikely for two reasons.

First, as shown by the most recent systematic review and meta-analysis, even with pharmaceutical product, counseling and health education under study conditions, only 7% remain abstinent at 6 months, 5% at 12 months and less than 2% at 20 months (Attachment C1). These dismal results rule out dependence on such products as a cornerstone of tobacco control policy.

Second, as shown by Zhu et al, spontaneous quit rates for smokeless tobacco products are about triple the spontaneous quit rates for conventional cigarettes (Attachment A4). Thus, as noted above, in the discussion of the goal of the tobacco free society, getting smokers to switch to something other than cigarettes could enhance overall nicotine quit rates and accelerate our movement toward a tobacco free society.

### ***E-cigarettes could serve as gateway to use of conventional cigarettes***

Some have speculated that E-cigarettes as a pathway to smoking conventional cigarettes in persons who would otherwise not use nicotine or would have quit nicotine use altogether. With regard to this scenario, Neither AAPHP nor FDA nor others opposing E-cigarettes have found evidence documenting persons transitioning from E-cigarettes to conventional cigarettes.

### ***Objections by Special Interest Groups***

The proposed reclassification **is opposed by the Campaign for Tobacco Free Kids (CTFK)** and other non-profit organizations in the mistaken belief that a harm reduction approach based on commercially available tobacco products would balloon the numbers of children and youth initiating tobacco use, and once initiated, they would then transition to cigarettes. The only data supporting this anticipated scenario is conditioned by a legally mandated warning on the smokeless tobacco product that leads most users of smokeless tobacco to erroneously believe that smokeless tobacco is as hazardous as cigarettes (Attachments A11-13).

The newly adopted FDA/Tobacco law encourages makers of conventional cigarettes to develop reduced-exposure products and market them as such with no requirement for scientific evidence that such reductions in exposure will translate to reduced risk (Section 911(g)(2)(A)(iii)). Neither CTFC nor the other non-profit organizations opposing the proposed harm reduction approach object to the harm-reduction approach written into the law, even though it will also involve harm reduction via commercially available tobacco products.

The harm reduction approach proposed in this petition was strongly **opposed by the major special interests** that shaped the current FDA/Tobacco law – the Altria/Philip Morris company who co-wrote the law with Matt Myers of CTFC, and the pharmaceutical interests that funded the CTFC advocacy for this legislation. These special interest groups opposed any federal action that might cut into the sales of their highly profitable cigarettes or smoking cessation products. This statement is in past tense because, in December of 2009, Altria submitted a comment to FDA requesting FDA consideration of “the substantial continuum of risk across different types of tobacco or nicotine-containing products.” (Attachment A14) This was apparently a follow-up to Altria’s acquisition of UST, America’s most prominent smokeless tobacco company.

Finally, some tobacco control activists have noted that we already have NRT products to address this issue, thus promoting the concept that switching to non-pharmaceutical tobacco products would serve no public health purpose. We disagree. NRT products have a dismal track record with regard

to smoking cessation (Attachment C1). The NRT products tend not to be acceptable to many smokers due to price, inadequate dosage of nicotine, limited access, and general lack of satisfaction.

## Impact of FDA July 22, 2009 Press Conference

As a direct result of the FDA July 22, 2009 press conference, many have concluded that E-cigarettes are as dangerous or more dangerous as conventional cigarettes and that they have attracted large numbers of teens to nicotine use who otherwise would have not initiated nicotine use. This has resulted in public statements, and political action to restrict or ban E-cigarettes. The strongly negative tone of the FDA press conference (Attachment B5B) created a situation in which people were encouraged to draw the incorrect conclusions noted above. One attachment has been added to this petition to document these interpretations (Attachment B4). This is a report from New Jersey GASP that summarizes the actions taken by others, mostly in response to the FDA press conference, as justification for their recommendations regarding E-cigarettes (Attachment B4).

## Sources of Additional Information on E-cigarettes

1. General information about electronic cigarettes can be found at the following e-mail contact and Internet sites:
  - a. Smokefree Pennsylvania: Bill Godshall [smokefree@compuserve.com](mailto:smokefree@compuserve.com)
  - b. American Association of Public Health Physicians: Joel Nitzkin, MD, MPH, DPA <http://www.aaphp.org/special/2009/20090829LtrDeyton.pdf>
  - c. American Council on Science and Health: President: Elizabeth Whelan, ScD, MPH <http://www.acsh.org/>
  - d. The Rest of the Story: Tobacco News and Analysis: Michael Siegel, MD, MPH <http://tobaccoanalysis.blogspot.com/>
  - e. TobaccoHarmReduction.org: Carl Phillips, MPP, PhD <http://tobaccoharmreduction.org/index.htm>
  - f. Tobacco Truth: Brad Rodu, DDS <http://rodutobaccotruth.blogspot.com/>
  - g. The Truth About E-Cigs : The MyInLife E-cigarette Company <http://truthaboutecigs.com/>
2. Vaping links (vaping is the term used by E-cigarette users for use of E-cigarettes (properly referred to as “nicotine vaporizers” (from [www.vaporsclub.com/links.html](http://www.vaporsclub.com/links.html) as downloaded 12/15/2009)
  - a. [www.VapersForum.com](http://www.VapersForum.com) – fun and informative place to learn about vaping
  - b. [www.VapersInternational.org](http://www.VapersInternational.org) - research organization to study vaping
  - c. [www.righttovape.com](http://www.righttovape.com)
  - d. [www.ecassoc.org](http://www.ecassoc.org) – E Cigarette Association (manufacturers)
3. To shop for E-cigarettes: (from [www.vaporsclub.com/links.html](http://www.vaporsclub.com/links.html) as downloaded 12/15/2009)
  - a. [www.PureSmoker.com](http://www.PureSmoker.com)
  - b. [www.eliquidplanet.com](http://www.eliquidplanet.com)
  - c. [www.myvaporstore.com](http://www.myvaporstore.com)
  - d. [www.JuicyLiquid.com](http://www.JuicyLiquid.com)
  - e. [www.RockyMountainVapor.com](http://www.RockyMountainVapor.com)
  - f. [www.BestEcig.com](http://www.BestEcig.com)
  - g. [www.totallywicked-liquid.com](http://www.totallywicked-liquid.com)
  - h. [www.E-cigs.co.uk](http://www.E-cigs.co.uk)
  - i. [www.MidwestVapor.com](http://www.MidwestVapor.com)
  - j. [www.WidowsBeadwork.com](http://www.WidowsBeadwork.com)
  - k. [www.JohnsonCreekSmokeJuice.com](http://www.JohnsonCreekSmokeJuice.com)

4. Sites for reviews of different models of electronic cigarettes (from [www.vaporsclub.com/links.html](http://www.vaporsclub.com/links.html) as downloaded 12/15/2009)
  - a. [www.e-cigreview.com](http://www.e-cigreview.com)
  - b. [www.e-cigreviews.com](http://www.e-cigreviews.com)
  - c. [www.vaportalk.com](http://www.vaportalk.com)
  - d. [www.esmoker-forever.com](http://www.esmoker-forever.com)

## ***Annotated index to attached reference materials.***

### ***Attachment A: Harm Reduction References***

1. **AAPHP Resolution and White Paper: The Case for Harm Reduction for control of tobacco-related illness and death**, October 26, 2008 (from [www.aaphp.org](http://www.aaphp.org) web site). This well documented 37 page report does not directly address E-cigarettes, but makes the case for a harm reduction initiative based on commercially available tobacco products to achieve substantial personal and public health benefits not otherwise obtainable.
2. Rodu B; Phillips CV: **Switching to smokeless tobacco as a smoking cessation method: evidence from the 2000 National Health Interview Survey**. Harm Reduction Journal 5:18 (2008)
3. Philips CV: **Debunking the claim that abstinence is usually healthier for smokers than switching to a low-risk alternative, and other observations about anti-tobacco-harm-reduction arguments**. Harm Reduction Journal 6:29 doi 10-1186/1477-7517-6-29 2009
4. Nitzkin: J: **Promoting Snus Will Save Lives in the USA** – an article posted on the Tobacco Issues Page of the [www.aaphp.org](http://www.aaphp.org) web site in response to the paper by Zhu et al, Tobacco Control, 2008 “**Quitting cigarettes completely or switching to smokeless tobacco: do U.S. Data replicate the Swedish Results**” This paper is remarkable in that the data show considerable potential benefit to switching to smokeless tobacco, but the abstract declares this point to be “unproven” on the basis that it has not been subjected to a controlled clinical trial. February 6, 2009 (from [www.aaphp.org](http://www.aaphp.org) web site)
5. Fagerstrom K: **The nicotine market: An attempt to estimate the nicotine intake from various sources and the total nicotine consumption in some countries**. Nicotine & Tobacco Research, 7:3, pp 343-350, June 2005. In this paper Fagerstrom presents an approach to determining the amount of nicotine consumed by the population by type of tobacco product – from cigars to cigarettes, smokeless tobacco products and NRTs. He then provides estimates for a number of European countries based on this approach.
6. Godshall E-mail 12/29/09 5:12PM Godshall used the formula and data from the Fagerstrom paper to estimate the percentages of nicotine intake in the USA from cigarettes, smokeless and NRT products.
7. Rodu B, Godshall WT: **Tobacco harm reduction: an alternative cessation strategy for inveterate smokers**. Harm Reduction Journal 3:37 (2006). This literature review describes the traditional and modern smokeless products, their prevalence and use in the United States and Sweden and the epidemiologic evidence for their low health risks, both in absolute terms and in comparison with smoking. This review does not consider E-cigarettes or tobacco-extracts. It covers smokeless tobacco products.
8. <http://www.harmreduction.org> This web site, developed and maintained by Dr. Carl Philips of the University of Alberta and Dr. Brad Rodu of the University of Louisville promotes

itself as “The leading source of information of safer alternatives for smokers who cannot or do not wish to quit using nicotine. Attachment A8 is a print out of the home page as it appeared 11/10/2009.

9. Rodu B, Cole P: **Nicotine Maintenance for inveterate smokers**. Technology, Vol 6, pp 17-21, 1999. This paper makes the case for encouraging inveterate smokers to switch to less harmful nicotine delivery products.
10. Petition by the NY state health commissioner to FDA requesting that NRT products be made more readily available and at lower cost. Downloaded from <http://www.regulations.gov/search/Regs/home.html#docketDetail?R=FDA-2008-P-0116>
11. O'Connor RJ, Hyland A, Giovino G, Fong GT, Cummings KM. **Smoker awareness of and beliefs about supposedly less harmful tobacco products**. Am J Prev Med 2005; 29: 85-90 Abstract only  
[http://www.ncbi.nlm.nih.gov/pubmed/16005803?itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_ResultsPanel.Pubmed\\_RVDocSum&ordinalpos=6](http://www.ncbi.nlm.nih.gov/pubmed/16005803?itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum&ordinalpos=6)
12. Cummings KM. **Informing Consumers about the Relative Health Risks of Different Nicotine Delivery Products**, presented at the National Conference on Tobacco or Health, New Orleans, LA, 2001.
13. O'Connor RJ, MCNEILL A, BORLAND R, et al. **Smokers' beliefs about the relative safety of other tobacco products: findings from the ITC Collaboration**. Nic & Tob Res 2007; 9: 1033-42. Abstract only  
[http://www.ncbi.nlm.nih.gov/pubmed/17943619?itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_ResultsPanel.Pubmed\\_RVDocSum&ordinalpos=2](http://www.ncbi.nlm.nih.gov/pubmed/17943619?itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum&ordinalpos=2)
14. Altria comment to FDA Dockets Management 12/22/2009 requesting that FDA recognize that smokeless tobacco products are less hazardous than cigarettes
15. Gartner CE, Hall WD, Vos T, Bertram MY, Wallace AL, Limm SS: **Assessment of Swedish snus for tobacco harm reduction: an epidemiological modeling study**. Lancet 369(9578) 2010-4, 2007. There was little difference in health-adjusted life expectancy between smokers who quit all tobacco and those who switched to snus. Current smokers who switch to snus rather than continuing to smoke can realize substantial health benefits. Abstract only
16. Ramstrom LM, Foulds J: **Role of snus in initiation and cessation of tobacco smoking in Sweden**. Tobacco Control 15:210-214 2006. Use of snus in Sweden is associated with a reduced risk of becoming a daily smoker and an increased likelihood of stopping smoking.
17. **Smoking-attributable mortality, Years of Potential Lief Lost and Productivity Losses – United States, 200-2004**. MMWR Weekly November 14, 2008 57(45); 1226-1228  
<http://www.cdc.gov/mmwr/preview/mmwrhtm/mm5745a3.htm> “During 2000-2004, an estimated 443,000 persons in the United States died prematurely each year as a result of smoking or exposure to secondhand smoke. This figure is higher than the average annual estimate of approximately 438,000 deaths during 1997-2001.”
18. Smoking continues gradual decline among U.S. teens, smokeless tobacco threatens a comeback. Press release December 14, 2009 from the Monitoring the Future program at the University of Michigan. <http://www.monitoringthefuture.org/pressreleases/09cigpr.pdf>  
Annual reductions in the percentage of teens initiating smoking have slowed in recent years.



19. Murrelle L et al: **Hypotheses and fundamental study design characteristics for evaluating potential reduced-risk tobacco products. Part I: Heuristic.** Regulatory Toxicology and Pharmacology (2009), doi:10.1016/j.yrph.2009.12.002. In this paper, the authors explore the numbers of participants and numbers of years of observation needed to explore possible benefit from reduced risk tobacco products in reducing the risk of lung cancer. Depending on the product and end points being sought, duration of study ranged from five to more than fifteen years. Documenting the risk-reducing effect of a potential reduced-risk tobacco product by means of a long-term prospective study of smokers, switchers and quitters, could, depending on the expected level of risk reduction from the reduced risk tobacco product, require observations on 8,000 to more than 100,000. subjects. The authors of this study did not comment on the ethics, feasibility, or practicality of multi-year studies with such large numbers of participants.
20. Pankow JF, Watanabe KH, Tocalino PL, Luo W; Austin DF: **Calculated Cancer Risks for Conventional and “Potentially Reduced Exposure Product” Cigarettes.** Cancer Epidemiol Biomarkers Prev 16(3) pages 584-592 (2007). This paper makes the case that since the major carcinogens in cigarette smoke only account for less than 2% of the lung cancer caused by cigarettes, reducing their concentration in cigarette smoke will be unlikely to reduce this cancer risk by any noticeable amount.
21. The home page of the Tobacco Control Research Branch of the National Cancer Institute has, as its opening line, “The vision of the TCRB is a world free of tobacco use and related cancer and suffering.” <http://www.cancercontrol.cancer.gov/tcrb/about.html>. This item is included as an attachment to this petition to document the commitment of federal agencies and others to the concept of a tobacco free society. This commitment has been commonly interpreted as ruling out any consideration of use of any commercially available non-pharmaceutical tobacco product in a harm reduction mode.

### ***Attachment B: Electronic Cigarette References***

1. Ben Thomas Group LLC: **Study to Determine the Presence of TSNAs in NJOY Vapor.** A report to Scottera, Inc, dba NJOY December 9, 2009. Ben Thomas Group, LLC, 11200 Westheimer Rd, Suite 900, Houston TX 77042. This paper affirms the safety of the NJOY product.
2. **Experiences of Electronic Cigarette Users Suggests that These Could Be Life-Saving Devices and that They are Effective for Smoking Cessation.** Commentary on Dr. Siegel’s tobacco policy blog, at: <http://tobaccoanalysis.blogspot.com/2009/08/experiences-of-electronic-cigarette.html>. Rcd as E-mail Message from M Siegel, 8/7/2009 9:38AM; with introduction edited by J. L. Nitzkin 2/27/2010 to adapt to FDA petition guidelines. The passionate testimonials of of electronic cigarette users suggest that these devices are effective in helping smokers to quit and stay off cigarettes. These are all the comments from electronic cigarette users in response to Dr. Whelan’s *Washington Times* [op-ed piece](#). They are taken from the *Washington Times* [site](#) as well as the *Digg* [site](#) for this article. Dr Siegel has not omitted any comments from electronic cigarette users, which is remarkable because there is not a single comment from a user who has not found these devices to be satisfactory as a substitute for conventional cigarettes.
3. Judge Leon’s 1/14/2010 opinion ordering FDA to allow importation of Smoking Everywhere and NJOY E-cigarette products as downloaded from [https://ecf.ded.uscourts.gov/cgi-bin/show\\_public\\_doc?2009cv0771-54](https://ecf.ded.uscourts.gov/cgi-bin/show_public_doc?2009cv0771-54). The Reuters description of this opinion reads, in part, as follows:

A U.S. judge on Thursday granted a preliminary injunction barring the Obama administration from trying to regulate electronic cigarettes (*as drug-device combinations*) and prevent them from being imported into the United States.

In a sharply worded decision, U.S. District Judge Richard Leon scolded the Food and Drug Administration for trying to assert jurisdiction over the cigarettes, which are battery-powered or rechargeable devices that vaporize a liquid nicotine solution.

"This case appears to be yet another example of FDA's aggressive efforts to regulate recreational tobacco products as drugs or devices," he said in granting an injunction barring the FDA from regulating the cigarettes as a drug-device combination.

4. **New Jersey GASP report on Electronic Cigarettes (E-Cigarettes)**

<http://www.njgasp.org/E-Cigs%20White%Paper.pdf> -- This nine page report erroneously is dated January 11, 2009 (should be January 11, 2010) (as downloaded 2/4/2010). This report is included to show the impact the July 22, 2009 FDA press conference had on many tobacco-related organizations who then, based on this severely flawed FDA report concluded that E-cigarettes are extremely harmful, should be banned; and even present significant hazard to non-smokers. On page 6 it cites calls for E-cigarettes to be banned. These calls were issued by the American Lung Association, American Cancer Society, American Heart Association and Campaign for Tobacco Free Kids – all on the basis of the FDA press conference. On page 6, based on the FDA report, it states as a fact that “E-cigarettes appeal to youth.” Later in the report it cites multiple localities and even foreign countries taking action against E-cigarettes. Other sources of information showed that each of these that were subsequent to the FDA July 22, 2009 press conference were as a result of the press conference.

5. **FDA Analysis and Responses to FDA Press Release**

- a. News Events links to July 22, 2009 Press “to discuss potential health risks associated with electronic cigarettes.”
- b. July 22, 2009 press release transcript – verbatim transcript condemning E-cigarettes as contaminated with carcinogens and being marketed to minors
- c. FDA E-cigarette laboratory analysis serving as basis for July 22 press conference – very limited study for contaminants of a few Smoking Everywhere and Njoy E-cigarette fluid and headspace vapor, with no comparisons to NRT products or cigarette smoke.

<http://www.fda.gov/downloads/Drugs/ScienceResearch/UCM173250.pdf>

- d. **Scientific Review of FDA Report-** evaluation of FDA study prepared for NJOY by Exponent Health Services pointing out major deficiencies in FDA study design and interpretation of data.  
[http://www.njoythefreedom.com/contactcommerce/images/press\\_releases/Response%20to%20the%20FDA%20Summary.pdf](http://www.njoythefreedom.com/contactcommerce/images/press_releases/Response%20to%20the%20FDA%20Summary.pdf)
- e. **Prominent Doctors Specializing in Tobacco Harm Reduction Question FDA Study- report** by inLife summarizing criticisms of FDA report by prominent

researchers and public health physicians.

<http://www.standardnewswire.com/news/162574365.html>

- f. AAPHP letter to Dr. Deyton urging correction of misleading information in July 22 press conference.
  - g. Siegel M (Blog post 7/22/2009): **Tobacco-Specific Carcinogens Found in Nicotine Replacement Products; Will Anti-Smoking Groups Call for Removal of these Products from the Market? Despite Laboratory Finding of Carcinogens in Nicotine Replacement Medications, FDA Fails to Hold Press Conference to Express Concern About Potential Dangers of Nicotine Replacement Products.** This Blog entry criticizes FDA for condemning E-cigarettes on basis of trace carcinogens without also condemning NRT products for similar contamination.  
<http://tobaccoanalysis.blogspot.com/>
  - h. Siegel M (Blog post 7/30/2009): **Comparison of Carcinogen Levels Shows that Electronic Cigarettes are Much Safer than Conventional Ones.** This Blog entry shows TSN levels in selected electronic cigarettes, NRTs, snus, smokeless tobacco and cigarettes. <http://tobaccoanalysis.blogspot.com/2009/07/comparison.html>.
  - i. Siegel M (from Blog): **List of Identified, Known Carcinogens in Electronic Cigarettes vs. Conventional Cigarettes.** This Blog entry shows no carcinogens in electronic cigarettes beyond trace quantities, and 57 in conventional cigarettes.  
<http://tobaccoanalysis.blogspot.com/2009/07/list-of-identified-known-carcinogens-in.html>.
6. Liquid and Vapor Analyses
- a. **Safety Report on the Ruyan E-cigarette Cartridge and Inhaled Aerosol**  
Study shows TSNA levels in vaporized nicotine liquid is below what would be considered carcinogenic. Report includes both laboratory analyses and literature review. Report done by Health New Zealand Ltd.  
<http://www.healthnz.co.nz/RuyanCartr...t30-Oct-08.pdf>
  - b. **e-cigs.co.uk** – study of one bottle of “e-juice XX High 36mg/ml rated Nicotine Solution provided by Hertfordshire Training Standards showing concentrations of major ingredients by GC MS. The liquid conformed to manufacturing specs. Considered hazardous due to nicotine content, authors urged warning labels regarding ingestion, skin contact, and to keep out of reach of children.  
<http://www.e-cigs.co.uk/docs/E249A.pdf>. Bulk E-cigarette liquid is commonly used by vapers (E-cigarette users) to refill the cigarette cartridges. This is easily done and is considerably less expensive than buying more cartridges.
  - c. **InLife** (Alliance Technologies) – two studies of Regal Cartridge Liquid by GCMS; first for major ingredients, second for TSNA and TSIs  
<http://truthaboutecigs.com/science/8.pdf>  
<http://truthaboutecigs.com/science/9.pdf>
  - d. **esmoke.net** – Precision Testing Labs studies of eSmoke LLC liquid – 3 certificates showing no detectable diethylene glycol and one sheet showing no detectable contamination by a long list of semivolatiles.  
<http://www.esmoke.net/batch/090124/PGDrumGCFID.pdf> (PG Raw Material)  
<http://www.esmoke.net/batch/090124/GLDrumGCFID.pdf> (Glycerin Raw Material)

<http://www.esmoke.net/batch/090124/090124-GCFID.pdf> (GC/FID)  
<http://www.esmoke.net/batch/090124/090124-GCMS.pdf> (GC/MS)

- e. **Totally Wicked/TECC** – due diligence GC-MS analysis of 3 nicotine cartridges to confirm major constituents and their relative concentrations  
[http://www.theelectroniccigarette.co...ogy\\_report.pdf](http://www.theelectroniccigarette.co...ogy_report.pdf)
- f. **Gamucci** – due diligence GC-MS analysis of 4 nicotine cartridges to confirm major constituents and their relative concentrations  
<http://www.ecigaretteschoice.com/GamucciLabStudy.pdf>
- g. **Instead** – due diligence GC-MS analysis of 2 nicotine cartridges and vapor to confirm major constituents and their relative concentrations  
<http://www.e-cig.org/pdfs/Instead-ELiquid-Report.pdf>
- h. **SuperSmoker** – lab analysis of the vapor from 20 SuperSmoker cigarettes, cigars and cartridges to document compliance with German and FDA GRAS standards of major ingredients. Attachment is summary report.  
<http://www.supersmokerjp.com/images/...anslatiion.pdf>
- i. **Propylene Glycol Studies** – a Vapers Club review of the literature and EPA assessments of the safety of Propylene Glycol, in response to the FDA condemnation of E-cigarettes as untested and of unknown safety. Vapers Club is a group of E-cigarette users organized to try to keep E-cigarettes on the American Market. They are not associated with any manufacturer or vendor.  
<http://www.vapersclub.com/pg.html>
- j. Siegel M (from Blog): **No tobacco-specific nitrosamines or diethylene glycol detected in inLife electronic cigarettes: Do anti-smoking groups still want ex-smokers to return to the real thing?** – This Blog entry sees the scare instilled into the American public by the FDA July 22 press release as damaging to the health of the public. : <http://tobaccoanalysis.blogspot.com/2010/01/no-tobacco-specific-nitrosamines-or.html>.

### ***Attachment C: NRT Product References***

***JLN Note: The following references are provided in the context of this petition to document both the long term safety of nicotine replacement or inhalation and the relative ineffectiveness of Nicotine Replacement Therapy (NRT) re ultimate cessation of nicotine use. Attachments E6 and E7 address serious problems with some of the initial studies leading to the FDA approval of NRT products. Taken together, this set of attachments supports our impression that NRT therapy cannot stand as a cornerstone of a tobacco harm reduction initiative that could be expected to reduce overall illness and death rates from cigarettes.***

1. Moore D, Aveyard P, Connock M, Wang D, Fry-Smith A, Barton P: **Effectiveness and safety of nicotine replacement therapy assisted reduction to stop smoking: systematic review and meta-analysis.** BMJ 338:b1024 2009. This paper documents the dismal track record of pharmaceutical NRT products in securing long-lasting cessation of cigarette smoking. The abstract cites a 93.25% failure rate of NRT products after 6 months (phrased as a 6.25% success rate). The 98.4% failure rate at 20 months is cited in the study, but not mentioned in the abstract
2. Waldum HL et al: **Long term effects of inhaled nicotine.** Life Sci. 58(16) 1339-46 1966. Study on long term (2 year) inhalation of nicotine by rats showing no ill effect.  
<http://www.ncbi.nlm.nih.gov/pubmed/8614291>

3. Murray RP, Connett, JE, Zapawa M: **Does nicotine replacement therapy cause cancer? Evidence from Lung Health Study** – abstract only – smoking predicts cancer, NRT use does not <http://ntr.oxfordjournals.org/cgi/content/abstract/11/9/1076>
4. Ossip DJ et al: **Adverse effects with use of nicotine replacement therapy among quitline clients** – abstract only; adverse effects mild, few quit due to adverse effects; distribution of over the counter nicotine through quitlines declared safe. <http://ntr.oxfordjournals.org/cgi/content/abstract/11//408>
5. Sumner II W: **Estimating the health consequences of replacing cigarettes with nicotine inhalers** – abstract only; spreadsheet projection of health consequences assuming nicotine accounts for 1/3 of tobacco related illness and death shows substantial health benefit (JLN note: other research indicates nicotine accounts for less than 2% of tobacco related illness and death – so expected public health benefit much more substantial than estimated in this study) <http://tobaccocontrol.bmj.com/content/12/2/124.abstract>
6. Siegel M (from Blog): **New study shows that at least two-thirds of patients receiving placebo in “double blind” NRT trials know that they are receiving placebo.** This blog entry casts doubt on conclusions regarding effectiveness of nicotine replacement therapy. <http://tobaccoanalysis.blogspot.com/2009/07/new-study-shows-that-at-least-two.html>
7. Siegel M (from Blog): **Effectiveness of nicotine replacement therapy needs to be re-examined.** This Blog entry lists ten problems, including but not limited to conflicts of interest, bias and blinding failures that permeate much of the literature in favor of NRT therapy. <http://tobaccoanalysis.blogspot.com/2009/07/in-my-view-effectiveness-of-nicotine.html>

## C. Environmental impact

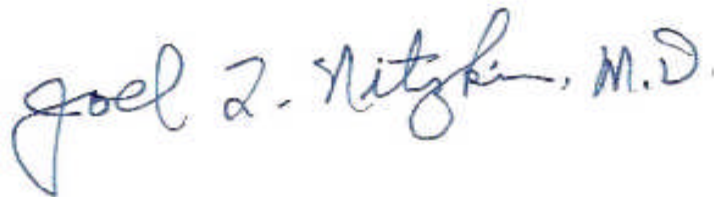
In accordance with the provision of CFR Title 21, Subpart C (Categorical Exclusions) Section 25.30 (General) paragraph (i) – I (Joel L. Nitzkin, MD – signatory to this petition) claim exclusion for need for environmental impact statement on basis that what we are requesting is limited to “corrections and technical changes in regulations.”

## D. Economic Impact

(CFR Title 21 specifies that an economic impact statement is required only when requested by the Commissioner following review of the petition.)

## E. Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition and attachments include all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are favorable to the petition.

Handwritten signature of Joel L. Nitzkin, M.D. in blue ink.