Robert M. Califf, M.D.
Commissioner of Food and Drugs
Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993-0002

April 25, 2023

Dear Dr. Califf:

Reagan-Udall Foundation evaluation of FDA's tobacco program - a response

We are academics and experts with many years of experience in tobacco and nicotine science and policy. We are writing to comment on the Reagan-Udall Foundation evaluation of the Food and Drug Administration's (FDA) tobacco program, and very much welcome the constructive response from the Director of the Center for Tobacco Products, Dr. Brian King. We summarize our points in this letter and expand on our proposed approach in the attached briefing.

In the 2023 State of the Union fact sheet on the Cancer Moonshot, the President committed to tackling cancer and prioritized *smoking* as its most avoidable cause. This mission and focus align well with the vision of the Center for Tobacco Products and should unite all parties with a sincere interest in achieving tangible public health outcomes.

To support the President's agenda, we suggest that FDA shape its tobacco program around four interdependent regulatory pillars to reduce smoking as deeply and rapidly as possible.

1. *To degrade the attractiveness and addictiveness of cigarettes and other combustible tobacco products*. FDA should use its powers to control ingredients, addictive agents, emissions, exposures, packaging, warnings, marketing, and retailer behaviors.

2. *To promote transition pathways to smoke-free status*. FDA should authorize a wide range of low-risk nicotine products that will allow smokers low-risk alternatives and an off-ramp from smoking. Using its wider regulatory powers, FDA should promote smoking cessation with better evidence-based treatments.

3. *To control risks arising from the ongoing use of smoke-free nicotine products.* The FDA should use its powers to ensure that non-combustible tobacco products, while not risk-free, are *safe enough* and have an acceptable risk threshold. It should create a system of standards and soft standards ("comply or justify") that would expedite the pre-market application process.

4. *To protect young people from tobacco-related health and welfare risks.* FDA should take a holistic view of the interests of young people, especially those at the highest risk from tobacco or substance use, and recognize young people benefit in multiple ways when the adults in their lives quit smoking.

As Reagan-Udall points out, FDA's approach to tobacco requires careful navigation of trade-offs and unintended consequences arising from its interventions - and that applies to the four-part strategy set out above. These trade-offs should be made explicit and grounded in minimizing disease risks to the extent possible.

In addition, such a strategy should be underpinned by four further supportive actions:

1. *Education. Undertake a concerted communications effort to better align public perceptions with scientific insight.* There are widespread misperceptions about the significant differences in the risks of combustible and non-combustible products and public misunderstandings about the role of nicotine in behavior and disease. FDA is well positioned to correct misperceptions about nicotine to accelerate the decline of smoking.

2. *Efficiency. Make immediate improvements in the efficiency, transparency, predictability, and proportionality of the PMTA process*. Process re-engineering will reduce pressure on staff and litigation risks. It means, for example, relying more on standardization, post-market surveillance, and expediting authorization for product updates.

3. *Enforcement. Build a rational regulatory regime and then enforce it*. FDA should combine a more rational, transparent, and risk-proportionate system for authorizing smoke-free products with stricter enforcement action against unauthorized products, rogue marketing practices, and illegal sales to under-21s. A more orderly, well-regulated market will reduce, though not eliminate, the need for enforcement.

4. *Engagement. Proactively engage stakeholders.* FDA should be open to a wide range of perspectives on these issues and demonstrate a willingness to consult and engage widely, including through the Tobacco Products Scientific Advisory Committee (TPSAC). FDA could publish or sponsor objective scientific assessments and help build consensus towards a common base of knowledge.

We hope you will take our views as a positive contribution to the further development of the FDA as an effective regulator of tobacco and nicotine products. We would also like to engage in constructive dialogue. To that end, we would welcome the opportunity to meet with relevant FDA leadership and discuss these matters.

We are copying this letter to Dr. King and will make it publicly available.

Yours sincerely,

David Abrams, Ph.D.
Professor of Social and Behavioral Sciences
School of Global Public Health
New York University

Scott D. Ballin, J.D.
Former Vice President and Legislative Counsel to the American Heart Association
Former Chairman of the Coalition on Smoking OR Health (ACS, AHA, ALA)
Advisor to the UVA Institute for Engagement and Negotiation

Clive D. Bates, M.A., M.Sc.
Director, Counterfactual Consulting
Former Director, Action on Smoking and Health London,
United Kingdom

Neal L. Benowitz M.D.
Professor of Medicine Emeritus
University of California San Francisco
Zuckerberg San Francisco General Hospital

K. Michael Cummings, Ph.D., MPH
Professor, Department of Psychiatry & Behavioral Sciences
Medical University of South Carolina

Clifford E. Douglas, J.D.
Adjunct Professor
Director, Tobacco Research Network
University of Michigan School of Public Health
Former Tobacco Control Policy Advisor
U.S. Assistant Secretary for Health and U.S. Surgeon General
Former Vice President, Tobacco Control, American Cancer Society

Jonathan Foulds, Ph.D.
Professor, Department of Public Health Sciences
Interim Chief, Division of Health Services and Behavioral Research
Professor, Department of Psychiatry and Behavioral Health
Penn State Cancer Institute

Thomas J. Glynn, Ph.D.
Adjunct Lecturer
Prevention Research Center, School of Medicine, Stanford University
Former Director, Cancer Science and Trends, American Cancer Society
Former Associate Director, Cancer Control Science Program, U.S. National Cancer Institute

Martin Jarvis, D.Sc., OBE
Emeritus Professor of Health Psychology
University College London,
United Kingdom

Lynn T. Kozlowski, Ph.D.
Former Dean
Professor of Community Health and Health Behavior
School of Public Health and Health Professions
University at Buffalo

David Levy, Ph.D.
Professor of Oncology
School of Medicine
Georgetown Lombardi Comprehensive Cancer Center
Georgetown University

David Mendez, Ph.D.
Associate Professor
Department of Health Management and Policy
School of Public Health
University of Michigan

Robin Mermelstein, Ph.D.
Distinguished Professor, Liberal Arts and Sciences
Psychology Department
Director, Institute for Health Research and Policy
Co-Director, Center for Clinical and Translational Science
University of Illinois at Chicago

Rafael Meza, Ph.D.
Distinguished Scientist
BC Cancer Research Institute
Adjunct Professor
University of Michigan

Tom Miller, J.D.
Former Iowa Attorney General
Des Moines, Iowa

Ethan Nadelmann, J.D., Ph.D.
Founder & Former Executive Director
Drug Policy Alliance
New York

Raymond Niaura, Ph.D.
Interim Chair of the Department of Epidemiology
Professor, Social and Behavioral Sciences
College of Global Public Health
New York University

Michael F. Pesko, Ph.D.
Associate Professor of Economics
Andrew Young School of Policy Studies | Dept. of Economics
Georgia State University

Vaughan W. Rees, Ph.D.
Senior Lecturer on Social and Behavioral Sciences
Director, Center for Global Tobacco Control
Department of Social and Behavioral Sciences
Harvard T.H. Chan School of Public Health

Steven A. Schroeder, M.D.
Professor Emeritus,
Department of Medicine
University of California, San Francisco

David Sweanor, J.D.
Advisory Committee Chair,
University of Ottawa Centre for Health Law, Policy and Ethics
Adjunct Professor, Faculty of Law
University of Ottawa,
Canada

Jamie Tam, MPH, Ph.D.
Assistant Professor
Department of Health Policy and Management
Yale School of Public Health

Kenneth E. Warner, Ph.D.
Avedis Donabedian Distinguished University Professor Emeritus
Dean Emeritus
University of Michigan School of Public Health

Daniel Wikler, Ph.D.
Mary B. Saltonstall Professor of Ethics and Population Health
Department of Global Health & Population
Harvard T.H. Chan School of Public Health

Briefing: Reagan-Udall Foundation evaluation of FDA's tobacco program – a response

Table of Contents

Introduction

We welcome the Reagan-Udall Foundation's operational evaluation of the FDA's tobacco program.[1] We commend your initiative in commissioning the evaluation and welcome the constructive and open-minded response from the Center for Tobacco Products.[2] We hope the Reagan-Udall findings will prompt a strategic reassessment. To that end, we are writing with comments on the Reagan-Udall findings and suggested directions for FDA's program. In response to the main recommendation, we propose an updated strategic framework that builds on the 2017 Comprehensive Plan.

The central concern of the Foundation's experts was the absence of a coherent regulatory strategy for the Center for Tobacco Products (CTP).

> CTP must invest the time, now, with staff and public input, to create and implement a Strategic Plan that identifies the Center's strategic objectives and plots an operational roadmap of the steps CTP will take over the next five years to achieve those objectives.

Proposed four-part strategic framework for tobacco regulation

Goal: a relentless focus on reducing serious diseases and premature death

Consistent with the vision of CTP,[3] the purpose of the tobacco program should be to reduce the burden of tobacco-related disease and death as deeply and rapidly as possible. This goal is aligned with President Biden's priorities as outlined in the briefing for the 2023 State of the Union address.[4]

> **Tackling the biggest single driver of cancer deaths in this country – smoking.** The Administration is preparing further action to help people avoid smoking in the first place and support Americans who want to quit.

We concur with the Administration's focus on *smoking* as the primary driver of cancer and other serious tobacco-related diseases. The tobacco program would have four interrelated elements. We list these below and expand in the following paragraphs.

1. To degrade the attractiveness and addictiveness of cigarettes and other combustible tobacco products.
2. To promote transition pathways to smoke-free status.
3. *To control risks arising from the ongoing use of smoke-free nicotine products.*
4. To protect young people from tobacco-related health and welfare risks.

---

[1] Silvis, L., Axelrad, J., Flanagan, K., Frizzera, C., & Gutierrez, A. (2022). *Operational Evaluation of FDA's Tobacco Program*. Reagan-Udall Foundation December 2022. https://bit.ly/3JDg2gH

[2] Brian King, Director of FDA's Center for Tobacco Products.An All-Center Approach: CTP's Response to the Reagan-Udall Foundation Evaluation Report https://bit.ly/42YfuZV 24 February 2023. Actions to Address Recommendations from the Reagan-Udall Evaluation of CTP, 24 February 2023. https://bit.ly/40N2Zi2

[3] CTP vision: To make tobacco-related disease and death part of America's past, not America's future, and, by doing so, ensure a healthier life for every family. https://bit.ly/CTPVision

[4] White House Briefing: FACT SHEET: In State of the Union, President Biden to Outline Vision to Advance Progress on Unity Agenda in Year Ahead, February 7, 2023. https://bit.ly/3I8uFrb

1. To degrade the attractiveness and addictiveness of cigarettes and all other combustible tobacco products

Around 3,000 lawfully available cigarette products continue to dominate the consumer nicotine market.[5] They are used by over 30 million adult smokers, causing 480,000 deaths every year - about 1 in 6 deaths - leaving 16 million living with smoking-related diseases.[6] Yet the regulation of these products is comparatively light compared to the heavy burdens of the pre-market application process for much safer non-combustible nicotine products. This disproportionate and distorting regime must become more "risk-proportionate." This means increasing regulatory controls on harmful combustibles and making the regulation of safer, non-combustible products more efficient and proportionate.

FDA has several options for rulemaking and communications to achieve this aim. Using its power under Section 907 of the Tobacco Control Act, *Tobacco Product Standards*,[7] FDA could introduce a broader range of controls on ingredients or emissions. These could include the regulation of significant toxicants and addictive agents to reduce the toxic burden, limit addictiveness, and control abuse liability or aspects of product appeal. Using its powers under Section 906,[8] FDA could address aspects of cigarette marketing, including packaging and appearance, and impose more detailed or impactful consumer information.

The federal government as a whole should support action to limit the appeal of smoking, including through tax policy that is more in line with other high-income countries.[9] Such measures will be effective if, and only if, smokers are motivated to transition to a low-risk smoke-free status rather than to access illicit smoking products or to find workarounds. There must be diverse, competitive, and lawful low-risk options available for smokers to switch to. The success of rules to control the addictiveness or appeal of cigarettes will be contingent on the supportive measures that influence the behavioral pathways followed by smokers in response to toughened cigarette regulation. Tobacco product rulemaking cannot be separated from policies that affect the behavioral response to the rule.

2. To promote transition pathways to smoke-free status

FDA should aggressively prioritize achieving smoking cessation and smoke-free status for those at great risk of experiencing health problems due to smoking (i.e., those with pre-existing smoking-related health conditions and those with mental health or substance use disorders). This could incorporate CDER licensing of improved smoking cessation treatments and authorizing a diverse range of smoke-free alternatives to cigarettes. It could mean using its education and communication resources to reset the highly inaccurate public perceptions of risk and misunderstanding of nicotine and encourage switching to smoke-free alternatives for those who want to continue using nicotine. We must recognize that people who smoke will follow different pathways to smoke-free status. For many, stopping smoking

[5] Cris Delnevo, Monitoring the Evolving Tobacco/Nicotine Marketplace: Lessons Learned and Future Priorities to Reduce Tobacco-Caused Morbidity and Mortality, SRNT Public Health Theme Lecture, 2022. Dr. Delnevo identifies 2,840 unique cigarette products in Nielson data for 2021. https://bit.ly/413movr (at 12 minutes)

[6] CDC, Current Cigarette Smoking Among Adults in the United States, accessed April 2023. https://bit.ly/3y0dlOX Note CDC attributes 1 in 5 deaths to smoking, but based on the 2,854,833 deaths registered in 2019, 1 in 6 is more appropriate.

[7] Section 907 of the Federal Food, Drug, and Cosmetic Act - Tobacco Product Standards https://bit.ly/3JZt3zS

[8] Section 906 of the Federal Food, Drug, and Cosmetic Act - General Provisions Respecting Control of Tobacco Products https://bit.ly/3zmea5F

[9] Numbeo, Price Rankings by Country of Cigarettes 20 Pack (Marlboro) (Markets), 2023. https://bit.ly/3G5pdUF

will feel more like an evolution of their consumer smoking behavior as they become "accidental quitters."[10] [11]

3. To control risks arising from the ongoing use of smoke-free nicotine products

The demand for nicotine will be more persistent than the demand for cigarettes. Nicotine use has a long history and is likely to persist on account of actual or perceived benefits to the user.[12] [13] While significantly less risky than smoked products, smoke-free products still impose controllable risks on the user. These should be reduced to the extent possible but consistent with enabling such products to displace smoking and meet the needs of consumers. The aim should be a diverse market of lawfully sold and regulated products with *acceptable* risks – mindful of the excess risks associated with illicit trade and informal manufacturing and supply. The regulation of the product itself should focus on the users' interest in protection from chemical, electrical, thermal, and mechanical risks. In contrast, regulation designed to protect youth and non-users should focus less on product design and more on marketing, branding, packaging, and compliance with age and other point-of-sale restrictions.

Once established, such restrictions must be enforced. Currently, manufacturers who invest financial and human resources in compliance face competition from companies that do not even try to comply. We discuss enforcement as a supporting measure below.

4. To protect young people from tobacco-related health and welfare risks

No responsible adult wants young people to smoke, vape, or use nicotine in any form. This is the case for most youth risk behaviors. Despite adult disapproval, there is widespread risk-taking among a subset of adolescents. The strategy should adopt a more sophisticated real-world view of young people and their risk behaviors. It should recognize that some adolescents would likely become smokers or choose to use nicotine as adolescents, just as they use alcohol or other drugs. Other teenagers will engage in transient experimentation without long-term consequences.[14] Any understanding of youth vaping should consider both the frequency of use and propensity to use tobacco.[15] For some youth, vaping could be a diversion from smoking.[16] [17] Youth smoking has fallen at an accelerated rate as vaping has

---

[10] Kasza, K. A., Edwards, K. C., Kimmel, H. L., et al. (2021). Association of e-Cigarette Use With Discontinuation of Cigarette Smoking Among Adult Smokers Who Were Initially Never Planning to Quit. *JAMA Network Open*, *4*(12). https://doi.org/10.1001/JAMANETWORKOPEN.2021.40880

[11] Notley, C., Ward, E., Dawkins, L., & Holland, R. (2018). The unique contribution of e-cigarettes for tobacco harm reduction in supporting smoking relapse prevention. *Harm Reduction Journal*, *15*(1), 1–12. https://doi.org/10.1186/s12954-018-0237-7

[12] Benowitz, N. L. (2009). Pharmacology of Nicotine: Addiction, Smoking-Induced Disease, and Therapeutics. *Annual Review of Pharmacology and Toxicology*, *49*, 57. https://doi.org/10.1146/ANNUREV.PHARMTOX.48.113006.094742

[13] Newhouse, P. A. (2019). Therapeutic Applications of Nicotinic Stimulation: Successes, Failures, and Future Prospects. *Nicotine & Tobacco Research*, *21*(3), 345–348. https://doi.org/10.1093/NTR/NTY189

[14] Polosa, R., Casale, T. B., & Tashkin, D. P. (2022). A Close Look at Vaping in Adolescents and Young Adults in the United States. *The Journal of Allergy and Clinical Immunology: In Practice*, *10*(11), 2831–2842. https://doi.org/10.1016/J.JAIP.2022.06.005

[15] Glasser, A. M., Johnson, A. L., Niaura, R. S., Abrams, D. B., & Pearson, J. L. (2021). Youth Vaping and Tobacco Use in Context in the United States: Results from the 2018 National Youth Tobacco Survey. *Nicotine and Tobacco Research*, *23*(3), 447–453. https://doi.org/10.1093/ntr/ntaa010

[16] Sokol, N. A., & Feldman, J. M. (2021). High School Seniors Who Used E-Cigarettes May Have Otherwise Been Cigarette Smokers: Evidence From Monitoring the Future (United States, 2009–2018). *Nicotine & Tobacco Research*, *23*(11), 1958–1961. https://doi.org/10.1093/NTR/NTAB102

[17] Selya, A. S., & Foxon, F. (2021). Trends in electronic cigarette use and conventional smoking: quantifying a possible 'diversion' effect among US adolescents. *Addiction*, add.15385. https://doi.org/10.1111/add.15385

increased,[18] [19] leading to substantial overachievement of Healthy People targets for youth smoking.[20] FDA should acknowledge that when prevention efforts fail, as should be expected in high-risk youth, it would be preferable that they use a safer non-combusted nicotine product rather than cigarettes.[21] No practical barrier can keep accurate, usable risk communications for adults away from youth. Adolescent experimentation with adult behaviors is inevitable but often transient and of little long-term consequence. It is not realistic to classify all youth as non-smokers for the purposes of regulating smoke-free products without considering what pathways they would follow in the absence of smoke-free alternatives.

The tobacco-related welfare of young people is also often contingent on parents or significant adults. Adults affect the welfare of children and adolescents through role modeling smoking, the impact of smoking on the household budget, and smoking-related harms, including caring responsibilities, grief, and secondhand smoke exposure. Young people grow up to be adults and may value having safer options when they are older. It is impossible to neatly separate youth and adult populations from a public health policy perspective.

We recommend that FDA takes a holistic view of the interests of young people, recognizing and carefully weighing benefits and detriments arising from the changing landscape of regulated nicotine products. Interventions should focus on age restrictions and controls on packaging, trademarks, and branding that are disproportionately attractive to youth.

Recognizing inter-relationships between the elements of a strategy

The interrelationships between these four elements are critical. A strategy strongly emphasizing *smoking* cessation must offer sound pathways to abstinence or smoke-free alternatives. An approach to smoking cessation that works through smoke-free alternatives must be subject to safeguards to discourage youth use and ensure products are acceptably safe. However, standards to control the risks of smoke-free products should maintain the value of these products as alternatives to cigarettes – the perfectly safe product that no one is willing to use has no public health impact. There must be a balance between risk and likelihood of use.[22] Equally, an approach to youth protection from vaping should not be so stringent that it favors the incumbent cigarette trade, imposes significant harm on adult or adolescent smokers, or leads to the engagement of young people in illicit trade or more dangerous workarounds. Unintended perverse consequences should be a primary consideration in designing a regulatory system. While these interrelationships should be a

[18] Foxon, F., & Selya, A. S. (2020). Electronic cigarettes, nicotine use trends and use initiation ages among US adolescents from 1999 to 2018. *Addiction*, *115*(12), 2369–2378. https://doi.org/10.1111/add.15099

[19] Levy, D. T., Warner, K. E., Cummings, K. M., Hammond, D., Kuo, C., Fong, G. T., Thrasher, J. F., Goniewicz, M. L., & Borland, R. (2019). Examining the relationship of vaping to smoking initiation among US youth and young adults: a reality check. *Tobacco Control*, *28*(6), 629–635. https://doi.org/10.1136/tobaccocontrol-2018-054446

[20] Healthy People 2030. The target for youth cigarette smoking in 2030 (3.4%) had been *achieved by 2020* (3.3%), down from the 2018 baseline of 5.4%. https://bit.ly/3KoNGa5. The Healthy People 2020 target was to reach 16.0% by 2020 from a baseline of 19.5% in 2009 https://bit.ly/3GaaS9z With an outturn of 3.3% in 2020, the average linear rate of decline in youth cigarette between 2009 and 2020 (1.47 percentage points per year) was *4.6 times* greater than the rate required to meet the Healthy People 2020 target (0.32 percentage points per year). The average exponential rate of decline (17.5% per year) was *9.6 times* greater than the rate required to meet the Healthy People 2020 target (1.8% per year).

[21] Villanti, A. C., Niaura, R. S., Abrams, D. B., & Mermelstein, R. (2019). Preventing Smoking Progression in Young Adults: the Concept of Prevescalation. *Prevention Science : The Official Journal of the Society for Prevention Research*, *20*(3), 377–384. https://doi.org/10.1007/S11121-018-0880-Y

[22] Kozlowski, L. T., Strasser, A. A., Giovino, G. A., Erickson, P. A., & Terza, J. v. (2001). Applying the risk/use equilibrium: use medicinal nicotine now for harm reduction. *Tobacco Control*, *10*(3), 201–203. https://doi.org/10.1136/TC.10.3.201

significant consideration during a strategy-forming process, the rigor and robustness will need to be validated throughout five years of implementation. We suggest regular stakeholder engagement and assessment of the routine performance of a strategic framework, but also as it faces novel risks or opportunities.

Balancing risks and benefits and making trade-offs

The Reagan-Udall evaluation highlighted a range of unavoidable trade-offs in making determinations under the "Appropriate for the Protection of Public Health" (APPH) standard.

> This lack of clarity, transparency, and communication extends to questions about: how the Agency intends to balance individual risk/benefit against population risk/benefit while carrying out its public health mission; how the Agency will weigh concerns about youth uptake of nicotine products against the harm-reduction potential of non-combustible tobacco products, how the Agency views the science that must inform these decisions

We agree with the Reagan-Udall assessment that much of this is unclear and inconsistent in FDA's approach to tobacco and nicotine regulation and its operationalization of the APPH test. To reconcile these trade-offs, we recommend a balanced approach to the science along the lines proposed by fifteen past presidents of the Society for Research in Nicotine and Tobacco (SRNT).[23]

In making its determinations, FDA must consider the following:

- The interests of adult smokers as well as risks arising from youth uptake of vaping.
- The interest of young people in *adult* smoking cessation, including parents and other significant adults.
- The interests of adolescent vapers who would otherwise become smokers.
- A realistic weighting of the harm to adult or adolescent vapers compared to risks to adult or adolescent smokers based on the likelihood that the behavior will lead to serious disease and premature death.
- The economic and population trend evidence suggests the net effect of vaping at the population level is to displace smoking and, overall, to contribute to a decline in smoking prevalence.[24] E-cigarettes function as an economic substitute for cigarettes.[25]
- The potential unintended detrimental consequences of well-intentioned regulatory actions, including *de facto* bans on flavored e-liquids. Given the relative risks, only a minimal unintended increase in smoking, through reduced switching or quitting, could easily outweigh any benefits arising from reduced vaping.

[23] Balfour, D. J. K., Benowitz, N. L., Colby, S. M., Hatsukami, D. K., Lando, H. A., Leischow, S. J., Lerman, C., Mermelstein, R. J., Niaura, R., Perkins, K. A., Pomerleau, O. F., Rigotti, N. A., Swan, G. E., Warner, K. E., & West, R. (2021). Balancing Consideration of the Risks and Benefits of E-Cigarettes. *American Journal of Public Health*, *111*(9), 1661–1672. https://doi.org/10.2105/AJPH.2021.306416

[24] Selya, A., Wissmann, R., Shiffman, S., Chandra, S., Sembower, M., Joselow, J., & Kim, S. (2023). Sales of Electronic Nicotine Delivery Systems (ENDS) and Cigarette Sales in the USA: A Trend Break Analysis. *Journal of Consumer Policy*, *46*(1), 79. https://doi.org/10.1007/S10603-022-09533-4

[25] Selya, A., Foxon, F., Chandra, S., & Nealer, E. (2023). Meta-analysis of e-cigarette price elasticity. *F1000Research 2023 12:121*, *12*, 121. https://doi.org/10.12688/f1000research.129233.1

Supporting measures

The four strategic pillars proposed above should be accompanied by four supporting measures listed below.

1. *Education*: undertake a concerted communications effort to better align public perceptions with scientific insight.
2. *Efficiency*: make immediate improvements in the efficiency, transparency, predictability, and proportionality of the PMTA process.
3. *Enforcement*: build a rational regulatory regime and then enforce it.
4. *Engagement:* proactively engage stakeholders.

1. Education: undertake a concerted communications effort to better align public perceptions with scientific insight

Risk perceptions influence choices made by tobacco and nicotine users. With reliable information, people can make choices in their best interests. There is *never* an ethical case to manipulate risk perceptions with false or misleading information to achieve a favored behavioral outcome. Not only is this likely to have unintended adverse consequences (more smoking), it violates the public health principle of autonomy and erodes trust in public health agencies and advice.[26]

For FDA to execute a strategy that reduces tobacco-related disease at the greatest possible rate, the public will need to understand the conceptual foundations of measures like lowering nicotine levels in cigarettes and encouraging smoking cessation by switching to smoke-free nicotine products.

It is concerning, therefore, that Americans have serious misperceptions about the relative risks of smoking, vaping, and smokeless tobacco,[27] [28] and there is widespread misunderstanding of the role of nicotine in causing disease.[29] Despite significant communications budgets, these perceptions have steadily deteriorated and departed from science-based findings. Adverse perceptions can underpin harmful behaviors, for example, by making people who smoke more reluctant to switch to e-cigarette use.[30] [31]

---

[26] Brown, R. C. H., & de Barra, M. (2023). A Taxonomy of Non-honesty in Public Health Communication. *Public Health Ethics*. https://doi.org/10.1093/PHE/PHAD003

[27] HINTS. (2020). *Compared to smoking cigarettes, would you say that electronic cigarettes are...* Health Information National Trends Survey. https://bit.ly/3ZsrNel Only 2.6% say e-cigarettes are "much less harmful" than cigarettes. 62.2% say just as harmful, more harmful or much more harmful.

[28] HINTS. (2017). *Do you believe that some smokeless tobacco products, such as chewing tobacco and snuff, are less harmful than cigarettes?* Health Information National Trends Survey (2017) https://bit.ly/3GcBiaz Only 13.4% believe that smokeless tobacco is less harmful than cigarettes.

[29] HINTS. (2019). *How much do you agree or disagree that the nicotine in cigarettes is the substance that causes most of the cancer caused by smoking?* Health Information National Trends Survey. https://bit.ly/3JZE7wY 56.5% incorrectly agree or strongly agree that nicotine causes most cancer caused by smoking. A further 19.5% don't know.

[30] Persoskie, A., O'Brien, E. K., & Poonai, K. (2019). Perceived relative harm of using e-cigarettes predicts future product switching among US adult cigarette and e-cigarette dual users. *Addiction (Abingdon, England)*, *114*(12), 2197–2205. https://doi.org/10.1111/ADD.14730

[31] Kim, S., Shiffman, S., & Sembower, M. A. (2022). US adult smokers' perceived relative risk on ENDS and its effects on their transitions between cigarettes and ENDS. *BMC Public Health*, *22*(1), 1–13. https://doi.org/10.1186/S12889-022-14168-8/TABLES/4

We are concerned that communications targeted at youth go beyond what can be justified scientifically and that there are instances where specific messaging (for example, EVALI or gateway claims) have adversely and inappropriately influenced risk perceptions.[32]

Further, FDA generally accepts that tobacco products exist on a risk continuum and with a qualitative step between combustible and non-combustible products. FDA also acknowledges that there are misperceptions about the health impacts of nicotine. However, to our knowledge, the Centre for Tobacco Products has not conducted any mass communication or educational activity to rectify these misperceptions. In a refreshed strategy, that should change.

We believe the FDA and CDC should establish measurable goals to create more realistic and actionable risk perceptions to support individual behavior change and underpin a credible strategy for tobacco and nicotine.

2. Efficiency: make immediate improvements in the efficiency, transparency, predictability, and proportionality of the PMTA process

There is a clear asymmetry between the low regulatory burdens facing cigarettes and the high barriers to entry for novel and reduced-risk nicotine products. The FDA's interpretation of its duties may create a regulatory protection for the incumbent cigarette trade and function as a barrier to the rapid reduction of smoking.

We recommend that the PMTA regime be simplified and made more proportionate by the following:

- Develop and communicate a principled, transparent, proportionate, and legally defensible strategy for APPH determinations. If applicants are clear on what is expected and how their applications will be evaluated, there will likely be fewer applicants and better-quality applications. *A robust regulatory strategy is the structural solution to the backlogs, litigation, and overwhelming demands on FDA staff and applicants*.

- Aim to create routine and expedited pathways through evaluation for products that are broadly similar and already well-established in the market.[33] By avoiding unnecessary repetition, FDA could reserve its scientific and assessment resources for novel products that present either novel risks or new opportunities. FDA should be able to prioritize innovations that are likely to advance the public health agenda, for example, by reaching particular at-risk populations, highly dependent smokers, or nudging dual users into exclusive use of low-risk products.

- Improve the transparency of FDA's evaluation criteria and how the agency maintains consistency between products, assessors, and over time. Any guidance to assessors (e.g., internal reviewer guides, briefs on the state of the science) should be made public and readily available to applicants.

[32] Pesko, M. F., Cummings, K. M., Douglas, C. E., Foulds, J., Miller, T., Rigotti, N. A., & Warner, K. E. (2022). United States public health officials need to correct e-cigarette health misinformation. *Addiction*. https://doi.org/10.1111/ADD.16097

[33] The legal options for achieving this are beyond the scope of this briefing. It is possible this could be achieved through the expansion of existing pathways, like supplemental PMTAs, expanding bridging options, or through the creation of new pathways to illuminate a route forward for discrete categories of products. Our purpose here is to argue that this should be the *intent,* and that FDA should seek lawful means to deliver on it.

- Use guidance to provide advisory standards-based pathways through the PMTA assessment. Such 'soft standards' or 'heuristics' would not be mandatory *tobacco product standards* under the Tobacco Control Act. Applicants and evaluators would use them to expedite and simplify the technical evaluation process by capitalizing on commonly accepted scientific findings. The approach would be "comply or justify," meaning that additional evidence and scrutiny would be required for products that did not meet these soft standards.

- Such 'soft standards' could also inform priorities for the exercise of enforcement discretion. For example, a soft standard that creates a presumption against using cartoons or childish branding would signal manufacturers not to include such imagery in pre-market applications (or be prepared to justify it) and to expect priority enforcement action in the absence of a PMTA.

- Develop a range of mandatory tobacco product standards under the Tobacco Control Act Section 907. This approach should help to standardize assessments and avoid the cost and waste of applications that will fail.[34]

- *Pre-market* assessment should focus on risks to the individual (toxicity, safety, abuse liability). Where individual risks are likely to be much lower, population and behavioral effects should be assessed *post-market* using real-world data. If adverse effects emerge, FDA retains the power to take corrective action, including removing products from the market.

- Use a single market-wide post-market surveillance system funded by user fees rather than imposing significant surveillance burdens on each applicant. A single surveillance system will provide a better insight into population effects, effects arising at category rather than product level, and capture products without authorization.

- Introduce a simplified system for evaluating incremental improvements to authorized products so American consumers can benefit sooner from product innovations. This should apply to both the PMTA process for authorizations and the MRTP pathway for modified risk claims. FDA's processes should encourage pro-health innovation, not obstruct innovation or deny Americans access to the best technologies available worldwide.

- Provide applicants with meaningful information on the progress of their applications with estimated decision dates. For many businesses, FDA's decisions are mission-critical and may be the difference between business viability and failure. They are entitled to timely assessments and realistic expectations about decision-making.

- Engage consistently with applicants to address reasonable application deficiencies so that these can be remedied with a view to FDA granting marketing orders rather than as a reason for abrupt denial. FDA should be aiming for a regulated competitive market with a diverse range of compliant products.

[34] Yagi, B., Lushniak, B., & Miller, B. (2023). Appropriate for the Protection of the Public Health: Why We Need Electronic Nicotine Delivery System Product Standards. *SSRN Electronic Journal*. https://doi.org/10.2139/SSRN.4383394

In addition, FDA should benchmark its processes against the requirements of good regulatory practice set out in relevant Executive Orders.[35] In doing so, FDA should revisit the Regulatory Impact Analysis for the 2016 deeming rule to reassess value for money and efficiency in the light of experience and outturns.[36]

3. Enforcement: build a rational regulatory regime and then enforce it

FDA should use its powers to provide meaningful consumer and public health protections but also to promote fair competition between regulated entities in compliant products. There is little value in regulation without enforcement, and a regulator that tolerates non-compliance is fundamentally unfair to those who have invested financial and human resources in achieving compliance.

However, excessive, arbitrary, and unfair regulation creates widespread non-compliance, unstainable enforcement burdens, costly challenges through litigation, and potential loss of trust and support for regulation. The balancing act for FDA is to match an efficient, transparent, and proportionate regulatory regime with effective enforcement. The regulation must be reasonable and its enforcement manageable. The recent history of regulation following the 2016 Deeming Rule does not strike this balance.

Until a rational regulatory framework is in place, the scale of *de facto* non-compliance will make it necessary to take targeted enforcement action. We recommend the following order for enforcement priorities:

- Activity by criminal networks or well-organized illicit supply chains. It is essential to suppress the growth of illegal supply networks in advance of further rulemaking,
- Age-related restrictions, including effective communication of Tobacco 21 and mandating ID checks at point-of-sale for all tobacco products,
- Removal of products where guidance or standards would mean that the product would be unlikely to be authorized for sale in the United States
- Removal of products for which no pre-market application has ever been made,
- Removal of products for which a pre-market application has been made and rejected.

4. Engagement: proactively engage stakeholders to build consensus and secure buy-in

We would like to see FDA use its good offices and convening power to try to nurture a more supportive external environment. CTP could use its convening power to bring together experts, activists, and academics to seek common ground and narrow and articulate differences.

[35] Office of Management and Budget, The White House. Regulatory Matters. https://bit.ly/3znTxGa Relevant Executive Orders on good regulatory practice include EO 12866 (Regulatory planing and review), 13563 (Improving Regulation and Regulatory Review), 13579 (Regulation and Independent Regulatory Agencies), 13610 (Identifying and Reducing Regulatory Burdens)

[36] DHHS/FDA (2016) Deeming Tobacco Products to be Subject to the Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act; [...] Docket No. FDA-2014-N-0189 Final Regulatory Impact Analysis May 2016 https://bit.ly/3HI3guG

In 2018, the then CTP Director, Mitchell Zeller, posed six questions that would shape attitudes to nicotine and regulation.[37] These questions remain relevant today and mostly remain unanswered in the mainstream of tobacco control. Today's CTP leadership could update those questions and try to build a consensus on the answers.

FDA could play an 'honest broker' role in assessing and synthesizing research findings on controversial subjects[38] - for example, setting out a factual assessment of the EVALI outbreak or claims about gateway effects.[39] In 2021, 42 tobacco and nicotine policy experts called on the FDA to commission a follow-up to the 2001 Institute of Medicine Report, *Clearing the Smoke*, which forms a basis for tobacco harm reduction policy in the United States.[40] A recent FOIA request shows that the FDA conducts or commissions high-quality scientific assessments for internal use.[41] Such reviews are valuable to all stakeholders and provide a common base of knowledge. They should be made public.

FDA could use the Tobacco Products Scientific Advisory Committee (TPSAC)[42] more creatively and routinely. For example, TPSAC could be asked for advice on regulatory strategy at the category level rather than on a product-by-product basis. TPSAC's deliberations and findings could help to establish external consensus and buy-in to well-founded FDA regulatory policy and determinations.

Conclusion

We have summarized our proposals in the attached cover letter. We have set out a four-part strategic framework for tobacco and nicotine regulation focused on radically reducing the disease risk and premature deaths arising from smoking, the availability of attractive pathways out of smoking, proportionate regulation of low-risk alternatives to cigarettes, and the protection of youth. It is essential to recognize the inter-relationships between the elements of the strategy and to be candid and explicit about trade-offs between different regulatory goals. In addition to a four-part strategic framework, we advocate four supporting measures. These would improve risk communication, make a step change in process efficiency, take a more rational and manageable approach to enforcement, and use FDA's formidable reputation to build consensus and buy-in.

The American public deserves and should expect a transparent, proportionate, and science-based regulatory system for tobacco and nicotine products. We hope the proposals contained in this briefing will assist FDA in implementing reform in response to the Reagan-Udall evaluation of the Center for Tobacco Products.

---

[37] Zeller, M. (2019). The Future of Nicotine Regulation: Key Questions and Challenges. *Nicotine & Tobacco Research : Official Journal of the Society for Research on Nicotine and Tobacco*, *21*(3), 331–332. https://doi.org/10.1093/ntr/nty200

[38] Gluckman, P. D., Bardsley, A., & Kaiser, M. (2021). Brokerage at the science–policy interface: from conceptual framework to practical guidance. *Humanities and Social Sciences Communications 2021 8:1*, *8*(1), 1–10. https://doi.org/10.1057/s41599-021-00756-3

[39] Pesko, M. F., Cummings, K. M., Douglas, C. E., Foulds, J., Miller, T., Rigotti, N. A., & Warner, K. E. (2022). United States public health officials need to correct e-cigarette health misinformation. *Addiction*. https://doi.org/10.1111/ADD.16097

[40] National Tobacco Reform Initiative. FDA/CTP should request that the NASEM conduct a follow -up review of the landmark Clearing the Smoke -Assessing the Science Base for Tobacco Harm Reduction, October 2021 https://bit.ly/40RO1HQ

[41] FDA Office of Science. (2020). *Interdisciplinary OS State of the Science on Electronic Nicotine Delivery Systems (ENDS).* https://bit.ly/3KmCACg FOIA request by the American Vapor Manufacturers, 2023.

[42] FDA, Tobacco Products Scientific Advisory Committee, https://bit.ly/3K1dTtl