

# Electronic cigarettes: Safety concerns and regulatory issues

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Is there anything such as safe smoking? This is a claim made by manufacturers of electronic cigarettes, who promote their products as smoking alternatives. The wide availability and aggressive marketing of these products may leave health care providers and patients asking an important public health question. Are electronic cigarettes the same lethal vice through a more modern vehicle or are they a safer alternative to smoking?

Historically, tobacco products, such as conventional cigarettes, are some of the most unregulated products on the market. In 1996, the Food and Drug Administration (FDA) attempted to assert jurisdiction over tobacco products under the Food, Drug, and Cosmetic Act of 1938.<sup>1</sup> However, this was met by great resistance, particularly by the tobacco industry. Ultimately, the courts determined that FDA did not have legal jurisdiction over tobacco products. After this ruling, all FDA tobacco regulations were dropped (Leggett CC, Food and Drug Administration, personal communication, 2002). However, on June 29, 2009, president Obama signed the Family Smoking

Prevention and Tobacco Control Act.<sup>2</sup> This new legislation grants FDA the authority to regulate tobacco products. The FDA is now starting to collaborate with public health leaders to develop and implement regulations.<sup>3</sup>

Independent of the new tobacco legislation, FDA has regulatory jurisdiction over nicotine replacement therapies and other non-nicotine-containing oral medications that are marketed as smoking-cessation aids. These medications and nicotine-containing skin patches, chewing gums, oral inhalers, and nasal sprays have demonstrated safety and efficacy through controlled clinical trials and have indications that are approved by FDA. Advertising for electronic cigarettes suggests that these products can be used as safe alternatives to conventional cigarettes, a message that may be misleading for both health care providers and patients.

**Design characteristics.** Although various brands of electronic cigarettes exist, most share the same general design (Figure 1). These non-flammable products are driven by microtechnology with three general

components: a nicotine cartridge, an atomization chamber with a membrane to suspend the ingredients, and a smart chip with a rechargeable lithium battery.

Manufacturers claim that the product's nicotine cartridge also contains water, propylene glycol, and other ingredients (e.g., flavorings). Some products emit an aroma that emulates tobacco or other scents; others are odorless. Unlike conventional cigarettes, these products do not contain tobacco or tar. However, FDA's Division of Pharmaceutical Analysis has recently analyzed samples of two brands of electronic cigarettes. The identified ingredients include diethylene glycol (a component of antifreeze) and nitrosamine (a known carcinogen).<sup>4</sup> Since these results are limited to products from two companies, no one can be certain of the type and quantity of ingredients that may be found in other brands of electronic cigarettes.

The tip of the delivery device has an indicator light that turns red as you inhale. Upon inhalation, the nicotine cartridge becomes heated, and the atomization chamber creates mist that resembles the smoke from conventional cigarettes. The nicotine-containing mist is not inhaled by the user and quickly evaporates. The actual effects, including effects of secondary exposure, of the vapor are unknown. In contrast to the few named ingredients used in the electronic cigarette cartridge, the top manufacturers of conventional tobacco cigarettes reportedly use a combined total of 599 ingredients in the production process.<sup>5</sup>

Although most electronic cigarette products appear to be tobacco free, health care providers and pa-

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Figure 1. Basic design of an electronic cigarette.



tients must remember that nicotine alone is highly addictive and has been associated with adverse events. Based on product design, it appears that electronic cigarettes are intended to deliver addictive levels of nicotine, which could lead to adverse effects. Upon inhalation, nicotine is carried deep into the lungs and absorbed quickly into the bloodstream. Chronic systemic exposure to nicotine has been found to contribute to accelerated coronary artery disease, acute cardiac ischemic events, and hypertension. Other potential adverse effects of nicotine include stroke, delayed wound healing, reproductive toxicity, peptic ulcer disease, and esophageal reflux.<sup>6</sup>

**Regulatory perspective.** The electronic cigarettes that have been investigated by FDA are not subject to the Family Smoking Prevention and Tobacco Control Act.<sup>7</sup> Thus, they do not fit within the regulatory scheme that Congress has established for tobacco products.

FDA has indicated that electronic cigarettes are intended to be manipulated and used in ways similar to how a smoker manipulates and uses conventional cigarettes. Moreover, like conventional cigarettes, electronic cigarettes are intended primarily for the delivery of volatilized chemical substances, which often include nicotine. Since FDA is not aware of any data establishing that such products are generally recognized among scientific experts as safe and effective, these products are new drugs, as defined by the Federal Food, Drug,

and Cosmetic Act of 1938,<sup>1</sup> requiring approval of a new drug application (NDA) to be legally marketed in the United States. Without an approved NDA, the marketing of the various brands of electronic cigarettes reviewed by FDA is subject to enforcement action within the United States.

Although general regulatory statements can be made, in order to make a definitive determination of the regulatory status of any drug and device combination product, FDA must review a complete description of the product's design, function, formulation, labeling and promotion (including statements and representations on the Internet), and any other information (e.g., patents) used to describe the product's intended uses.

FDA continues to evaluate the regulatory status of electronic cigarettes on a case-by-case basis. Although no electronic cigarette has received FDA-approved labeling, manufacturers continue to make unfounded claims. Examples of these statements include "It's a better way to smoke. It is free of tar and carbon monoxide, therefore, healthier. There is no danger of secondhand smoke."<sup>7</sup> Since no clinical trials have been conducted with these products, it is unclear how electronic cigarettes actually affect the body's structures and functions or if they mitigate or treat the symptoms of nicotine addiction. FDA requires all nicotine-delivery products intended for use by humans, with the exception of conventional tobacco products, to be clinically proven for safety and efficacy and regulated.

Currently, electronic cigarettes are sold in all 50 states and in over 25 other countries. They are available online and at several retail locations across the United States. It is not uncommon for unscrupulous marketers to introduce unregulated products into the market without FDA's review or approval. One of the first steps in targeting unapproved products is the issuance of an import alert, which allows for the refusal of entry of several brands of electronic cigarettes offered for importation into the United States.<sup>8</sup> However, with limited FDA resources and creative manufacturers who misbrand their products, some products may continue to enter the United States.

**Information for health care providers.** Based on consumer inquiries to FDA, electronic cigarettes appear to be viewed by the general public as an aid to smoking cessation. This misconception needs to be addressed by health care providers. The goal is to stop or prevent smoking, not to seek an unproven alternative that may delay a smoker's desire to quit or encourage the initiation of smoking behavior if a product is perceived as a safer alternative to conventional cigarettes. These products may be attractive to minors who may be drawn to the technology, flavoring, and accessibility.

Until FDA review and approval of electronic cigarettes prove otherwise, smokers should be encouraged to seek nicotine replacement therapies or non-nicotine-containing oral medications with FDA-approved labeling.

In the interest of public health, health care providers should advise patients that electronic cigarettes are not a proven, safer alternative to conventional cigarettes. For this reason, the use of these product as a harm-reduction strategy or smokeless alternative in public settings should be discouraged.

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