e-Cigarette Use Among Youth and Young Adults - Introduction

Although conventional cigarette smoking has declined markedly over the past several decades among youth and young adults in the United States (U.S. Department of Health and Human Services [USDHHS] 2012), there have been substantial increases in the use of emerging tobacco products among these populations in recent years (Centers for Disease Control and Prevention [CDC] 2015c). Among these increases has been a dramatic rise in electronic cigarette (e-cigarette) use among youth and young adults. It is crucial that the progress made in reducing cigarette smoking among youth and young adults not be compromised by the initiation and use of e-cigarettes. This Surgeon General's report focuses on the history, epidemiology, and health effects of e-cigarette use among youth and young adults; the companies involved with marketing and promoting these products; and existing and proposed public health policies regarding the use of these products by youth and young adults.

E-cigarettes include a diverse group of devices that allow users to inhale an aerosol, which typically contains nicotine, flavorings, and other additives. E-cigarettes vary widely in design and appearance, but generally operate in a similar manner and are composed of similar components (Figure 1.1). A key challenge for surveillance of the products and understanding their patterns of use is the diverse and nonstandard nomenclature for the devices (Alexander et al. 2016). These devices are referred to, by the companies themselves, and by consumers, as "e-cigarettes," "e-cigs," "cigalikes," "e-hookahs," "mods," "vape pens," "vapes," and "tank systems." In this report, the term "e-cigarette" is used to represent all of the various products in this rapidly diversifying product category. The terms may differ by geographic region or simply by the prevailing preferences among young users. For example, some refer to all cigarette-shaped products as "e-cigarettes" or as "cigalikes," and some may refer to the pen-style e-cigarettes as "hookah pens" or "vape pens" (Richtel 2014; Lempert et al. 2016).

Figure 1.1 Diversity of e-cigarette products

Source: Photo by Mandie Mills, CDC.

This report focuses on research conducted among youth and young adults because of the implications of e-cigarette use in this population, particularly the potential for future public health problems. Understanding e-cigarette use among young persons is critical because previous research suggests that about 9 in 10 adult smokers first try conventional cigarettes during adolescence (USDHHS 2012). Similarly, youth e-cigarette experimentation and use could also extend into adulthood; however, e-cigarette use in this population has not been examined in previous reports of the Surgeon General. The first Surgeon General's report on the health consequences of smoking was published in 1964; of the subsequent reports, those published in 1994 and 2012 focused solely on youth and young adults (USDHHS 1994, 2012). More recently, the 2012 report documented the evidence regarding tobacco use among youth and young adults, concluding that declines in cigarette smoking had slowed and that decreases in the use of smokeless tobacco had stalled. That report also found that the tobacco industry's advertising and promotional activities are causal to the onset of smoking in youth and young adults and the continuation of such use as adults (USDHHS 2012). However, the 2012 report was prepared before e-cigarettes were as widely promoted and used in the United States as they are now. Therefore, this 2016 report documents the scientific literature on these new products and their marketing, within the context of youth and young adults. This report also looks to the future by examining the potential impact of e-cigarette use among youth and young adults, while also summarizing the research on current use, health consequences, and marketing as it applies to youth and young adults.

Evidence for this report was gathered from studies that included one or more of three age groups. We defined these age groups to be young adolescents (11–13 years of age), adolescents (14–17 years of age), and young adults (18–24 years of age). Some studies refer to the younger groups more generally as *youth.* Despite important issues related to e-cigarette use in adult populations, clinical and otherwise (e.g., their potential for use in conventional smoking cessation), that literature will generally not be included in this report unless it also discusses youth and young adults (Farsalinos and Polosa 2014; Franck et al. 2014; Grana et al. 2014).

Given the recency of the research that pertains to e-cigarettes, compared with the decades of research on cigarette smoking, the "precautionary principle" is used to guide actions to address e-cigarette use among youth and young adults. This principle supports intervention to avoid possible health risks when the potential risks remain uncertain and have been as yet partially undefined (Bialous and Sarma 2014; Saitta et al. 2014; Hagopian et al. 2015). Still, the report underscores and draws its conclusions from the known health risks of e-cigarette use in this age group.

Historical Background

Understanding the role of e-cigarettes requires understanding the long history of tobacco use in the United States, including the role of nicotine delivery, the multiple examples of "reduced-harm" products and associated health claims, and the impact of using tobacco products on the public's health. Since the late nineteenth century, when the "modern" cigarette came into use, scientists and public health officials have linked cigarette smoking to a remarkable number of adverse effects, and it is now recognized as the primary cause of premature death in the United States (USDHHS 2014). Correspondingly, for a century, manufacturers, scientists, entrepreneurs, and public health leaders have promoted or recommended product changes that might remove some of the harmful elements in cigarette smoke. E-cigarettes are among the latest products.

E-cigarettes are designed for users to inhale nicotine, flavorings, and other additives through an aerosol. The claims and marketing strategies employed by the e-cigarette companies, and the efforts made by others to develop scientific and regulatory tools to deal with these new products, both contribute to the current discourse on e-cigarettes. Many lessons for assessing the potential (and future) consequences of these products can be learned from examining the relevant experiences of the past century, especially the introduction of novel products (including e-cigarettes as well as other tobacco and nicotine products) and the claims of reduced exposure to toxins made by the industry and elsewhere.

Early Efforts to Modify Cigarettes

In the 1880s and 1890s, entrepreneurs promoted novel products that allegedly blocked nicotine and other constituents of conventional cigarettes believed to be poisonous. Dr. Scott's Electric Cigarettes, advertised in *Harper's Weekly*, claimed not only to light without matches but also to contain a cotton filter that "strains and eliminates the injurious qualities from the smoke," including nicotine (*Harper's Weekly* 1887). Nicotine delivery was essential to the development of the modern cigarette in the twentieth century; early on, this substance was thought to be addicting and thus vital to retaining customers. In 1913, the Camel brand was a new kind of cigarette that introduced high-nicotine content by using burley tobacco, which was generally too harsh to inhale into the lungs, but was made more inhalable through the addition of casings (e.g., sugars, licorice) (Tindall 1992; Proctor 2011). In 1916, American Tobacco introduced its Lucky Strike blended cigarette, and in 1918 Liggett & Myers (L&M) reformulated its Chesterfield brand to make it more palatable to users. As the market grew, advertisements for major brands routinely included health-related statements and testimonials from physicians. During the 1930s and 1940s, prominent advertising campaigns included claims like "Not a cough in a carload" (Old Gold) (Federal Trade Commission [FTC] 1964, p. LBA-5); "We removed from the tobacco harmful corrosive ACRIDS (pungent irritants) present in cigarettes manufactured in the old-fashioned way" (Lucky Strike) (FTC 1964, p. LBA-2); and "Smoking Camels stimulates the natural flow of digestive fluids … increases alkalinity" (Camel) (FTC 1964, p. LBA-1a). Thus, early modifications to the cigarette were made so that it was more palatable, had a higher nicotine delivery and uptake, and could be marketed as "safe" (FTC 1964; Calfee 1985).

Filters, Tar Reduction, and Light and Low-Tar Cigarettes

The landmark 1964 Surgeon General's report on smoking and health concluded that cigarette smoking contributed substantially to mortality from certain specific diseases, including lung cancer (U.S. Department of Health, Education, and Welfare 1964). Although the 1964 report considered the topic, it found the evidence insufficient to assess the potential health benefits of cigarette filters. Cigarettes with filters became the norm by the 1960s, and marketing them with an overt message about harm reduction became the standard (National Cancer Institute [NCI] 1996). However, the Surgeon General convened another group of experts on June 1, 1966, to review the evidence on the role played by the tar and nicotine content in health. The group concluded that "[t]he preponderance of scientific evidence strongly suggests that the lower the 'tar' and nicotine content of cigarette smoke, the less harmful are the effects" (Horn 1966, p. 16,168). Subsequent studies have repeatedly failed to demonstrate health benefits of smoking light and low-tar cigarettes versus full-flavor cigarettes (Herning et al. 1981; Russell et al. 1982; Benowitz et al. 1983, NCI 2001).

Over the years, the tobacco industry used multiple methods to reduce the machine-tested yields of tar and nicotine in cigarettes as a way to claim "healthier" cigarettes. Beginning in the 1970s, tobacco companies advertised the tar and nicotine levels for their cigarettes, which encouraged smokers to believe, without substantiation,

they could reduce their risk of exposure to these constituents (Cummings et al. 2002; Pollay and Dewhirst 2002). In 1996, the FTC issued a statement that it would allow cigarette companies to include statements about tar and nicotine content in their advertising as long as they used a standardized machine-testing method (Peeler 1996).

The Role of Nicotine and Nicotine Delivery

Although the public health community understood early on that nicotine was the primary psychoactive ingredient in cigarette smoke, before the 1980s, little was known about the importance of nicotine in the addiction process beyond what the cigarette manufacturers had learned from their own research. Some scientists warned that due to nicotine addiction, a reduction in nicotine yields, along with decreases in tar, could lead smokers to change their smoking behavior, such as by smoking a greater number of cigarettes to maintain their nicotine intake or changing their behavior in more subtle ways, such as varying the depth of inhalation or smoking more of the cigarette (Jarvis et al. 2001; National Cancer Institute 2001; Thun and Burns 2001). Not until the 1970s and 1980s, as researchers studying other forms of drug abuse began to apply their research methods to cigarette smoking, did it become apparent that nicotine was similar in its addictive capability to other drugs of abuse, such as heroin and cocaine (USDHHS 1981, 1988). As described in the 1988 Surgeon General's report and in subsequent research, symptoms associated with nicotine addiction include craving, withdrawal, and unconscious behaviors to ensure consistent intake of nicotine (USDHHS 1988; al'Absi et al. 2002; Hughes 2007).

Although the tobacco industry has long understood the importance of nicotine to maintain long-term cigarette smokers through addiction, public health officials did not fully appreciate this in a broad sense until the 1988 Surgeon General's report, *The Health Consequences of Smoking: Nicotine Addiction* (USDHHS 1988).

FDA and Nicotine Regulation

In 1988 (and again in 1994), the Coalition on Smoking OR Health and other public-interest organizations petitioned FDA to classify low-tar and nicotine products as drugs and to classify Premier, the short-lived "smokeless cigarette product" from R.J. Reynolds, as an alternative nicotine-delivery system (Stratton et al. 2001). The Coalition on Smoking OR Health cited indirect claims made through advertising and marketing as evidence of R. J. Reynolds's intent to have the product used for the mitigation or prevention of disease (Slade and Ballin 1993). Meanwhile, FDA launched an investigation into the practices of the tobacco industry, including the manipulation of nicotine delivery. FDA asserted its jurisdiction over cigarettes and smokeless tobacco and issued certain rules governing access to and promotion of these products (*Federal Register* 1996). On March 21, 2000, the U.S. Supreme Court ruled 5-4 that Congress had not yet given FDA the necessary statutory authority to issue any rules pertaining to tobacco products (Gottlieb 2000; *FDA v. Brown & Williamson Tobacco Corp.* 2000). The subsequent debate over control of nicotine products, including their potential impact on youth, ultimately led to the passage of the 2009 *Family Smoking Prevention and Tobacco Control Act,* which gave FDA authority to regulate tobacco products. Thus, discussions about the introduction of novel nicotine-containing tobacco products in the market during the 1980s and 1990s helped shape the current regulation of tobacco and nicotine products.

New products introduced in the 1990s or later included modified tobacco cigarettes (e.g., Advance, Omni); cigarette-like products, also called cigalikes (e.g., Eclipse, Accord); and smokeless tobacco products (e.g., Ariva, Exalt, Revel, snus). Advance, made by Brown and Williamson, was test-marketed with the slogan "All of the taste … Less of the toxins." Vector launched a national advertising campaign for its Omni cigarette with the slogan "Reduced carcinogens. Premium taste." In addition to the question of whether the claims were supported by sufficient evidence, scientists and tobacco control leaders raised concerns about the potential for adverse consequences associated with novel nicotine and tobacco products marketed for harm reduction, such as a reduction in cessation rates or increased experimentation by children (Warner and Martin 2003; Joseph et al. 2004; Caraballo et al. 2006). Studies have shown that smokers are interested in trying novel "reduced-exposure" products and perceive them to have lower health risks, even when advertising messages do not make explicit health claims (Hamilton et al. 2004; O'Connor et al. 2005; Caraballo et al. 2006; Choi et al. 2012; Pearson et al. 2012).

At FDA's request, the Institute of Medicine (IOM [now the National Academy of Medicine]) convened a committee of experts to formulate scientific methods and standards by which potentially reduced-exposure products (PREPs), whether the purported reduction was pharmaceutical or tobacco related, could be assessed. The committee concluded that "[f]or many diseases attributable to tobacco use, reducing risk of disease by reducing exposure to tobacco toxicants is feasible" (Stratton et al. 2001, p. 232). However, it also cautioned that "PREPs have not

yet been evaluated comprehensively enough (including for a sufficient time) to provide a scientific basis for concluding that they are associated with a reduced risk of disease compared to conventional tobacco use" (Stratton et al. 2001, p. 232). The committee added that "the major concern for public health is that tobacco users who might otherwise quit will use PREPs instead, or others may initiate smoking, feeling that PREPs are safe. That will lead to less harm reduction for a population (as well as less risk reduction for that individual) than would occur without the PREP, and possibly to an adverse effect on the population" (Stratton et al. 2001, p. 235). Subsequently, in 2006, Judge Kessler cited these findings in her decision which demanded the removal of light and low-tar labeling due to the misleading nature of these claims (*United States v. Philip Morris* 2006).

The E-Cigarette

Invention of the E-Cigarette

An early approximation of the current e-cigarette appeared in a U.S. patent application submitted in 1963 by Herbert A. Gilbert and was patented in August 1965 (U.S. Patent No. 3,200,819) (Gilbert 1965). The application was for a "smokeless nontobacco cigarette," with the aim of providing "a safe and harmless means for and method of smoking" by replacing burning tobacco and paper with heated, moist, flavored air. A battery-powered heating element would heat the flavor elements without combustion (Gilbert 1965). The Favor cigarette, introduced in 1986, was another early noncombustible product promoted as an alternative nicotine-containing tobacco product (United Press International 1986; Ling and Glantz 2005).

The first device in the recent innovation in e-cigarettes was developed in 2003 by the Chinese pharmacist Hon Lik, a former deputy director of the Institute of Chinese Medicine in Liaoning Province. Lik's patent application described a kind of electronic atomizing cigarette (Hon 2013). With support from Chinese investors, in 2004 the product was introduced on the Chinese market under the company name Ruyan (Sanford and Goebel 2014). The product gained some attention among Chinese smokers early on as a potential cessation device or an alternative cigarette product.

The e-cigarette was part of the U.S. market by the mid-2000s, and by 2010 additional brands started to appear in the nation's marketplace, including Ruyan and Janty (Regan et al. 2013). Ruyan gained a U.S. patent for its product with the application stating that the product is "an electronic atomization cigarette that functions as substitutes (sic) for quitting smoking and cigarette substitutes." (U.S. Patent No. 8,490,628 B2, 2013). In August 2013, Imperial Tobacco Group purchased the intellectual property behind the Ruyan e-cigarette for $75 million. As of 2014 an estimated 90% of the world's production of e-cigarette technology and products came from mainland China, mainly Guangdong Province and Zhejiang Province (Barboza 2014).

Sales of e-cigarettes in the United States have risen rapidly since 2007. Widespread advertising via television commercials and through print advertisements for popular brands, often featuring celebrities, has contributed to a large increase in e-cigarette use by both adults and youth since 2010 (Felberbaum 2013; King et al. 2013; Regan et al. 2013). Additionally, marketing through social media, as well as other forms of Internet marketing, has been employed to market these devices (Huang et al. 2014; Kim et al. 2014).

In 2013, an estimated 13.1 million middle school and high school students were aware of e-cigarettes (Wang et al. 2014). According to data from the National Youth Tobacco Survey, in 2011 the prevalence of current e-cigarette use (defined as use during at least 1 day in the past 30 days) among high school students was 1.5%; prevalence increased dramatically, however, to 16% by 2015, surpassing the rate of conventional-cigarette use among high school students (CDC 2016b; see Chapter 2). This equates to 2.4 million high school students and 620,000 middle school students having used an e-cigarette at least one time in the past 30 days in 2015 (CDC 2016b).

These trends have led to substantial concern and discussion within public health communities, including state and national public health agencies, professional organizations, and school administrators and teachers. A primary concern is the potential for nicotine addiction among nonsmokers, especially youth and young adults, and that this exposure to nicotine among youth and young adults is harmful. The diversity and novelty of e-cigarette products on the market and ongoing product innovations make assessments of the biological effects of current e-cigarettes under actual conditions of use—such as their long-term harmfulness—difficult to measure. Unanswered questions remain about the risk profile of these devices, their potential use by young people as a first step to other nicotine products, and their total impact on public health. There are diverging opinions about the potential public health impact of these new products. Some public health scientists have highlighted the potential for alternative

nicotine products to serve as a substitute for conventional cigarettes and thus a harm reduction tool (Henningfield et al. 2003; Abrams 2014). Others have cautioned that the use of alternative nicotine products might become a bridge that may lead to greater tobacco product use—including dual- or multiple-product use—or initiate nicotine addiction among nonsmokers, especially youth (Cobb et al. 2010; Wagener et al. 2012; Benowitz and Goniewicz 2013; Britton 2013; Chapman 2013; Etter 2013; USDHHS 2014). Current evidence is insufficient to reject either of these hypotheses.

E-Cigarette Products

Components and Devices

E-cigarette devices are composed of a battery, a reservoir for holding a solution that typically contains nicotine, a heating element or an atomizer, and a mouthpiece through which the user puffs (Figure 1.2). The device heats a liquid solution (often called e-liquid or e-juice) into an aerosol that is inhaled by the user. E-liquid typically uses propylene glycol and/or glycerin as a solvent for the nicotine and flavoring chemicals

Flavors and E-Cigarettes

The e-liquids in e-cigarettes are most often flavored; a study estimated that 7,700 unique flavors exist (Zhu et al. 2014) and that most of them are fruit or candy flavors (Figure 1.3). A content analysis of the products available via online retail websites documented that tobacco, mint, coffee, and fruit flavors were most common, followed by candy (e.g., bubble gum), unique flavors (e.g., Belgian waffle), and alcoholic drink flavors (e.g., strawberry daiquiri) (Grana and Ling 2014). Some retail stores are also manufacturers that create custom flavors, which increases the variety of flavors available.

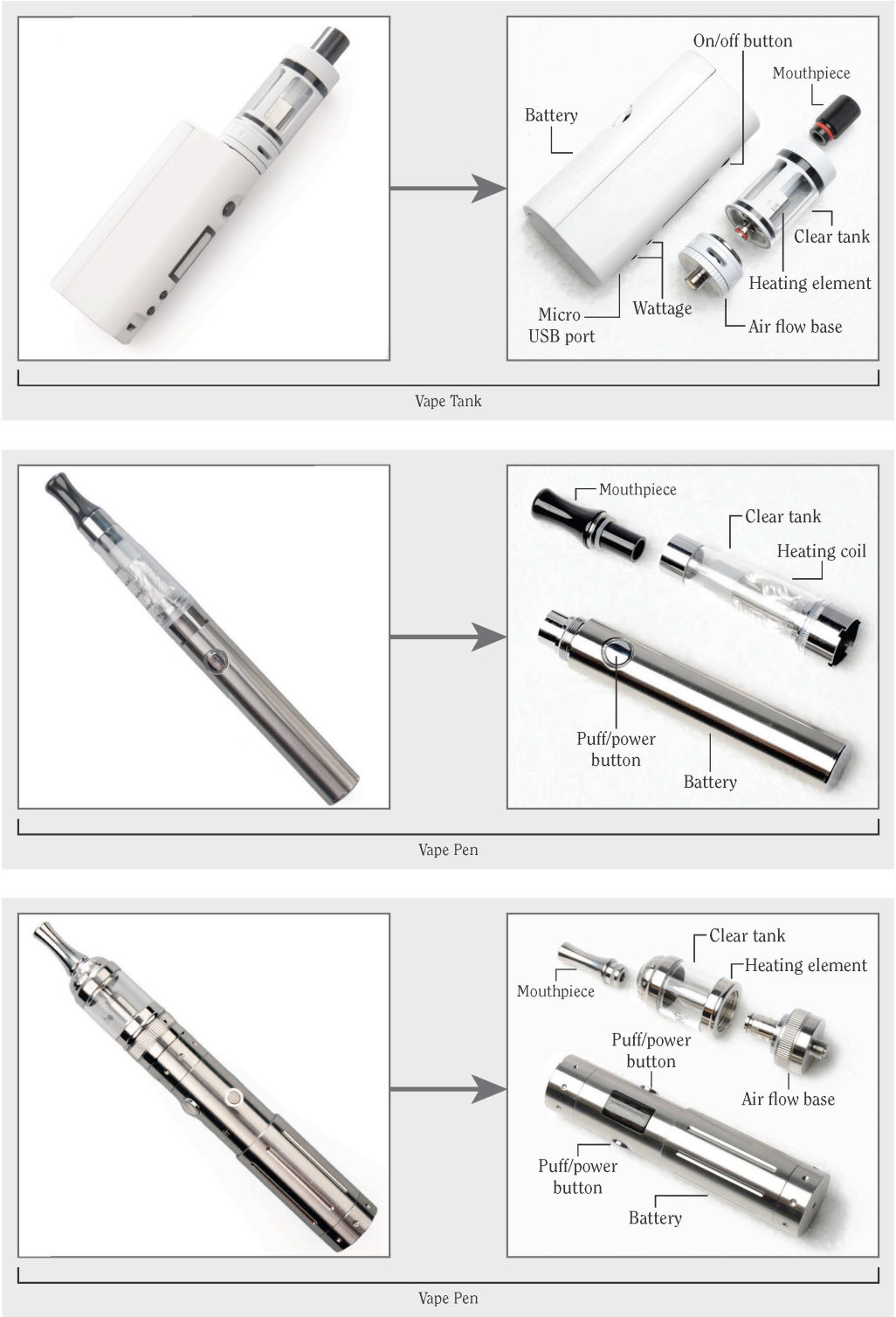
The widespread availability and popularity of flavored e-cigarettes is a key concern regarding the potential public health implications of the products. The concern, among youth, is that the availability of e-cigarettes with sweet flavors will facilitate nicotine addiction and simulated smoking behavior—which will lead to the use of conventional tobacco products (Kong et al. 2015; Krishnan-Sarin et al. 2015). Flavors have been used for decades to attract youth to tobacco products and to mask the flavor and harshness of tobacco (USDHHS 2012). Industry documents show that tobacco companies marketed flavored little cigars and cigarillos to youth and to African Americans to facilitate their uptake of cigarettes (Kostygina et al. 2014). Companies also intended flavored smokeless tobacco products to facilitate "graduation" to unflavored products that more easily deliver more nicotine to the user (USDHHS 2012). Various studies have shown that youth are more likely than adults to choose flavored cigarettes and cigars (CDC 2015b). Concern over these findings led Congress to include a ban on characterizing flavors for cigarettes, other than tobacco or menthol, in the Tobacco Control Act. A similar concern exists about e-cigarettes, and this concern is supported by studies indicating that youth and young adults who have ever used e-cigarettes begin their use with sweet flavors rather than tobacco flavors (Kong et al. 2015; Krishnan-Sarin et al. 2015). Notably, 81.5% of current youth e-cigarette users said they used e-cigarettes "because they come in flavors I like" (Ambrose et al. 2015).

E-Cigarette Devices

First-generation e-cigarettes were often similar in size and shape to conventional cigarettes, with a design that also simulated a traditional cigarette in terms of the colors used (e.g., a white body with tan mouthpiece). These devices were often called cigalikes, but there were other products designed to simulate a cigar or pipe. Other cigalikes were slightly longer or narrower than a cigarette; they may combine white with tan or may be black or colored brightly. These newer models use a cartridge design for the part of the device that holds the e-liquid, which is either prefilled with the liquid or empty and ready to be filled. The user then squeezes drops of the e-liquid onto a wick (or bit of cotton or polyfil) connected to the heating element and atomizer (Figure 1.4). As e-cigarettes have become more popular, their designs have become more diverse, as have the types of venues where they are sold (Noel et al. 2011; Zhu et al. 2014).

Second-generation devices include products that are shaped like pens, are comparatively larger and cylindrical, and are often referred to as "tank systems" in a nod to the transparent reservoir that holds larger amounts of e-liquid than previous cartridge-containing models. Third- and fourth-generation devices represent a diverse set of products and, aesthetically, constitute the greatest departure from the traditional cigarette shape, as many are square or rectangular and feature customizable and rebuildable atomizers and batteries. In addition, since the beginning of the availability of e-cigarettes and their component parts, users have been modifying the devices or building their own devices, which are often referred to as "mods." The differences in design and engineering of the products are key factors in the size, distribution, and amount of aerosol particles and the variability in levels of chemicals and nicotine present in the e-liquid/aerosol and delivered to the user (Brown and Cheng 2014).

Figure 1.2 Parts of an e-cigarette device



Source: Photo by Mandie Mills, CDC.

Figure 1.3 Examples of e-liquid flavors

Source: Photo by Mandie Mills, CDC.

Figure 1.4 E-liquids being poured into an e-cigarette device

Source: Photo by Mandie Mills, CDC.

E-Cigarette Product Components and Risks

One of the primary features of the more recent generation of devices is that they contain larger batteries and are capable of heating the liquid to a higher temperature, potentially releasing more nicotine, forming additional toxicants, and creating larger clouds of particulate matter (Bhatnagar et al. 2014; Kosmider et al. 2014). For instance, one study demonstrated that, at high temperatures (150°C), exceedingly high levels of formaldehyde—a carcinogen (found to be 10 times higher than at ambient temperatures)—are present that are formed through the heating of the e-liquid solvents (propylene glycol and glycerin), although the level of tolerance of actual users to the taste of the aerosol heated to this temperature is debated (Kosmider et al. 2014; CDC 2015a; Flavor and Extract Manufacturers Association of the United States 2015; Pankow et al. 2015). There is also concern regarding the safety of inhaling e-cigarette flavorings. Although some manufacturers have claimed their flavorants are generally recognized as safe for food additives (i.e., to be used in preparing foods for eating), little is known about the long-term health effects of inhaling these substances into the lungs (CDC 2015a).

Many devices can be readily customized by their users, which is also leading to the concern that these devices are often being used to deliver drugs other than nicotine (Brown and Cheng 2014). Most commonly reported in the news media, on blogs, and by user anecdote

is the use of certain types of e-cigarette-related products for delivering different forms of marijuana (Morean et al. 2015; Schauer et al. 2016). The tank systems, for example, have been used with liquid tetrahydrocannabinol (THC) or hash oil. Some personal vaporizer devices can be used with marijuana plant material or a concentrated resin form of marijuana called "wax." One study describes the use, in Europe, of e-cigarette devices to smoke marijuana (Etter 2015).

The various e-cigarette products, viewed as a group, lack standardization in terms of design, capacity for safely holding e-liquid, packaging of the e-liquid, and features designed to minimize hazards with use (Yang et al. 2014). All of these design features may have implications for the health impact of e-cigarette use. Notably, from 2010 to 2014, calls to poison control centers in the United States about exposures related to e-cigarettes increased dramatically. According to the American Association of Poison Control Centers (2015), 271 cases were reported in 2011, but 3,783 calls were reported in 2014. Among all calls, 51% involved exposure among children younger than 5 years of age (CDC 2014). Most poisonings appear to have been caused by exposure to nicotine-containing liquid (CDC 2014). The lack of a requirement for child-resistant packaging for e-liquid containers may have contributed to these poisonings. Since these data were released, one death in the United States has been confirmed in a child who drank e-liquid containing nicotine (Mohney 2014). Additionally, serious adverse reactions, including at least two deaths, have been reported to FDA in cases that could be attributed to the use of e-cigarettes (FDA 2013). This increase in poisonings prompted the *Child Nicotine Poisoning Prevention Act of 2015* (2016), which was enacted in January 2016. This law requires any container of liquid nicotine that is sold, manufactured, distributed, or imported into the United States to be placed in packaging that is difficult to open by children under 5 years of age.

Secondary risks are also of concern regarding e-cigarettes, including passive exposure to nicotine and other chemicals, and adverse events due to device malfunction. Nicotine is a neuroteratogen, and its use by pregnant women exposes a developing fetus to risks that are well documented in the 50th-anniversary Surgeon General's report on smoking (USDHHS 2014) and include impaired brain development (England et al. 2015) and other serious consequences. Finally, another consequence of the lack of device regulation is the occurrence of battery failures and subsequent explosions. Explosions have typically occurred during charging, resulting in house and car fires, and sometimes causing injuries to those involved. From 2009 to late 2014, 25 incidents of explosions and fires involving e-cigarettes occurred in the United States (Chen 2013; U.S. Fire Administration 2014; FDA 2013).

E-Cigarette Companies

E-cigarette companies include manufacturers, wholesalers, importers, retailers, distributors, and some other groups that overlap with these entities (Barboza 2014; Whelan 2015). Currently, most of the products are manufactured in Shenzhen, Guangdong Province, China (Cobb et al. 2010; Grana et al. 2014; Zhu et al. 2014). One study placed the number of brands at 466 in January 2014 and found a net increase of 10.5 brands per month (Zhu et al. 2014). All the major tobacco companies (e.g., Reynolds American, Altria; Table 1.1) and many smaller, independent companies are now in the business. When e-cigarettes first entered the U.S. market, they were sold primarily by independent companies via the Internet and in shopping malls at kiosks where those interested could sample the products. A unique feature of the e-cigarette industry, compared to other tobacco and nicotine products, is the recruitment of visitors to their websites as "affiliates" or distributors to help market the products and, in turn, receive commissions on sales (Grana and Ling 2014; Cobb et al. 2015). For example, some companies offer a way for users to earn a commission by advertising the products (e.g., a banner ad is placed on one's website, and when someone clicks on the link and subsequently purchases a product, the website owner gets a percentage commission). Some companies also offer rewards programs for recruiting new customers or for brand loyalty, with website users earning points for free or reduced-price products (Richardson et al. 2015).

E-cigarettes are now in widespread national distribution through convenience stores, tobacco stores, pharmacies, "big box" retail chains such as Costco, online retailers, and shops devoted to e-cigarette products (often called "vape shops") (Giovenco et al. 2015; Public Health Law Center 2015). The "vape shops" offer a place to buy customizable devices and e-liquid solutions in many flavors and sometimes include a café or other elements that promote socializing, essentially making such places like a lounge. With the rapid increase in distribution and marketing in the industry, sales have increased rapidly and were projected to reach $2.5 billion in 2014 and $3.5 billion in 2015, including projections for retail and online channels, as well as "vape shops" (Wells Fargo Securities 2015).

Table 1.1 Multinational tobacco companies with e-cigarette brands

Company	E-cigarette brand
Altria (NuMark)	MarkTen, Green Smoke
Philip Morris International	Heat-not-burn, IQOS brand (Vape Ranks 2014) E-cigs, Nicolites by Nicocigs (Philip Morris International 2014)
Reynolds (Reynolds Vapor Company)	VUSE
Lorillard (Lorillard Vapor Company)	blu (until 2015)
Imperial Tobacco (Fontem Ventures)	Puritane (formerly Ruyan) blu (acquired in 2015)
British American Tobacco	Vype
Swisher	E-swisher
Japan Tobacco International (JTI)	E-Lites, offered in the United Kingdom by Zandera Ltd., which was acquired by Japan Tobacco Inc. in 2014 (Japan Tobacco Inc. 2014) Ploom (tobacco pods in heat-not-burn) and Ploom PAX (used for vaporizing marijuana) (Japan Tobacco Inc. 2015)

The advertising and marketing of e-cigarette products has engendered skepticism among public health professionals and legislators, who have noted many similarities to the advertising claims and promotional tactics used for decades by the tobacco industry to sell conventional tobacco products (Campaign for Tobacco-Free Kids 2013; CDC 2016a). Indeed, several of the e-cigarette marketing themes have been reprised from the most memorable cigarette advertising, including those focused on freedom, rebellion, and glamor (Grana and Ling 2014). E-cigarette products are marketed with a variety of unsubstantiated health and cessation messages, with some websites featuring videos of endorsements by physicians (another reprisal of old tobacco industry advertising) (Grana and Ling 2014; Zhu et al. 2014). Unlike conventional cigarettes, for which advertising has been prohibited from radio and television since 1971, e-cigarette products are advertised on both radio and television, with many ads featuring celebrities. E-cigarettes also are promoted through sports and music festival sponsorships, in contrast to conventional cigarettes and smokeless tobacco products, which have been prohibited from such sponsorships since the Master Settlement Agreement in 1998. E-cigarettes also appear as product placements in television shows and movies (Grana et al. 2011; Grana and Ling 2014).

Another key avenue for e-cigarette promotion is social media, such as Twitter, Facebook, YouTube, and Instagram. As is true in the tobacco industry, the e-cigarette industry organizes users through advocacy groups (Noel et al. 2011; Harris et al. 2014; Saitta et al. 2014; Caponnetto et al. 2015). The extensive marketing and advocacy through various channels broadens exposure to e-cigarette marketing messages and products; such activity may encourage nonsmokers, particularly youth and young adults, to perceive e-cigarette use as socially normative. The plethora of unregulated advertising is of particular concern, as exposure to advertising for tobacco products among youth is associated with cigarette smoking in a dose-response fashion (USDHHS 2012).

Federal Regulation of E-Cigarettes

A "Two-Pronged" Approach to Comprehensive Tobacco Control

Since the passage of the Tobacco Control Act in 2009, FDA has had the authority to regulate the manufacturing, distribution, and marketing of tobacco products sold in the United States. FDA had immediate jurisdiction over cigarettes, roll-your-own cigarette tobacco, and smokeless tobacco. In May 2016, FDA asserted jurisdiction over products that meet the statutory definition of a tobacco product, including e-cigarettes, except accessories of these products (*Federal Register* 2016). That regulation is currently under litigation.

The IOM's 2007 report, *Ending the Tobacco Problem: A Blueprint for the Nation,* established a "two-pronged" strategy for comprehensive tobacco control: (1) full implementation of proven, traditional tobacco control measures such as clean indoor air laws, taxation, and countermarketing campaigns; and (2) "strong federal regulation of tobacco products and their marketing and distribution" (Bonnie et al. 2007, p. 1).

Included in FDA's broad authority are the restriction of marketing and sales to youth, requiring disclosure of ingredients and harmful and potentially harmful constituents, setting product standards (e.g., requiring the reduction or elimination of ingredients or constituents), requiring premarket approval of new tobacco products and review of modified-risk tobacco products, and requiring health warnings. The standard for FDA to use many of its regulatory authorities is whether such an action is appropriate for the protection of public health (*Federal Food, Drug, and Cosmetic Act*, § 907(a)(3)(A)). The public health standard in the Tobacco Control Act also requires FDA to consider the health impact of certain regulatory actions at both the individual and population levels, including their impact on nonusers, and on initiation and cessation (*Federal Food, Drug, and Cosmetic Act*, § 907(a)(3)(B)).

Importantly, the Tobacco Control Act preserves the authority of state, local, tribal, and territorial governments to enact any policy "in addition to, or more stringent than" requirements established under the Tobacco Control Act "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" (*Federal Food, Drug, and Cosmetic Act*, § 916(a)(1)). This preservation of state and local authority ensures the continuation of more local-level, comprehensive tobacco control. However, the statute expressly preempts states and localities from establishing or continuing requirements that are different from or in addition to FDA requirements regarding standards for tobacco products, premarket review, adulteration, misbranding, labeling, registration, good manufacturing practices, or modified-risk tobacco products (*Federal Food, Drug, and Cosmetic Act*, § 916(a)(2)(A)). But this express preemption provision does not apply to state and local authority to impose requirements relating to the "sale, distribution, possession, information reporting to the State, exposure to, access to, the advertising and promotion of, or use of, tobacco products by individuals of any age . . ." (*Federal Food, Drug, and Cosmetic Act*, § 916(a)(2)(b)). The interaction of these complex provisions related to federal preemption of state law has been the subject of challenges by the tobacco industry to state and local laws. Thus far, courts have upheld certain local ordinances restricting the sale of flavored tobacco products (*National Association of Tobacco Outlets, Inc. v. City of Providence* 2013; *U.S. Smokeless Tobacco Manufacturing Co. v. City of New York* 2013).

Legal Basis for Regulating E-Cigarettes as Tobacco Products

In the United States, e-cigarettes can be regulated either as products marketed for therapeutic purposes or as tobacco products. Since the advent of e-cigarettes in the United States around 2007, manufacturers have had the option to apply to FDA's Center for Drug Evaluation and Research (CDER) or Center for Devices and Radiological Health (CDRH) for approval to market e-cigarettes for therapeutic purposes; as of August 2016, no e-cigarette manufacturers have received approval through this avenue.

In 2008 and early 2009, FDA detained multiple shipments of e-cigarettes from overseas manufacturers and denied them entry into the United States on the grounds that e-cigarettes were unapproved drug-device combination products (FDA 2011). Sottera, Inc., which now does business as NJOY, challenged that determination (*Smoking Everywhere, Inc. and Sottera, Inc., d/b/a NJOY v. U.S. Food and Drug Administration, et al.* 2010; Bloomberg Business 2015). Between the filing of the lawsuit and a decision on the motion for preliminary injunction, Congress passed the Tobacco Control Act and the President signed it into law. The Tobacco Control Act defines the term "tobacco product," in part, as any product, including component parts or accessories, "made or derived from tobacco" that is not a "drug," "device," or "combination product" as defined by the *Federal Food, Drug, and Cosmetic Act* (21 U.S.C. 321(rr)) (*Family Smoking Prevention and Tobacco Control Act* 2009, § 101(a)). The District Court subsequently granted a preliminary injunction relying on the Supreme Court's decision in Brown and Williamson (1996) and the recently enacted Tobacco Control Act. FDA appealed the decision and the U.S. Court of Appeals for the D.C. Circuit held that e-cigarettes and, therefore, other products "made or derived from tobacco" are not drug/device combinations unless they are marketed for therapeutic purposes, but can be regulated by FDA as tobacco products under the Tobacco Control Act (*Sottera, Inc. v. Food & Drug Administration* 2010).

On September 25, 2015, FDA proposed regulations to describe the circumstances in which a product made or derived from tobacco that is intended for human consumption will be subject to regulation as a drug, device, or a combination product. The comment period for this proposed regulation closed on November 24, 2015.

Most e-cigarettes marketed and sold in the United States today contain nicotine made or derived from tobacco. Although some e-cigarettes claim that they contain nicotine not derived from tobacco, or that they contain no nicotine at all (Lempert et al. 2016), there may be reason to doubt some of these claims. Currently, synthetic nicotine and nicotine derived from genetically modified, nontobacco plants are cost-prohibitive for e-cigarette manufacturers, although technological advances could eventually increase the cost-effectiveness of using nicotine that was not derived from tobacco (Lempert et al. 2016). The health effects of passive exposure to e-cigarettes with no nicotine, as well as their actual use and the extent of exposure to these products, have just begun to be studied (Hall et al. 2014; Marini et al. 2014; Schweitzer et al. 2015) and some states and localities are taking steps to regulate e-cigarettes that do not contain nicotine or tobacco (Lempert et al. 2016).

Deeming Rule

The Tobacco Control Act added a new chapter to the *Federal Food, Drug, and Cosmetic Act*, which provides FDA with authority over tobacco products. The new chapter applied immediately to all cigarettes, cigarette tobacco, roll-your-own tobacco, and smokeless tobacco; and the law included "any other tobacco products that the Secretary of Health and Human Services by regulation deems to be subject to this chapter" (*Federal Food, Drug, and Cosmetic Act*, §901 (b)). Therefore, to regulate e-cigarettes as tobacco products, FDA was required to undertake a rulemaking process to extend its regulatory authority to include e-cigarettes.

Consequently, in May 2016, through its Center for Tobacco Products (CTP), FDA issued a rule—often referred to as the "deeming rule"—to extend its authority over all products meeting the definition of a tobacco product, except accessories of the newly deemed products. This rule extended FDA's tobacco product authorities to include e-cigarettes and their components and parts (e.g., nicotine cartridges), but also to such products as cigars, pipe tobacco, nicotine gels, waterpipe/hookah tobacco, and dissolvables not already regulated as smokeless tobacco products (*Federal Register* 2016). This regulation is currently under litigation. The deeming rule subjects e-cigarettes to Tobacco Control Act provisions, including:

- Prohibitions on adulterated and misbranded products;
- Required disclosure of existing health information, including lists of ingredients and documents on health effects;
- Required registration of manufacturers;
- Required disclosure of a list of all tobacco products, including information related to labeling and advertising;
- Premarket review of new tobacco products (i.e., those not on the market on February 15, 2007);
- Restrictions on products marketed with claims about modified risk.

In addition to the aforementioned Tobacco Control Act provisions applicable to all deemed tobacco products, the Tobacco Control Act grants FDA authority to undertake a broad range of other actions on specific classes of products. In its deeming rule, FDA included the following additional actions for tobacco products, including e-cigarettes:

- Minimum age restrictions to prevent sales to minors;
- Requirements to include a nicotine warning; and
- Prohibitions on vending machine sales, unless in a facility that never admits youth.

Future Regulatory Options

E-cigarette manufacturers have the option to apply to FDA to authorize the marketing of their products or to be able to manufacture and sell tobacco products marketed with modified-risk claims, in addition to the existing option to apply to FDA's CDER or CDRH for approval to market their products for therapeutic purposes. FDA also has authority to undertake a number of actions if the Secretary of USDHHS finds such actions to be appropriate for the protection of public health, including:

- Product standards, including restrictions on flavors;
- Restrictions on promotion, marketing, and advertising, and prohibitions on brand-name sponsorship of events;
- Minimum package sizes;
- Prohibitions on self-service displays;

- Child-resistant packaging and the inclusion of health warnings; and
- Regulation of nicotine levels in products.

Despite this broad authority, FDA is prohibited from certain regulatory actions, even if those actions may be appropriate for the protection of public health. Specifically, FDA generally cannot restrict tobacco use in public places, levy taxes on tobacco products, prohibit sales by a specific category of retail outlet (e.g., pharmacies), completely eliminate nicotine in tobacco products, require prescriptions for tobacco products unless it is marketed for therapeutic purposes, or establish a federal minimum age of sale for tobacco products above 18 years of age. Thus, even if FDA fully exercises all of its existing authority over e-cigarettes, regulation will still need to be complemented at the state and local levels, including efforts previously shown to be effective for conventional tobacco products, such as comprehensive smokefree laws at the state and local levels, pricing strategies, raising the minimum age of sales to minors to 21, and high-impact countermarketing campaigns. In the current context of rising rates of use by youth, localities and states can also implement policies and programs that minimize the individual- and population-level harms of e-cigarettes (see Chapter 5).

Summary

This chapter presents the major conclusions of this Surgeon General's report and the conclusions of each chapter. E-cigarettes are presented within their historical context, with an overview of the components of these devices and the types of products. In 2016, FDA announced its final rule to regulate e-cigarettes under the *Family Smoking Prevention and Tobacco Control Act.* The chapter outlines options for the regulation of e-cigarettes, particularly as they relate to youth and young adults, based on successful smoking policies. The need to protect youth and young adults from initiating or continuing the use of nicotine-containing products forms a strong basis for the need to regulate e-cigarettes at the local, state, and national levels in the future.

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