DAVID A. KESSLER MD

July 31, 2019

Senator Richard J. Durbin
Democratic Whip
711 Hart Senate Office Building
Washington, DC 20510

Dear Senator Durbin,

I very much appreciate your asking me for my views on the specific design of JUUL and how it may be leading to initiation in non-smokers. After discussion with your staff, because of the public health importance of this issue, in addition to setting out my views in this letter, I am also setting them out in the form of an op-ed.

As you know well, over 3.6 million American kids are using e-cigarettes.[1] Use of the most popular brand, JUUL, has resulted in an alarming increase among middle and high school students.[2] This should not be a surprise.

JUUL's founders state that the product is not intended for youth and that it was designed with the adult smoker in mind.[3] While that is important, it misses an essential point.

Based on what we know about cigarettes, the unique design of JUUL may facilitate initiation by young people.[4] The JUUL design seems like a page out of the tobacco industry's playbook.

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[1] Surgeon General's Advisory of E-cigarette Use Among Youth, "In 2018, more than 3.6 million U.S. youth, including 1 in 5 high school students and 1 in 20 middle school students, currently use e-cigarettes," https://e-cigarettes.surgeongeneral.gov/; FDA. *Vaporizers, E-Cigarettes, and other Electronic Nicotine Delivery Systems (ENDS)* https://www.fda.gov/tobacco-products/products-ingredients-components/vaporizers-e-cigarettes-and-other-electronic-nicotine-delivery-systems-ends

2 CDC. *Sales of JUUL e-cigarettes skyrocket, posing danger to youth*. October 2, 2018, https://www.cdc.gov/media/releases/2018/p1002-e-Cigarettes-sales-danger-youth.html

3 https://www.juul.com; Matthew Perrone and Richard Lardner, AP, July 26, 2019: *Juul exec: Never intended electronic cigarette for teens*

4 See text below. See also Talih S, Salman R, El-Hage R, *et al* Characteristics and toxicant emissions of JUUL electronic cigarettes. *Tobacco Control*. Published Online First: 11 February 2019. doi: 10.1136/tobaccocontrol-2018-054616, "JUUL consists of two main components: a liquid-containing and heating coil-containing pod, and a USB-rechargeable battery. JUUL's product literature states that the nicotine in the pod is salt based (i.e., protonated rather than freebase, FB). Protonated nicotine has long been associated with greatly reduced airway irritation compared with FB nicotine and therefore may be more easily inhaled, particularly by new tobacco users."

Twenty-five years ago, we went inside the tobacco industry to understand what it knew about nicotine, its addictive properties, and how it was manipulated.[5] That investigation led to Congress giving FDA authority to regulate both traditional and e-cigarettes.[6]

In internal tobacco company memoranda that date back almost fifty years, tobacco developers discussed how to design new brands of cigarettes that would be particularly attractive to the young smoker, while ideally, at the same time, appealing to all smokers.[7]

The industry recognized that attracting young smokers was key to its success. The tobacco industry understood that there were differences between "presmokers," "learners," and "confirmed smokers." As the industry stated, for the "pre-smoker," and "learner" the physical effects of smoking are quite unpleasant.[8] Once that learning period is over, the addictive properties of nicotine override that unpleasantness.

The industry figured out that a key design element for a successful youth brand was to reduce nicotine's harshness.[9] They determined that an important physical characteristic of the brand was smoothness.[10] Marlboro cigarettes were initially held up by Philip Morris'

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https://www.researchgate.net/publication/331041011_Characteristics_and_toxicant_emissions_of_JUUL_ electronic cigarettes; CDC, op.cit. "Juul…also uses nicotine salts, which can allow high levels of nicotine to be inhaled more easily and with less irritation;" CDC, Tobacco Use by Youth is Rising, February 11, 2019, "Juul also has a high nicotine content, among the highest of the any cigarette – e-cigarette on the U.S. market. The devices also use nicotine salt which can allow high amounts of nicotine to be inhaled more easily and with less irritation than the free-base nicotine that's used in most other e-cigarettes on the market."

5 David A. Kessler, M.D., Ann M. Witt, Philip S. Barnett, Mitchell R. Zeller, Sharon L. Natanblut, Judith P. Wilkenfeld, Catherine C. Lorraine, Larry J. Thompson, and William B. Schultz, The Food and Drug Administration's Regulation of Tobacco Products. *N Engl J Med* 1996; 335:988-994

[6] Pub.L. 111-31 Family Smoking Prevention and Tobacco Control Act

[7] RJR, Teague, Claude E. *Research Planning Memorandum on Some Thoughts on Tobacco Smoke Flavors and Mouth-Feel.* 1973 February 12. Philip Morris Records. https://www.industrydocuments.ucsf.edu/docs/ffcg0189

[8] Ibid pg. 2

[9] For a discussion of nicotine's aversive properties see Fowler, C. D., & Kenny, P. J. (2014). Nicotine aversion: Neurobiological mechanisms and relevance to tobacco dependence vulnerability. *Neuropharmacology, 76 Pt B*(0 0), 533–544. doi:10.1016/j.neuropharm.2013.09.008; Wayne GF, Connolly GN, How cigarette design can affect youth initiation into smoking: Camel cigarettes 1983–93, *Tobacco Control* 2002;11: i32-i39 [available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1766065/pdf/v011p00i32.pdf]; RJR Tague, op. cit.

[10] RJR, Teague, op. cit.; Wayne GF, op. cit.

competitors inside the industry as the best positioned cigarette for young people. Joe Camel soon followed.

To reduce nicotine's harshness, the tobacco industry studied the effects of organic acids (which when combined with nicotine produces nicotine salts, which scientists call "protonated" nicotine). As early as 1954, the tobacco industry studied the effects of adding organic acids to burley tobacco blends and found that many significantly improved "smoothness" of the smoke.[11] Industry developers focused on smoothness in designing a new cigarette for what the industry called "first time smokers."[12] A published study of industry documents concluded that "product design changes which make cigarettes more palatable, easier to smoke, or more addictive are also likely to encourage greater uptake of smoking."[13]

Today, e-cigarettes are typically made with nicotine that comes from extracts from tobacco. Nicotine in this extract is in the "freebase" or unprotonated form, which is harsh when inhaled.[14] Prior to JUUL, e-cigarettes generally contained 1-2.4% nicotine extract,[15] which was in the freebase form. JUUL increased the nicotine compared to other e-cigarettes, using up to

[11] C. Thompson, RDR 1954, No. 11 cited in *Review the use of organic acids and nicotine salts in tobacco burning cigarettes with enhanced nicotine yield.* 1990 April 06. RJ Reynolds Records. At page 2 https://www.industrydocuments.ucsf.edu/docs/lmmn0097

[12] McCarthy, RF. *Harshness workshop*. RJR Tobacco Company. December 10, 1985. Bates No: 507166417-6420 quoted on pg. i34 in Wayne op. cit. "Historically, RJR products have been perceived and rated as being harsher than their respective Philip Morris counterparts . . . Given the corporate emphasis placed on competitive younger adults as being a source of new and future business, it has been recognized and agreed upon that significant improvements in the harshness ratings of Winston King, Winston Lights, Camel Filler, and Camel Lights must be realized in order to increase acceptance among the aforementioned smoker group."

[13] Ibid pg. i37. "Internal documents suggest a strong link between the effects of product design and market share among YAS. [Young Adult Smokers]. According to internal industry research, all brands successful among YAS (including Marlboro and Newport) first demonstrated increased product smoothness or mildness. Camel's success among YAS in the late 1980s followed product design changes affecting the brand's smoothness and harshness attributes, which coincided with introduction of the "Smooth Character" (Joe Camel) advertising campaign;" In 1986, as part of the development of R.J. Reynold's smokeless tobacco product, Premier, the industry further explored ways to improve "harshness" by using numerous organic acids for "smoothing" effects." *Review the use of organic acids and nicotine salts in tobacco burning cigarettes with enhanced nicotine yield.* 1990 April 06. RJ Reynolds Records. At page 2 https://www.industrydocuments.ucsf.edu/docs/lmmn0097

[14] US US20060018840A1 [0062] "Free-base nicotine has a harsh, unpleasant taste. In contrast, nicotine salt forms are less harsh and have a less unpleasant taste."

[15] Truth Initiative: https://truthinitiative.org/research-resources/emerging-tobacco-products/how-much-nicotine-juul

5% nicotine[16] without the harshness, by turning, as the industry had studied decades earlier, to organic acids.[17] JUUL developed prototypes that were treated with organic acids, specifically benzoic acid to form nicotine salts.[18] According to an interview the team that designed JUUL, using these nicotine salts (rather than "free base nicotine") allowed JUUL to "increase the nicotine concentration from two percent to five percent without being unpalatable." By using organic acids, the problem with harshness was addressed.[19]

There are additional characteristics of JUUL's design that may facilitate initiation among young people. They include the use of flavor additives.[20] JUUL used several categories of flavors, tobacco, mint, fruit, and dessert. Some of these flavors can mask off notes and chemical sensations. Tobacco industry documents show the appeal of flavors including sweet taste to young people.[21] JUUL recently stopped selling some flavors in retail establishments.[22] In addition, the small size of the vapor cloud (small but with high nicotine) limits detection in schools.[23]

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[16] Ibid.; CDC, *Tobacco Use by Youth is Rising*, February 11, 2019 "Juul also has a high nicotine content, among the highest of the any cigarette – e-cigarette on the U.S. market. The devices also use nicotine salt which can allow high amounts of nicotine to be inhaled more easily and with less irritation than the free-base nicotine that's used in most other e-cigarettes on the market." https://www.cdc.gov/media/releases/2019/t0211-tobacco-youth-rising.html

[17] Nitasha Tiku, *Startup behind the Lambo of vaporizers just launched an intelligent e-cigarette*, Apr 21, 2015, https://www.theverge.com/2015/4/21/8458629/pax-labs-e-cigarette-juul; David Pierce, *This might just be the first great e-cig*, Wired, 4.21.15 https://www.wired.com/2015/04/pax-juul-ecig/

[18] US 2016/0044968 A [0128], *Nicotine Salt Formulations for Aerosol Devices and Methods thereof*, Feb. 18, 2016, https://patentimages.storage.googleapis.com/66/19/9e/97712c8ace61e2/US20160044968A1.pdf

[19] Tiku op. cit.

[20] See: Esther E. Omaiye, Kevin J. McWhirter, Wentai Luo, James F. Pankow, Prue Talbot. High Nicotine Electronic Cigarette Products: Toxicity of JUUL Fluids and Aerosols Correlates Strongly with Nicotine and Some Flavor Chemical Concentrations. *Chem Res Toxicol.* 2019 Jun 17; 32(6): 1058–1069. Published online 2019 Apr 17. doi: 10.1021/acs.chemrestox.8b00381

[21] Wayne, op. cit.

[22] https://newsroom.juul.com/2018/11/13/juul-labs-action-plan/

[23] Sheila Kaplan, *JUUL Targeted Schools and Youth Camps, House Panel on Vaping Claims*, The New York Times July 25, 2019. https://www.nytimes.com/2019/07/25/health/juul-teens-vaping.html; Sheila Kaplan, *JUUL's New Product: Less Nicotine, More Intense Vapor,* November 27, 2018 https://www.nytimes.com/2018/11/27/health/juul-ecigarettes-nicotine.html.

Each JUUL cartridge delivers 200 puffs, compared to the approximately 10-15 puffs of a traditional cigarette[24]. There are no built in "speed bumps" as when a cigarette naturally extinguishes after a dozen or so puffs. As a pediatrician, I am concerned not only about nicotine addiction, but about the possibility of increased daily nicotine consumption leading to nicotine toxicity.

I had hoped there could be a substitute for traditional cigarettes that offers a less risky nicotine delivery system for those who are addicted to nicotine, could not quit smoking, and need an "off ramp" from smoking and nicotine addiction.

Unfortunately, the explosive growth of JUUL use by children and adolescents has made such a resolution impossible. We cannot allow another entire generation of young people to become addicted to nicotine.

Marked reduction in the initiation of young people to JUUL must be the first order of business. Those who support the use of e-cigarettes for adults who are addicted should support clamping down on brands that facilitate the initiation of use by young people. JUUL should put all its clinical studies and consumer perception surveys in the public domain. Now that Philip Morris has a 35% stake in this youth-appealing product it should tell regulators and the public what it knows about engineering to reduce harshness and increase nicotine's "kick." [25] This will

[24] https://www.juul.com/calculator "One 5% strength JUUL pod is designed to replace one pack of cigarettes in both amount (20 cigarettes ~ 200 puffs) and nicotine strength."; Gideon St. Helen, Kathryn C. Ross, Delia A. Dempsey, Christopher M. Havel, Peyton Jacob, III, Neal L. Benowitz, Nicotine Delivery and Vaping Behavior During *ad Libitum* E-cigarette Access *Tob Regul Sci.* 2016 Oct; 2(4): 363–376. doi: 10.18001/TRS.2.4.8. Available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5381821/

[25] Sheila Kaplan and Matt Richtel, *Juul Closes Deal with Tobacco Giant Altria.* The New York Times Dec. 20, 2018. Available at https://www.nytimes.com/2018/12/20/health/juul-reaches-deal-with-tobacco-giant-altria.html; As JUUL's 2016 patent points out, there is still controversy about the role of ammonia technology in cigarette design. Ammonia was used in reconstituted tobacco as a "processing aid" and "flavorant." While Brown and Williamson was convinced that ammonia technology was important in Marlboro to increase "impact" and "satisfaction." Philip Morris denied its importance in nicotine transfer efficiency. See, PMUSA, Philip Morris USA, SJ. Jeff Seeman E, C, Binder 1997. Philip Morris Records. https://www.industrydocuments.ucsf.edu/docs/xpch0061; Brown & Williamson Tobacco Corp, Root Technology. A

give FDA information to encourage the development of products that help smokers quit but do not lead to initiation by children and adolescents. Last week the founder of JUUL testified to Congress that "we don't want any underage consumer using this product." They need to change the design of their product so it does not facilitate initiation by young people. If JUUL does not, the only appropriate pathway to market its product is a smoking cessation drug under the Federal Food, Drug and Cosmetic Act.[26]

The words Addison Yeoman, the general counsel for the tobacco company, Brown & Williamson, wrote in 1963 are equally applicable today, "we are, then, in the business of selling nicotine, an addictive drug…." [27]. A long and tragic history has taught us that nicotine addiction begins as a pediatric disease.[28]

Sincerely,

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Handbook for Leaf Blenders and Product Developers 1991 February; 2012 March 29. Philip Morris Records. Unknown. https://www.industrydocuments.ucsf.edu/docs/hzyn0189

[26] Section 910 (c)(4), Tobacco Control Act. For JUUL's application, which is now due in approximately 10 months, it must establish a net public health benefit taking into account, among other factors, whether it will increase the likelihood that those who do not use tobacco products will start using such products. If JUUL's design facilitates initiation of people who do not use tobacco products, it would have difficulty being approved as a new tobacco product. If JUUL cannot get approval as a new tobacco product, the only other regulatory pathway would be as an over the counter or prescription drug, if JUUL could establish its safety and effectiveness as a smoking cessation product.

[27] Yeaman, A., *Implications Of Battelle Hippo I & II And The Griffith Filter*: July 17 1963 https://www.industrydocuments.ucsf.edu/tobacco/docs/#id=hrwh0097 pg. 4.

[28] D. A. Kessler, S. L. Natanblut, J. P. Wilkenfeld, C. C. Lorraine, S. L. Mayl, I. B. Bernstein, L. Thompson. Nicotine addiction: a pediatric disease. *J Pediatrics*. 1997 Apr; 130(4): 518–524. Abstract available at https://www.jpeds.com/article/S0022-3476(97)70232-4/abstract