Juul Labs®

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November 7, 2022

By Email

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cc: Lauren Silvis, J.D., Chair

Re: Operational Evaluation of FDA's Tobacco Program

Dear Ms. Winckler:

On behalf of Juul Labs, Inc. (JLI or the Company; we or our), we submit this long-form comment in support of the Reagan-Udall Foundation's (Reagan-Udall) external review of the Food and Drug Administration's (FDA or the Agency) Center for Tobacco Products (CTP) and tobacco-regulatory programs. In parallel, we also have provided comments through Reagan-Udall's stakeholder portal on its website.

We are encouraged by Reagan-Udall's review of CTP's programs for application review, regulations and guidance, compliance and enforcement, and stakeholder communications. These are core regulatory programs that, when operated efficiently and according to the law, ensure that FDA protects and promotes public health based on science and evidence. Here, we focus on CTP's review of product applications, specifically premarket tobacco product applications (PMTAs) for new products. Through the PMTA process, the Agency has the statutory authority and mandate to protect public health through science-based decision-making. For novel products, that should mean advancing tobacco harm reduction through product innovation and regulation.

That is not happening today. The PMTA process has been mired in opacity, inefficiency, unpredictability. Other premarket pathways — like substantial equivalence (SE) reports and SE exemption requests — seem to be working to introduce new combustible products to the market. But we are no closer to establishing an efficient, predictable, and transparent review for less harmful, noncombustible alternatives to reduce tobacco-related death and disease and further public-health objectives.

I. INTRODUCTION

JLI is the manufacturer of the JUUL System, a closed, cartridge-based electronic nicotine delivery system (ENDS) that utilizes proprietary heating technology to aerosolize and deliver nicotine without combustion. Our company and products exist for one reason: To advance tobacco harm reduction by transitioning adult smokers from combustible cigarettes to potentially less harmful, noncombustible alternatives.

While nicotine is addictive and can be harmful, it is not directly responsible for tobacco-caused cancer, lung disease, and heart disease. By providing adult smokers (who otherwise cannot or will not quit) a less harmful form of nicotine delivery and moving them down the continuum of risk, unprecedented public-health gains can be made while marginalizing the most lethal consumer product ever marketed — the combustible cigarette.

Our mission aligns with a central objective of the Family Smoking Prevention and Tobacco Control Act (Tobacco Control Act): "[T]o promote cessation to reduce disease risk and the social costs associated with tobacco-related diseases."[1] Ending cigarette use will not and cannot occur unless there is a robust marketplace of scientifically-substantiated, less harmful alternatives for adult smokers. It follows that well-studied noncombustible products, including ENDS, should be a priority for review and authorization under the Tobacco Control Act given their potential to advance public health.

Unfortunately, minimal progress has been made. Combustible cigarettes continue to comprise more than 75% of the total market for tobacco products and continue to be used by approximately 31 million Americans, resulting in approximately 480,000 preventable deaths each year.[2] Meanwhile, FDA has authorized only forty-two "less harmful" new products, which really includes just twelve distinct brands.[3] One of those is a combustible cigarette, albeit with "very low nicotine."[4] For ENDS products, the Agency has authorized only twenty-three new products, which really includes just seven distinct brands.[5] This

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[1] Pub. L. No. 111-31 § 3(4), 123 Stat. 1776, 1782 (2009).

[2] Cornelius, M., et al., *Tobacco Product Use Among Adults – United States, 2020*, MORBIDITY & MORTALITY WEEKLY REP., (Mar. 18, 2022), *71*(11):397-405; CDC, *Tobacco-Related Mortality*, (Apr. 28, 2020), https://www.cdc.gov/tobacco/data_statistics/fact_sheets/health_effects/tobacco_related_mortality/index.htm; Passport – Euromonitor International, U.S. Retail Sales (2021), retrieved from https://www.portal.euromonitor.com/. While combustible cigarettes comprise approximately 75% of the total tobacco market, all combustible products (including cigarettes, cigars, cigarillos, and roll-your-own tobacco) comprise approximately 85% of the market.

[3] FDA Premarket Tobacco Product Marketing Granted Orders, retrieved from https://www.fda.gov/tobacco-products/premarket-tobacco-product-applications/premarket-tobacco-product-marketing-granted-orders. .

[4] FDA TPL Review of 22nd Century Group Inc.'s PMTAs PM0000491–PM0000492, (Dec. 17, 2019).

[5] FDA Premarket Tobacco Product Marketing Granted Orders, retrieved from https://www.fda.gov/tobacco-products/premarket-tobacco-product-applications/premarket-tobacco-product-marketing-granted-orders.

represents less than 4% of the total ENDS market.[6] Combustible cigarettes continue to dominate the market in the United States, while less harmful ENDS products remain unauthorized — with many stuck in an uncertain regulatory purgatory.

One of the key factors that has hampered the proper implementation of the Tobacco Control Act has been CTP's program management and operations. This dysfunction has been particularly apparent in CTP's review of PMTAs for new products. For applicants of ENDS products, like JLI, CTP's review of PMTAs has been a veritable black box that seemingly shifts for policy outcomes. From early guidance and rulemaking through its substantive review of PMTAs, CTP has failed to engage consistently and meaningfully with regulated entities; a pillar of all other FDA product centers. Further, it appears that CTP may have diverted resources from its review of innovative, less harmful products toward the authorization of legacy, more harmful combustible ones (i.e., cigarettes).

In the discussion below, we speak not only from our own experiences with the PMTA process but generally on where we see persistent challenges that warrant a course correction of priorities, program, and process. Until these changes are made, we do not see a viable path forward for regulatory progress on tobacco harm reduction that is grounded in science and adherent to the law.

Given these operational challenges, we also offer a solution based on learnings from other FDA regulatory programs. Specifically, we urge consideration of a reformed user-fee model for tobacco products — one focused on accountability and transparency in the review of product applications. This new model should reflect the goals-letter framework that has been successful in supporting FDA's regulation and application review for medical products. Our recommendations aim to modernize and improve CTP's regulatory programs and processes and ensure science-based decision-making to foster innovation and protect and promote public health.

To further support Reagan-Udall's review of CTP's application-review program, we include relevant materials from CTP's decision on our PMTAs. Below is a brief chronology of events:

- July 29, 2020: JLI submitted PMTAs for its currently marketed JUUL products and a new device with age-verification technology to better restrict underage access.

- June 23, 2022: FDA issued a marketing denial order (MDO) for all products covered by JLI's July 2020 PMTAs.

[6] Internal analysis based on syndicated market data from Information Resources, Inc. (IRI) for tracked channels through the third quarter of 2022. Tracked channels are limited to convenience, food/grocery, and drug. Based on internal estimates for tracked and non-tracked channels, JLI believes that authorized ENDS products comprise approximately 1.0–1.5% of the ENDS market.

- June 24, 2022: JLI sought judicial relief in the United States Court of Appeals for the District of Columbia Circuit, which granted a temporary administrative stay of the MDO on the same day.

- July 5, 2022: FDA issued an administrative stay of the MDO under 21 C.F.R. § 10.35 and initiated supervisory review of its marketing decision under 21 C.F.R. § 10.75, based on "scientific issues unique to this application that warrant additional review."

- July 29, 2022: JLI submitted its own § 10.75 request for supervisory review of the MDO, which FDA has accepted and is pending review.

Our 10.75 appeal presents first-hand insights on the PMTA process for JUUL products and our position that FDA's decision, in the backdrop of immense political pressure to deny the applications, was substantively and procedurally flawed.

Driven by stakeholder interest in JLI's PMTAs and FDA's decision, on October 21, 2022, we made our 10.75 appeal and the Agency's MDO and technical project lead (TPL) memorandum publicly available on juullabsscience.com. We have enclosed the same materials in this submission to highlight additional program- and process-related issues impacting the review of PMTAs (Appendices 1–3).

II. BOTH CONGRESS AND FDA HAVE RECOGNIZED THE IMPORTANCE OF BRINGING INNOVATIVE, LESS HARMFUL PRODUCTS TO THE MARKET TO REDUCE TOBACCO-RELATED DEATH AND DISEASE

In enacting the Tobacco Control Act in 2009, Congress sought "to promote cessation to reduce disease risk and the social costs associated with tobacco-related diseases."[7] Part of FDA's regulatory mandate under the Tobacco Control Act is to "provide new and flexible enforcement authority to ensure that there is effective oversight of the tobacco industry's efforts to develop, introduce, and promote less harmful tobacco products."[8]

The Tobacco Control Act established three marketing pathways for new tobacco products:

- SE reports for products that have the same characteristics as predicate products already on the market;

- SE exemption requests for products modified by adding or deleting a tobacco additive, or increasing or decreasing the quantity of an existing tobacco additive; and

[7] Pub. L. No. 111-31 § 3(4), 123 Stat. 1776, 1782 (2009).

[8] *Id.*

- PMTAs.

The PMTA is the primary pathway to market for novel products like ENDS.[9] The Tobacco Control Act also grandfathered all products that were commercially marketed in the United States as of February 15, 2007, effectively grandfathering only preexisting, legacy tobacco products like combustible cigarettes from premarket review. [10]

The PMTA process is set out in § 910 of the Tobacco Control Act. The pathway incorporates a harm-reduction framework by requiring applicants to submit information showing "whether such tobacco product presents less risk than other tobacco products."[11] Section 910 also requires the denial of an application if it does not meet the statutory "appropriate for the protection of the public health" (APPH) standard.[12] Finding that a new product is APPH requires FDA to consider the risks and benefits to both users and nonusers, the likelihood that existing adult users of tobacco products will stop using them, and the likelihood that nonusers of tobacco products will start using those products.[13]

Further, § 910 imposes postmarket surveillance and reporting requirements for authorized products,[14] and the Agency has implemented extensive postmarket-reporting regulations to help ensure that that marketing of a product after authorization remains APPH.[15] Among others, FDA requires an applicant to provide information such as labeling, advertising, marketing, promotional materials, and marketing plans not previously submitted to the Agency and do so at least 30 days before using those materials.[16]

The PMTA pathway became applicable to ENDS products through regulatory action. On enactment, the Tobacco Control Act applied by its terms to only "cigarettes, cigarette tobacco, roll-your-own tobacco, and smokeless tobacco," while authorizing the Agency to extend the statute's reach "to any other tobacco products . . . by regulation."[17] In 2016, FDA finalized a regulation (the Deeming Rule) that applied the Tobacco Control Act to any and all tobacco products including ENDS.[18] At the time, a large number of ENDS products were already on the market, and the rule meant that manufacturers of those products would

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[9] 81 Fed. Reg. at 28994.

[10] FDCA § 910(a)(2)(B) [21 U.S.C. § 387j(a)(2)(B)].

[11] FDCA § 910(b)(1)(A) [21 U.S.C. § 387j(b)(1)(A)].

[12] FDCA § 910(c)(2)(A) [21 U.S.C. § 387j(c)(2)(A)].

[13] FDCA § 910(c)(4) [21 U.S.C. § 387j(c)(4)].

[14] FDCA § 910(f) [21 U.S.C. § 387j(f)].

[15] 21 C.F.R. § 1114.41.

[16] *See* 21 C.F.R. § 1114.31(b)(3); Premarket Tobacco Product Applications and Recordkeeping Requirements, 86 Fed. Reg. 55300, 55389 (Oct. 5, 2021) [hereinafter PMTA Rule].

[17] 21 U.S.C. § 387a(b).

[18] 79 Fed. Reg. 23,141 (Apr. 25, 2014) (proposed rule); 81 Fed. Reg. 28,973 (May 10, 2016) (final rule).

have to obtain marketing authorization from the Agency to remain on the market.[19] For ENDS products, that requires a PMTA.

FDA couched this premarket-review requirement in the Tobacco Control Act's express purpose of introducing less harmful products. The Agency stated that forcing ENDS products through the PMTA pathway would "allow FDA to monitor product development and changes and to prevent more harmful or addictive products from reaching the market" and to "incentivize development of tobacco products that pose less risk to human health by limiting market access for more-risky competitor products."[20] Since the APPH standard compares new tobacco products to the current market, FDA further assumed that "over time, the premarket authorities will move the market toward less-risky tobacco products."[21]

Critically, in 2017, FDA announced a comprehensive framework for tobacco and nicotine regulation which reaffirmed the importance of bringing more innovative and less harmful products to the market. This comprehensive framework recognized "the potential for innovation to lead to less harmful products" and the need to "strike the right balance between FDA fulfilling its vital consumer protection role while also fostering innovation[.]"[22] It also emphasized the importance of "reducing the addictiveness of combustible cigarettes while recognizing and clarifying the role that potentially less harmful tobacco products could play in improving public health."[23] FDA's approach at that time aimed to "make it possible for current adult smokers who still seek nicotine to get it from alternative and less harmful sources."[24]

More recently, FDA recognized that ENDS are one of the most promising types of alternative tobacco products, with significant potential to switch adult smokers from

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[19] *See, e.g.*, 81 Fed. Reg. at 28,977 ("Manufacturers of newly deemed products that are "new tobacco products" as defined in section 910(a)(1) of the FD&C Act will be required to obtain premarket authorization of their products through one of three pathways—SE., exemption from SE., or premarket tobacco product applications (sections 905 and 910 of the FD&C Act).").

[20] Deeming Tobacco Products To Be Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act; Restrictions on the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Products, 81 Fed. Reg. 28973, 28999 (May 10, 2016) [hereinafter Deeming Rule].

[21] *Id.* at 28999.

[22] Scott Gottlieb, Speech — Protecting American Families: Comprehensive Approach to Nicotine and Tobacco (July 28, 2017), https://www.fda.gov/news-events/speeches-fda-officials/protecting-american-families-comprehensive-approach-nicotine-and-tobacco-06282017.

[23] Scott Gottlieb, A Nicotine-Focused Framework for Public Health, by FDA Commissioner Scott Gottlieb and CTP Director Mitchell Zeller in the New England Journal of Medicine (September 21, 2017), https://www.nejm.org/doi/full/10.1056/NEJMp1707409?query=featured_home.

[24] FDA Statement, Statement from FDA Commissioner Scott Gottlieb, M.D., on pivotal public health step to dramatically reduce smoking rates by lowering nicotine in combustible cigarettes to minimally or non-addictive levels, (March 15, 2018), https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm601039.htm.

combustible cigarettes to a less harmful form of nicotine delivery. Informed by the science, FDA recognized that ENDS products are preferable to cigarettes as "the aerosol that is exhaled by users of some e-cigarettes . . . may not pose as much harm as smoke emitted from combusted tobacco products"[25] since "the exposure to toxins is likely to be lower than from a traditional cigarette."[26] Indeed, the Agency's few marketing granted orders (MGOs) for ENDS products recognize that such products present lower overall toxicological risk to users compared to combustible cigarettes due to lower abuse liability — i.e., the ability to promote continued use, addiction, or dependence — and significant reductions in harmful and potentially harmful constituents (HPHC) in ENDS aerosols.[27]

III. FDA'S IMPLEMENTATION OF THE TOBACCO CONTROL ACT AND PMTA PATHWAY HAS BEEN PLAGUED BY DYSFUNCTION

FDA's actual implementation of the Tobacco Control Act has not followed the public-health priorities discussed above.

Over time, CTP has been able to provide an efficient review of new combustible products (including cigarettes) allowing them to remain and expand on the market. In fiscal years 2020–2022 alone, CTP issued SE orders for 120 new cigarette products and accepted SE reports for an additional 259 new cigarette products.[28] Since 2015, CTP's median time to issue an SE order for new cigarette products has taken less than a year (260 days).[29] Perhaps most notably, in 2018, CTP simply abandoned the review of approximately 1,500 SE reports — most of which were for new cigarette products — and

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[25] Deeming Tobacco Products To Be Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act; Restrictions on the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Products, 81 Fed. Reg. 28973, 29032 (May 10, 2016).

[26] Ned Sharpless, Remarks by Dr. Sharpless, Acting Commissioner of Food and Drugs, on the 10th Anniversary of the Tobacco Control Act (Jun. 24, 2019), https://www.fda.gov/news-events/speeches-fda-officials/remarks-dr-sharpless-acting-commissioner-food-and-drugs-10th-anniversary-tobacco-control-act.

[27] *See* TPL Review for NJOY LLC DAILY ENDS Products, at 6, https://www.fda.gov/media/159136/download; TPL Review for R.J. Reynolds Vapor Company Vuse Vibe and Ciro ENDS products, at 6, https://www.fda.gov/media/158374/download; TPL Review for Logic Technology Development LLC, at 6, https://www.fda.gov/media/158754/download; TPL Review for R.J. Reynolds Vapor Company Vuse Solo ENDS products, at 6, https://www.fda.gov/media/153017/download.

[28] *See* FDA, Tobacco Product Applications: Metrics & Reporting, (Aug. 2, 2022), https://www.fda.gov/tobacco-products/market-and-distribute-tobacco-product/tobacco-product-applications-metrics-reporting.

[29] *See* FDA, Marketing Orders for SE, (May 31, 2022), https://www.fda.gov/tobacco-products/substantial-equivalence/marketing-orders-se (comparing application submission dates to SE issuance dates).

used its enforcement discretion to allow those products to remain on the market without even evaluating their public-health impact.[30]

At the same time, CTP has stalled its review of PMTAs for new, less harmful alternatives to cigarettes. In fiscal years 2020–2022, CTP has accepted PMTAs for over six million ENDS products, but has issued MGOs for only twenty-three.[31] Since 2015, CTP's median time to issue an MGO is 751 days[32] — more than four times the review period required by the Tobacco Control Act[33] and significantly longer than CTP's assumption that substantive review would require 1,800–7,200 hours of work (75–300 days).[34] Moreover, the review of PMTAs from ENDS manufacturers with the largest market share, which was supposed to be prioritized, remains significantly behind schedule and is not estimated to be complete until June 30, 2023.[35]

Given this history, we believe that Reagan-Udall's review should focus on specific aspects of CTP's review of PMTAs for new products: (i) CTP's failure to issue timely guidance and rules for the submission of PMTAs; (ii) CTP's failure to conduct its review of PMTAs in a predictable and transparent manner; and (iii) the resultant de facto freeze of the ENDS market, which till this day remains stalled and serves as a barrier to the innovation of less harmful alternatives for adult smokers.

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[30] FDA Update on Provisional Substantial Equivalence (SE) Review Process, CTP Newsroom, (Apr. 5, 2018), https://www.fda.gov/tobacco-products/ctp-newsroom/fda-update-provisional-substantial-equivalence-se-review-process.

[31] *See* FDA, Tobacco Product Applications: Metrics & Reporting, (Aug. 2, 2022), https://www.fda.gov/tobacco-products/market-and-distribute-tobacco-product/tobacco-product-applications-metrics-reporting.

[32] *See* FDA, Premarket Tobacco Product Marketing Granted Orders, (June 10, 2022), https://www.fda.gov/tobacco-products/premarket-tobacco-product-applications/premarket-tobacco-product-marketing-granted-orders (comparing application submission dates to MGO issuance dates). NJOY LLC submitted its applications for Daily ENDS products on March 30, 2020, and FDA Issued its MGO on June 10, 2022 (802 days review time). R.J. Reynolds Vapor Company submitted its applications for Vuse Vibe and Ciro ENDS products on April 2, 2020, and FDA Issued its MGO on May 12, 2022 (770 days review time). NJOY LLC submitted its applications for ACE ENDS products on March 10, 2020, and FDA Issued its MGO on April 26, 2022 (777 days review time). Logic Technology Development LLC submitted its applications August 19, 2019, and FDA Issued its MGO on March 24, 2022 (948 days review time); R.J. Reynolds Vapor Company submitted its applications for Vuse Solo ENDS products on October 10, 2019, and FDA Issued its MGO on October 12, 2021 (733 days review time).

[33] *See* 21 U.S.C. § 387j(c)(1)(A).

[34] FDA, Premarket Tobacco Product Applications and Recordkeeping Requirements, Final Regulatory Impact Analysis, at 50 (Oct. 5, 2021), https://www.fda.gov/media/152622/download.

[35] *See* Status Report at 3, *Am. Acad. of Pediatrics v. FDA*, No. 8:18-cv-883-PWG, Dkt. 205 (D. Md. May 13, 2022) [hereinafter Status Report].

A. CTP Has Moved Glacially in Establishing the PMTA Process and Requirements for Submission and Review

On May 10, 2016, the day the Deeming Rule was finalized, there were no regulations or final guidance defining the PMTA pathway that had just become mandatory for the continued marketing of deemed products. That same day, CTP issued its first draft guidance on recommendations for submitting PMTAs for ENDS products.[36]

That solitary draft guidance was not remotely sufficient to enable ENDS manufacturers to prepare meaningful technical and scientific submissions. Thus, in 2017, when FDA announced its comprehensive framework for tobacco and nicotine regulation, it acknowledged that the need for additional guidance was so great that it justified extending the compliance period by several years. The Agency explained that the extension would "provide manufacturers additional time to develop higher quality, more complete applications informed by additional guidance from the agency" and to "afford the agency time to explore clear and meaningful measures to make tobacco products less toxic, appealing and addictive."[37] Accordingly, FDA announced that it would "issue foundational rules to make the product review process more efficient, predictable, and transparent for manufacturers."[38]

Despite that 2017 promise, CTP issued no new guidance relating to PMTAs for ENDS until it finalized the 2016 draft in June 2019.[39] While CTP revised several of its guidance documents to include information relevant to ENDS products, none of those specified the requirements for PMTAs.[40]

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[36] Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems; Draft Guidance for Industry; Availability; Agency Information Collection Activities; Proposed Collection; Comment Request, 81 Fed. Reg. 28781 (May 10, 2016).

[37] FDA News Release, FDA Announces Comprehensive Regulatory Plan to Shift Trajectory of Tobacco-related Disease, Death, (July 27, 2017), https://www.fda.gov/news-events/press-announcements/fda-announces-comprehensive-regulatory-plan-shift-trajectory-tobacco-related-disease-death.

[38] *Id.*

[39] FDA, Guidance for Industry, Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems, (June 2019), https://www.fda.gov/media/127853/download.

[40] *See* FDA, Guidance for Industry, Small Entity Compliance Guide, FDA Deems Certain Tobacco Products Subject to FDA Authority, Sales and Distribution Restrictions, and Health Warning Requirements for Packages and Advertisements (Revised)*, (Oct. 2020), https://www.fda.gov/media/143049/download; FDA, Guidance for Industry and Investigators, Meetings with Industry and Investigators on the Research and Development of Tobacco Products (Revised*), (June 2020), https://www.fda.gov/media/83420/download; FDA, Guidance for Industry, Enforcement Priorities for Electronic Nicotine Delivery Systems (ENDS) and Other Deemed Products on the Market Without Premarket Authorization (Revised)*, (Apr. 2020), https://www.fda.gov/media/133880/download; FDA, Guidance for Industry, Listing of Ingredients in Tobacco Products (Revised)*, (Nov. 2018), https://www.fda.gov/media/101162/download; FDA, Guidance for Industry and FDA Staff, "Harmful and Potentially Harmful Constituents" in Tobacco Products as Used in Section 904(e) of the Federal Food, Drug, and Cosmetic Act (Revised)*, (Aug. 2016), https://www.fda.gov/media/80109/download.

In September 2019, CTP finally issued proposed regulations to codify PMTA requirements. In October 2021, these regulations were finalized and thus binding — over one year after applications for currently marketed products were due.[41] CTP has issued only two other guidance documents relevant to PMTAs for ENDS products: one draft guidance relating to analytical testing method validation and verification (2021)[42] and one final guidance relating to tobacco product perception and intention studies (2022).[43]

Other key areas remain untouched. For instance, CTP has not proposed regulations for Tobacco Product Manufacturing Practice (TPMP) requirements, despite industry-driven proposals having been available for public comment since 2013 for legacy products and 2017 for ENDS products.[44] Nor has CTP proposed regulations for investigational tobacco products (ITPs) — or even finalized its revised 2019 draft guidance — to support the research and development of novel products that can reduce tobacco-related harms.[45] The Tobacco Control Act requires both sets of regulations, among others, to be issued.

In addition to complicating manufacturers' efforts to prepare comprehensive and compliant submissions, the lack of clear and timely guidance has caused real harm to the PMTA program. Multiple lawsuits have been filed against FDA alleging that it moved the goalposts by imposing new requirements after applicants submitted their PMTAs in reliance on the Agency's prior statements. One court of appeals recently agreed and vacated an MDO, while FDA itself has rescinded several MDOs for overlooking critical information in the applications.[46] Within two weeks of issuing an MDO for JLI's PMTAs, the

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[41] Premarket Tobacco Product Applications and Recordkeeping Requirements, 86 Fed. Reg. 55300, 55301 (Oct. 5, 2021) ("The rule requires an applicant to submit detailed information regarding the physical aspects of its new tobacco product and full reports of information regarding investigations that may show the health risks of the new tobacco product and whether it presents the same or different risks compared to other tobacco products.").

[42] FDA, Guidance for Industry, Validation and Verification of Analytical Testing Methods Used for Tobacco Products, (Dec. 2021), https://www.fda.gov/media/155033/download.

[43] FDA, Tobacco Products: Principles for Designing and Conducting Tobacco Product Perception and Intention Studies, (Aug. 2022), https://www.fda.gov/media/143322/download.

[44] Tobacco Product Manufacturing Practice; Request for Comments, 82 Fed. Reg. 5513 (Nov. 22, 2017).

[45] FDA, Draft Guidance for Industry and Investigators, Use of Investigational Tobacco Products, (Feb. 2019), https://www.fda.gov/media/94052/download. This draft guidance was revised from the initial draft guidance issued in September 2015. This is of concern — because they are still operating on draft guidance for ITPs, manufacturers cannot conduct clinical and actual-use studies of new products in the United States. In contrast, FDA has put a tremendous amount of effort into its post-market requirements, *see* 21 C.F.R. § 1114.41, which is ironic given the lack of guidance to obtain authorization in the first place.

[46] *See Bidi Vapor LLC v. FDA*, 2022 WL 3594073, at *8 (11th Cir. Aug. 23, 2022) (remanding review of the applicants' PMTAs to FDA for complete review; concluding that "it was arbitrary and capricious for [FDA] to ignore the relevant marketing and sales-access-restriction plans" where "[t]he 2020 [ENDS Enforcement Priorities] Guidance did not state that existing marketing and sales-access-restriction plans were categorically ineffective for electronic nicotine-delivery systems other than flavored, cartridge-based products" and "the tobacco companies submitted marketing and sales-access-restriction plans that conformed with the recommendations for their kinds of products in the 2020 [ENDS Enforcement Priorities] Guidance"); *see e.g.*, Emergency Motion for A Stay Pending Review, at 18-20 (Oct. 17, 2021), *filed in Gripum,*

Agency stayed its marketing decision given "scientific issues unique to this application that warrant additional review."

B. CTP's Review Process for PMTAs Has Been Opaque and Inconsistent

To be even reasonably effective, the review process for a PMTA must be iterative and cooperative. Much like FDA's review of premarket applications for other regulated products (e.g., new drugs and medical devices). FDA's tobacco regulations embody this: They allow CTP to freely communicate with applicants through "conversations, letters, electronic communications, or meetings" about issues arising during the review process.[47] CTP may request that an applicant amend its PMTA to complete its review.[48] CTP also may issue deficiency letters (i.e., requests for additional information) to applicants.[49] In its proposed PMTA Rule, CTP noted that it "on average issues four deficiency letters" per submission.[50] By the time CTP finalized the PMTA Rule, it stated that it "on average issue[s] two deficiency letters" per submission.[51]

CTP's experience with non-ENDS products reflects that approach. Several scientific reviews accompanying MGOs for non-ENDS products show that CTP had multiple, iterative engagements during the review of those PMTAs, including through meetings, information requests, and deficiency letters.

- Philip Morris International's heated-tobacco product (IQOS) had two meetings, four information requests, and twelve amendments;
- Swedish Match's smokeless tobacco products (General Snus) had three meetings, two information requests, and eleven amendments; and
- 22nd Century's very-low-nicotine cigarettes (Moonlight) had six meetings and fourteen amendments.

But CTP's review of PMTAs for ENDS products has not been consistent with this approach, let alone iterative. CTP issued only one deficiency letter for R.J. Reynolds's 2019

LLC v. FDA, 21-2840 (7th Cir. 2021); Emergency Motion for A Stay Pending Review And for Expedited Consideration, at 12-14 (Oct. 6, 2021), *filed in Wages And White Lion Invs. v. FDA*, 21-60766 (5th Cir. 2021).

[47] 21 C.F.R. § 1114.25.

[48] 21 C.F.R. § 1114.9(a).

[49] 21 C.F.R. § 1114.27(a)(3).

[50] Proposed Rule, Premarket Tobacco Product Applications and Recordkeeping Requirements, 84 Fed. Reg. 50566, 50627 (Sept. 25, 2019).

[51] Final Rule, Premarket Tobacco Product Applications and Recordkeeping Requirements, 86 Fed. Reg. 55300, 55402 (Oct. 5, 2021).

PMTAs and 2020 PMTAs and for both of NJOY's 2020 PMTAs.[52] For Juul Labs' PMTAs, there also was only one deficiency letter.

Presumably due to the pressures of an accelerated timeline imposed on the review of PMTAs for on-market products, CTP's approach with ENDS products has been more limited.[53] The resulting risk of Type II error is not just theoretical — it seems to be bearing out in real time where CTP has provided applicants with little opportunity to address identified deficiencies. We are aware of at least eight other instances in the past year where CTP's approach has led to the issuance of MDOs that were subsequently rescinded (in full or in part) or at least stayed pending further review.[54]

The increased risk also should be particularly concerning where it applies to products that are widely used by adults who are former cigarette smokers. Although CTP has authorized a few ENDS products with the potential to reduce harm compared to combustible cigarettes, those currently make up less than 4% of the total ENDS market.[55]

CTP's marketing decisions prompt the question (and risk) on whether it will fail to authorize products that have the most potential to benefit public health. Instead, CTP should follow the iterative process for review that it has previously developed and followed for prior PMTAs and that is necessary to assure its product-specific decisions serve its public-health objectives.

C. CTP's Inefficient Review of PMTAs Has Resulted in a De Facto Freeze of the ENDS Market, Hampering the Innovation of Less Harmful Alternatives

In enacting the Tobacco Control Act, Congress did not intend to lock in the tobacco-product market as it existed in 2009 — or, for that matter, in 2016. As noted above, one of the Tobacco Control Act's express purposes was to ensure the effective oversight of "the

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[52] TPL Review, R.J. Reynolds Vapor Company, (May 12, 2022), https://www.fda.gov/media/158374/download; TPL Review, R.J. Reynolds Vapor Company, 5, 34 (Oct. 12, 2021), https://www.fda.gov/media/153017/download; TPL Review, NJOY LLC, at 4 (Apr. 26, 2022), https://www.fda.gov/media/157959/download; TPL Review, NJOY LLC, at 4 (June 10, 2022), https://www.fda.gov/media/159136/download.

[53] *See* Am. Acad. of Pediatrics v. FDA, Case No. PWG-18-883, 379 F. Supp. 3d 461 (D. Md. 2019); *see also* Norcia N. (2020), CTP's Office of Science (OS) Premarket Application Review Prioritization Plan, *Scribd*, retrieved at from https://www.scribd.com/document/575749534/CTP-s-Office-of-Science-OS-Premarket-Application-Review-Prioritization-Plan?secret_password=e79TH5ywGHVX4QlsN23O#download&from_embed (disclosing a redacted version of CTP's original PMTA review prioritization plan).

[54] FDA Premarket Tobacco Product Marketing Denial Orders, retrieved from https://www.fda.gov/tobacco-products/market-and-distribute-tobacco-product/tobacco-products-marketing-orders#Marketing%20Denial.

[55] Internal analysis based on syndicated market data from Information Resources, Inc. (IRI) for tracked channels through the third quarter of 2022. Tracked channels are limited to convenience, food/grocery, and drug. Based on internal estimates for tracked and non-tracked channels, JLI believes that authorized ENDS products comprise approximately 1.0–1.5% of the ENDS market.

tobacco industry's efforts to develop, introduce, and promote less harmful tobacco products."[56] The PMTA pathway was created with that end in mind.

Since the Deeming Rule, however, there has been an effective years-long ban on innovation and both the introduction of new ENDS and the modification of existing ENDS. When FDA promulgated the Deeming Rule in 2016, ENDS products had already developed into a market comprising as many as 11,000 products.[57] The Agency recognized that the effect of deeming all these existing products — plus thousands of others — subject to the Tobacco Control Act would be to render them "suddenly noncompliant with the statute."[58] To mitigate the disruption from this regulatory action, FDA adopted compliance periods during which newly deemed products could remain on the market while manufacturers prepared premarket applications and underwent premarket review.[59]

When it established this policy, FDA appeared to be aware of the de facto freeze and the harm that could flow if the market remained frozen for an extended period. Thus, the Agency recognized the need "to reduce and prevent backlogs of marketing applications pending FDA review" and to "act as expeditiously as possible with respect to all new applications."[60] FDA claimed that its policy would achieve these goals by giving manufacturers sufficient time to "provide high quality applications" and thus "provid[ing] FDA with a more manageable flow of incoming applications to be reviewed, allowing the agency to more quickly make decisions on applications."[61]

Moreover, the compliance policy applied only to "newly deemed products that were on the market on the effective date of this final rule."[62] This meant that manufacturers could not even modify products because, under CTP's understanding of the statute, any modification would result in a new tobacco product that had not been on the market as of the Deeming Rule's effective date and required regulatory authorization before marketing.[63]

The following year, however, CTP's failure to timely issue regulations and guidance caused the Agency to more than double the length of the compliance periods. In July 2017,

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[56] Pub. L. No. 111-31 § 3(4), 123 Stat. 1776, 1782 (2009).

[57] *See* FDA Mem. in Opp'n to Summary Judgment at 35, *Am. Acad. of Pediatrics v. FDA*, No. 8:18-cv-883-PWG, Dkt. 36-1 (D. Md. August 7, 2018).

[58] *See id.* at 1; *see also Am. Acad. of Pediatrics v. FDA*, 379 F. Supp. 3d 461, 470 (D. Md. 2019) (noting that the Deeming Rule applied to approximately 25,000 products already on the market).

[59] *See* 81 Fed. Reg. at 29011.

[60] *See id.* at 29013.

[61] *See id.* at 29012.

[62] *See id.*

[63] *See* 21 U.S.C. § 387j(a)(2); 86 Fed. Reg. at 55392.

FDA extended the deadline for PMTAs for noncombustible tobacco products, including ENDS, to August 8, 2022.[64]

The resulting reality is that since the Deeming Rule, ENDS manufacturers have been virtually locked from innovating to introduce new products or improve existing ones. This is evident in the fact that the only ENDS products to have received MGOs are those that were on the market at the time of the Deeming Rule. This situation is plainly contrary to the scheme Congress established in the Tobacco Control Act and is both unsustainable and scientifically unsound — particularly for a product category that FDA has recognized "is likely less hazardous for an individual user than continued smoking of traditional cigarettes."[65]

The de facto market freeze took on outsized significance when the COVID-19 pandemic and other factors combined to create global supply shortages that hindered access for ENDS products' essential electronic components. CTP's "no modifications" position left ENDS manufacturers with pending PMTAs no viable options to make changes to their marketed products.

Unless priorities, program management, and processes change to efficiently review PMTAs going forward, this and similar problems will persist, hampering both the maintenance of existing ENDS products and the introduction of new, less harmful alternatives to combustible cigarettes.

IV. A CASE STUDY ON DYSFUNCTION: CTP'S HANDLING OF JLI'S PMTAS

On July 29, 2020, JLI submitted PMTAs for its currently marketed products and a new product with embedded age-verification technology to better restrict underage access. These PMTAs included information, data, and analysis from over 110 scientific studies across nonclinical (75+ studies), clinical (14 studies), and behavioral (21 studies) research programs to provide a comprehensive dataset on the health risk and net-population impact associated with the use of JUUL products. JLI also assessed its products relative to combustible cigarettes, an FDA-authorized heated tobacco product (IQOS), and other marketed ENDS products.

On health risks, among other findings, the JUUL System presented at least a 98% reduction in harmful and potentially harmful constituents (HPHCs) compared to combustible cigarettes, presented at least an 82% reduction in HPHCs compared to IQOS, and showed a reduction in biomarkers of exposure (BOE) to toxicants among adult

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[64] FDA, Press Release, *FDA Announces Comprehensive Regulatory Plan To Shift Trajectory Of Tobacco-Related Disease, Death*, (July 17, 2017), https://www.fda.gov/news-events/press-announcements/fda-announces-comprehensive-regulatory-plan-shift-trajectory-tobacco-related-disease-death; FDA, Guidance for Industry, Extension of Certain Tobacco Product Compliance Deadlines Related to the Final Deeming Rule, at 3 (rev. Aug. 2017). Deadlines for other products and application types were extended until either August 8, 2021, or August 8, 2022, depending on the type of product and/or application type. *See id.* at 3.

[65] 81 Fed. Reg. at 29035.

smokers who completely switched to the JUUL System that was on par with no tobacco use at all.

On net-population impact, among other findings, over 90% of JUUL users were current or former smokers and over 50% of JUUL purchasers completely switched from combustible cigarettes within twelve months. For the remaining 50% that did not switch completely, over 80% reduced their cigarette consumption by 50% or more and thus significantly reduced their exposure to HPHCs and other toxicants in cigarette smoke.

These lines of evidence converge on the conclusion that use of the JUUL System presents substantially less risk than combustible cigarettes for adult smokers and, based on JLI's understanding of the literature, is the most effective alternative product to get smokers off cigarettes.

On June 23, 2022, FDA issued an MDO for all of JLI's PMTAs.

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According to public statements, CTP prioritized PMTA reviews for ENDS manufacturers with the greatest market share, identifying JLI as the top market share and thus a top priority.[66] Despite this supposed prioritization of the Company's PMTAs, CTP took two years to render a decision. When it finally did, CTP issued a decision that reflected a failure to fairly and completely review the applications.

JLI asked FDA for a temporary stay of the MDO within hours of its marketing decision, explaining that the Company "was already experiencing harms that were likely irreparable and were expected to continue and worsen." FDA declined JLI's request, forcing it to petition the U.S. Court of Appeals for the D.C. Circuit for emergency injunctive relief.[67] In response, CTP took the highly unusual steps of agreeing to stay the MDO and voluntarily initiating an internal review of the marketing decision under 21 C.F.R. § 10.75 based on "scientific issues unique to this application that warrant additional review."[68] That decision implicitly concedes that the nearly two years CTP took to review JLI's applications resulted in a deficient review and a deficient order.

A multi-year campaign of intense political pressure from at least sixty members of Congress defined the environment in which JLI's PMTAs were reviewed. For example, on June 29, 2021, Representative Krishnamoorthi and Senator Durbin sent a letter to the Acting Commissioner demanding that FDA review all documents JLI had produced to the

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[66] Holman, M, CTP, Office of Science (OS) Premarket Application Review Prioritization Plan, (Aug. 31, 2020).

[67] *See* Redacted Motion for Stay Pending Review, at 11 (June 27, 2022) (citing Public Appendix 482), *filed in JUUL Labs, Inc. v. FDA*, 22-1123, (D.C. Cir. 2022).

[68] E-mail from CTP to JLI, (July 5, 2022) (attached as Exhibit A to the parties' Joint Motion to Hold Case in Abeyance Pending Completion of Agency Proceedings and to Withdraw Emergency Motion to Stay, (July 6, 2022), *filed in JUUL Labs, Inc. v. FDA*, 22-1123 (D.C. Cir. 2022)).

Office of the Attorney General of North Carolina in connection with a state settlement, "before ruling on a JUUL PMTA application."[69] On July 19, 2021, Senator Durbin tweeted that FDA "needs to finally do the right thing and take . . . JUUL off the market."[70] On March 9, 2022, fifteen Senators wrote to the Commissioner falsely describing the JUUL System as a "flavored" ENDS product and demanding that FDA rescind its policy of enforcement discretion and remove JUUL products from the market.[71] A similar letter followed on May 20, 2022, with eleven Senators demanding that FDA rescind its policy of enforcement discretion and remove JUUL products from the market.[72]

The day before the MDO was issued to JLI, Senator Durbin issued a public statement advancing the extraordinary assertion that the Commissioner should either deny JLI's PMTAs or resign.[73] As one observer noted, "FDA simply could not have authorized" JLI's PMTA without provoking a backlash from Congress and that would have "threatened the agency's funding."[74]

During the nearly two-year review period of its PMTAs, JLI received just one substantive request for additional information on its PMTAs in the form of a deficiency letter in March 2021. In June 2021, JLI responded by addressing each question with additional information, data, and analysis to support CTP's review. From June 2021 until the MDO in June 2022, CTP did not raise any other questions or otherwise engage substantively with JLI. This limited engagement is in direct contrast to FDA's usual, iterative process that defines a full and complete review of product applications generally.

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[69] Press Release, Chairman Krishnamoorthi & Senator Durbin Urge FDA To Review New and Disturbing Evidence From North Carolina That JUUL Deliberately Marketed High-Nicotine Products to American Youth (June 29, 2021), https://tinyurl.com/2p93jkt5.

[70] Richard Durbin (@senatordurbin), TWITTER (July 19, 2021), https://tinyurl.com/bdha6h5s ("A big decision indeed. After dangerous delays, the @US_FDA needs to finally do the right thing and take addictive, kid-friendly products like JUUL off the market.").

[71] Letter from Richard Durbin et al. to Robert Califf, Comm'r of Food and Drugs (Mar. 9, 2022), https://tinyurl.com/4pswntvx (stating Agency is six months past court-ordered deadline to regulate e-cigarettes).

[72] Letter from Richard Durbin et al. to Robert Califf, Comm'r of Food and Drugs (May 20, 2022), https://tinyurl.com/5629bxxj (requesting FDA remove all unauthorized e-cigarettes from market immediately).

[73] Press Release, Richard Durbin, Durbin Investigation Finds More Than 750,000 Kids Have Picked Up Vaping Since FDA's Missed Deadline to Regulate E-Cigarettes, (June 22, 2022), https://tinyurl.com/3h3yd7uv.

[74] Grace Kay, *Experts say the FDA ban on Juul e-cigarettes could be the 'opening gun' for a crackdown on the entire industry*, BUS. INSIDER (June 23, 2022), https://tinyurl.com/y399uy5p. FDA has not formally reported internal allegations of potential political interference because FDA "do[es] not have procedures that define political interference in scientific decision-making or describe how it should be reported and addressed." GAO Report to Congressional Addressees, Scientific Integrity, HHS Agencies Need to Develop Procedures and Train Staff on Reporting and Addressing Political Interference, (Apr. 2022), https://www.gao.gov/products/gao-22-104613.

A day before the MDO, JLI already knew of the marketing decision — but not from CTP. In a stunning breach of confidentiality regulations,[75] the decision was leaked to *The Wall Street Journal* on or before June 22. The resulting article reported that "[FDA] is preparing to order Juul Labs Inc. to take its e-cigarettes off the U.S. market, according to people familiar with the matter" and that "FDA could announce its decision as early as this week."[76] CTP announced its decision the next day. To date, we have received no indication that FDA is investigating this breach of confidentiality.

The MDO itself provided four deficiencies that collectively formed the basis for the marketing decision and which purportedly precluded a determination of APPH for all JUUL products. The deficiencies all relate to a subset of toxicological data provided by JLI.

JLI maintains that the MDO is flawed both substantively and procedurally. The MDO incorrectly and incompletely concluded that, based on a limited and narrow toxicology review, CTP-OS was precluded from determining that the marketing of the JUUL System is APPH. For each alleged deficiency, the MDO erred by overlooking key information, incorrectly analyzing the information it did consider, and inequitably holding the PMTAs to a new and different standard compared to similarly-situated applicants. The alleged deficiencies, if anything, were limitations that warranted additional engagement and review and could have been reconciled with information already provided in the PMTAs. Far from justifying a denial, the marketing decision reflected an analysis that failed to conduct a complete, holistic, and fair review of the body of science and evidence in JLI's PMTAs.

Of course, the MDO had real-world consequences. Upon hearing news of the MDO, JLI's wholesalers indicated that they had already ceased or intend to cease distribution of JLI's products. Similarly, retailers removed JLI's inventory from their shelves, instructing stores not to place any new orders for JUUL products. Adding to the disruption, key retailers were duped by unknown individuals masquerading as FDA officials, who delivered counterfeit documents purporting to order retailers to stop selling JLI's products. Although FDA later issued a statement disavowing responsibility for this conduct,[77] we have received no indication whether the Agency is investigating this clear violation of federal law.

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To say that there were procedural and program irregularities in the review of JLI's PMTAs would be an understatement.

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[75] *See* 21 C.F.R. § 1114.47(b).

[76] Maloney, J., *FDA to Order Juul E-cigarettes Off U.S. Market*, THE WALL STREET J. (June 22, 2022), https://www.wsj.com/articles/fda-to-order-juul-e-cigarettes-off-u-s-market-11655904689?mod=Searchresults_pos4&page=2.

[77] FDA, CTP Statement, (June 24, 2022), https://www.fda.gov/tobacco-products/ctp-newsroom/ctp-statement.

V. A NEW MODEL TO ADDRESS DYSFUNCTIONS IN THE PMTA PROCESS AND ENSURE EFFICIENCY, PREDICTABILITY, AND TRANSPARENCY GOING FORWARD

CTP's implementation of the Tobacco Control Act has been plagued by dysfunction, resulting in an opaque, inefficient, and unpredictable review of PMTAs. In our view, a lack of effective program management and operational capabilities have been contributing factors. CTP seems to have used what resources it does have to prioritize keeping combustible cigarettes on the market while its review of PMTAs for ENDS and other less harmful alternatives has been delayed and, in some cases, stalled. Nor has CTP been held accountable for its lack of adherence to the statute and slow and untimely review of PMTAs.

As a result, CTP has become further distanced from the Tobacco Control Act's central objective to "promote cessation to reduce disease risk and the social costs associated with tobacco-related diseases." Over thirteen years ago, the Tobacco Control Act was enacted. Today, combustible cigarettes continue to be used by approximately 31 million Americans, result in approximately 480,000 preventable deaths each year, and comprise approximately 75% of the total tobacco market.[78] In those thirteen-plus years, FDA has authorized just forty-two less harmful new products and only twenty-three new ENDS products representing less than 4% of the total ENDS market. And even these PMTA reviews have taken years — well beyond the statutory requirement of 180 days.

A recent status report filed by FDA estimates it will take CTP until June 30, 2023, to complete a subset of the pending applications for currently marketed products.[79] In another case, FDA has stated that "it estimates that it will complete re-review of petitioner's collaborators' applications in or about January 2024, and that it will complete re-review of petitioner's application in or about January 2025[,]" attributing the delay to the volume of pending applications and FDA's current prioritization plan.[80] Products not yet on the market are even further back in the queue.

These challenges are ripe and systemic in the application-review program. There may not be one single solution to the problem. But there needs to be a course correction if the Tobacco Control Act and PMTA process will serve as a viable means to tobacco harm reduction in the United States.

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[78] Cornelius, M., et al. (2022, Mar. 18). Tobacco Product Use Among Adults – United States, 2020, *Morbidity and Mortality Weekly Report, 71*, 399; Center for Disease Control. (2020, April). *Tobacco-Related Mortality*; Passport – Euromonitor International. (2021). U.S. Retail Sales. Retrieved from https://www.portal.euromonitor.com/. While combustible cigarettes comprise approximately 75% of the total tobacco market, all combustible products (including cigarettes, cigars, cigarillos, and roll-your-own tobacco) comprise approximately 85% of the total tobacco market. *See id.*

[79] *See* Status Report at 3.

[80] *See* Joint Status Report at 2, *My Vape Order, Inc. v. FDA*, No. 21-71302, Dkt. 53 (9th Cir. July 19, 2022).

As a starting point, Reagan-Udall's external review should trigger a complete audit of the PMTA program as currently managed by CTP. This audit should include a review of whether the Tobacco Control Act, regulations, and guidance are being followed; whether principles of sound scientific assessment and good regulatory practices are being applied; whether adequate safeguards are in place to protect against political interference and ensure science-based decision-making; and whether processes and checks are established to comply with the Administrative Procedure Act. Once completed, such an audit coupled with Reagan-Udall's report should result in necessary program changes. Until that occurs, CTP should avoid making further marketing decisions on pending applications. CTP can continue to exercise enforcement discretion for currently marketed products that are compliant with FDA laws, regulations, and policy and do not pose an acute health risk, while significantly enhancing its enforcement activities against those products that continue to evade its regulatory authorities.

In addition, we believe these systemic challenges are best addressed by reforming the tobacco user-fee program to ensure a proper allocation of funding and, more importantly, transparency and accountability for timely and fair reviews of current and future product applications. While we appreciate that such reform requires legislation, we lay out our thinking and the benefits of such a model for FDA's tobacco-regulatory programs below.

Tobacco user fees are assessed only on the six product categories expressly listed in § 919 of the Tobacco Control Act: cigarettes, cigars, chewing tobacco, roll your own, pipe tobacco, and snuff.[81] Manufacturers of ENDS and some other deemed products are not required to pay user fees under current law.[82] And CTP is not required to tie its allocation of user fees to any intended purpose — including the review of premarket applications, let alone the introduction of less harmful products, or other statutory mandates.[83] Even with the fees provided by other product categories, CTP appears to lack the requisite capabilities to meet FDA's policy goals of reducing tobacco-related death and disease through the premarket review of new products.

Requiring user fees for all tobacco products, including ENDS, may provide CTP with resources more commensurate with its responsibilities, including application review. But money alone is not enough. CTP currently receives approximately $712 million annually from tobacco user fees without any accountability on how those funds are allocated.

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[81] *See* GAO, Report to Congressional Requesters, Tobacco User Fees, Further Action Needed to Ensure Calculations Are Based on Complete and Accurate Data, (Oct. 17, 2019), https://www.gao.gov/products/gao-20-34.

[82] FDA has stated that Section 919(b)(2)(B)(iv) of the FDCA does not allow user fees to be imposed on products outside the six listed classes. *See* Requirements for the Submission of Data Needed To Calculate User Fees for Domestic Manufacturers and Importers of Cigars and Pipe Tobacco, 81 Fed. Reg. 28707, 28710 (May 10, 2016).

[83] *See* FDA, Report to the House Committee on Appropriations on Tobacco Product User Fees, https://www.fda.gov/tobacco-products/rules-regulations-and-guidance/reports-congress#sectionUserFees (available for

Rather, there needs to be a directed shift in priorities, program management, and processes. A goals-letter framework that includes performance goals and resource allocation — modeled on the medical product user-fee programs — will establish better program and operations management. Such a goals-letter framework for all tobacco products will promote efficiency, predictability, and transparency for the review of product applications and ensure accountability to statutory requirements.

The goals-letter frameworks under the Prescription Drug User Fee Act (PDUFA), the Generic Drug User Fee Amendments (GDUFA), the Medical Device User Fee Amendments (MDUFA), and the Biosimilar User Fee Act (BsUFA) provide a model for reforming the tobacco user-fee program.

These user-fee programs operate hand-in-glove with process and performance goals and transparency and accountability assurances delineated through a robust stakeholder input process. [84] Specifically, the goals-letter framework requires FDA to consult with the House Committee on Energy and Commerce; the Senate Committee on Health, Education, Labor, and Pensions; scientific and academic experts; health-care professionals; representatives of patient and consumer advocacy groups; and regulated industry. Along with requiring negotiations with regulated industry, the goals-letter framework requires FDA to provide notice for and hold a public meeting on reauthorization and future recommendations and solicit and publish public comments. The PDUFA, MDUFA, and GDUFA goals-letter framework requires FDA to hold periodic consultations with representatives of patient and consumer advocacy groups while FDA negotiates with regulated industry. Under statutory sunset provisions, the PDUFA, MDUFA, GDUFA, and BsUFA goals-letters must be resubmitted every five years for reauthorization of user fees assessments by FDA.

Congress had three main objectives in establishing the goals-letter framework for medical product user fees. And they are the same objectives that ought to guide reform of the tobacco user-fee program: (i) to increase the efficiency, predictability, consistency, and transparency of FDA's review of applications; (ii) to ensure that FDA's benefits from user fees would be tied directly to supporting the development of new products; and (iii) to encourage collaboration between FDA and industry, the public, and Congress in setting these goals.

First, to ensure that user fees promoted innovation, Congress aimed to increase efficiency, predictability, consistency, and transparency for the review of product applications. Accordingly, Congress tied review times under the performance goals to user fees. PDUFA, the first of the medical products user-fee programs, expressly provided that the user fees it authorized "will be dedicated toward expediting the review of human drug applications as set forth in the goals identified in the letters" from FDA to Congress.[85] MDUFA was later enacted to give the Center for Devices and Radiological Health access to

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[84] *See* 21 U.S.C. § 379j-43(f)(1)-(6) (GDUFA); 21 U.S.C. § 379h-2(f)(1)-(6) (PDUFA); and 21 U.S.C. § 379j-1(b)(1)-(6) (MDUFA); and 21 U.S.C. § 379j-53(f)(1)-(3) (BsUFA).

[85] Prescription Drug User Fee Act of 1992, Pub. L. No. 102-571, § 102(3), 106 Stat. 4491, 4491.

similar resources as the Center for Drug Evaluation and Research under PDUFA "so that they can provide "thorough, effective reviews, in less time."[86] FDA has stated in rulemaking that "the ultimate goal was for FDA to clear and approve safe and effective medical devices more rapidly"[87] and reduce the average total time for product reviews.[88] Similarly, when later enacting BsUFA, Congress was motivated to "ensure that FDA can facilitate the development and evaluation of biosimilar products" by creating "a transparent, predictable and balanced regulatory framework for the review and approval of biosimilars accompanied by reasonable performance goals and a dedicated independent funding stream[.]"[89]

Second, assessing user fees under a goals-letter framework ensure that FDA's benefits from user fees would be tied directly to supporting the development of new products. When first enacting the framework under PDUFA, Congress was concerned with the "key question" about "which activity should be included or supported by the user fee[.]" "Since user fees must be dedicated to the new drug approval process, we consider the establishment of performance goals . . . to be essential."[90] Congress also was concerned that "there is a substantial risk that the new money will be used to prop up existing activities."[91] Goals-letter performance standards are required "to ensure that new funds are being used to improve FDA's review of new drug and biologic products."[92] Tying user fees to performance goals also is "intended to support a new emerging industry" that "provided new and effective treatment options[.]"[93]

And third, the goals-letter framework was established to encourage collaboration between FDA and industry, the public, and Congress in setting these goals and reauthorizing the program. The sunset provision enacted first under PDUFA was created to

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[86] Medical Device User Fee and Modernization Act of 2002, 148 Cong. Rec. H. 7153, 7163 (Oct. 7, 2002) (Statement of Mr. Greenwood).

[87] Medical Device User Fee Amendments; Public Meeting; Request for Comments, 81 Fed. Reg. 69829, 69831 (Oct. 7, 2016).

[88] Medical Device User Fee Act; Public Meeting, 77 Fed. Reg. 16239, 16242 (Mar. 20, 2012).

[89] Hearing Before the Subcommittee on Health of the Committee on Energy and Commerce, Searial No. 112-136 (Apr. 18, 2012), (Statement of Sara Radcliffe, Executive Vice President for Health for the Biotechnology Industry Organization).

[90] Hearing Before the Subcommittee on Health and the Environment, Serial No. 102-16, 17-18 (Aug. 10, 1992) (Statement of Mr. Lerner).

[91] Hearing Before the Subcommittee on Health and the Environment, Serial No. 102-16 (Aug. 10, 1992) (Statement of Mr. Beier, VP, Government Affairs, Genentech, Inc.).

[92] Hearing of the Committee on Labor and Human Resources, S. Hrg. 102-1171 (Sept. 22, 1992) (Statement of Mr. Skaletsky, Chairman of Enzytech).

[93] Hearing Before the Subcommittee on Health of the Committee on Energy and Commerce, Serial No. 112-114, (Feb. 9, 2012) (Statement of Janet Woodcock); *see also* Biosimilar User Fee Act; Public Meeting, 80 Fed. Reg. 58259 (Sept. 28, 2015) ("BsUFA's intent is to provide additional revenues so that FDA can hire more staff, improve systems, and establish a better managed biosimilar biological product review process to make biosimilar biological product therapies available to patients sooner without compromising review quality.").

evaluate whether FDA was meeting its performance goals and "to allow the public, the industry which would be paying the fees, and Congress to decide whether the program should be continued."[94] Under the goals-letter framework, FDA "hold[s] itself responsible for the goals[,]" but a partnership with industry ensures FDA meets its milestones.[95]

A goals-letter framework for all tobacco products, including ENDS, would promote these same goals for CTP's review of product applications. A specific allocation of user fees should be tied directly to performance goals for the review of product applications — not only to increase efficiency, predictability, and transparency for PMTA reviews but also to advance FDA's broader goal of reducing tobacco-related harm. This framework should safeguard the allocation of user fees for reviewing less harmful and more innovative products, rather than diverting funds to keeping more harmful combustible cigarettes on the market. Finally, this framework would not only encourage, but require collaboration among key stakeholders including FDA and industry, the public, and Congress.

VI. CONCLUSION

JLI remains committed to engage with FDA through the PMTA process, in recognition of the unique role that it plays in determining whether JLI's products are appropriate for the protection of public health. Going forward, we hope that under improved CTP program management and operations, we can establish a structure and commitments at CTP that enable an efficient, predictable, and transparent review of PMTAs with increased program and personnel accountability. A regulatory program that is based on science and evidence, grounded in its statutory authorities, and without the appearance of political interference and policy-driven outcomes.

Respectfully submitted,

Enclosures: Appendix 1 – JLI's 10.75 appeal
Appendix 2 – FDA's MDO of JLI's PMTAs
Appendix 3 – FDA's TPL memorandum accompanying the MDO

[94] Hearing of the Committee on Labor and Human Resources, S. Hrg. 102-1171 (Sept. 22, 1992) (Statement of Commissioner Kessler).

[95] *Id.*