



SCIENTIFIC EVIDENCE ON ELECTRONIC NICOTINE DELIVERY SYSTEMS (ENDS)

June 2015

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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 typically provide doses of nicotine and other additives to the user in an aerosol.¹
 - *Note that this brief refers to e-cigarettes specifically if the surveillance data referred to asked about e-cigarettes specifically, rather than the full class of ENDS products.*
- 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 that do not make therapeutic claims, including e-cigarettes, 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 provisions, such as establishing a product standard prohibiting flavors, could require additional rule-making.²
- Furthermore, FDA 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
 - Section 916, however, 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.

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 more than doubled from 2010 (3.3%) to 2013 (8.5%).⁵
 - 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%).⁶ As a result, in 2014, an estimated 2.4 million U.S. middle and high school students were current users of e-cigarettes.⁶
- 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 263,000.⁷
- 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.⁷
- These surveillance data also suggest that the majority of adults and youth who use e-cigarettes also use conventional cigarettes.^{1,8,9} For example, during 2012–2013, 76.8% of adult current e-cigarette users were also current conventional cigarettes smokers.⁹

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 do not make therapeutic claims are not yet 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.¹⁰
 - 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).¹¹
 - 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 lower levels than in conventional cigarettes.¹²

- 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”).¹³ However, GRAS status applies to additives for particular food uses, and does not apply to products that are not food.
- Although nicotine exposure in the absence of combustion is less hazardous than exposure to combusted conventional tobacco products, nicotine itself is not without risk.^{14,15}
 - Nicotine is addictive.¹⁰
 - Nicotine exposure during certain periods of development can impair the development of brain circuits and neurons, changing the way the brain works.^{10,16,17}
 - Pregnant women can transfer nicotine to their developing fetus, which can be toxic to the fetus, leading to adverse pregnancy and infant outcomes.^{10,17}
 - 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.^{10,17,18,19,20}
 - 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.^{21,22}
- 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.”¹⁰

II. Toxicant Exposure to Non-Users

- The health effects of ENDS may not be limited to users.^{23,24,25}
- ENDS aerosol is not “water vapor.” It typically contains nicotine and can contain additional toxins, and thus, it is not as safe as clean air.²⁶
- Although some ENDS have been shown to emit volatile organic compounds and dangerous toxins such as acetaldehydes, including acrolein, these are generally emitted at lower levels than by cigarettes.¹⁴ 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 THC, the active ingredient in marijuana, and other psychoactive substances.²⁷
- 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.
- In addition, FDA does not regulate the use of ENDS use, particularly in public places, and 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 0–5.²⁸ 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 2014.²⁸

- 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 using certain ENDS products 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.^{29,30} Importantly, the health risks of secondhand exposure to such self-mixed concoctions are unknown.

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 conventional 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.”¹⁰
 - The 2014 Surgeon General’s Report also 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 conventional cigarette smokers.¹⁰
- In the current context, conventional cigarettes and other combusted tobacco products are widely available, heavily marketed, inexpensive, and appealing to young people.¹⁰ In this context of widespread marketing and availability of conventional cigarettes and other combustible tobacco products, there are a number of potential adverse consequences of ENDS on tobacco use patterns.¹⁰
 - Among youth, risks include:
 - Aforementioned concerns about nicotine addiction and consequences of nicotine on brain development;
 - Initiation of the use of cigarettes or other combusted tobacco products as a result of introduction to inhalation of nicotine delivered via ENDS;
 - Exposure to ENDS marketing and use that normalizes a behavior that looks very similar to smoking; and
 - Use of combusted and noncombustible tobacco products at the same time (“dual use”).^{10,31}
 - 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.^{4,31} Again, a recent study found that among never-smoking youth who had ever used an e-cigarette, their intention to smoke conventional cigarettes was nearly double that of youth who had never used e-cigarettes (43.9% v. 21.5%, respectively).⁷
 - 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.^{4,31}
- Among adults, potential adverse consequences include:
 - Initiation of nicotine addiction among non-tobacco users and potential for progression to combusted tobacco use;
 - Long-term dual use among current smokers, which may result in delayed quitting; and
 - Relapse of smoking among former smokers.¹⁰

- 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.^{32,33}

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.²²
- There is currently no conclusive scientific evidence that ENDS promote long-term cessation, especially at the population level.^{34,35,36,37,38,39,40,41,42}
- 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. 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.”¹⁰
- 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.³¹¹
 - 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.”¹⁰

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.⁴³ Therefore, clean air—free of both smoke and ENDS aerosol—remains the standard to protect health.
- The majority of e-cigarette users also smoke conventional cigarettes.^{1,9} 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.⁴⁴

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 conventional 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 conventional 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.

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