TESTIMONY

OF

MITCHELL ZELLER, J.D., DIRECTOR, CENTER FOR TOBACCO PRODUCTS
FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE
COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS
U.S. SENATE

"EXAMINING THE RESPONSE TO LUNG ILLNESSES AND RISING YOUTH ELECTRONIC CIGARETTE USE"

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Introduction

Good morning, Chairman Alexander, Ranking Member Murray, and Members of the Committee. Thank you for the opportunity to be here today to discuss the Food and Drug Administration's (FDA or the Agency) regulation of electronic nicotine delivery systems, or ENDS, which include e-cigarettes, and the Agency's role in the ongoing investigation into vaping product use associated lung injury. I am Mitch Zeller, Director of the U.S. Food and Drug Administration's Center for Tobacco Products.

I appreciate the opportunity to be here today to provide an update on FDA's regulation of ENDS, and to provide an update on FDA's efforts to investigate the illnesses associated with the use of vaping products.

In my testimony I will begin with some background on FDA's tobacco product regulatory authorities. I will then address the history of our regulation of e-cigarettes and where we find ourselves today, confronting the epidemic levels of youth use of e-cigarettes. Finally, I will discuss FDA's role in the federal and state investigation of the cases of lung injury.

Background

Let me start with some background on our tobacco regulatory authorities.

Tobacco use is the single largest preventable cause of disease and death in the United States. Each year, more than 480,000 people in the United States die prematurely from diseases caused by cigarette smoking and exposure to tobacco smoke. In 2009, Congress passed the Family Smoking Prevention and Tobacco Control Act (Tobacco Control Act), which amended the Federal Food, Drug, and Cosmetic Act (FD&C Act) to authorize FDA to oversee the manufacture, marketing, distribution, and sale of tobacco products and protect the public from the harmful effects of tobacco product use. This authority gave FDA comprehensive tools to

protect the public from the harmful effects of tobacco use through science-based tobacco product regulation.

Through premarket review, FDA evaluates new tobacco products based on applicable public health standards that include, for example, a consideration of the risks and benefits of the tobacco product to the population as a whole, including users and non-users. Similarly, when developing certain regulations such as product standards or restrictions on tobacco sales and advertising, the law requires FDA to apply a public health approach that considers the effect of the regulatory action on the population as a whole, not just on individual users, taking into account the likelihood of initiation and cessation of tobacco use.

Under the statute, FDA had immediate authority to regulate cigarettes, cigarette tobacco, roll-your-own tobacco, and smokeless tobacco. The Tobacco Control Act also authorized FDA to "deem" other "tobacco products" (which include "any product made or derived from tobacco that is intended for human consumption" that is not a drug, device, or combination product under the FD&C Act, "including any component, part, or accessory" of that product) to be subject to the Agency's regulatory authority in Chapter IX of the FD&C Act.

It's important to note FDA's initial efforts to regulate e-cigarettes more than a decade ago, long before the rise in youth use and the multi-state lung injury outbreak. Between 2008 and 2010, FDA attempted to regulate e-cigarettes as unapproved drug/device combination products. FDA's action was challenged, and ultimately the U.S. Court of Appeals for the D.C. Circuit ruled that while FDA could choose to regulate e-cigarettes and other products "made or derived from tobacco" under its new tobacco authorities, it could not regulate these products under FDA's drug and device authority unless they were marketed for therapeutic purposes. *Sottera, Inc. v. Food and Drug Administration*, 627 F.3d 891 (D.C. Cir. 2010).

Publication of the final deeming rule brought e-cigarettes under FDA's regulatory authority for tobacco products. That rule was issued on May 10, 2016, deeming additional products that meet the statutory definition of a "tobacco product," except for accessories of such products, to be subject to FDA's regulatory authority. Deemed products include ENDS, cigars, pipe tobacco,

nicotine gels, waterpipe (or hookah) tobacco, and any future tobacco products. The deeming rule, and FDA's regulation of these products, took effect on August 8, 2016.

Regulatory Requirements for ENDS Products

When the deeming rule took effect in August 2016, many of the regulatory and legal requirements that had been in place for manufacturers of cigarettes, smokeless tobacco, cigarette tobacco, and roll-your-own tobacco since 2009, as well as several new requirements specific to deemed products, became applicable to makers of e-cigarettes and other ENDS products. These include:

- Registering domestic establishments and submitting lists of products manufactured at those establishments, including all labeling and representative samples of advertisements;
- Submitting tobacco health documents;
- Submitting ingredient listings;
- Marketing new tobacco products only after FDA review; and
- Marketing products with direct or implied claims of reduced risk only if FDA confirms that scientific evidence supports the claim and determines that providing a marketing authorization for the product will, among other things, benefit the health of the population as a whole.

In addition, under the deeming rule, the following regulatory provisions also apply to deemed tobacco products, including ENDS products:

- Minimum age restriction (18 years or older) and identification requirements to prevent sales to underage youth;
- Requirements to bear certain health warnings on packages and advertisements (including certain ENDS components, such as e-liquids) such as, "WARNING: This product contains nicotine. Nicotine is an addictive chemical." and
- Prohibition of vending machine sales, unless in a facility that never admits youth.

To provide time for industry to come into compliance with some of the new regulatory requirements triggered by the final deeming rule, FDA announced an enforcement policy with staggered timeframes. Some of the requirements, such as the federal minimum age of purchase (18 years or older), were enforced immediately when the deeming rule took effect on August 8, 2016, while, through an exercise of enforcement discretion, FDA temporarily deferred enforcement of other provisions such as premarket review of "new" tobacco products.

Premarket Review of ENDS

All deemed products, including ENDS, became subject to the premarket authorization requirements in the Tobacco Control Act on August 8, 2016. All "new tobacco products" are required to obtain authorization from FDA before they can be legally marketed. Pursuant to the Tobacco Control Act, a "new tobacco product" is one that was not commercially marketed as of February 15, 2007, or that was modified after February 15, 2007.

FDA's initial compliance policy for premarket review stated that the Agency did not intend to enforce the requirements of premarket review against manufacturers of newly-regulated new tobacco products that were on the market as of August 8, 2016, as long as they submitted marketing applications and received authorization within specific timeframes. As a result, FDA anticipated that many ENDS products would remain on the market without premarket authorization for up to three years.

In July 2017, FDA announced a new comprehensive plan for tobacco and nicotine regulation that would serve as a multi-year roadmap in an effort to significantly reduce tobacco-related disease and death. The comprehensive plan was announced in part to afford the Agency time to explore other meaningful measures, beyond premarket review, to make combustible tobacco products less toxic, less appealing, and less addictive. One aspect of the plan involved striking a balance between conducting reasonable oversight through regulation and encouraging development of innovative tobacco products that may be less harmful than cigarettes. The Agency announced that it planned to issue an updated compliance policy to defer some enforcement timelines described in the preamble to the final deeming rule.

Since that announcement, FDA has been hard at work on rules, guidances, and other communications that will help manufacturers develop higher quality applications, including the issuance of the following:

- Substantial Equivalence pathway proposed rule
- Premarket Tobacco Application for ENDS final guidance
- Premarket Tobacco Application proposed rule
- Vape shops final guidance
- Regular meetings with manufacturers to provide guidance on premarket authorization processes
- Regular meetings with retailers on e-cigarette policies of particular importance for retailers such as efforts to prevent youth sales and the availability of free educational resources for retailers to assist them in preventing youth sales
- Draft guidance on Developing Nicotine Replacement Therapy Drug Products
- Draft guidance on Nonclinical Testing of Orally Inhaled Nicotine-Containing Drug Products Guidance for Industry

The July 2017 announcement led to publication of the August 2017 Compliance Policy, which was later the subject of litigation. In May 2019, a U.S. District Court in Maryland vacated FDA's August 2017 Compliance Policy. In July 2019, the court issed a further order directing FDA to require that applications for deemed "new tobacco products" such as e-cigarettes, cigars, pipe tobacco, and hookah tobacco, that were on the market as of August 8, 2016, be filed with FDA no later than May 12, 2020. The court order also provided for a one-year period during which products with timely filed applications might remain on the market pending FDA review, but subsequently clarified that its order does not restrict the Agency's authority to enforce the premarket review provisions against deemed products prior to May 12, 2020, or during the one-year review period.

As the Committee considers the issues related to e-cigarette use today, it is important to remember that no ENDS product in the United States is on the market legally. To be legally marketed as a tobacco product, the product would need to obtain premarket authorization from the Agency. The product would undergo FDA scientific review, and (assuming that the product

is being reviewed through the Premarket Tobacco Application pathway) the Agency would have to find that the product meets the applicable statutory standard for marketing—for example, that the product is appropriate for the protection of the public health. Alternatively, an ENDS product that is intended for therapeutic purposes (e.g., smoking cessation) would need to be reviewed and approved under FDA's drug authorities to be legally marketed as a drug. Currently, there is no FDA-authorized or FDA-approved ENDS product on the market.

FDA's Aggressive Actions to Address the Youth Epidemic of ENDS Product Use

At the time FDA issued the August 2017 Compliance Policy to modify the enforcement discretion policies regarding premarket authorization, nationally representative data suggested that youth use of e-cigarettes had declined.[1] While no level of youth use is acceptable, FDA took this directional data into consideration, along with the potential benefits some of these products might provide to some addicted individual adult smokers seeking to make a complete transition away from combustible cigarettes.

The Agency was engaged in a public health balancing act. Given the then-existing evidence suggesting a decline in youth use, and with the potential for FDA to pursue other bold measures, in part by reducing the addictiveness of combustible cigarettes while temporarily delaying the likely immediate market exit of newly deemed tobacco products that could be potentially less harmful to individual users, FDA determined that the balancing of public health considerations argued in favor of a different comprehensive approach to nicotine and tobacco regulation.

However, only a year after we announced the 2017 comprehenseive plan, the National Youth Tobacco Survey (NYTS) in 2018 showed a new and significant increase in youth use of e-cigarettes. FDA collaborates with CDC to administer the survey to middle and high school students each year. The survey provides important data that allow us to understand current youth tobacco product use in a larger historical context.

[1] Jamal A, Gentzke A, Hu SS, et al. Tobacco Use Among Middle and High School Students — United States, 2011–2016. MMWR Morb Mortal Wkly Rep 2017;66:597–603. *https://www.cdc.gov/mmwr/volumes/66/wr/mm6623a1.htm?s_cid=mm6623a1_w*. The NYTS defines e-cigarettes as "battery-powered devices that provide nicotine and other additives to the user in the form of an aerosol."

Between 2017 and 2018, current (past 30-day) e-cigarette use among high school students increased 78 percent, from 11.7 percent to 20.8 percent.[2] Current e-cigarette use among middle school students increased by 48 percent over the same time period, from 3.3 percent to 4.9 percent.[3] Moreover, evidence demonstrated that youth are especially attracted to flavored ENDS products. Data from the 2018 NYTS showed that, in just one year, current use of flavored e-cigarettes increased substantially among high school students who were current e-cigarette users, from 60.9 percent in 2017 to 67.8 percent in 2018.[4] In addition, the proportion of current e-cigarette users in high school who reported use on 20 or more days of the past 30 days increased from 20.0% in 2017 to 27.7% in 2018.

FDA and CDC recently published 2019 NYTS data in the *Journal of the American Medical Association* (JAMA).[5] Unfortunately, the data show that current e-cigarette use among youth has continued at its alarming increase, with 27.5% of high school students and 10.5% of middle school students reporting current use of e-cigarettes. The data also showed that more than five million U.S. middle and high school students are current e-cigarette users. Further, most of those middle and high school students who exclusively use e-cigarettes are using flavored products. And the survey shows that 34.2 percent of current high school e-cigarette users in 2019 are using the product frequently (use on 20 or more days in the last 30 days). In total, 1.6 million middle school and high school current e-cigarette users were frequent users, with nearly one million using e-cigarettes daily.

As in previous years, the 2019 NYTS shows a disturbing rate of youth use of non-tobacco flavored e-cigarettes. In particular, the data show that among current exclusive e-cigarette users, nearly three quarters of those in high school and more than half of those in middle school used flavored e-cigarettes. The most commonly reported flavors were fruit, menthol or mint

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[2] *Id.*

[3] *Id.*

[4] Cullen, K.A., B.K. Ambrose, A.S. Gentzke, et al., "Notes from the Field: Increase in e-cigarette use and any tobacco product use among middle and high school students – United States, 2011-2018," *Morbidity and Mortality Weekly*, 67(45);1276-1277 (2018).

[5] *https://jamanetwork.com/journals/jama/fullarticle/2755265*

(evaluated as a single category), and candy, desserts, or other sweets.[6] Importantly, findings from another study, the 2019 Monitoring the Future (MTF) survey—also published in JAMA on November 5, 2019—give us a more granular picture of flavor preferences as they relate to this public health balancing act. These findings indicate that youth preference for menthol- and tobacco-flavored products is much *lower* than that for mint- and fruit-flavored products. This recent analysis was limited to youth who indicated they had specifically used the JUUL brand.

We are committed to doing everything we can to prevent kids from using tobacco products and will continue to develop a policy approach that aligns with that concern. Additionally, we are taking a number of other actions to help address the youth use epidemic:

- FDA has been holding retailers and manufacturers accountable for marketing and sales practices that have led to increased youth accessibility and appeal of e-cigarettes. For example, since the effective date of the Deeming Rule in August 2016, FDA has issued more than 10,000 warning letters to, and filed more than 1,500 civil money penalty complaints against, retailers, both online and in brick-and-mortar retail stores, for sales of ENDS and their components to youth.
- FDA has sent letters to over 100 companies seeking information on over 130 brands, including ENDS products, to determine whether those products were not marketed as of August 8, 2016, and therefore not subject to any previous FDA compliance policy. To date, FDA has issued warning letters to six ENDS companies notifying them of the need to remove a combined total of more than 140 products from the market.
- The Agency has issued warning letters, many in collaboration with the Federal Trade Commission (FTC), that resulted in the removal of dozens of e-liquid products resembling kid-friendly foods, such as juice boxes, cereal, and candy.
- On September 9, 2019, FDA issued a warning letter[7] to JUUL Labs Inc. for marketing unauthorized modified risk tobacco products by engaging in labeling, advertising, and/or other activities directed to consumers, including a presentation given to youth at a school,

[6] Cullen KA, Gentzke AS, Sawdey MD, et al., "E-Cigarette Use Among Youth in the United States, 2019," *JAMA*.
[7] The warning letter is available at: *https://www.fda.gov/news-events/press-announcements/fda-warns-juul-labs-marketing-unauthorized-modified-risk-tobacco-products-including-outreach-youth*.

by marketing it for reduced risk or harm from using the product compared to cigarette smoking. Concurrently, the Agency issued a second letter expressing its concern and requesting additional information about several issues raised by Congress regarding JUUL's outreach and marketing practices, including those targeted at students, tribes, health insurers and employers.

- FDA has also continued to invest in campaigns to educate youth about the dangers of e-cigarette use. Last year, FDA launched "The Real Cost" Youth E-Cigarette Prevention Campaign[8]—a comprehensive effort targeting nearly 10.7 million youth, aged 12-17, who have used e-cigarettes or are open to trying them. The campaign features hard-hitting advertising on TV, digital and social media sitespopular among teens, as well as posters with e-cigarette prevention messages in high schools across the nation.
- FDA joined forces with Scholastic to develop educational resources for middle and high school teachers and administrators. These materials have been distributed to more than 1 million middle and high school educators. Our work with Scholastic continues and more resources will be made available in Spring 2020.
- The Agency also developed posters and resources for doctors, youth groups, religious institutions, state and local public health agencies, and others on the dangers of youth e-cigarette use and has worked to advance discussion and understanding around how to help those kids who are already addicted to e-cigarettes quit.

We will continue to take vigorous actions aimed at ensuring e-cigarettes and other tobacco products are not being marketed or sold to kids. In addition, we will continue to expand our public education efforts to get the word out to youth about the harms of e-cigarettes.

Investing in Research to Learn More About the Health Impacts of ENDS Products

FDA is funding several research projects assessing the health impact of e-cigarettes, including the FDA and NIH Population Assessment of Tobacco and Health (PATH) Study. The PATH Study is a national, longitudinal cohort study of almost 46,000 youth and adults in the United States that collected its first wave of data in 2013 and is following study participants over time to

[8] More information is available at: *https://www.fda.gov/tobacco-products/real-cost-campaign.*

learn how and why people start using tobacco products, quit using them, and start using them again after they have quit, as well as how different tobacco products affect health (such as cardiovascular and respiratory health) over time. The PATH Study is tracking potential behavioral and health impacts, including collecting biospecimens to analyze for biomarkers of exposure and harm.[9]

In 2016, FDA awarded a contract to National Academy of Sciences, Engineering and Medicine (NASEM) to "conduct an in-depth evaluation of the available evidence of health effects from electronic nicotine delivery systems (ENDS) and make recommendations for future federally funded research." This work included convening a multi-disciplinary committee of 13 members that met several times and holding an open meeting to obtain input from a wide range of stakeholders. The committee's methodology included: a comprehensive literature search and review; a quality assessment and evidence synthesis to assess causality for health effects; and an application of a framework for levels of evidence. Over 800 peer-reviewed scientific studies were evaluated and the consensus report, "Public Health Consequences of E-Cigarettes," was released by NASEM in January 2018.[10] Among the conclusions in the NASEM report is that teens who experiment with an e-cigarette are more likely to try conventional cigarettes compared to teens who never used an e-cigarette.

As noted in the NASEM report, assessing the long-term health effects of e-cigarettes is challenging given the range of devices and constituents. For example, products can vary widely in terms of device type, mechanism, ingredients and the characteristics of aerosol generation. Variables of ENDS that could affect health impact include factors such as: exposure to metals (including heavy metals), heating capacity, voltage, e-liquid substrates, nicotine concentration, flavors and flavoring ingredients, and use of other ingredients or contaminants with unknown inhalation effects. A specific ENDS product's health impact is also likely to be significantly affected by user behaviors (and we know that many ENDS users also use other tobacco products in addition to e-cigarettes, known as dual use or poly-use). Assessing the short-term health

[9] More information on the PATH Study can be found at *https://www.fda.gov/tobacco-products/research/fda-and-nih-study-population-assessment-tobacco-and-health.*
[10] More information can be found at *http://nationalacademies.org/hmd/Reports/2018/public-health-consequences-of-e-cigarettes.aspx.*

effects is also challenging for these same reasons. To help understand the individual and population impact of ENDS, FDA is currently funding more than 115 studies assessing the short- and long-term health effects of e-cigarettes including nicotine dependence, cardiovascular and pulmonary toxicity, potential carcinogenesis, effects of maternal use during pregnancy, and effects in the oral cavity.[11]

Investigation of Severe Respiratory Injury Associated with Vaping Products

FDA is also deeply concerned by the recent outbreak of severe respiratory lung injuries and reported deaths that are linked to use of vaping products. Investigating this crisis is a top priority for FDA, and the Agency is working very closely with CDC and state officials. The Agency is committed to taking appropriate actions to protect the public as the facts emerge. FDA is not pursuing any actions associated with personal use of any vaping products; our interest is in the supply chain. Every day we are gathering more information, and every day we seek to use that information to better understand the relationship between any specific products or substances and the reported illnesses. To date, most patients have reported a history of using vaping products containing tetrahydrocannabinol (THC). Many patients have reported using products containing THC and products containing nicotine. Some have reported the use of e-cigarette products containing only nicotine. We are following all potential leads and are doing all we can to move this complex investigation forward.

In recent months, this outbreak has possibly sickened, by the most recent CDC data, 2,051 people from 49 states, the District of Columbia, and one U.S. Territory. Sadly, 39 deaths have been confirmed in 24 states and the District of Columbia. These illnesses do not appear to be due to infectious diseases, but rather appear to be associated with a chemical exposure from vaping products. Patients generally report a gradual start of symptoms including breathing difficulty, gastrointestinal symptoms, and/or chest pain before hospitalization. Many patients have reported recent use of vaping products containing THC. Although these cases seem similar, it is not clear if they have a common cause, or if they involve different diseases with similar

[11] More information can be found on the FDA website at *https://www.fda.gov/tobacco-products/research/ctp-supported-tobacco-regulatory-research-projects.*

presentations. The investigation has not identified any specific product or substance that is linked to all cases.

On September 6, 2019, FDA activated an Incident Management Group (IMG) to coordinate FDA's activities for the investigation into these reports. The IMG is comprised of subject matter experts from numerous FDA centers and offices, such as clinicians, toxicologists, pharmacologists, epidemiologists, chemists, engineers, consumer safety and criminal investigators, and computational scientists. FDA is focused on better understanding whether there is a relationship between any specific products or substances and the reported cases. It is important to stress that identifying any compounds present in the samples is but one piece of the puzzle and will not necessarily answer questions about causality, which makes our ongoing work critical.

FDA's work includes collecting critical details about the products or substances involved, where they were purchased and how they were being used and analyzing product samples. To date, FDA laboratories have received over 1,000 samples from 25 states for this investigation with roughly 850 of these samples connected to patients. Overall, 595 of the samples collected from patients have undergone some level of testing. The Agency is also working to link samples with specific patients, directly linking 509 samples to 69 patients. Eighty percent of these include links to THC products and of these 75% of cases included products with vitamin E acetate as a diluent. Connecting the products and how they were used to specific patients is critically important to our investigation to determine, to the extent possible, the cause or causes of these injuries.

FDA continues reaching out directly to the states that have submitted samples and is providing them high-level aggregate data in the form of status reports on preliminary analytical findings. Additionally, as the investigation continues to evolve, FDA and CDC are ensuring that information is shared seamlessly between the two agencies. FDA has assigned staff to CDC's Emergency Operations Center. Likewise, CDC has assigned staff to our IMG to facilitate collaboration. We continue to work closely on sample collection and joint testing plans for

aerosol and e-liquid. The agencies also continue to share epidemiologic and product testing data to aid in linking of case patients to product testing results.

Importantly, last week CDC reported on the first analysis of human lung fluid in 29 samples from individuals in 10 states. Vitamin E acetate was found in all 29 samples. THC was found in three samples from individuals who reported they only used a nicotine-containing vaping product. More work needs to be done to get to the bottom of what substance or substances is causing these illnesses and deaths, but these findings will help us get closer to the answers we and CDC are seeking.

We are working to communicate with the public when we have information to share in a frequent and transparent way. FDA has warned consumers to avoid buying vaping products of any kind "on the street" and to refrain from vaping THC or modifying/adding any substances to products purchased in stores. FDA also encourages the public to submit detailed reports of any unexpected tobacco- or vaping-related product issues to FDA via the online Safety Reporting Portal, which can be found on our website (or at *www.safetyreporting.hhs.gov*).

Conclusion

Thank you for the opportunity to testify today about FDA's tobacco product regulatory work and our efforts to investigate vaping product use associated lung injury. FDA is committed to the evolving investigation and to protecting and improving the public health.

I am happy to answer any questions you may have.