November 6, 2019

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Dear Dr. Tanski:

Thank you for appearing before the Subcommittee on Health on Wednesday, October 16, 2019, at the hearing entitled "Legislation to Reverse the Youth Tobacco Epidemic." We appreciate the time and effort you gave as a witness before the Subcommittee.

Pursuant to Rule 3 of the Committee on Energy and Commerce, members are permitted to submit additional questions to the witnesses for their responses, which will be included in the hearing record. Attached are questions directed to you from me and other members of the Committee. In preparing your answers to these questions, please address your responses to the member who has submitted the questions using the Word document provided with this letter.

To facilitate the publication of the hearing record, please submit your responses to these questions by no later than the close of business on **Thursday, November 21, 2019**. As previously noted, your responses to questions in this letter will be included in the hearing record. Your written response should be transmitted by email in the Word document provided with this letter to Josh Krantz, Policy Analyst with the Committee, at josh.krantz@mail.house.gov. You do not need to send a paper copy of your responses to the Committee. Using the Word document provided for submitting your responses will also help maintain the proper format for incorporating your answers into the hearing record.

Thank you for your prompt attention to this request. If you need additional information or have other questions, please have your staff contact Mr. Krantz at (202) 225-5056.

Sincerely,

Frank Pallone, Jr.
Chairman

Attachments

cc: Hon. Greg Walden, Ranking Member
Committee on Energy and Commerce

Hon. Anna G. Eshoo, Chairwoman
Subcommittee on Health

Hon. Michael C. Burgess, Ranking Member
Subcommittee on Health

Attachments—Additional Questions for the Record

Subcommittee on Health
Hearing on
"Legislation to Reverse the Youth Tobacco Epidemic"
October 16, 2019

Susanne Tanski, M.D.

Member, American Academy of Pediatrics

The Honorable Lisa Blunt Rochester (D-DE)

1. A study published by the Journal of the American Medical Association found that e-cigarette use by adults is stable, and in some cases, declining. Just 2% of adults ages 45-64 used e-cigarettes in 2018, but a staggering 1 out of 11 students in 8th grade reported using an e-cigarette in the past 30 days. Why do you think youth usage is growing at a faster rate than adult usage?

   The rate of youth usage has grown faster than in adults essentially because of lack of regulation of these products, which generated inappropriate appeal to the youth market.

   Marketing: When these products as a class were introduced to the market with a (relative) lack of marketing restrictions, their claims implied safety with terms like "water vapor", "…produces no smoke and no ash, only vapor, making it the smarter alternative to regular cigarettes." (blu e-cigarettes) "Give the gift of better health." (White Cloud e-cigarettes) They also appealed to a youth market with celebrities such as Jenny McCarthy encouraging people to "take back their freedom…without the guilt." (blu e-cigarettes) E-cigarette companies took to social media (Twitter, Facebook and Instagram), hired social media influencers and encouraged participation in social media campaigns such as "#DoIt4JUUL" or to post on YouTube. Images of celebrities echoed across social media when celebrities were seen vaping (such as Robert Pattinson of "Twilight" fame in 2012). E-cigarettes were also advertised on TV (notably NJOY in Superbowl ads in 2013 and 2015) or seen on TV programming (such as Leonardo DiCaprio vaping at the Screen Actor Guild awards in 2016, or Katherine Heigl "ER" on the David Letterman show in 2010). This generated interest and excitement among the population of people who frequent these media venues, for whom the target audience was not and is not 45-64 year olds.

   Flavors: E-cigarettes come in a wide array of flavors, which are known to be appealing to youth and to influence the perception of harm. Many decades of research had indicated the harm of flavors to the public health by promoting initiation of tobacco product use among youth. This body of research was sufficiently persuasive that the 2009 Family Smoking Prevention and Tobacco Control act banned combustible cigarettes and several other tobacco products from characterizing flavors

other than menthol.[1] In a national study (Population Assessment of Tobacco and Health [PATH]), investigators found that flavor was a primary reason for using a given tobacco product, specifically among youth, and that current flavored product use was higher among youth (80%) than adults (38.5% of 45-64 year olds).[2] In a recent longitudinal study of California youth, 93.8% of high school youth in 10-12th grade used a non-traditional flavor (such as fruit, candy, dessert, etc.) (traditional flavors included tobacco, mint, menthol or flavorless). Use of a non-traditional flavor was associated with greater odds of continued vaping 6 months later.[3]
Nicotine: Nicotine is a highly addictive psychoactive drug. Nicotine exposure during the vulnerable adolescent period of development is more likely to lead to addiction than for exposure at any other developmental stage. The characteristics of nicotine deliver found in newer e-cigarettes is more likely to reinforce vaping behavior and lead to addiction (see response to Question 5).

To put some population numbers to this, using data from the US census bureau for population estimates by age group, the above noted *JAMA* article for vaping rates among adults in 2018,[4] and new 2019 prevalence data regarding middle and high school current vaping,[5] only 3.2% of the total US adult population is vaping, compared to 27.5% of high schoolers. The rate is only 2% among 45-64 year olds, and 7.6% among 18-24 year olds. (Conceivably, these 18-24 year olds may have started in high school and have now aged into that age group).
If numbers are split out by adolescents and young adults vs older, using age 25 as a cut point, there are **7.6 million vapers under the age of 25**, **and 5.8 million vapers who are 25 and up**. This is indeed an adolescent and young adult phenomenon.

2. What is youth perception about the safety of combustible cigarettes? And what's youth perception of the safety of e-cigarettes?

   Consistently, youth perceive cigarettes as harmful with a dose-response for risk, and as more harmful than e-cigarettes across multiple studies.[6-8] Research from the Monitoring the Future and the Truth Initiative has similarly found that a majority of youth perceive that e-cigarettes are much safer than cigarettes, and many are unaware that they have any addiction potential. For example, Monitoring the Future data (2017) showed that up to 80% of youth (8th, 10th and 12th graders) did not perceive vaping as harmful. Truth found that 63% of youth were unaware that JUUL always contained nicotine, the addictive component of tobacco products.[9]

3. What differences are you seeing between youth cigarette users and youth e-cigarette users? For example, you mention that you see youth e-cigarette users waking up in the middle of the night to use vaping products, but did not see similar behavior in youth cigarette users.

   First, youth e-cigarette users are a different demographic and risk profile than traditional combusted e-cigarette users. From Monitoring the Future data, researchers reported that risk factors for cigarette use include older age, male gender, White race, lacking college plans, having less-educated parents, having experienced highly stressful events, and having a lower perception of harm from cigarettes.[10] In a PATH

study analysis, e-cigarette users (compared to cigarette users) had lower odds of other tobacco use or marijuana use, lower GAIN (Global Appraisal of Individual Needs) substance use scores, higher academic achievement, and less exposure to others smoking.[11] In FDA focus groups, they noted that e-cigarette users are "popular and social, aspirational, athletic and academically driven."[12]

Patterns of use are also different, based on anecdotal evidence, however no studies of trajectories or patterns of e-cigarette use have yet been published. There have been many reports from pediatricians, parents and adolescents regarding such concerning behaviors as waking in the night to vape, indicating significant levels of addiction. Given the product characteristics of current vaping devices, it is easier to consume higher levels of nicotine than from combusted tobacco cigarettes. The tempo to frequent use also appears significantly shortened than it was for cigarettes. With cigarettes, there was an average of 23 months of use prior to daily use.[13] Anecdotally, adolescents report transitions to daily use in a far shorter time course. Research is clearly needed to better describe and quantify patterns of use.

4. While in the absence of premarketing applications having been submitted to the FDA, it is hard to know for certain how many or which chemicals are in each e-cigarette, but there have been some studies published about the impacts of vegetable glycerin; propylene glycol; cinnamaldehyde; acrolein; and heavy metals including tin, nickel and lead.

   a. Can these chemicals damage lungs, especially the lungs of youth?

   Yes.

   b. What are some of the known consequences of exposure to inhaling these chemicals?

   There are known and unknown harms from inhalation aerosols of these various chemicals, made more complex by the fact that the *delivery* of these chemicals varies based on the device and e-juice characteristics (see response to Question 5). Simply put, the ingredient list on a bottle of e-juice is quite different from the chemical constituents that are delivered to the lungs of the user. There are many dozens of articles that have assessed the impacts of each of these chemicals/substances, so this is an overly simple reply. A more complete answer would best be by a chemist with more detailed understanding.

   The solvents that are used in e-juice solutions generally contain a combination of vegetable glycerin and propylene glycol. **Propylene glycol** is present in many foods, cosmetics, and even the FDA-approved nicotine inhaler. The short and long term health effects of inhalation of vaporized propylene glycol are not yet known. When heated to high temperatures and vaporized, however, propylene glycol breaks down into thermal degradation by-products which include acrolein and formaldehyde.

   Cinnamaldehyde is a flavorant that falls in the class of an aromatic aldehyde. Aromatic aldehydes have been found in several studies to suppress the function of a specific cell type in the lung called a macrophage, which is a critical part of the immune system.[14]

Additional studies have found that this chemical also impairs the ability of cilia to move, which has impact on the ability to clear mucous.[15]

Acrolein is one of the most common aldehydes present in cigarette smoke, and has been found in aerosols from e-cigarettes. From the heavily-referenced introduction of a 2017 study, the investigators state, "Low-molecular-weight aldehydes are estimated to be the most toxic constituents of tobacco products and tobacco smoke. Three toxic aldehydes acetaldehyde, acrolein, and formaldehyde have been ranked by the Institute of Medicine as the most significant cardiovascular (CV) toxins in tobacco smoke. These aldehydes are present in cigarette smoke (700−800 μg/cigarette in mainstream smoke), cigars, and waterpipes (hookah and narghile) and are also present in electronic cigarette (e-cigarette) aerosols. Although levels of some aldehydes are lower in e-cigarette aerosols than those in the smoke of conventional tobacco, a "safe level" of exposure has not been established. Many studies have shown that acute exposure to even low levels of acrolein can induce dyslipidemia, vascular injury, endothelial dysfunction, and platelet activation, whereas chronic exposures accelerate cardiovascular disease (CVD). Indeed, over 92% of the theoretical cardiopulmonary disease (noncancer) risk due to smoking is attributed to just the three aforementioned aldehydes, that is, acrolein, 88.5%; acetaldehyde, 2.4%; and formaldehyde, 0.4%."[16]

5. How does an e-cigarette delivery method allow more nicotine to get to the user?

E-cigarettes use a variety of **engineering** and e-liquid product characteristics to deliver the complex aerosol to the lungs of the user, that does vary by the product type. The "Box-Mod" type of e-cigarettes, which are refillable and have varying power levels that can be changed by the user, can deliver higher (or lower) levels of nicotine based on the differences in temperature and resistance at the coil.[17] In this way, the same "strength" of labelled nicotine e-juice can therefore deliver a wider range of nicotine to the user. Changes to the strength of the nicotine e-juice can also alter the amount of nicotine delivered and change the range of dose. In addition, there is no cue for dosing as there is with a combusted tobacco cigarette, so users may consume higher levels of nicotine within a vaping session due to the depth and frequency of puffing. Therefore, many users get an equivalent nicotine dose that would be seen in "chain smoking" cigarettes (which was the practice of lighting a cigarette from the former cigarette and smoking sequential cigarettes in a short time period.)

The **flavors** in the e-juice have also contributed to increased nicotine delivery by masking the harsh taste of nicotine, allowing deeper and more frequent inhalation of the aerosol (see response to Question 1).

Finally, the **innovation** of e-juice changing from "free base nicotine (FB)" with a more basic pH to a more pH-neutral protonated nicotine-salt based solution, developed and patented by Pax labs, was a game changer for nicotine delivery in an e-cigarette. Their innovation, allegedly inspired by tobacco documents from RJ Reynolds[18] and documented within their patent application,[19] involved buffering the alkaline pH with a

benzoic acid salt and testing a variety of solutions for acceptability to the users and a dose of nicotine delivery that closely resembles that of a combusted tobacco cigarette.[19] New research has suggested that nicotine delivery in the protonated nicotine salt-based solution used in JUUL delivers a markedly different experience. "Per-puff, nicotine emissions from the JUUL are equivalent to 1–10 puffs of closed system devices previously studied. Additionally, compared with previously studied ECIGs whose emissions contain predominantly FB nicotine new ECIG users will likely find inhaling JUUL aerosol less aversive due to its low FB fraction. This factor may contribute to the alarming uptake of JUUL products by adolescents, while the relatively high JUUL nicotine emissions may contribute to their continued use and eventual dependence."[20]

6. What's the typical withdrawal like when an adolescent tries to stop using e-cigarettes and how does it compare to what clinicians see when adolescents try to quit combustible cigarettes?

   Withdrawal from nicotine is characterized by behavioral, cognitive and physiological symptoms and signs. These include irritability and anger, anxiety and depressed mood, difficulty concentrating, restlessness, sleep disturbance and increased appetite.

   There is no data in the scientific literature to describe any differences in withdrawal between these two sources of nicotine. Severity/intensity of symptoms of nicotine withdrawal is related to the level of addiction to nicotine, which is related to frequency and intensity of use. If you have a cigarette user and an e-cigarette user who are each using a similar amount of nicotine and for the same duration of time, they could be expected to have similar levels of withdrawal. There are many individual characteristics that impact withdrawal (gender, comorbid mental health issues, comorbid substance use), but this would not be likely to be differential based on nicotine delivery via combusted vs. vaped inhalation.

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