United States Senate
WASHINGTON, DC 20510

13 December 2023

Dr. Robert M. Califf
Commissioner of Food and Drugs
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Dr. Califf:

We write to urge the U.S. Food and Drug Administration (FDA) Center for Tobacco Products (CTP) to reform the application review process for harm-reduced products. Given the public health function the CTP is meant to serve, we also write to request information about its policies and actions to ensure it is acting efficiently in a way that is based on science and evidence.

According to the Centers for Disease Control and Prevention (CDC), cigarette smoking is the leading cause of preventable disease and death in the United States, where nearly 31 million Americans smoke cigarettes.[1] Less than eight percent of smokers will successfully quit smoking each year, while thousands will start smoking every day.[2] Combustible cigarette smoking is on the decline[3] due in part to the availability of harm reduction alternatives.[4] Congress recognized the importance of harm reduction when it passed the bipartisan Family Smoking Prevention and Tobacco Control Act of 2009 (the "Act"), which charged the FDA with establishing one of the most comprehensive approaches to tobacco harm reduction in the world. The Act requires the CTP to make application determinations within 180 days, yet the agency routinely fails to meet this requirement.

For the FDA to meet its harm reduction goals, it must have a functioning authorization process. Since 2009, more than 26 million premarket tobacco product applications (PMTAs) have been submitted for new tobacco products in the U.S.[5] Of those 26 million applications, the CTP has authorized fewer than 50.[6] Remarkably, it has also authorized a total of only 16 Modified Risk

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[1] Centers for Disease Control and Prevention, "Current Cigarette Smoking Among Adults in the United States," https://www.cdc.gov/tobacco/data_statistics/fact_sheets/adult_data/cig_smoking/index.htm

[2] Centers for Disease Control and Prevention, "Smoking Cessation: Fast Facts," https://www.cdc.gov/tobacco/data_statistics/fact_sheets/cessation/smoking-cessation-fast-facts/index.html

[3] Centers for Disease Control and Prevention, "Current Cigarette Smoking Among Adults in the United States," https://www.cdc.gov/tobacco/data_statistics/fact_sheets/adult_data/cig_smoking/index.htm

[4] Fagerström, K. Can alternative nicotine products put the final nail in the smoking coffin? *Harm Reduct J* 19, 131 (2022): https://doi.org/10.1186/s12954-022-00722-5

[5] U.S. Food and Drug Administration, "FDA Makes Determinations On More than 99% of the 26 Million Tobacco Products For Which Applications Were Submitted" (15 March 2023), https://www.fda.gov/tobacco-products/ctp-newsroom/fda-makes-determinations-more-99-26-million-tobacco-products-which-applications-were-submitted

[6] U.S. Food and Drug Administration, "Premarket Tobacco Product Marketing Granted Orders," https://www.fda.gov/tobacco-products/premarket-tobacco-product-applications/premarket-tobacco-product-marketing-granted-orders

Tobacco Products (MRTPs) for only four unique products and their accessories.[7] This miniscule authorization rate is not in keeping with the CTP policy acknowledging that tobacco products fall on a continuum of risk. The availability of scientifically substantiated, authorized-PMTAs or MRTPs could potentially improve health outcomes for smokers currently using riskier products.

The CTP has previously attributed its backlog to staffing shortages, but CTP's staff has more than doubled over the past decade, from 426 employees in 2013 to more than 1,100 today.[8] Since 2009, the FDA has also had the authority to assess and collect user fees from tobacco manufacturers and importers, with those fees being $712 million annually since 2019.[9] Given these significant resources, there is no reason why the CTP should be so drastically out of step with the Act's requirements.

The independent Reagan Udall Foundation (RUF) published a December 2022 review of the CTP, finding it has been struggling as a regulator. Specifically, the RUF recommended that "CTP should develop a more clear and predictable framework for high-quality PMTA and MRTP application submission and reviews."[10] In light of the RUF's recommendations that the CTP clarify its policy goals and act more quickly on PMTA and MRTP applications, we request the following information:

1. Does the agency prioritize its review of PMTAs or MRTPAs, and if so, what criteria does the CTP apply in that prioritization process?
2. If the FDA does not prioritize its review of PMTAs or MRTPAs, do you agree there should be a prioritization strategy?
3. There are FDA programs in place in other Centers that enable accelerated review of certain products that have the potential to benefit public health (e.g., breakthrough designation). Has the CTP considered whether and how such a concept could be integrated into its review program for tobacco products?
4. Does the CTP support a supplemental PMTA process, and if so, what is the agency doing to (1) encourage use of the supplemental PMTA pathway and (2) implement ways to expedite decision-making on supplemental applications?
5. Given the FDA's acknowledgment of a continuum of risk in nicotine-containing products, what is the agency doing to raise public awareness of the difference in risk between product categories and to encourage smokers to switch to less harmful products?
6. The CTP's assessment of whether a PMTA product is "appropriate for the protection of public health" includes an evaluation of the extent or likelihood that a product promotes complete switching or a significant reduction in combustible cigarette use in adult smokers. What specific scientific criteria does the CTP consider in this assessment, and how does it weigh or balance each of them in its final determination?

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[7] U.S. Food and Drug Administration, "Modified Risk Granted Orders," https://www.fda.gov/tobacco-products/advertising-and-promotion/modified-risk-granted-orders

[8] U.S. Food and Drug Administration, "Mitch Zeller Reflects on Experiences as Director of FDA Center for Tobacco Products," Answer to Question #3, https://www.fda.gov/tobacco-products/about-center-tobacco-products-ctp/mitch-zeller-reflects-experiences-director-fda-center-tobacco-products

[9] U.S. Food and Drug Administration, "Tobacco Product User Fees: Report in Response to the Consolidated Appropriations Act, 2021," p. 2, footnote (Nov. 2021): https://www.fda.gov/media/155617/download

[10] Reagan-Udall Foundation for the FDA, "Operational Evaluation of Certain Components of FDA's Tobacco Program," p. 19 (Dec. 2022): https://reaganudall.org/sites/default/files/2022-12/Tobacco%20report%20210pm.pdf

7. Does the CTP apply any criteria to determine whether to provide applicants an opportunity to address application deficiencies before issuing a Refuse to Accept (RTA) decision? If so, what are those criteria?
8. An article from the Society for Research on Nicotine and Tobacco recently called on the FDA to set a definition for premium cigars, saying that the failure to do so had prevented the agency from directing appropriate resources to riskier categories of tobacco products. Does the FDA agree with this approach and with establishing a separate category for premium cigars to promote risk-appropriate research and regulation?

Please respond within 30 days of the date of this letter. We look forward to your responses to these important questions.

Sincerely,

Rand Paul, M.D.
United States Senator

Joe Manchin III
United States Senator

Ted Budd
United States Senator