CTP should advance and finalize a rule setting a product standard for a maximum allowable level of nicotine in tobacco products

Docket No. FDA–2023–N–2873
Developing FDA's Center for Tobacco Products' Strategic Plan

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FDA announced[1] a Public Meeting and Listening Session and an opportunity to submit written public comments to obtain feedback on five proposed strategic goals it is using to develop a strategic plan for FDA's Center for Tobacco Products' (CTP) comprehensive Strategic Plan. CTP proposed four cross-cutting themes – (1) health equity; (2) science; (3) transparency; and (4) stakeholder engagement – in proposing the following five goals:

1. Develop, advance, and communicate comprehensive and impactful tobacco regulations and guidance;
2. Ensure timely, clear, and consistent product application review to protect public health;
3. Ensure compliance of regulated industry and tobacco products utilizing all available tools, including robust enforcement actions;
4. Improve public health by enhancing knowledge and understanding of CTP tobacco product regulation and the risks associated with tobacco product use; and
5. Advance operational excellence.

This comment addresses the first goal and urges CTP to initiate a rulemaking and finalize a rule setting a product standard that would establish a maximum nicotine level to reduce the addictiveness of cigarettes and certain other combusted tobacco products. ***This is one of the most important specific actions that CTP could initiate and finalize in the next five years that, with proper implementation, could have great impact in significantly reducing premature disease and death. The sooner a maximum nicotine level standard is implemented, the more lives will be saved.***

[1] US Food and Drug Administration, CTP Newsroom, Listening Session: Developing FDA's Center for Tobacco Products' Strategic Plan, August 22, 2023 (July 21, 2023). Available: https://www.fda.gov/tobacco-products/ctp-newsroom/listening-session-developing-fdas-center-tobacco-products-strategic-plan-08222023?utm_campaign=ctp-ruf&utm_content=landingpage&utm_medium=email&utm_source=govdelivery&utm_term=stratcomms#Proposed%20Strategic%20Goals

- In March 2018, FDA issued an Advance Notice of Proposed Rulemaking (ANPRM) to obtain information to inform the development of a tobacco product standard setting a maximum allowable nicotine level for cigarettes. FDA's rationale for this proposed standard was and remains sound: "Because tobacco-related harms ultimately result from addiction to the nicotine in such products, causing repeated use and exposure to toxicants, FDA is considering taking this action to reduce the level of nicotine in these products so they are minimally addictive or nonaddictive, using the best available science to determine a level that is appropriate for the protection of the public health… We envision the potential circumstance where nicotine levels in cigarettes do not spur or sustain addiction for some portion of potential smokers. This could give addicted users the choice and ability to quit more easily, and it could help to prevent experimenters (mainly youth) from initiating regular use and becoming regular smokers."[2]
- In response to FDA's request for comment on this proposed standard, we submitted public comments in July 2018 that support the goal of setting a maximum nicotine level, which we incorporate by reference.[3, 4]
- In one of our comments,[3] we argued that the FDA should adopt a tobacco product standard setting a nicotine level to be achieved in a single step for all combusted tobacco products. The scientific evidence supports a specific standard for all combusted tobacco products, with a nicotine level for the standard implemented in a single step. The tobacco companies have already shown that it is technically possible to implement such a standard. In implementing this standard there are substantial risks of adversely affecting risk perceptions, especially among youth, that could lead to increased use of nicotine products not covered by the new standard. Effectively countering these adverse effects needs to be part of the standard and associated public education from the beginning to prevent the tobacco industry from taking advantage of this standard to expand its market resulting in net population harm. ***Lowering the nicotine delivery of all combusted tobacco products – not just cigarettes – if written and enforced vigorously in a way that anticipates tobacco industry efforts to thwart the intent of the standard, holds promise for improving public health.***
- The original proposal to reduce the nicotine content in cigarettes was published by Neal Benowitz and Jack Henningfield in 1994.[2] The rationale for that proposal was primarily to prevent youth who experimented with cigarette smoking from becoming addicted adult smokers. While most youth who try cigarettes begin for social reasons and indicate that they do not intend to remain smokers as adults, when surveyed five years later most have become addicted smokers and are unable to quit. A non-addicted person cannot truly appreciate what drug addiction is like, and therefore cannot make a reasonably informed consent to take that risk. Cigarettes are manufactured with nicotine content and delivery levels that will sustain addiction, based on tobacco company research. Thus, a young person who begins smoking

[2] FDA, Tobacco Product Standard for Nicotine Level of Combusted Cigarettes, March 16, 2018. Available: https://www.regulations.gov/document/FDA-2017-N-6189-0001

[3] Glantz SA, Benowitz N, Chaffee, B et al. Tobacco Product Standard for Nicotine Level: The FDA Should Set a Nicotine Level to be Achieved in a Single Step for All Combusted Tobacco Products, Docket No. FDA-2017-N-6189, July 12, 2018. Available: https://www.regulations.gov/comment/FDA-2017-N-6189-7029

[4] Glantz SA, Chaffee B, Gotts J, et al. Tobacco Product Standard for Nicotine Level: Protecting Against Unintended Consequences by Expending the Scope of the Rule to All Inhaled Recreational Nicotine Products, Docket No. FDA-2017-N-6189, July 12, 2018. Available: https://www.regulations.gov/comment/FDA-2017-N-6189-7020

for social reasons may transition to smoking for the pharmacologic effects of nicotine and ultimately become an addicted adult smoker. Cigarettes that deliver nicotine in levels that produce addiction are unreasonably dangerous in part because consent to their use by youth is impossible. Thus, reducing nicotine levels will likely significantly reduce the probability likelihood that a youth experimenting with cigarettes or other combustible tobacco products would become addicted.

- The advisory committee to the World Health Organization supported nicotine reduction in 2015, reporting that nicotine reduction decreases the acquisition of smoking and progression to addiction among experimenters, limits the number of cigarettes smoked by some smokers, increases the number of addicted smokers who stop smoking, and reduces the number of those who relapse.[5]
- Another beneficial effect of reducing nicotine would be to promote quitting in addicted adult smokers. Most smokers want to quit smoking and wish they had never started. Reducing the nicotine content of cigarettes to non-addicting levels would result in smokers finding their cigarettes to be much less satisfying and likely quitting smoking. For smokers with a high degree of nicotine dependence, it was proposed that non-combustible forms of nicotine would be readily available so that smokers would not have to suffer severe withdrawal symptoms or lose any perceived benefits of nicotine for mood modulation or other self-medication for psychiatric reasons. The original proposal was to gradually reduce the nicotine content of cigarettes over time, to simulate a tapering process that is commonly used to detoxify people from other drugs of abuse. However, more recent scientific evidence supports a rapid reduction of nicotine levels for better overall public health benefit.[6,7,8]
- In June 2022, FDA announced[9] plans to develop a proposed product standard that would establish a maximum nicotine level to reduce the addictiveness of cigarettes and certain other combusted tobacco products. FDA said the goal of the potential rule would be to "reduce youth use, addiction and death." "This proposed rule is a tobacco product standard that would establish a maximum nicotine level in cigarettes and certain finished tobacco products. Because tobacco-related harms primarily result from addiction to products that repeatedly expose users to toxins, FDA would take this action to reduce addictiveness to certain tobacco products, thus giving addicted users a greater ability to quit. This product standard would also help to prevent experimenters (mainly youth) from initiating regular use, and, therefore,

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[5] World Health Organization. (2015). Advisory note: global nicotine reduction strategy: WHO Study Group on Tobacco Product Regulation. World Health Organization. https://apps.who.int/iris/handle/10665/189651

[6] Li Q, Chen X, Li X, Gorowska M, Li Z, Li Y. The Effects of Immediate vs Gradual Reduction in Nicotine Content of Cigarettes on Smoking Behavior: An Ecological Momentary Assessment Study. Front Psychiatry. 2022 May 11;13:884605. doi: 10.3389/fpsyt.2022.884605. PMID: 35633808; PMCID: PMC9130591.

[7] Klemperer EM, Luo X, Jensen J, al'Absi M, Cinciripini PM, Robinson JD, Drobes DJ, McClernon J, Strasser AA, Strayer LG, Vandrey R, Benowitz NL, Donny EC, Hatsukami DK. Smoking abstinence and cessation-related outcomes one month after an immediate versus gradual reduction in nicotine content of cigarettes. Prev Med. 2022 Dec;165(Pt B):107175. doi: 10.1016/j.ypmed.2022.107175. Epub 2022 Jul 20. PMID: 35870575.

[8] Hatsukami DK, Luo X, Jensen JA, al'Absi M, Allen SS, Carmella SG, Chen M, Cinciripini PM, Denlinger-Apte R, Drobes DJ, Koopmeiners JS, Lane T, Le CT, Leischow S, Luo K, McClernon FJ, Murphy SE, Paiano V, Robinson JD, Severson H, Sipe C, Strasser AA, Strayer LG, Tang MK, Vandrey R, Hecht SS, Benowitz NL, Donny EC. Effect of Immediate vs Gradual Reduction in Nicotine Content of Cigarettes on Biomarkers of Smoke Exposure: A Randomized Clinical Trial. JAMA. 2018 Sep 4;320(9):880-891. doi: 10.1001/jama.2018.11473. PMID: 30193275; PMCID: PMC6372240.

[9] https://www.fda.gov/news-events/press-announcements/fda-announces-plans-proposed-rule-reduce-addictiveness-cigarettes-and-other-combusted-tobacco

from becoming regular smokers. The proposed product standard is anticipated to benefit the population as a whole while also advancing health equity by addressing disparities associated with cigarette smoking, dependence, and cessation."

- In its Spring 2023 unified regulatory agenda,[10] FDA announced that it plans to issue a proposed rule by December 2023.
- In any case, FDA has had more than enough time and has gathered enough evidence since Benowitz and Henningfield first wrote about this in 1994 to finalize a product standard setting a maximum level of nicotine.
- In addition to combustible tobacco products, FDA should consider setting limits on nicotine in e-cigarettes, oral nicotine products, and other tobacco products. Other countries have limits on the amount of nicotine in e-cigarettes,[11] and the UK limit restricts e-liquids to a nicotine strength of no more than 20mg/ml.[12]
- However, many products being marketed in the US including e-cigarette products and pouches are available with egregiously high levels of nicotine, and the trend has been towards increasing nicotine strength starting when JUUL popularized nicotine salts.[13] For example, disposable flavored Elf Bar e-cigarette products that are extremely popular with kids are marketed on their website with the claim, "Each BC5000 EBCREATE disposable vape contains +5000 puffs and have a 40mg nicotine strength."[14] And some oral nicotine products produced elsewhere have 30 mg/g,[15] 50 mg/g,[16] and even as much as 150mg/g.[17]
- An August 2023 study[18] found that disposable e-cigarettes sold in the US nearly tripled in nicotine strength, quintupled in e-liquid capacity, and dropped in price by nearly 70% between 2017 and 2022.[19]
- Since the rationale for the original Benowitz and Henningfield proposal was primarily to prevent youth who experimented with cigarette smoking from becoming addicted adult smokers, FDA should conduct research to determine what level of nicotine in e-cigarettes and other oral nicotine products might assist smokers in cigarette cessation without

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[10] https://www.reginfo.gov/public/do/eAgendaViewRule?pubId=202304&RIN=0910-AI76

[11] Snell LM, Nicksic N, Panteli D, Burke S, Eissenberg T, Fattore G, Gauci C, Koprivnikar H, Murauskiene L, Reinap M, Barnes AJ. Emerging electronic cigarette policies in European member states, Canada, and the United States. Health Policy. 2021 Apr;125(4):425-435. doi: 10.1016/j.healthpol.2021.02.003. Epub 2021 Feb 18. PMID: 33663799; PMCID: PMC8025686.

[12] E-cigarettes: regulations for consumer products. GOV.UK. Published July 12, 2022. Accessed August 24, 2023. https://www.gov.uk/guidance/e-cigarettes-regulations-for-consumer-products.

[13] Jackler RK, Ramamurthi D. Nicotine arms race: JUUL and the high-nicotine product market. *Tobacco Control* 2019;**28:**623-628.

[14] https://mipod.com/collections/elf-bar-disposable-vapes/products/elf-bar-bc5000-sampler-pack

[15] https://snusdaddy.com/pablo-red-super-strong-slim-all-white

[16] https://snusdaddy.com/pablo-exclusive-50-mg-strawberry-cheesecake

[17] https://snuscore.com/products/iceberg-dragonfire?pr_prod_strat=copurchase&pr_rec_id=36c73b6b5&pr_rec_pid=8121705496805&pr_ref_pid=8206690943205&pr_seq=uniform

[18] Diaz MC, Silver NA, Bertrand A*, et al*
Bigger, stronger and cheaper: growth in e-cigarette market driven by disposable devices with more e-liquid, higher nicotine concentration and declining prices
Tobacco Control Published Online First: 03 August 2023. doi: 10.1136/tc-2023-058033

[19] https://truthinitiative.org/research-resources/emerging-tobacco-products/bigger-stronger-and-cheaper-disposable-e-cigarettes

increasing abuse liability for youth, and consider setting a limit on nicotine for all tobacco products.