IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MARYLAND

AMERICAN ACADEMY OF PEDIATRICS, *et al.*,

Plaintiffs,

v.

UNITED STATES FOOD AND DRUG ADMINISTRATION, *et al.*,

Defendants.

Civil Action No. 8:18-cv-883-PWG

DEFENDANTS' REMEDY BRIEF

INTRODUCTION

The FDA believes that the recent "epidemic-level rise in youth e-cigarette use" is a "mounting public health crisis."[1] It agrees that this crisis demands a robust regulatory response, including through enforcement of the Tobacco Control Act's premarket review provision. And, as reflected in its March 2019 draft guidance, it is taking steps to accelerate enforcement of that provision, particularly with respect to the products driving this crisis: e-cigarettes targeted to youth or easily accessible to them, especially those in kid-friendly fruit or candy flavors. *See* Defs.' Notice (Mar. 15, 2019) (ECF No. 59). To address this public health crisis, the FDA is committed to finalizing that guidance within 120 days.

Nevertheless, bedrock principles of administrative law constrain the Court's authority to enter the specific relief that Plaintiffs request. Having already set aside the challenged August 2017 guidance—the remedy authorized by the terms of the Administrative Procedure Act—the Court should simply remand to the FDA to permit it to choose a course of action consistent with the Court's opinion. But even if the Court determines to go further, it should not enter the specific relief that Plaintiffs request, and certainly not on the dramatically accelerated timetable they suggest. In particular, requiring premarket applications for all deemed products—an expected 5,424 to 6,764 applications—to be submitted within 4 months would create massive administrative burdens at the agency that would ultimately be counterproductive. More importantly, such a precipitous deadline would threaten to abruptly clear the market of e-cigarette products, creating a "genuine risk" that adult former smokers addicted to nicotine would "migrat[e] from potentially less harmful ENDS products [*i.e.*, e-cigarettes] back to combustible tobacco products"—a "public health outcome that should be avoided if at all possible, while still achieving the public health benefits of earlier premarket review for

[1] FDA, *Statement from FDA Commissioner Scott Gottlieb, M.D., on advancing new policies aimed at preventing youth access to, and appeal of, flavored tobacco products, including e-cigarettes and cigars* (Mar. 13, 2019), at https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-advancing-new-policies-aimed-preventing-youth-access.

deemed products, especially with respect to curtailing youth use." Declaration of Mitchell Zeller, Director, Center for Tobacco Products, FDA ("Zeller Decl.") ¶ 12.

Thus, should the Court order premarket applications to be submitted by a date certain, it should set that deadline no sooner than 10 months from the date of its decision, along with a one-year period for FDA review. *See id.* ¶ 13. That would strike a better balance among public health considerations, and allow the agency some time to prepare to absorb a flood of applications significantly sooner than anticipated. It would also permit the FDA to finalize the March 2019 draft guidance setting forth its enforcement priorities in the meantime. That is "one of the most critical public health steps that [the] FDA can take to curb youth vaping," Zeller Decl. ¶ 11, and the agency plans to complete it within 120 days.

DISCUSSION

I. The Court should not go beyond vacating the August 2017 guidance.

In this case, Plaintiffs challenged a single, discrete agency action: the issuance of an August 2017 guidance document describing the FDA's intention to temporarily defer enforcement of the Tobacco Control Act's (TCA) premarket review provision with respect to a subset of deemed products. Compl. ¶ 30. The relief they sought was accordingly narrow: they asked the Court to declare the guidance unlawful, and to "[v]acate [it] and set [it] aside." *Id.* ¶¶ (a)–(b) (prayer for relief). And the Court has now granted that relief, holding that the guidance exceeded the agency's statutory authority, was improperly issued without notice and comment, and must therefore be vacated. Mem. Op. at 44, 53 (ECF No. 73); Order at 1 (ECF No. 74).

Under longstanding principles of administrative law, that should be the end of the matter. By its terms, the Administrative Procedure Act (APA) authorizes courts only to "set aside" unlawful agency action. 5 U.S.C. § 706(2); *see* Compl. ¶¶ 93, 102, 104, 118. And "[u]nlike a district court managing a 'garden variety civil suit,' a district court reviewing a final agency action" under the APA

"'does not perform its normal role' but instead 'sits as an appellate tribunal.'" *Palisades Gen'l Hosp. v. Leavitt*, 426 F.3d 400, 403 (D.C. Cir. 2005). "Thus, under settled principles of administrative law, when a court reviewing agency action determines that an agency made an error of law, the court's inquiry is at an end: the case must be remanded to the agency for further action consistent with the correct legal standards." *Id.* Relief in an APA case is therefore ordinarily "limited only to vacating the unlawful action," and courts should not enjoin an agency to implement a specific remedy that "preclud[es] future agency decisionmaking." *Hill Dermaceuticals v. FDA*, 709 F.3d 44, 46 n.1 (D.C. Cir. 2013).

Nevertheless, Plaintiffs now ask the Court to do just that. They urge the Court to enter an injunction requiring that: (1) premarket applications be submitted within 120 days; (2) products with timely applications on file be allowed to remain on the market for no more than one year pending FDA review; (3) the FDA take "any and all actions necessary" to ensure that "no" newly deemed product remains on the market "without being subject to FDA enforcement action"; and (4) the FDA make quarterly reports about the number of premarket applications it has processed and the "number and nature of enforcement actions it has commenced." Pls.' Proposed Order at 1–2 (ECF No. 78-1). But absent unusual circumstances not present here,[2] it is inappropriate to issue an injunction imposing specific duties on the agency—a principle that courts have adhered to time and again.

For example, in *Hill Dermaceuticals*, the court considered a challenge to the FDA's approval of a supplemental new drug application for a generic corticosteroid. In rejecting the challenge, the court

[2] This case bears no resemblance to the few Plaintiffs cite where courts entered injunctive relief. Pls.' Remedy Br. at 7, 9. In *NAACP v. HUD*, 817 F.2d 149 (1st Cir. 1987), for example, the court found that "over time, HUD's pattern of activity" reflected a failure to enforce the nondiscrimination policies of the Fair Housing Act, despite a demonstrated history of racial segregation in housing in Boston. *Id.* at 151 (citing 42 U.S.C. § 3608(e)(5)). Similarly, in *Thompson v. HUD*, No. 95-309, 2006 WL 581260 (D. Md. Jan. 10, 2006), the agency's "long-term practice" and "pattern of actions" "perpetuated Region-wide segregation" in housing in the Baltimore area. *Id.* at *4. And in *Cobell v. Norton*, 240 F.3d 1081 (D.C. Cir. 2001), the court cited "the government's 'historical record of recalcitrance' in performing its trust duties" toward Native Americans. *Id.* at 1108. There is nothing comparable here.

criticized the plaintiff for requesting "injunctive relief[] seeking to enjoin the FDA from approving [the generic competitor's] new drugs." 709 F.3d at 46 n.1. It explained: "where a district court reviews agency action under the APA, it acts as an appellate tribunal, so the appropriate remedy for a violation is 'simply to identify a legal error and then remand to the agency.'" *Id.* Thus, any relief "would need to be limited only to vacating the unlawful action, not precluding future agency decisionmaking." *Id.*

Similarly, in *Palisades*, the plaintiff hospital claimed that the Department of Health and Human Services had failed to correct certain data, leading to improperly low reimbursement rates, and urged the court to "exercise its equitable powers" to award it "make-whole relief including an adjusted reimbursement." 426 F.3d at 401, 403. The court concluded that the "district court had no jurisdiction to order specific relief": although it could "vacate the Secretary's decision rejecting the hospital's revised wage data and . . . remand for further action consistent with its opinion," it "did not . . . have jurisdiction to order reclassification based upon those adjusted wage data or an adjusted reimbursement payment." *Id.*; *see also, e.g.*, *Bennett v. Donovan*, 703 F.3d 582 (D.C. Cir. 2013) ("We do not hold, of course, that HUD is required to take this precise series of steps, nor do we suggest that the district court should issue an injunction to that effect. Appellants brought a complaint under the Administrative Procedure Act to set aside an unlawful agency action, and in such circumstances, it is the prerogative of the agency to decide in the first instance how best to provide relief.").

These cases point the way here. The Court has held that the August 2017 guidance exceeded the FDA's statutory authority and was improperly issued without notice and comment. But the remedy is not to issue an injunction constraining the agency to undertake a judicially prescribed course of action, as Plaintiffs now argue. It is instead to remand to the FDA to permit it to choose a course consistent with the Court's opinion, as Plaintiffs previously suggested. *See* Pls.' Letter Mot. to Reconsider at 1 (ECF No. 63) ("if the Court strikes down the operative Guidance, FDA would know the legal rules it must follow to make its forthcoming guidance valid"). That is particularly true given

the range of remedial options open to the FDA, which Congress has recognized as the "regulatory agency with the scientific expertise" to "evaluate scientific studies supporting claims about the safety of products" and "make[] decisions about how whether and how [tobacco] products may be marketed." TCA § 2(44). The Court should not substitute its judgment for the scientific expertise of the agency on these matters.

Moreover, an injunction would be particularly anomalous here given that Plaintiffs make no attempt to meet the standard prerequisites for such relief. "An injunction is an equitable remedy that 'does not follow from success on the merits as a matter of course.'" *SAS Institute, Inc. v. World Programming Ltd.*, 874 F.3d 370, 384 (4th Cir. 2017) (citation omitted). Rather, Plaintiffs must show that: (1) they have suffered irreparable injury; (2) remedies available at law are inadequate; (3) a remedy in equity is warranted considering the balance of hardships; and (4) the public interest would not be disserved by a permanent injunction. *Id.* Here, Plaintiffs fail to show that any harm to them is irreparable—a traditional prerequisite to any injunction, whether preliminary or final. *Bethesda Softworks, LLC v. Interplay Entm't Corp.*, 452 F. App'x 351, 354 (4th Cir. 2011). They assert harm from a "deprivation of information" to be made available upon approval of premarket applications. Mem. Op. at 18. But presumably they already have sufficient information to counsel their patients and the public to avoid e-cigarettes and cigars. *See* Pls.' Remedy Br. at 1 (arguing that these products are "highly addictive and harmful"). And under their own remedial proposal, Plaintiffs would not receive the additional information they seek here for some 17 months: 4 months for the submission of premarket applications, a year for review, and an additional month for information to be released, *see* Pls.' Remedy Br. at 8; 21 U.S.C. § 387j(a)(4)(B), so they provide no reason to think they would be irreparably harmed by not having that information for some hypothetical period of time beyond that point. *See, e.g.*, *Elec. Privacy Info. Ctr. v. Presidential Advisory Comm'n on Election Integrity*, 266 F. Supp. 3d 297, 319 (D.D.C. 2017) (it "cannot be" "that whenever a statute provides for potential disclosure, a

party claiming entitlement to that information in the midst of a substantial public debate would be entitled to a finding of irreparable informational injury").

The equities and public interest also tilt against injunctive relief. *See Nken v. Holder*, 556 U.S. 418, 435 (2009) (these "factors merge when the Government is the opposing party"). To "set aside" the challenged guidance, as contemplated by the text of the APA, 5 U.S.C. § 706(2), would adequately remedy their asserted harm. And Plaintiffs' proposed timeframe could adversely affect the public health by abruptly clearing the market of e-cigarette products, creating a genuine risk that former smokers addicted to nicotine could migrate back to conventional cigarettes. Zeller Decl. ¶ 15; *see Weinberger v. Romero-Barcelo*, 456 U.S. 305, 312–13 (1982) ("[C]ourts of equity should pay particular regard for the public consequences in employing the extraordinary remedy of injunction."). Plaintiffs' request for this extraordinary form of relief should therefore be rejected.

II. Plaintiffs' proposed 120-day deadline for the submission of premarket applications could adversely affect the public health and would be administratively infeasible.

If the Court nevertheless enters an injunction requiring premarket applications to be submitted by a date certain, it should not adopt the 120-day deadline that Plaintiffs propose. As explained in the attached declaration of Mitchell Zeller, Director of the FDA's Center for Tobacco Products, that precipitous deadline "would cause significant public health concerns, as well as implementation challenges." Zeller Decl. ¶ 15. It could suddenly clear the market of thousands of e-cigarette products, raising the risk that some former smokers addicted to nicotine might migrate back to conventional cigarettes, and is likely to flood the agency with thousands of low-quality applications that would strain agency resources and significantly delay processing. *Id.* ¶¶ 15, 18. Thus, if the Court orders a deadline for the submission of premarket applications, it should set that deadline no sooner than 10 months from the date of its decision (with a one-year period for FDA review, without limiting the agency's discretion to take enforcement action in the meantime). These dates, while still significantly accelerated, would at least reduce the expected abrupt and massive market exit of e-cigarette products,

and give the FDA an opportunity to administratively prepare for and review a massive influx of applications sooner than anticipated. Critically, they would also allow the agency to finalize the March 2019 draft guidance setting forth its enforcement priorities in the interim—particularly with respect to e-cigarettes targeted to minors or sold in ways that heighten the risk of youth access. In the FDA's judgment, finalizing that guidance is "one of the most critical public health steps that [the agency] can take to curb youth vaping," *id.* ¶ 11, and it plans to do so within 120 days, *id.* ¶ 10. And it is the FDA, not Plaintiffs, who are in the best position to balance the important public health and agency resource considerations interests at stake.

"First and foremost, from the public health perspective," a 120-day deadline would "likely" lead to a "mass market exit of ENDS products." Zeller Decl. ¶ 15. Because e-cigarette products are relatively novel, their manufacturers are likely to seek premarket authorization by filing a "premarket tobacco application" (PMTA)—the most complex of the three possible pathways. *See* Defs.' Br. at 5–6 (ECF No. 36-1) (describing premarket pathways); *see also* Zeller Decl. ¶ 5(d). There are currently no authorized PMTAs for e-cigarette products, and the FDA believes that Plaintiffs' proposed 120-day deadline would lead to "mass market exit"—a "significant public health concern." Zeller Decl. ¶ 15. To be sure, the "[o]verall population level impact" of e-cigarettes "remains uncertain today, especially given youth uptake of ENDS." *Id.* But for "cigarette smokers who completely switch to ENDS, these products may be less harmful at an individual level than combustible tobacco products." *Id.* The "mass market exit" of e-cigarette products thus "would limit the availability of a potentially less harmful alternative for adult smokers seeking to transition or stay away from combustible tobacco products." *Id.* In the FDA's judgment, "[d]ramatically and precipitously reducing availability of these products could present a serious risk that adults, especially former smokers, who currently use ENDS products and are addicted to nicotine would migrate to combustible tobacco products, even if particular ENDS products ultimately receive marketing authorization and return to the market later."

Id. "And although there has been great recent progress in declining use of cigarettes for all age groups," the FDA is "concerned that these declines could be slowed or reversed in the case of very sudden and very dramatic reductions in availability." *Id.* The FDA's expert judgment on this issue merits substantial deference. *See, e.g.*, *West Virginia v. EPA*, 362 F.3d 861, 871 (D.C. Cir. 2004) ("We will give an extreme degree of deference to the agency when it is evaluating scientific data within its technical expertise.").

Second, on top of this public health concern, Plaintiffs' proposed 120-day deadline would likely inundate the agency with low-quality applications that would strain agency resources and result in significant delays. For starters, the FDA would be receiving an estimated 5,424 to 6,764 premarket applications. Zeller Decl. ¶ 19. When the deeming rule was issued in May 2016, there were approximately 20,504 to 25,704 deemed tobacco products on the market, including 4,640 to 8,800 e-cigarette products and 7,500 cigars. RIA at 84 tbl.9. The FDA expected the manufacturers of about 5,424 to 6,764 of those products, including some 1,610 to 2,950 e-cigarette products and 2,625 cigars, to apply for premarket review. *Id.* Although the August 2017 guidance explained that the agency generally intended to defer enforcement of the premarket review provision until 2021 or 2022, manufacturers were not precluded from submitting applications earlier—in fact, the agency has repeatedly encouraged them to do so. *See, e.g.*, Press Release, FDA, *Statement from FDA Comm'r Scott Gottlieb, M.D., On New Steps to Address Epidemic of Youth E-Cigarette Use* (Sept. 12, 2018) (there is "no excuse for manufacturers not to file applications with the FDA because the agency hasn't told them what they are expected to do").[3] Nevertheless, given the sheer number of products at issue, requiring all manufacturers to submit premarket applications within 120 days would be counterproductive.

[3] *Available at* https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-new-steps-address-epidemic-youth-e-cigarette-use; *see also* Press Release, FDA, *Statement From FDA Comm'r Scott Gottlieb, M.D., On Proposed New Steps to Protect Youth by*

The PMTA pathway requires a manufacturer to establish that the product is "appropriate for the protection of the public health," 21 U.S.C. § 387j(c)(2)(A), considering "the risks and benefits to the population as a whole, including users and nonusers of the tobacco product, and taking into account—(A) the increased or decreased likelihood that existing users of tobacco products will stop using such products; and (B) the increased or decreased likelihood that those who do not use tobacco products will start using such products," *id.* § 387j(c)(4). By statute, a PMTA must include, among other things:

- "full reports of all information, published or known to, or which should reasonably be known to, the applicant, concerning investigations which have been made to show the health risks of such tobacco product and whether such tobacco product presents less risk than other tobacco products;"
- "a full statement of the components, ingredients, additives, and properties, and of the principle or principles of operation, of such tobacco product;" and
- "a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and, when relevant, packing and installation of, such tobacco product."

Id. § 387j(b)(1); *see also* Zeller Decl. ¶¶ 20–21. A PMTA must also include an adequate environmental assessment (or a claim of categorical exclusion). 25 C.F.R. § 25.15. To assist manufacturers in navigating these requirements, in May 2016 the FDA released a 50-page draft guidance document for

Preventing Access to Flavored Tobacco Products and Banning Menthol in Cigarettes (Nov. 15, 2018) (expressing hope that FDA would "soon see manufacturers of ENDS [Electronic Nicotine Delivery Systems] products preparing, with FDA input as appropriate, premarket tobacco product applications (PMTAs) to demonstrate that their products meet the public health standard in the Tobacco Control Act"), *at* https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-proposed-new-steps-protect-youth-preventing-access; Press Release, FDA, *Statement From FDA Comm'r Scott Gottlieb, M.D., On Advancing New Policies Aimed At Preventing Youth Access to, and Appeal of Flavored Tobacco Products, Including E-Cigarettes and Cigars* (Mar. 13, 2019) ("manufacturers need not wait to submit premarket tobacco product applications for ENDS products, flavored or otherwise"), *at* https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-advancing-new-policies-aimed-preventing-youth-access.

the submission of PMTAs for e-cigarette products.[4] The final, 52-page version of that guidance document was released on June 11, 2019.[5]

To date, the FDA has received few PMTAs that meet even the basic requirements for them to be considered properly filed. As of April 30, 2019, the agency had received 401 PMTAs, 373 of which were for deemed products. Zeller Decl. ¶ 5(d). Of those 373, more than 99% (369/373) were closed as insufficient to accept or file, largely for failure to include an environmental assessment, and the manufacturers have not refiled corrected versions. *Id.* Overall, just 12 PMTAs have been authorized, for smokeless tobacco and noncombustible, "heated" cigarettes (which differ from e-cigarettes in that they vaporize actual tobacco, rather than an e-liquid). *See id.* And only 4 PMTAs remain pending for deemed products, none of them for e-cigarette products. *Id.* Moreover, as part of the premarket authorization process, tobacco manufacturers routinely consult with FDA, similar to the analogous process for new drug or device applications under the Federal Food, Drug, and Cosmetic Act (FDCA). *See id.* ¶ 5(d). Yet only a handful of manufacturers—"fewer than 10"—"have sought pre-submission meetings with FDA to discuss potential premarket applications for ENDS products." *Id.* ¶ 15.

Perhaps the best analogue to this expected influx of premarket applications took place in March 2011, in the days preceding a statutory deadline for manufacturers to submit "provisional" substantial equivalence (SE) applications. *See* 21 U.S.C. § 387j(a)(2)(B) (discussed in Defs.' Br. at 34). In total, manufacturers submitted nearly 3,600 provisional SE applications—about 3,000 of them (more than 83%) "within the last several days leading up to" the deadline. Zeller Decl. ¶ 19. While

[4] FDA, Draft Guidance for Industry, *Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems* (May 2016), *at* https://www.fda.gov/media/97652/download.

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

the "FDA has put many more systems in place since then, and has created a robust application review process within CTP's Office of Science, there is no doubt that the agency will be flooded with applications in the final days leading up to any court-ordered submission deadline" entered here. *Id.*

Such a large number of premarket applications would threaten to overwhelm the FDA's resources if submitted *en masse* by a deadline much earlier than the agency had anticipated. This resource problem is likely to be compounded by the fact that "[m]any applicants will be newly regulated entities lacking experience with FDA"—which is particularly likely for e-cigarette products, which are relatively novel. *Id.* ¶ 18. "[B]ased on [the agency's] experience to date, the applications are anticipated to be lower in quality and less complete than current-day applications for other FDA-regulated products." *Id.* A "large volume of incomplete or haphazard applications in which the information is not clearly presented or is missing data will cause further delay because it will divert valuable agency resources into the painstaking effort of reviewing those submissions and communicating deficiencies." *Id.* ¶ 18.

Finally, the FDA only recently published the final version of its guidance document for the submission of PMTAs for e-cigarette products, *see supra* at 9–10, and is still in the process of issuing a rule concerning PMTAs. *See* Zeller Decl. ¶ 4(d). Of course, "manufacturers may submit premarket applications for these products at any time, and there is no legal barrier to filing." *Id.* ¶ 16. "Indeed, CTP has accepted, filed, and authorized applications through each of the available pathways based on statutory criteria even in the absence of rules or product-specific guidance." *Id.* But such guidance can assist manufacturers in preparing applications that are of high enough quality to facilitate efficient review. *See id.*

For all of these reasons, Plaintiffs' proposed 120-day deadline for the submission of premarket applications would threaten to harm the public health and is administratively infeasible. Indeed, it is the FDA's "firm belief" that such an accelerated deadline would "create[] a genuine risk of migration

from potentially less harmful ENDS products back to combustible tobacco products within the population of addicted adult smokers who have completely switched to ENDS." *Id.* ¶ 12. "This is a public health outcome that should be avoided if at all possible, while still achieving the public health benefits of earlier premarket review for deemed products, especially with respect to curtailing youth use." *Id.*

Thus, should the Court order premarket applications to be submitted by a date certain—and it should not, *see supra* at 2–6—under no circumstances should it set that deadline sooner than 10 months from the date of its decision (with a one-year period for FDA review, without limiting the agency's discretion to take enforcement action in the meantime). *See* Zeller Decl. ¶ 13.[6] While perhaps not the dates that the FDA would select if permitted to exercise its own discretion, such a deadline would at least reduce the expected abrupt and massive market exit; avoid flooding the FDA with thousands of premarket applications on a nearly immediate basis; and allow the agency at least some time to prepare to receive and review applications much more quickly than it had anticipated. *See id.* ¶¶ 15, 16. It would also enable manufacturers to strengthen their applications based on the recently issued PMTA guidance. *See id.* ¶ 16. And this relief would permit the FDA to finalize the March 2019

[6] Plaintiffs also ask the Court to order that products with timely premarket applications on file be allowed to remain on the market for no more than one year pending FDA review. *See* Pls.' Proposed Order ¶ 2. The original compliance policy, set forth in the preamble to the final deeming rule, contained a similar one-year compliance period for products with timely premarket applications. 81 Fed. Reg. 28,974, 29,011 (May 10, 2016) ("Unless FDA has issued an order denying or refusing to accept the submission, products for which timely premarket submissions have been submitted will be subject to a continued compliance period for 12 months after the initial compliance period[.]"). That policy also provided that, "if at the time of the conclusion of the continued compliance period," authorization has not yet been granted but "the applicant has provided the needed information and review of a pending marketing application has made substantial progress toward completion, FDA may consider, on a case-by-case basis, whether to defer enforcement of the premarket authorization requirements for a reasonable time period." *Id.* at 29,012. If the Court determines to enter an injunction limiting the compliance period for products with timely premarket applications on file to one year, it should not disturb the FDA's discretion to similarly defer enforcement on a case-by-case basis with respect to specific products in light of the relevant circumstances.

draft guidance setting forth its enforcement priorities in the meantime, which it plans to do within 120 days. *Id.* ¶ 10. Notably, that draft guidance proposes that the FDA would target several categories of deemed products for earlier enforcement of the premarket review provision—including e-cigarette products targeted to minors or sold in ways that heighten the risk of youth access. *See* Defs.' Notice (Mar. 15, 2019) (ECF No. 59). And that enforcement could take place before any deadline for the submission of premarket applications that the Court were to order.

III. The Court should not order the FDA to enforce the premarket review provision—a step that would raise significant separation of powers concerns.

In all events, the Court should flatly reject Plaintiffs' suggestion that it order the FDA to take "any and all actions necessary" to ensure that "no" newly deemed product remains on the market "without being subject to FDA enforcement action," Pls.' Proposed Order ¶ 1, and make quarterly reports about the number of premarket applications it has processed and the "number and nature of enforcement actions it has commenced," *id.* ¶ 4. The FDCA contains no private right of action, which is effectively what Plaintiffs seek. *See* 21 U.S.C. § 337(a); *Buckman Co. v. Pls.' Legal Comm.*, 531 U.S. 341, 349 n.4 (2001). Moreover, such an order would plainly intrude on the prerogatives of the executive branch and raise significant separation of powers concerns.

The Court has held that, under the Tobacco Control Act, "the FDA '*must*' require filings from manufacturers and approve or deny those filings." Mem. Op. at 33 (citations omitted). But it is one thing to say that the agency must require the submission of premarket applications and adjudicate any applications submitted. It would be quite another to order the agency to take enforcement action against noncompliant products—and the Court's opinion rightly stopped short of doing so.

As Defendants have explained, a tobacco product that is marketed without a necessary premarket authorization is considered "adulterated" or "misbranded." Defs.' Br. at 6 (quoting 21 U.S.C. §§ 387b(6), 387c(a)(6)). The FDA "is *authorized* to conduct examinations and investigations" to enforce these and other provisions of the FDCA, 21 U.S.C. § 372(a)(1)(A) (emphasis added), and

violations may lead to enforcement action, including the seizure of offending products, *id.* § 334 (products "shall be *liable* to be proceeded against" (emphasis added)), injunctions against manufacturers, distributors, and retailers, *id.* § 332, and potentially criminal prosecution, *id.* §§ 331(a)–(c), 333(a), 336. These enforcement provisions are *precisely the same* as those at issue in *Heckler v. Chaney*, 470 U.S. 831 (1985), where the Supreme Court held that they "commit *complete discretion* to the Secretary to decide how and when they should be exercised." *Id.* at 835 (emphasis added). Thus, even if the Court enters a deadline for the submission of premarket applications, it should not purport to order the agency to take enforcement action against manufacturers that fail to meet that requirement.

The "basic principle" underlying the separation of powers doctrine is that "one branch of the Government may not intrude upon the central prerogatives of another." *Loving v. United States*, 517 U.S. 748, 757 (1996). Under Article II, the power to "take care that the laws be faithfully executed" is "entrusted to the executive branch—and only to the executive branch." *Baltimore Gas & Elec. Co. v. FERC*, 252 F.3d 456, 459 (D.C. Cir. 2001) (citing U.S. Const. art. II, § 3). "One aspect of that power is the prerogative to decline to enforce a law, or to enforce the law in a particular way." *Id.* Thus, "[w]hen the judiciary orders an executive agency to enforce the law it risks arrogating to itself a power that the Constitution commits to the executive branch." *Id.* Indeed, "*Chaney*'s recognition that the courts must not require agencies to initiate enforcement actions may well be a requirement of the separation of powers commanded by our constitution." *Id.*

That is reason enough to reject Plaintiffs' requested relief. But here, Plaintiffs offer more, as they would have the Court intrude even further into the executive sphere. Plaintiffs seek not only to compel the FDA to take enforcement action, but also for the Court to second-guess the nature, scope, and thoroughness of the agency's enforcement efforts. Indeed, their remedy brief and proposed order make clear that Plaintiffs envision an invasive inquiry into the FDA's decisionmaking process, including quarterly reports on: (a) "all steps" the agency is taking to enforce the premarket review

provision; (b) the "number of applications . . . it has received"; (c) the "status of its processing of those applications"; (d) the "number of . . . enforcement actions it has commenced"; and (e) the "nature" of those enforcement actions. Pls.' Proposed Order ¶ 4. Presumably, then, Plaintiffs anticipate continual judicial supervision of the FDA's processing of an expected 5,424 to 6,764 premarket applications, and intend to ask the Court to manage the agency's enforcement efforts should they be thought unsatisfactory.

Such inquiries fall outside the judicial role—a province that "a district judge must be careful not to exceed" "when the government is challenged for not bringing as extensive an action as it might." *United States v. Microsoft Corp.*, 56 F.3d 1448, 1462 (D.C. Cir. 1995).[7] In *Microsoft*, for example, the district court refused to enter a consent decree after the government declined to provide it with details akin to those sought by Plaintiffs here, such as (a) the "broad contours of the investigation"; (b) the "conclusions reached by the Government" about the company's practices; (c) why "areas were bargained away" during settlement discussions; and (d) what the government's future investigative plans were. *Id.* at 1455. The D.C. Circuit reversed—and reassigned the case—explaining that the district "judge's demand that he be informed [of these matters] indicates that the judge impermissibly arrogated to himself the President's role to 'take care that the laws be faithfully executed.'" *Id.* at 1457 (quoting U.S. Const. art. II, § 3). This Court should decline Plaintiffs' invitation to similarly encroach on the executive power.

CONCLUSION

For the foregoing reasons, the Court should decline to issue further relief in this case.

[7] Nor do Plaintiffs cite any relevant support for requiring agencies to report their *enforcement* activities to a court. *See* Pls.' Remedy Br. at 9. In *Cobell*—the only case they cite—reporting requirements were imposed for a breach of trust, and only in light of a "history of destruction of documents," "government malfeasance," and a "longstanding inability or unwillingness of government officials to discharge their fiduciary obligations." 240 F.3d at 1109.

Dated: June 12, 2019

Respectfully submitted,

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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MARYLAND

AMERICAN ACADEMY OF PEDIATRICS, *et al.*, Plaintiffs, v. UNITED STATES FOOD AND DRUG ADMINISTRATION, *et al.*, Defendants.	Civil Action No. 8:18-cv-883-PWG

DECLARATION OF MITCHELL ZELLER

I, Mitchell Zeller, declare as follows:

1. I am the Director of the Center for Tobacco Products ("CTP"), United States Food and Drug Administration ("FDA"), a position I have held since March 2013. In this role, I direct the development and implementation of programs and policies for regulating the manufacture, marketing, and distribution of tobacco products. In my capacity as Director of CTP, I am fully familiar with the instant matter and the facts stated herein.

2. I have dedicated my career to working on FDA issues (nearly 37 years), including the last 25 years focused on tobacco regulation. I am a graduate of Dartmouth College and the American University Washington College of Law. I began my career as a public interest attorney in 1982 at the Center for Science in the Public Interest working on FDA food safety and nutrition issues. In 1988, I served as counsel to the Human Resources and Intergovernmental Relations Subcommittee of the House of Representatives Government Operations Committee, where I conducted oversight of enforcement of federal health and safety laws, including human and animal drugs, dietary supplements, and food policies at FDA. In 1993, I joined the staff of

then-FDA Commissioner, Dr. David Kessler, M.D., on a two-week assignment to examine the practices of the tobacco industry. This assignment led to my serving as associate commissioner and director of FDA's first Office of Tobacco Programs where I led FDA's efforts to craft the agency's 1996 tobacco regulations. In this capacity, I represented FDA before Congress, federal and state agencies, and served as an official United States delegate to the World Health Organization Working Group for the Framework Convention on Tobacco Control. In 2000, I left FDA to continue my work in tobacco control as executive vice president of the American Legacy Foundation, where my responsibilities included marketing, communications, strategic partnerships, and creating the foundation's first Office of Policy and Government Relations. I later joined Pinney Associates as senior vice president in 2002, where I remained until I took my current position as Director of CTP. In that role, I provided strategic planning and communications advice on domestic and global health policy issues involving the treatment of tobacco dependence and the regulation of tobacco products and pharmaceuticals.

3. The Family Smoking Prevention and Tobacco Control Act, Pub. L. No. 111-31, 123 Stat. 1776 (2009) ("TCA") gave FDA authority to "deem" additional tobacco products subject to Chapter IX of the FDCA through notice and comment rulemaking. On May 10, 2016, FDA issued the "deeming rule," which subjected all other tobacco products (except accessories) to the requirements in Chapter IX of the FDCA, including electronic nicotine delivery systems ("ENDS") and cigars. 81 Fed. Reg. 28,974.

4. FDA has used and will continue to use its authority under the TCA and the deeming rule to address serious concerns about tobacco products, including youth use of ENDS and flavored cigars. We are committed to keeping tobacco products out of the hands of youth, and have used our authority and resources forcefully to prevent youth access, curb the marketing

of tobacco products aimed at youth, and educate teens and their families about the health risks of vaping and other tobacco product use. Specifically, since early 2018, these actions have included: (1) in May 2018, issuing 17 warning letters to manufacturers and retailers for selling e-liquids that resembled kid-friendly food products, which prompted all of the recipients to stop selling the violative products;[1] (2) in summer 2018, conducting a nationwide undercover investigation that resulted in over 1,300 warning letters and civil money penalty actions against retailers who illegally sold ENDS products to minors;[2] (3) in January 2019, holding a public hearing to discuss strategies to eliminate youth use of ENDS with a focus on the role of drug therapies to help young people quit using e-cigarettes and other tobacco products;[3] (4) in March and April 2019, publicly admonishing thirteen national chain stores and franchises with high rates of violations for illegal sales of tobacco products to minors, and requesting plans that describe how these retailers will address and mitigate illegal sales to minors;[4] (5) in June 2019, sending four warning letters jointly with the Federal Trade Commission for violations related to online posts by social media influencers;[5] and (6) continuing robust public education efforts to prevent youth use of tobacco, including expanding its tobacco prevention campaign—called "The Real Cost"—to ENDS products with messaging that has been seen by teens nearly 500 million times.[6] Other CTP actions to address youth use are described in a March 2019 draft

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[1] *See* FDA News Release, *available at* https://www.fda.gov/news-events/press-announcements/fda-warns-more-companies-stop-misleading-kids-e-liquids-resemble-kid-friendly-foods-part-youth.

[2] *See* FDA News Release, *available at* https://www.fda.gov/news-events/press-announcements/fda-takes-new-steps-address-epidemic-youth-e-cigarette-use-including-historic-action-against-more.

[3] *See* Eliminating Youth Electronic Cigarette and Other Tobacco Product Use: The Role for Drug Therapies Public Hearing, Jan. 18, 2019, https://www.fda.gov/news-events/fda-meetings-conferences-and-workshops/eliminating-youth-electronic-cigarette-and-other-tobacco-product-use-role-drug-therapies-public.

[4] *See* https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-forceful-new-actions-focused-retailers-manufacturers.

[5] *See* https://www.fda.gov/news-events/press-announcements/fda-ftc-take-action-protect-kids-citing-four-firms-make-sell-flavored-e-liquids-violations-related.

[6] *See* https://www.fda.gov/tobacco-products/public-health-education-campaigns/real-cost-campaign.

guidance document.[7]

5. This case relates to the premarket review of deemed tobacco products that are new tobacco products as defined in 21 U.S.C. § 387j(a)(1). I describe the various pathways in which tobacco products may be legally marketed below:

a. Grandfathered Tobacco Products. Products that were commercially marketed in the United States as of February 15, 2007, are considered "grandfathered" and do not require prior authorization to be legally marketed. *See* 21 U.S.C. § 387j(a)(1). They also may serve as a predicate tobacco product for a substantial equivalence (SE) report, described below. FDA has made 1,651 grandfathered determinations for deemed products (e.g., cigars, pipe tobacco, and waterpipe tobacco).[8] Seeking an FDA grandfather determination is a voluntary process and there are likely many additional grandfathered products being marketed.

b. Substantial Equivalence (SE). A substantially equivalent tobacco product is a new tobacco product that has been found by FDA either to have the same characteristics as a predicate tobacco product or to have different characteristics than the predicate tobacco product, but, in the latter case, the substantial equivalence report submitted by the manufacturer demonstrates that it is not appropriate to regulate the new tobacco product under the Premarket Tobacco Application (PMTA) pathway because the product does not raise different questions of public health. 21 U.S.C. § 387j(a)(3)(A). A predicate tobacco product that an applicant can use is one that was commercially

[7] *See* Modifications to Compliance Policy for Certain Deemed Tobacco Products, Draft Guidance (Mar. 2019) at 5, *available at* https://www.fda.gov/media/121384/download.
[8] *See* Grandfathered Tobacco Products, *available at* https://www.fda.gov/tobacco-products/market-and-distribute-tobacco-product/grandfathered-tobacco-products (page last viewed June 12, 2019).

marketed in the United States as of February 15, 2007 (a grandfathered tobacco product), or has previously been found to be substantially equivalent by FDA, and is in compliance with the requirements in Chapter IX of the FDCA. FDA has issued guidance documents[9] and a proposed rule on April 2, 2019,[10] which address SE reports. As of April 30, 2019, FDA has authorized 1070 products with SE orders. For deemed products, FDA has received 313 SE reports and issued four orders authorizing SE reports.[11]

c. Substantial Equivalence Exemption. A new product may be exempt from the need to demonstrate substantial equivalence if it is modified by adding or deleting a tobacco additive or by increasing or decreasing the quantity of an existing tobacco additive, and such a modification would be a minor modification of a legally marketed product and an SE report is not necessary for the protection of public health. 21 U.S.C. § 387e(j)(3). As of April 30, 2019, FDA has issued 199 SE exemption orders, including 21 orders for deemed products.[12] FDA issued a final rule establishing procedures for requesting an exemption from the substantial equivalence requirements in 2011. *See* 76 Fed. Reg. 38,961 (Jul. 5, 2011). In addition, information about this pathway is available in the SE guidance documents referred to above.

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[9] *See* Section 905(j) Reports: Demonstrating Substantial Equivalence for Tobacco Products (Jan. 2011), available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/section-905j-reports-demonstrating-substantial-equivalence-tobacco-products. FDA has also issued another Guidance, Demonstrating the Substantial Equivalence of a New Tobacco Product: Responses to Frequently Asked Questions, most recently revised in December 2016 (available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/demonstrating-substantial-equivalence-new-tobacco-product-responses-frequently-asked-questions).

[10] *See Content and Format of Substantial Equivalence Reports; Food and Drug Administration Actions on Substantial Equivalence Reports*, 84 Fed. Reg. 12740 (Apr. 2, 2019).

[11] *See* https://www.fda.gov/tobacco-products/substantial-equivalence/marketing-orders-se (Jan. 29, 2019 order for Black & Mild Shorts). SE orders are generally publicly available at the website above, but commercially confidential information must be redacted before posting. Three of the four SE orders referred to above have not yet been posted.

[12] *See* SE Exemption Order for John Middleton Co., Black & Mild (Sept. 7, 2018), *available at* https://www.fda.gov/tobacco-products/exemption-substantial-equivalence/marketing-orders-exemption-se.

d. Premarket Tobacco Application (PMTA). All other new tobacco products must be authorized through the PMTA pathway, which requires applicants to demonstrate that the new tobacco product is appropriate for the protection of the public health, which is determined with respect to the risks and benefits to the population as a whole, including users and non-users of tobacco products, and taking into account the increased or decreased likelihood that existing users of tobacco products will stop using such products, and those who currently do not use tobacco products will start using such products. 21 U.S.C. § 387j(b), (c). FDA issued a guidance specifically for ENDS products, which are likely to be reviewed through the PMTA pathway, on June 11, 2019 ("PMTAs for ENDS Guidance").[13] The PMTAs for ENDS Guidance is intended to assist applicants to prepare PMTAs for these products and explains, among other things, when a PMTA is required, general procedures for review of an ENDS PMTA, what information the FDCA requires applicants to submit in a PMTA, and what information FDA recommends applicants submit in an ENDS PMTA to show whether permitting such new tobacco product to be marketed is appropriate for the protection of the public health. In addition, FDA intends to issue a proposed rule in the near future to further specify application contents and FDA's review and communication procedures under this pathway.[14] As of April 30, 2019, FDA has received 401 PMTA applications, 373 of which are for deemed products. FDA has authorized the marketing of 12 total products

[13] *See* Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems Guidance for Industry (June 2019), *available at* https://www.fda.gov/regulatory-information/search-fda-guidance-documents/premarket-tobacco-product-applications-electronic-nicotine-delivery-systems-ends.
[14] *See* Premarket Tobacco Product Application and Recordkeeping Requirements, RIN: 0910-AH44, *available at* https://www.reginfo.gov/public/do/eAgendaViewRule?pubId=201904&RIN=0910-AH44.

under two different product types (non-combustible cigarettes and smokeless tobacco),[15] and closed out 369 of the 373 applications it has received for deemed products as insufficient to accept or file, primarily for failure to file an adequate environmental assessment, as required by 21 C.F.R. § 25.15. Only four PMTA applications are pending with the agency at this time for deemed products, none of them for an ENDS product. Thus far, FDA has provided information about the PMTA application process through public seminars and workshops,[16] and regularly meets with sponsors to discuss FDA's expectations for these applications.

6. By statute, all deemed products require marketing authorization unless they are grandfathered. No deemed products had authorization when the deeming rule went into effect. Thus, when the deeming rule took effect on August 8, 2016, all deemed products on the market were suddenly noncompliant with the statute. Accordingly, in the preamble to the deeming rule, FDA announced a compliance policy under which, as an exercise of enforcement discretion, it intended to defer enforcement of various provisions for limited periods of time to give manufacturers time to come into compliance. With respect to premarket review, for products that were on the market as of August 8, 2016, FDA provided staggered compliance dates for submission of applications depending on the type and complexity of the application; in addition, if an application was submitted within the compliance period, the preamble further stated that the agency did not intend to initiate enforcement for lack of a marketing order from FDA for one year after submission while FDA reviewed the application. *Id.* at 28,977-78. As explained in the preamble, this policy was based on balancing complex and competing public health and resource

[15] *See* Premarket Tobacco Product Marketing Orders, *available at* https://www.fda.gov/tobacco-products/premarket-tobacco-product-applications/premarket-tobacco-product-marketing-orders.
[16] *See* Useful Links for PMTA, *available at* https://www.fda.gov/media/101179/download (Oct. 17, 2016).

considerations, primarily that products would remain available without having undergone scientific review, concerns regarding the effect that flavors have on use of tobacco products by youth and young adults, the potential for some net public health benefits if flavored ENDS remain available, the different risks posed by different classes of products, the fact that some flavored combusted products are grandfathered, the expected complexity of applications, efficiently managing the flow of incoming applications, and encouraging high-quality applications. *Id.*

7. In July 2017, FDA announced a new comprehensive approach to tobacco and nicotine. The approach included many components, the centerpiece of which was developing a regulation aimed at reducing nicotine in cigarettes to minimally addictive or non-addictive levels. In a world where cigarettes were minimally addictive or non-addictive, access to alternative and less harmful forms of nicotine would be essential. Other components included advancing rules to lay out what needs to be in SE and PMTA applications; determining whether and how FDA should regulate youth-appealing flavors in ENDS and other tobacco products; and seeking new information that may inform consideration of the regulation of so-called premium cigars. As one part of this comprehensive public health package, where each component was intended to work alongside the others in striking an appropriate balance, FDA stated that it would further defer enforcement of the premarket review provision for deemed products to encourage development of innovative tobacco products that had the potential to be less dangerous than cigarettes and to provide manufacturers additional time to develop higher quality applications informed by additional guidance and rules and products standards from the agency.

8. On August 8, 2017, FDA issued a revised guidance extending the compliance dates for the submission of premarket review applications for deemed products until August 8,

2021, for combustible new tobacco products (including cigars) and until August 8, 2022, for noncombustible new tobacco products (including most ENDS products)—but only for products that were on the market as of August 8, 2016. *See* Guidance for Industry: Extension of Certain Tobacco Product Compliance Deadlines Related to the Final Deeming Rule (Aug. 2017) ("Guidance"). The Guidance also indicated that FDA expected that these products would remain on the market while their premarket applications were under review (or were withdrawn).

9. In the summer of 2018, data from the annual National Youth Tobacco Survey showed a significant increase in youth use of ENDS products. This followed two years of a reduction or leveling off in youth ENDS prevalence rates. These data prompted FDA to consider revising the compliance policy for premarket review set forth in the Guidance. On March 13, 2019, FDA issued a draft guidance proposing to modify that compliance policy.[17] This new draft guidance reiterated that all deemed products without a marketing order (except "grandfathered" products on the market as of February 15, 2007) were on the market in violation of the statute and therefore potentially subject to enforcement. It outlined FDA's enforcement priorities to help address youth use, particularly youth use of certain flavored products. The draft guidance reflects a careful rebalancing of public health considerations based on new information. It revises the prior deferred-enforcement policy with respect to broad categories of e-cigarette and cigar products, and proposes prioritizing enforcement of the premarket review provisions against: e-cigarette products targeted to minors or likely to promote use by minors; flavored e-cigarette products (except tobacco, mint, and menthol flavors) offered for sale in ways that pose heightened risks of youth access; flavored e-cigarette products (except tobacco, mint, and menthol flavors) offered for domestic sale after August 8, 2021, for which the manufacturer has

[17] *See* Modifications to Compliance Policy for Certain Deemed Tobacco Products, Draft Guidance (Mar. 2019) at 5, *available at* https://www.fda.gov/media/121384/download.

not submitted a premarket application; and flavored cigars. Evidence shows that tobacco, mint and menthol flavors are preferred more by adults than minors, and in the draft guidance FDA noted it is concerned by the potential that adult former smokers who switched to ENDS could be at risk of migrating back to combustible products if there were an abrupt market exit of ENDS.[18]

Remedies

10. FDA has continued to invest significant resources into addressing the recent surge in youth ENDS use and developing the draft March 2019 guidance, and is committed to finalizing the guidance within 120 days. FDA has thus far received over 15,000 comments on the draft guidance and has reviewed the more substantial comments. FDA expects to complete consideration of the comments, draft the final guidance, and publish it on this highly accelerated 120-day timeframe.

11. The general framework of the March 2019 guidance, when finalized, would allow FDA to strike an appropriate balance of complex and competing public health and agency resource considerations, including addressing the rapid rise in youth use of ENDS versus the availability of potentially less harmful products for currently addicted adult users of combustible products. I believe that finalizing this guidance – which focuses on restricting youth access to flavored ENDS products – is one of the most critical public health steps that FDA can take to curb youth vaping.

12. I understand that plaintiffs seek a remedy that would order FDA "to ensure that no new tobacco product" that was subject to the Guidance's extended compliance dates "may

[18] *See* Schneller, L.M., M. Bansal-Travers, M.L. Goniewicz, et al., "Use of flavored electronic cigarette refill liquids among adults and youth in the US—Results from Wave 2 of the Population Assessment of Tobacco and Health Study (2014-2015)," *PLoS ONE* 13(8): e0202744 (2018), available at: https://doi.org/10.1371/journal.pone.0202744; Harrell, M.B., Weaver, S. R., Loukas, A., et al., "Flavored e-cigarette use: Characterizing youth, young adult, and adult users. *Preventive Medicine Reports*, 5, 33-40, (2017), doi: 10.1016/j.pmedr.2016.11.001.

remain on the market without being subject to FDA enforcement action" unless an application for premarket review has been received within 120 days of a remedial order from the Court. It is my firm belief that plaintiffs' proposed 120-day submission deadline creates a genuine risk of migration from potentially less harmful ENDS products back to combustible tobacco products within the population of addicted adult smokers who have completely switched to ENDS. This is a public health outcome that should be avoided if at all possible, while still achieving the public health benefits of earlier premarket review for deemed products, especially with respect to curtailing youth use.

13. If the Court nevertheless finds it necessary to enter an injunction requiring the submission of premarket applications by a date certain, it should not set a deadline sooner than 10 months from now—a date that I believe would at least make it feasible for more manufacturers to develop and submit complete and high quality applications, and for FDA to publish a proposed PMTA rule and be close to finalizing the SE and PMTA rules. It would also enable ENDS manufacturers to consider and strengthen their applications based on the final PMTA for ENDS guidance. Similarly, if the Court enters an injunction limiting the compliance period for products with timely premarket applications on file to one year, as Plaintiffs also request, it should not disturb the FDA's discretion to defer enforcement on a case-by-case basis with respect to applicants who have provided the needed information and made substantial progress toward completion, as was the case under the original compliance policy. *See* 81 Fed. Reg. at 29,012.

14. This approach, although not as accelerated as Plaintiffs' proposal, would better protect the public health. Products lacking an application after 10 months would be subject to enforcement, as would products lacking an authorization after a one-year review period.

Critically, in the interim, all deemed new products would be subject to enforcement in accordance with the priorities set forth in the March 2019 draft guidance, when finalized, even before the 10-month submission and one-year review time periods elapse.

15. Plaintiffs' proposed remedy, by contrast, would cause significant public health concerns, as well as implementation challenges. First and foremost, from the public health perspective, Plaintiffs seek to clear the market of any new and unauthorized deemed products for which no application is submitted within 120 days. Given the nearness of that deadline and the very limited number of companies (fewer than 10) that have sought pre-submission meetings with FDA to discuss potential premarket applications for ENDS products, I believe that, if plaintiffs' proposed remedy were granted, it is likely that there would be a mass market exit of ENDS products. For cigarette smokers who completely switch to ENDS, these products may be less harmful at an individual level than combustible tobacco products. It is possible some of these products may have a net positive effect on public health at a population level, depending on several factors, including patterns of use. Overall population level impact remains uncertain today, especially given youth uptake of ENDS. We do not yet know the general public health impact of these products, but it is likely that some ENDS products may reduce harm at the individual level and that some addicted adult smokers use these products with a goal to end use of combustible tobacco products. Given this, mass market exit of such products would limit the availability of a potentially less harmful alternative for adult smokers seeking to transition or stay away from combustible tobacco products. Dramatically and precipitously reducing availability of these products could present a serious risk that adults, especially former smokers, who currently use ENDS products and are addicted to nicotine would migrate to combustible tobacco products, even if particular ENDS products ultimately receive marketing authorization and return

to the market later. And, although there has been great recent progress in declining use of cigarettes for all age groups, I am concerned that these declines could be slowed or reversed in the case of very sudden and very dramatic reductions in availability.

16. Second, there are important programmatic and logistical considerations. Of course, manufacturers may submit premarket applications for these products at any time, and there is no legal barrier to filing. Indeed, CTP has accepted, filed and authorized applications through each of the available pathways based on statutory criteria even in the absence of rules or product-specific guidance. However, I am concerned that many ENDS manufacturers will be unlikely to submit quality PMTA applications (*e.g.*, applications that are sufficiently complete and organized to enable CTP to efficiently conduct the required scientific review) for deemed products within a 120-day period. Instead, a longer period of time (10 months) would be appropriate to help ensure that manufacturers are better able to prepare quality submissions. Their efforts will be aided by FDA's publication of the PMTAs for ENDS Guidance, which provides important recommendations to help this newly regulated segment of industry develop their applications. Most significantly, that guidance describes the types of information required by the statute for submission in a PMTA, provides recommendations for how to address specific public health concerns, and suggests ways to demonstrate that a product is appropriate for the protection of public health. I am concerned that 120 days is an insufficient amount of time to permit some manufacturers to consider and implement the recommendations in the guidance.

17. In addition, there will also be logistical impediments for CTP to receive and review large numbers of applications without being able to meaningfully prioritize among them. The Final Regulatory Impact Analysis (RIA) from 2016 estimates that manufacturers will apply for marketing authorization for 5,424 to 6,764 deemed products (of all types) in the initial

compliance period (two years). AR 23,995 (RIA at 84). Of these, an estimated 1,250 to 2,000 would be PMTAs for e-liquids, as well as 360-450 for ENDS delivery devices. *Id.* These numbers are based on estimates in the context of significant uncertainty, and it is possible that manufacturers will seek premarket authorization for many more products, particularly if the products' continued marketing is contingent on the filing of an application. One concern here is that low-quality applications, many of which could be time-consuming to review due to their poor quality, will be submitted merely to prolong marketing.

18. For ENDS PMTAs, these are first-ever applications for a previously novel and unregulated category of products. Thousands of these applications are expected to be submitted very close in time. This expectation is based on the dynamics of the deadline coming earlier than many applicants previously anticipated. It is also informed by our experience with provisional SE applications, as discussed below. Many applicants will be newly regulated entities lacking experience with FDA, and based on our experience to date, the applications are anticipated to be lower in quality and less complete than current-day applications for other FDA regulated products. A large volume of incomplete or haphazard applications in which the information is not clearly presented or is missing data will cause further delay because it will divert valuable agency resources into the painstaking effort of reviewing those submissions and communicating deficiencies. In addition, there may be technological challenges to accepting and processing large applications if they come in all at once, especially if the deadline were as soon as 120 days after a court order, allowing FDA less time to continue preparations.

19. For comparison, in 2011, at a parallel point in time with a submission deadline approaching, approximately 3,000 of 3,600 provisional SE applications were submitted within

the last several days leading up to a March 22, 2011 deadline.[19] While FDA has put many more systems in place since then, and has created a robust application review process within CTP's Office of Science, there is no doubt that the agency will be flooded with applications in the final days leading up to any court-ordered submission deadline. I expect that FDA will receive roughly 5,424 to 6,764 applications for three different authorization pathways. This will undoubtedly put a strain on the agency. Additional time to file applications would provide more planning time for FDA and applicants, more time to build out operational systems, and more time to issue guidance and rules to reduce the volume of low-quality applications.

20. Most ENDS products are relatively novel and are unlikely to be substantially equivalent to a valid predicate and so will need to be authorized through the PMTA pathway. Among other things, a PMTA application must include:

a. Full reports of all information concerning investigations which have been made to show the health risks of the new tobacco product and whether such product presents less risk than other tobacco products;

b. Full statement of the components, ingredients, additives, and properties, and of the principle(s) of operation of the new tobacco product; and

c. Full description of the methods used in, and the facilities and controls used for, the manufacture, processing, packing and installation of the new tobacco product.

21. In addition, some applications may need new nonclinical and clinical studies if the product's potential impact on the public health has not yet been sufficiently reviewed, though in some cases it may be possible to support a marketing order for an ENDS product without

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

conducting new nonclinical or clinical studies. For example, if there is an established body of evidence regarding the health impact (individual or population) of a product or a similar product that can be adequately bridged to product that is the subject of the application, such as data from the published literature or government-sponsored databases, these data may be sufficient to support a PMTA.

22. Plaintiffs' proposed 120-day deadline for the submission of premarket applications does not account for the sheer number of expected applications, the complexity of those applications and the scientific review process, or the public health and operational concerns I have described. I believe that a submission deadline at least 10 months away would reflect a much better balancing of the competing concerns and, though still accelerated, would at least reduce the potential for administrative disruption and the risk of a mass market exit that could adversely affect the public health.

I declare under penalty of perjury that the foregoing is true and correct to the best of my information, knowledge, and belief.

Dated: Silver Spring, Maryland

June 12, 2019

Mitchell Zeller -S

Digitally signed by Mitchell Zeller -S
Date: 2019.06.12 23:08:03 -04'00'

Mitchell Zeller
Director, Center for Tobacco Products
United States Food and Drug Administration