American Academy of Pediatrics

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Statement of

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On behalf of the

American Academy of Pediatrics

Before the

Food and Drug Administration

Public Hearing on

"Eliminating Youth Electronic Cigarette and Other Tobacco Product Use: The Role for Drug Therapies"

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Good morning. I want to start by thanking the Food and Drug Administration for convening this public meeting to discuss the role of drug therapies in eliminating youth use of electronic cigarettes, an issue that requires urgent public attention. My name is Dr. Susanne Tanski, and I am a pediatrician and tobacco control expert with over 17 years of experience researching tobacco issues and counseling youth who use tobacco products. In the past several years, this has included e-cigarettes and an evolving range of vaping products. I am the former chair of the American Academy of Pediatrics Tobacco Consortium, a group of tobacco researchers committed to addressing tobacco as a child health issue. The AAP is a nonprofit professional organization of over 67,000 primary care pediatricians, pediatric medical subspecialists, and pediatric surgical specialists. The Academy believes that all children should lead tobacco-free lives: free from the use of all tobacco products and free from exposure to secondhand smoke and vapor.

CURRENT TRENDS IN E-CIGARETTE USE/VAPING

As the FDA is well aware, recent trends in use of e-cigarettes by adolescents are quite concerning. According to data from the National Youth Tobacco Survey, current e-cigarette use among high school students increased by 78 percent over the last year and, among those in middle school, current use rose by 48 percent. In 2018, one in five high school students used an e-cigarette in the past month; looking at middle and high school students together, more than 3.7 million U.S. adolescents are current users of e-cigarettes. These youth are using e-cigarettes frequently, with 27% vaping 20 or more days in the last month. Looking at another nationally-representative U.S. survey, 2018 data from Monitoring the Future shows similar increases in vaping since 2017, including a 37 percent increase in reports of "any vaping"

in the past 12 months among high school seniors. These dramatic increases in e-cigarette use among adolescents are of grave concern, and the AAP appreciates Commissioner Gottlieb's recognition of these epidemic levels of youth e-cigarette use.

Pediatricians have seen the growing threat of e-cigarette use among their patients in recent years. The rise of a new generation of products like JUUL that are sleek, discrete, and available in appealing flavors has enticed teens to try these products in ever-growing numbers. What's more, these products deliver very high levels of nicotine, meaning that even brief experimentation is likely to put adolescents at risk for long-term dependence. For those teens already dependent on e-cigarettes, clinicians urgently require new solutions to safely and effectively help them stop using these and all tobacco products for good.

PREVENTION IS PARAMOUNT

Reversing these trends and, ultimately eliminating youth use of e-cigarettes, will require a multifaceted approach, and strong tobacco control policies must play the primary role. Let me say at the outset that while it is important to discuss how drug therapies can help adolescents who are already dependent on tobacco products, preventing youth use in the first place should be FDA's primary goal. We must all recognize that if an adolescent has developed a nicotine addiction as a result of vaping, we have already failed. FDA's recently announced regulatory actions regarding e-cigarettes do not go far enough and we urge much stronger action. Strong tobacco control policy aimed at keeping enticing products away from adolescents may be more effective in achieving adolescent cessation than medical interventions. Indeed, it is likely that nothing FDA does to advance tobacco dependence treatment for adolescents will be as powerful or effective as addressing the availability of flavored e-cigarette products that are attracting and sustaining youth use. We must prevent youth nicotine addiction before it starts.

CAN WE USE EVIDENCE FROM CIGARETTE CESSATION?

There is unfortunately virtually no data on how to treat an adolescent with e-cigarette dependence. As things currently stand, there is not a single randomized controlled trial that has tested strategies to help teens quit e-cigarettes, and there is a significant need for research in this area. We simply do not know yet if our traditional approach to cigarette cessation will apply to adolescent vaping cessation. In the absence of this data, we must be informed by what we do know about evidence-based strategies for helping teens quit traditional tobacco products.

Most teen cigarette smokers want to quit, though most struggle to do so and rates of relapse are high. While the evidence base is not large, research suggests that behavioral and psychosocial interventions delivered in schools, community settings and medical visits are somewhat effective at helping youth stop smoking.

The US Preventive Services Task Force (USPSTF) recommends the use of the 5As approach when counseling adolescent smokers about smoking cessation: Ask, Advise, Assess, Assist, Arrange. Research from the AAP's Julius B. Richmond Center of Excellence tested use of the 5As intervention by pediatricians in the primary care setting. This research suggests that the 5As, when delivered by pediatricians in health care settings, increases teens' likelihood of a quit attempt. At follow-up, however, most teens had relapsed, and there was not a significant impact on cessation at 6 months. Outside of the medical setting, a school nurse-based cessation program was found to be feasible and effective for

abstinence and short-term smoking reduction in adolescents, meeting teens' needs in a location in which they spend a great deal of time. Other techniques that focus on motivational interviewing and face-to-face counseling from health care providers have also been shown to increase quit attempts and aid in cessation. A 2015 state-of-the-art literature review by the AAP Tobacco Consortium found that while evidence for youth tobacco cessation is increasing, few findings are generalizable and adherence to treatment protocol is low.

Unfortunately, little research has been conducted assessing the effectiveness of pharmacologic therapies such as nicotine replacement therapy, varenicline, and bupropion for smoking cessation in adolescents. The research that has been done to date has been disappointing, finding that these treatment options are not particularly effective for adolescent cessation. While bupropion and NRT seem to increase cessation attempts and decrease daily intake of cigarettes in youth, they have not been shown to have an impact on long-term cessation. Crucially, adolescent adherence to treatment protocols for pharmacotherapy is low, which may impact the efficacy of these drugs in cessation for this population. Due to this insufficient evidence of efficacy, NRT for adolescent cessation was not recommended in the most recent USPSTF guidelines, and NRT has not been approved for use with patients under the age of 18. Studies have found that some adolescent tobacco users do elect to use NRT without physician guidance, indicating at least some interest in pharmacotherapy from adolescents. This is an important area for further investigation.

Beyond rigorous prevention policies, research to conclusively identify the most effective tobacco cessation modalities for adolescents addicted to e-cigarettes is an urgent need. In particular, we need the help of FDA to identify how best to treat young people who are already dependent on high-nicotine-delivery products like JUUL.

RESEARCH IS NEEDED

In order to better understand how to help adolescents quit e-cigarette use, we must understand the specific trajectories of e-cigarette use and related nicotine dependence in this age group. Our current understanding of nicotine dependence trajectories is based on experience with traditional tobacco products, and largely from traditional combusted cigarettes. We know that youth are uniquely susceptible to nicotine dependence and that symptoms of dependence develop faster in adolescents than in adults. Indeed, in youth the first symptoms of nicotine dependence can appear within days to weeks of the onset of occasional cigarette use, and well before the onset of daily smoking. Withdrawal symptoms have been shown to progress predictably from "wanting" to "needing" to "craving" cigarettes. As the lag time between the last cigarette smoked and the onset of withdrawal symptoms shortens, teens respond by smoking more frequently.

In contrast to traditional combusted cigarettes, we currently know very little about the trajectories of nicotine dependence for e-cigarettes. Further, we recognize that it is plausible that the dependence trajectory for young cigarette users may differ from that of e-cigarette users, and in particular users of JUUL and similar pod-based devices, due to higher nicotine delivery levels. Recently published research has documented high exposure to nicotine among teens who use JUUL and other pod-based systems. One study, published in September, looked at urinary cotinine concentration in teen users of pod-based systems and found that the concentration of urinary cotinine was higher in users of pod-based systems as compared to teens who used conventional combusted cigarettes. In a study currently in press, pod-based e-cigarette users had median cotinine levels significantly higher than non-pod users, and daily e-

cigarette users had significantly higher median cotinine concentrations than non-daily users. That higher cotinine levels correlate with higher nicotine intake and more frequent use corroborates teens' self-described addiction to these new products. Anecdotally, some young cigarette users have commented that JUUL has been harder to quit. These early and limited data suggest that adolescent users of JUUL and similar e-cigarettes may require unique cessation therapies.

PROMISING RESEARCH DIRECTIONS

With so many outstanding questions surrounding adolescent e-cigarette dependence, we strongly urge FDA to fund studies to better understand adolescent e-cigarette addiction, while also quickly identifying effective interventions for this population of e-cigarette users. We need to know the most effective interventions for adolescent e-cigarette users, whether they be drug therapies, behavioral interventions, or most likely, regimens that combine the two. We must also explore whether these interventions should be the same for adolescents at different points in the nicotine dependence trajectory and whether they should differ based on the severity of dependence. The very issue of measuring nicotine dependence in adolescent e-cigarette users is also likely to be a challenge, and researchers may need support in measuring dependence in a consistent way. There are self-report tools that exist, including the Hooked on Nicotine Checklist (HONC), to assess teen self-reported levels of dependence. However, this tool was originally designed to gauge cigarette use, and teens use e-cigarettes differently than traditional cigarettes. Pairing a self-report tool such as HONC with cotinine validation could be an effective measure of nicotine dependence, but it is certain to add cost and burden to research protocols. We urge the FDA to give this issue thought while investigating interventions for cessation.

Expanded research of nicotine replacement therapies and other drug therapies for adolescent e-cigarette cessation is needed. As mentioned, these products do not currently have an indication for adolescents because they have not been proven to be efficacious in the past. There have not been any trials for e-cigarette cessation with NRT; a randomized controlled trial of NRT in adolescents could be a useful line of study. It is also possible that modifications to the characteristics of currently available NRT products, such as changes to flavor to make them more palatable to adolescents, may help to improve regimen compliance and improve effectiveness. This should be explored as we look for treatment solutions to e-cigarette dependence among adolescents.

We are very aware that pharmacological studies in pediatric populations can be difficult, and drug companies often have little financial incentive to pursue drug development in children. Two pediatric drug laws, the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA), have been successful in greatly increasing the number of drugs with data on pediatric dosing, safety, and efficacy. We've learned a great deal about how to better study drugs in children, and we need to apply these lessons to treatments for nicotine dependence. For example, we know that while recruiting patients into pediatric drug trials is not easy, with the appropriate expertise, protocols, and the use of networks and multi-site trials, we have been able to enroll sufficient numbers to make meaningful progress. **We urge FDA to apply the lessons it has learned to drug therapies for nicotine dependence, and we also urge FDA to utilize the incentives and requirements provided by BPCA and PREA whenever appropriate to encourage additional drug study in this area.**

As industry interest in adolescent nicotine dependence treatment has not been robust, we recommend that FDA take the first steps and fund clinical trials that are large and include multiple enrollment sites in order to be sufficiently powered. The design of any trials and future label changes, if justified by the

evidence, must also recognize that teens have unique access issues that are different from adults. Some teens use tobacco products without their parents' knowledge, and accessing treatment may "out" them to their parents. As such, a teen's ability to confidentially access drug therapies may be critical to the ability to scale and disseminate any successful research interventions that do involve pharmacotherapy. If drug therapies are to be an effective intervention in eliminating youth use of e-cigarettes, **FDA will need to consider how to encourage safe and confidential access points for teens to obtain any evidence-based pharmacotherapies and treatments for nicotine cessation.**

As these changes are explored, we also urge FDA to ensure that any novel drug therapies or modifications to existing therapies developed to address the needs of young e-cigarette users also take into account the potential risks to nicotine-naïve adolescents and young adults. Currently approved NRT products are absorbed very slowly and therefore have a low abuse potential, even in adolescents, making them generally quite safe. **However, as FDA contemplates new formulations and novel products that could be useful in helping e-cigarette dependent adolescents, we encourage caution so accessible NRT products do not become attractive to those who have not already been exposed to nicotine.**

There are additional opportunities for immediate research that FDA should consider. FDA has recently announced sales restrictions on certain flavored e-cigarettes that are likely to decrease access to certain products for adolescents. FDA should consider funding a large observational study of youth who are current JUUL/e-cigarette users and track how they respond to this policy intervention. Reduced access through policy change is itself an intervention that can support cessation. As I said before, strong policy solutions aimed at keeping enticing products away from adolescents — addressing flavors, increasing the purchase age to 21, increasing tobacco taxes—are not only the best ways to prevent adolescent initiation, but are also probably also the best ways to encourage adolescent *cessation*. FDA can and must do more, and make certain that addressing pharmacological treatment for adolescent e-cigarette use is not a replacement for advancing the policies we know are effective for youth.

E-cigarette use among adolescents is a significant public health crisis. There is much we do not yet know when it comes to helping adolescents abstain from e-cigarette use permanently. However, we can use the evidence we do have from adolescent cigarette cessation to drive a research agenda that will help us quickly implement and test potential treatments for teens in real time. We look forward to working with FDA to help end adolescent e-cigarette use. Thank you again for holding this hearing, and for your time and attention.