



March 23, 2016

Office on Smoking and Health
U.S. Centers for Disease Control and Prevention
4770 Buford Highway
MS F-79
Atlanta, Georgia 30341-3717

Harry L. Chen, MD
Commissioner of Vermont Department of Health
108 Cherry Street
Burlington, Vermont 05402

Dear Dr. Chen,

Per your request, I am submitting this statement of scientific evidence regarding electronic nicotine delivery systems (ENDS; including e-cigarettes), including the health effects of ENDS aerosol. For the record, I am not submitting this statement for or against any specific legislative proposal.

Please note that I will use the term ENDS throughout this letter, except where I am referring to study results that looked at surveillance survey results for a particular product, such as e-cigarettes.

Current Status of ENDS Market and Product Regulation

E-cigarettes are part of a class of products also referred to as electronic nicotine delivery systems (ENDS), which are battery-powered devices that provide doses of nicotine and other additives to the user in an aerosol.¹ There are currently multiple types of ENDS on the U.S. market, including e-cigarettes, e-hookahs, hookah pens, vape pens, e-cigars, and others. Some of these products are disposable varieties, while others can be refilled or recharged for repeated use.

ENDS, including e-cigarettes, that are not marketed for a therapeutic purpose are currently not regulated by the U.S. Food and Drug Administration (FDA) under the Family Smoking Prevention and Tobacco Control Act (FSPTCA), although FDA issued a proposal in April 2014 to regulate them under its tobacco product authorities.² If finalized as written, the rule would establish, among other provisions: restrictions to prevent sales to minors, to prohibit free samples, and to prohibit vending machine sales, unless in a facility that never admits minors.² Additional restrictions, such as establishing a product standard prohibiting flavors, would require additional rule-making.²

Furthermore, FDA's proposed regulation does not address certain key policy interventions related to ENDS, such as use in public places.² Section 916 of the Federal Food, Drug, and Cosmetic Act preserves the authority of States and localities to enact, adopt, promulgate, and enforce laws, rules, regulations or other measures with respect to tobacco products that are in addition to, or more stringent than requirements established under Chapter IX of the Food, Drugs, and Cosmetics Act, including laws, rules, regulations, or other measures relating to or prohibiting the sale, distribution, possession, exposure to, access to, advertising and promotion of, or use of tobacco products by individuals of any age, information reporting to the State, or measures relating to fire safety standards for tobacco products.³ Notwithstanding that preservation of state and local authority, however, section

916 prescribes that no State or political subdivision of a State may establish or continue in effect with respect to a tobacco product any requirement which is different from, or in addition to, any requirement under the provisions of Chapter IX of the Federal Food, Drug, and Cosmetic Act relating to tobacco product standards, premarket review, adulteration, misbranding, labeling, registration, good manufacturing standards, or modified risk tobacco products.³

Additional national and—to the extent not preempted by federal law—state policies addressing retailer licensing, Internet sales, taxation, and marketing could further prevent youth use of ENDS and other tobacco products.⁴

The current landscape of ENDS—including product design and availability, sales, marketing, use, and related legislation—is one of rapid change and high variability. Significant questions remain regarding ENDS’ toxicity and impact on patterns of conventional tobacco use. This letter summarizes the available scientific literature regarding ENDS, including surveillance data on experimentation and recent use; the health effects of ENDS, including toxicant exposure to users and non-users and impacts on patterns of conventional tobacco use; effectiveness of ENDS for quitting conventional smoking; ENDS marketing; smokefree policies and ENDS; and evidence-based strategies to prevent and reduce tobacco use.

Current Patterns of ENDS Use

To date, surveillance questions on the use of ENDS have focused primarily on e-cigarettes. National surveys show rapid increases in adult and youth use of e-cigarettes. Results from the HealthStyles survey suggest that U.S. adult e-cigarette ever use nearly doubled from 2010 (3.3%) to 2013 (8.5%).⁵ In 2014, 12.6% of U.S. adults reported ever using an e-cigarette.⁶

Data from the National Youth Tobacco Survey show current (past 30 day) e-cigarette use increased in U.S. middle and high school students substantially from 2011 to 2014 (1.5% to 13.4%).⁷ As a result, in 2014, an estimated 2.4 million U.S. middle and high school students were current users of e-cigarettes.⁷

From 2011 to 2013, U.S. middle and high school students who had never smoked cigarettes but who had ever used an e-cigarette increased over three-fold, from approximately 79,000 to over 263,000.⁸ Furthermore, intention to smoke conventional cigarettes was 43.9% among U.S. middle and high school students who had ever used e-cigarettes, whereas only 21.5% of students who had never used e-cigarettes reported intending to smoke conventional cigarettes.⁸

These surveillance data also suggest that the majority of adults and youth who use e-cigarettes also use conventional cigarettes; approximately three-quarters of current adult e-cigarette users are also current conventional cigarette smokers.^{1,9,10}

Health Effects of ENDS

A discussion of the health effects of ENDS should consider the consequences of toxicant exposure for ENDS to both users and non-users, as well as potential impacts on patterns of use of other tobacco products.

I. Toxicant Exposure to Users

Since ENDS that are not marketed for a therapeutic purpose are not currently regulated as tobacco products under the FSPTCA, we have very little information about the ingredients of liquids (purity, impurities or stability), or the approximate exposure to harmful and potentially harmful constituents when using ENDS over the short-term or long-term. To date, manufacturers are not required to publish what chemicals are in the ENDS solution, or to perform or reveal results from systematic testing. Studies have demonstrated wide variability in design, operation, and contents and emissions of carcinogens, other toxicants, and nicotine from ENDS.¹¹ Depending on the brand, ENDS cartridges typically contain nicotine, a component to produce the aerosol (e.g., propylene glycol or

glycerol), and flavorings (e.g., fruit, mint, or chocolate).¹² Chemicals that pose health risks have also been documented in some ENDS, including tobacco-specific nitrosamines, aldehydes, metals, volatile organic compounds, phenolic compounds, polycyclic aromatic hydrocarbons, and tobacco alkaloids, but at much lower levels than in conventional cigarettes.¹³ Furthermore, some ENDS manufacturers claim that the use of food flavorings is safe because they meet the FDA definition of “Generally Recognized as Safe (“GRAS”).¹⁴ However, GRAS status applies to additives for particular food uses, and does not apply to products that are not food. Furthermore, a recent study of the flavoring chemicals in e-cigarettes indicates that 75% of the flavors tested contained diacetyl.¹⁵ Diacetyl is associated with bronchiolitis obliterans and other severe respiratory diseases known as “popcorn lung.”¹⁵

Although nicotine exposure in the absence of combustion is less hazardous than exposure to combusted conventional tobacco products, nicotine itself is not without risk.^{11,16,17} Nicotine is addictive.¹¹ Nicotine exposure during certain periods of development can impair the development of brain circuits and neurons, changing the way the brain works.^{11,18,19} Pregnant women can transfer nicotine to their developing fetus, which can be toxic to the fetus, leading to adverse pregnancy and infant outcomes.¹¹ The evidence is also suggestive that nicotine exposure during adolescence may have lasting adverse consequences for brain development, including cognitive maturation and effects on working memory and attention.^{11,19,20,21,22} For non-smokers, nicotine is an acute irritant, potentially causing headache, nausea, and discomfort; for former smokers, nicotine exposure can trigger cravings, jeopardizing their abstinence.^{23,24}

Because of the risks associated with nicotine, the 2014 Surgeon General’s Report concluded that “the evidence is sufficient to provide cautionary messages to pregnant women and women of reproductive age as well as adolescents about the use of nicotine-containing products such as [...] electronic cigarettes, and newer forms of nicotine-containing tobacco products, as alternatives to smoking.”¹¹

II. Toxicant Exposure to Non-Users

The health effects of ENDS may not be limited to users.^{25,26,27} ENDS aerosol is not “water vapor.” It contains nicotine and can contain additional toxins, and thus, it is not as safe as clean air.²⁸ Although some ENDS have been shown to emit volatile organic compounds and dangerous toxins such as acetaldehydes, including acrolein, these are generally emitted at much lower levels than by cigarettes.¹⁶ However, because there are hundreds of manufacturers and no manufacturing standards, there is no way to ensure that all ENDS have acceptably low levels of toxicants. Furthermore, some ENDS can be modified to deliver marijuana and other psychoactive substances.^{29,30,31} Therefore, air containing ENDS aerosol is less safe than clean air, and ENDS use has the potential to involuntarily expose children and adolescents, pregnant women, and non-users to aerosolized nicotine and, if the products are altered, to other psychoactive substances.

All ENDS have the potential to involuntarily expose children and adolescents, pregnant women, and non-users to aerosolized nicotine. In addition, the FSPTCA does not authorize FDA to directly regulate the use of ENDS products, such as by restricting their use in public places, to address the issue of involuntary exposure among bystanders to ENDS aerosol.

III. Additional Hazards

ENDS use can result in accidents and other potential health hazards. CDC recently reported that the number of calls to poison centers in the 50 states, the District of Columbia, and U.S. territories involving e-cigarettes rose from one per month in September 2010 to 215 per month in February 2014, and 51.1% of these e-cigarette-related poisonings were among young children ages 0–5.³² In the U.S., e-cigarettes account for a small proportion of total tobacco product sales, but were involved in nearly 42% of combined monthly cigarette and e-cigarette poison center calls in February 2014.³² Health-care providers; the public health community; e-cigarette manufacturers, distributors, sellers, and marketers; and the public should be aware that e-cigarettes have the potential to cause acute adverse health effects and represent an emerging public health concern.

An increasingly popular method of ENDS use is to self-mix the e-liquid—both the nicotine content and the flavorings—prior to use. In this way, individuals can produce a customized ENDS product. There are also reports in the news media about the potential for e-cigarettes to be altered to deliver other psychoactive substances such as THC, the active ingredient in marijuana.^{33,34} Importantly, the health risks of secondhand exposure to such self-mixed concoctions are unknown.

Furthermore, there have also been multiple reports of acute injuries from these products, including burns and explosions.³⁵

IV. Impact of ENDS on Patterns of Tobacco Use

There are a range of potential beneficial and harmful impacts of ENDS on patterns of use of cigarettes and other combusted tobacco products. The Surgeon General has stated that cigarettes and other combusted tobacco products are the “overwhelming cause [of] the burden of death and disease from tobacco use in the United States” and recommends that “rapid elimination of their use will dramatically reduce this burden.”¹¹ The 2014 Surgeon General’s Report notes that ENDS—in combination with rigorous surveillance and aggressive strategies to end combusted tobacco use—could help complement strategies to eliminate combusted tobacco use by allowing complete nicotine substitution among cigarette smokers.¹¹

In the current context, cigarettes and other combusted tobacco products are widely available, heavily marketed, inexpensive, and appealing to young people.¹¹ In this context of widespread marketing and availability of cigarettes and other combustible tobacco products, there are a number of potential adverse consequences of ENDS on tobacco use patterns.¹¹ Among youth, risks include: (1) aforementioned concerns about nicotine addiction and consequences of nicotine on brain development, (2) initiation of the use of cigarettes or other combusted tobacco products as a result of introduction to inhalation of nicotine delivered via ENDS, (3) exposure to ENDS marketing and use that normalizes a behavior that looks very similar to smoking, and (4) use of combusted and noncombustible tobacco products at the same time (“dual use”).^{9,13,19,36} The potential for ENDS to renormalize tobacco use is of concern, because adolescents are particularly vulnerable to visual cues to smoke and to social norms.^{4,36,36} Again, a recent study found that among never-smoking youth who had ever used an e-cigarette, their intention to smoke conventional cigarettes was 22.4% higher than among youth who had never used e-cigarettes (43.9% v. 21.5%, respectively).⁸ Furthermore, some longitudinal studies that have followed the same individuals over time have found that among never-smoking adolescents and young adults at baseline, those who use e-cigarettes are significantly more likely to progress to conventional cigarette smoking at follow-up than those who have not used e-cigarettes.^{37,38,39} To advance the public health goal of preventing youth initiation of tobacco use, youth should not be able to purchase or be exposed to marketing for any tobacco products, including ENDS.^{4,366,40}

Among adults, potential adverse consequences include: (1) initiation of nicotine addiction among non-tobacco users and potential for progression to combusted tobacco use; (2) long-term dual use among current smokers, which may result in delayed quitting; and (3) relapse of smoking among former smokers.¹¹

As noted above, current evidence shows that the majority of adults and youth who are using e-cigarettes are also using conventional cigarettes; among current e-cigarette users, the proportion of current cigarette smokers was 72% during 2010/2011 and 76.8% during 2012/2013.^{1,5} This is of concern because only cutting down on the number of cigarettes smoked does not significantly reduce tobacco-related health risks.^{41,42}

Evidence of Effectiveness for Quitting Smoking

To date, no ENDS, including e-cigarettes, have been approved as a smoking cessation aid by the Food and Drug Administration’s Center for Drug Evaluation and Research, and there is limited research on their effectiveness as a cessation aid.²⁴ There is currently no conclusive scientific evidence that ENDS promote long-term cessation, especially at the population level.^{43,44,45,46,47,48,49,50} Currently, seven types of FDA-approved prescription and non-prescription smoking cessation products are available, including nicotine replacement therapies. These products have been scientifically shown to be effective for smoking cessation, approved by the FDA for this use, and are

safe when used as directed. ENDS marketed as smoking cessation aids must be approved for such use by the FDA Center for Drug Evaluation and Research.

ENDS Marketing

Although conventional tobacco products have been banned from television advertising for decades, ENDS are now marketed on television and other mainstream media channels. In 2014, more than 18 million, or 7 out of 10 U.S. middle and high school youth, reported exposure to e-cigarette ads in retail stores, the Internet, TV/movies, and newspapers/magazines.⁴⁰ Youth exposure to e-cigarette advertising is especially prominent in retail stores, where 1 out of 2 youth reported seeing these ads.^{40,51}

Like the products themselves, marketing claims for ENDS vary widely. The 2014 Surgeon General's Report observed that ENDS marketing "has included claims of safety, use for smoking cessation, and statements that they are exempt from clean air policies that restrict smoking."¹¹ Moreover, some ENDS marketing uses tactics which the Surgeon General has found lead to youth smoking, including: candy-flavored products; youth-resonant themes such as rebellion, glamour, and sex; and celebrity endorsements and sports and music sponsorships.³⁶ This is of concern because the Surgeon General has found that "many changes in tobacco product form and marketing have been documented as efforts by the tobacco industry to contribute to tobacco use and addiction by fostering initiation among young people; making products easier and more acceptable to use; making and marketing products so as to address health concerns; and making and marketing products to perpetuate addiction through the use of alternate products, when smoking is not allowed or is socially unacceptable."¹¹

Smokefree Policies and ENDS

As mentioned earlier, air containing ENDS aerosol is less safe than clean air, and ENDS use has the potential to involuntarily expose children and adolescents, pregnant women, and non-users to aerosolized nicotine and, if the products are altered, to other psychoactive substances.⁵² Therefore, clean air—free of both smoke and ENDS aerosol—remains the standard to protect health.

The majority of e-cigarette users also smoke cigarettes.^{1,10} Permitting ENDS use in public places could perpetuate combusted tobacco use and, therefore, tobacco-related morbidity and mortality. For example, ENDS use in public places could make it easier for smokers to sustain their nicotine addiction in public places, without switching completely away from combusted tobacco use. There is no evidence to support any claim that policies that allow ENDS use in public places result in smokers switching to ENDS completely. Additionally, because some e-cigarettes are designed to mimic smoking, allowing ENDS use in places where smoking is prohibited could complicate enforcement of smokefree policies and renormalize tobacco use.⁵³

Conclusion

ENDS have a range of potential impacts on individual and population health, and significant questions remain regarding their toxicity and impact on patterns of conventional tobacco use. In contrast, considerable and conclusive evidence exists on the health harms of cigarettes and other combusted tobacco products among both users and non-users. Moreover, the scientific literature supports the safety and effectiveness of FDA-approved cessation aids when used as directed.

Given what we know about the harms of cigarettes and other combusted tobacco products, we should not lose sight of the importance of tobacco prevention and control. However, given what we also know about nicotine addiction, the harms of nicotine exposure—especially to the adolescent brain—and the fact that ENDS that do not make therapeutic claims are not currently regulated, the scientific evidence supports a public health approach to first "do no harm." Ensuring children and youth do not have access to ENDS, preventing ENDS use among children and youth, reducing the appeal of ENDS to children and youth, protecting nonusers from involuntary exposure to ENDS aerosol, and ensuring smokers who want to quit have access to proven cessation methods are all ways we can promote public health and protect vulnerable populations from potential harms.

Thank you for your attention to this important public health issue.

Thank you for your inquiry.

Sincerely,

A handwritten signature in blue ink that reads "Brian A. King". The signature is fluid and cursive, with a large initial "B" and a long, sweeping underline.

Brian A. King, PhD, MPH
Deputy Director for Research Translation
Office on Smoking and Health
Centers for Disease Control and Prevention
U.S. Department of Health and Human Services

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