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December 12, 2022

VIA CM/ECF

Office of the Clerk
United States Court of Appeals for the Third Circuit
21400 U.S. Courthouse
601 Market Street
Philadelphia, PA 19106

Re: Logic Technology Development LLC v. U.S. Food & Drug Administration
No. 22-3030

Dear Clerk:

Under FRAP 28(j), Petitioner Logic Technology Development LLC ("Logic") submits as supplemental authorities two memoranda from FDA's Center for Tobacco Products ("CTP"), that are part of the Administrative Record in this matter, but which FDA only made available to Logic on December 6, 2022, after the close of the stay briefing.

These new documents reveal the extraordinary fact that CTP's Office of Science ("OS") reversed its science-based recommendation to issue marketing granted orders for Logic's premarket tobacco product applications ("PMTAs") for its menthol-flavored electronic nicotine delivery systems ("ENDS") after receiving pressure from the new CTP Director and his office, the Office of Center Director ("OCD"). In the first memorandum (Ex.A), OS explains that it evaluated Logic's PMTAs, including its product-specific evidence, and concluded that authorization of the marketing of Logic's menthol-flavored ENDS was appropriate. Ex.A at 2. OS changed course only after the new CTP Director and OCD, to whom OS reports, concluded that menthol-flavored ENDS should be treated as a disfavored product category. Ex.A at 2–3. The second memorandum (Ex.B) reiterates the same policy shift, Ex.B at 3, and suggests that meetings were held to address the concerns of OS staff regarding the propriety of this decision-making process, Ex.B at 4, including concerns that the new approach would eliminate all non-tobacco-flavored ENDS, *see* Ex.B at 3 n.3.

These memoranda further support Logic's argument that FDA denied Logic's PMTAs for its menthol ENDS pursuant to an unpromulgated policy against the product category, not an evaluation of Logic's product-specific evidence. Dkt.8 at 14–21. That is, under new leadership,

OCD overruled OS's initial recommendations to approve Logic's products—recommendations that OS had based upon its science-based evaluation of Logic's submission—because OCD concluded that *all* menthol-flavored ENDS should be treated disfavorably, as a category. As Logic has explained, basing product-specific decisions on unpromulgated, across-the-board policies that were never subject to notice-and-comment rulemaking is arbitrary and capricious, in violation of the APA. *See* Dkt.8 at 14–21. This further demonstrates that Logic has shown a sufficient likelihood of success on the merits, entitling it to a stay. Dkt.30 at 7.

Sincerely,

/s/Misha Tseytlin
Misha Tseytlin

CC: All counsel of record (via CM/ECF)

Memorandum to File

Date: October 25, 2022

From: Benjamin Apelberg, Ph.D.
Deputy Director
Office of Science, Center for Tobacco Products

Digitally signed by Benjamin Apelberg -S
Date: 2022.10.25 15:51:01 -04'00'

Todd L. Cecil, Ph.D.
Acting Director
Office of Science, Center for Tobacco Products

Todd L. Cecil -S Digitally signed by Todd L. Cecil -S
Date: 2022.10.25 15:54:00 -04'00'

Subject: Development of the Approach to Evaluating Menthol-Flavored ENDS PMTAs

Introduction

The Director of the Office of Science (OS), Center for Tobacco Products (CTP), is among the CTP officials authorized to issue orders on pre-market tobacco product applications (PMTAs), and OS has been charged by the CTP Director with reviewing such applications. This memo describes how OS's thinking on the analytical approach to applications for menthol-flavored electronic nicotine delivery systems (ENDS) developed over time, taking into consideration, in particular, the peer-reviewed scientific literature related to menthol-flavored ENDS, regulatory policy, and discussions with CTP's Office of the Center Director (OCD).

Background

Just prior to September 9, 2020, CTP received more than 6.5 million PMTAs for ENDS products. In the year that followed, CTP conducted premarket review of the applications, analyzed existing scientific evidence, and issued deficiency letters for certain applications. In August 2021, OS began issuing marketing denial orders on certain PMTAs for ENDS with flavors other than tobacco or menthol, deferring decisions on menthol products to allow more time to consider whether there were any aspects unique to menthol-flavored ENDS that would affect the assessment of whether authorizing the marketing of such products would be appropriate for the protection of the public health (APPH). Specifically, OS needed more time to assess whether and to what extent any evidence in the peer-reviewed scientific literature might, in concert with evidence provided in specific product applications, support a finding of benefit from menthol-flavored ENDS for adult menthol-flavored cigarette smokers sufficient to outweigh the risk to youth from the marketing of such a product.

In considering this issue, OS conducted a thorough review of the scientific literature regarding menthol-flavored cigarette smokers and menthol-flavored ENDS use to determine whether it established that menthol-flavored ENDS provide a sufficient benefit for adult smokers relative to that of tobacco-flavored ENDS. OS concluded that the existing literature supports that menthol-flavored cigarette smokers show a preference for menthol-flavored ENDS relative to tobacco-flavored ENDS. But OS did not find that the current literature supports that use of menthol-flavored ENDS by adult smokers is associated with greater likelihood of complete switching or significant cigarette reduction relative to

tobacco-flavored ENDS. OS considered these findings from the literature together with product-specific evidence to assess the public health impact of particular menthol-flavored ENDS products.

Logic menthol-flavored ENDS PMTA

From late 2021 to August 2022, OS work related to menthol-flavored ENDS focused on the Logic menthol-flavored ENDS PMTA because, among other reasons, it was one of the applications for menthol-flavored ENDS furthest along in review. In the latter half of 2021, OS briefed OCD on its evaluation of the Logic menthol PMTA and OS's preliminary recommendation to authorize the marketing of the products. This briefing focused in particular on whether the differential preference for menthol-flavored ENDS among menthol-flavored cigarette smokers documented in the peer-reviewed literature could provide evidence to support a sufficient potential benefit for adult smokers.[a]

From a policy perspective, OS believed at the time that as long as menthol-flavored cigarettes remain on the market, menthol-flavored ENDS could be a direct substitute for them, providing a less harmful alternative for menthol-flavored cigarette smokers, who are less likely to successfully quit smoking than smokers of non-menthol-flavored cigarettes.[b] OS acknowledged that menthol-flavored ENDS appeal to youth but suggested the appeal may not be at the same level as some other flavors (e.g., fruit-flavored ENDS). Accordingly, at the time, OS considered the documented preference for menthol-flavored ENDS among adult menthol-flavored cigarette smokers to suggest a potential benefit: that menthol-flavored cigarette smokers would be more likely to try menthol-flavored ENDS (relative to tobacco-flavored ENDS), creating an opportunity for some to use menthol ENDS and ultimately transition away from combustible cigarettes. OS considered that this suggested potential benefit, in the form of increased opportunity for use and transition, coupled with product-specific evidence of some benefit to smokers (even if not greater than that of tobacco-flavored ENDS products), amounted to a likelihood of greater cessation or significant reduction in smoking that would outweigh the known risks to youth from the marketing of the products, sufficient to meet the legal standard for authorization. OCD raised questions about OS's recommendation, including questions about the role and sufficiency of the general scientific literature on adult menthol smokers' differential preference for menthol ENDS in demonstrating likely behavioral change, and underscored its concerns about the substantial appeal of menthol to youth. Given the importance of the Logic menthol-flavored ENDS PMTA decision in establishing a precedent for CTP's approach to assessing APPH for menthol-flavored ENDS, discussions of whether the available evidence supported a potential benefit to adult smokers continued over the course of several months into 2022.

A decision was still pending for the Logic PMTA in July 2022, when CTP transitioned to a new Center Director.[c] In mid-July 2022, OS conferred with the new Center Director and members of OCD about menthol-flavored ENDS and the Logic menthol-flavored ENDS PMTA. OS shared its views with the new

[a] On the question of potential benefit and Logic's PMTA, OS did not consider the differential preference for menthol ENDS in the literature in isolation, but instead in combination with Logic's product-specific evidence of significant reduction in cigarettes smoked per day. However, Logic's evidence did not include a statistical comparison between menthol-flavored ENDS and tobacco-flavored ENDS and all cohorts in Logic's studies reduced cigarettes smoked per day to a similar degree. The evidence therefore did not demonstrate a sufficient benefit from menthol-flavored ENDS use relative to tobacco-flavored ENDS use.
[b] See, for example, Mills et al., 2021. "The Relationship Between Menthol Cigarette Use, Smoking Cessation, and Relapse: Findings From Waves 1 to 4 of the Population Assessment of Tobacco and Health Study." Nicotine Tob Res. 23(6):966-975.
[c] Prior to the start date of the new Center Director, then-OS Director Matthew Holman recused himself from all OS duties as he sought employment outside of FDA. In his absence, the authors of this memo were asked to fill his role until he either returned or left the organization. In late July 2022, Dr. Holman left for employment in the private sector at Philip Morris International.

Center Director and engaged in an open discussion on topics including the general body of literature, Logic's clinical studies, risks to youth, and potential postmarketing requirements. After that meeting, the OCD Senior Science Advisor shared OCD's views with OS, articulating that, in light of the substantial risk to youth and the lack of robust evidence of actual differential use to quit or significantly reduce cigarettes per day, the approach to menthol-flavored ENDS should be the same as for other flavored ENDS, i.e., the products could be found to be APPH only if the evidence showed that the benefits of the menthol-flavored ENDS were greater than tobacco-flavored ENDS, which pose lower risk to youth.

OS, on its own initiative, then reassessed and decided it was reasonable and consistent to treat menthol-flavored ENDS PMTAs in the same way as other non-tobacco-flavored ENDS PMTAs regarding the evidence needed to show a potential benefit to adult smokers. Regarding youth risk, OS had already determined that menthol-flavored ENDS pose a substantial risk of youth use greater than tobacco-flavored ENDS and similar to flavors such as candy, desserts, sweets, and mint.[d] Accordingly, and based on new awareness and understanding of the OCD position by OS leadership at that time, OS determined it was scientifically appropriate and consistent to adopt the approach applied to other non-tobacco-flavored ENDS, which present a similar risk to youth. In particular, OS concluded that the literature did not demonstrate that menthol-flavored ENDS were differentially effective, relative to tobacco-flavored ENDS, in terms of promoting significant cigarette reduction or complete switching among adult smokers, and that it was scientifically appropriate to expect applicants to provide robust, product-specific evidence showing that their menthol-flavored products facilitate complete switching or significant reduction in smoking (behavior change) among adults greater than that facilitated by tobacco-flavored ENDS, which pose less risk to youth. See, e.g., Logic Menthol Technical Project Lead Review, Section 1.1. OS staff then applied this approach to the Logic application, as they will to other pending applications for menthol-flavored ENDS.

[d] For example, in the 2022 National Youth Tobacco Survey, 85.5% of high school and 81.5% of middle school ENDS users reported using non-tobacco-flavored ENDS, and the most commonly used flavor type was fruit (69.1%), followed by candy, desserts, and other sweets (38.3%), mint (29.4%), and menthol (26.6%). Cooper M, Park-Lee E, Ren C, Cornelius M, Jamal A, Cullen KA. Notes from the Field: E-cigarette Use Among Middle and High School Students - United States, 2022. MMWR Morb Mortal Wkly Rep. 2022;71(40):1283-1285.

Memorandum to File

Date: October 25, 2022

From: Brian A. King, PhD, MPH
Director, Center for Tobacco Products

Brian King Digitally signed by Brian King Date: 2022.10.25 18:23:33 -04'00'

Michele Mital
Deputy Director, Center for Tobacco Products

Michele Mital -S Digitally signed by Michele Mital -S Date: 2022.10.25 18:29:05 -04'00'

Subject: Process for Evaluating Menthol-Flavored ENDS PMTAs

Introduction

This memo summarizes FDA's Center for Tobacco Products' (CTP's) history and process in developing an approach for evaluating pre-market tobacco product applications (PMTAs) for menthol-flavored electronic nicotine delivery systems (ENDS). Like many other questions of first impression that CTP has been required to decide, establishing a process and analytical framework for these applications has involved novel and complex questions that overlap matters of science, law, and policy. CTP has engaged in substantial discussion and debate over these questions, which has involved some disagreements. This memo discusses the relevant authority and processes that CTP followed in resolving these foundational questions and the steps taken by CTP's Office of the Center Director (OCD) to improve internal communications.

Background

Under the Federal Food, Drug, and Cosmetic Act (FD&C Act), authority is granted to the Secretary of Health and Human Services to regulate tobacco products, including issuing orders on PMTAs. Sections 901(a) and 910(c). This authority has been delegated to the Commissioner of Food and Drugs and redelegated, with respect to orders on PMTAs, to the Director of CTP and the Director of CTP's Office of Science (OS), among others.[1] The Director of OS reports to the Director of CTP.

Delegation does not entail the cessation of supervisory oversight. The normal and historical practice at FDA is that supervisory oversight occurs even when authority has been delegated to subordinate officials. See, e.g., 21 CFR 10.75(a) ("A decision of an FDA employee, other than the Commissioner, on a matter, is subject to review by the employee's supervisor under the following circumstances: (1) At the request of the employee; (2) On the initiative of the supervisor; (3) At the request of an interested person outside the [A]gency; (4) As required by delegations of authority."). At each level of decision-making, a staff member reports to their supervisor, who in turn reports to their supervisor, on up the chain. As part of this reporting relationship, supervisors routinely discuss matters that are under review with their subordinates, and they, in turn, keep their supervisors informed about those matters. For many decisions, discussions can reach well above the level of delegated authority. The more significant

[1] See FDA Staff Manual Guides (SMG), Vol. II – Delegations of Authority, SMG 1410.10 (Aug. 26, 2016), available at https://www.fda.gov/media/81983/download; SMG 1410.1103 (Apr. 27, 2017), available at https://www.fda.gov/media/83160/download; see also FD&C Act, Section 1003(d)(2) (the Secretary executes the Act "through the Commissioner").

or noteworthy the matter, by reason of science, policy, law, or level of public interest, the more likely such discussions will occur up the supervisory chain.

This type of collaboration has been routinely employed in CTP's decisions on matters of first impression, which have arisen frequently given the newness of CTP's authorities. The Family Smoking Prevention and Tobacco Control Act (TCA), enacted on June 22, 2009, granted FDA new authority to regulate the manufacture, marketing, and distribution of tobacco products. ENDS products were included as part of FDA's tobacco authority beginning in 2016.[2] As relevant here, Section 910 of the FD&C Act requires that, for a new tobacco product to receive a PMTA marketing authorization, FDA must conclude, among other things, that permitting the product to be marketed would be appropriate for the protection of the public health (APPH). Section 910(c)(2)(A). The statute specifies that, in assessing APPH, FDA must consider the risks and benefits to the population as a whole, including both tobacco users and nonusers, taking into account the increased or decreased likelihood that existing users of tobacco products will stop using such products and the increased or decreased likelihood that those who do not use tobacco products will start using such products. Section 910(c)(4). Determining how best to implement these requirements into concrete processes, principles, and considerations involved interrelated questions of science, law, and policy, as well as questions of administrative process, that required extensive thought and discussion.

Accordingly, when such complex questions arise, it is not the role of OS to decide those questions independently from other parts of CTP and FDA. Instead, OS regularly presents its initial findings and conclusions to other senior leaders, including the Center Director, Deputy Director, Senior Science Advisor, and other members of OCD's Senior Leadership Team (SL), as well as other Office Directors within CTP. Consistent with processes used for other Centers across FDA, CTP also consults closely with the Office of the Chief Counsel and others within the Office of the Commissioner on these foundational questions. These types of deliberations stretch back to the very first days of product review under the TCA, including consideration of applications submitted through a variety of pathways, such as new products that manufacturers claim are substantially equivalent to products on the market, products to be marketed as modified risk, and applications for premarket authorization of new versions of cigarettes or smokeless tobacco. The questions involved in developing the framework under each pathway often involve significant discussion and debate, which at times have included disagreements.

In fact, FDA regulations recognize that, in the normal course of making regulatory decisions within the hierarchical structure typical of federal agencies, there will sometimes be "significant controversies" and "differences of opinion" in the recommended outcome on a particular matter. 21 CFR 10.70(b)(2)(i). The regulations provide an opportunity for an employee to record their "individual views," regardless of whether that recommendation is ultimately followed in the Agency's final decision. See 21 CFR 10.70(b)(2)(ii).

[2] "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 FR 28973 (May 10, 2016).

Discussion

Over the past two years, FDA has engaged in in-depth deliberation on the agency's approach to deciding menthol-flavored ENDS PMTAs, following the same general processes and procedures that have been followed for other regulatory decisions, as described above. As noted in the memorandum to file from current OS leadership, Benjamin Apelberg, Ph.D. and Todd L. Cecil, Ph.D., on the subject of "Development of the Approach to Evaluating Menthol-Flavored ENDS PMTAs" (OS memo), OS chose to focus its work on the Logic menthol-flavored ENDS PMTA, and the agency's deliberations led to the approach laid out in the Technical Project Lead Review (TPL) for the Logic menthol-flavored ENDS PMTA.

During deliberations, it became clear that there was not agreement within CTP on the approach for evaluating menthol-flavored ENDS. OCD took steps to consider and address staff views and to ensure that the process for decisions on PMTAs was driven by the science. In July 2022, shortly after becoming CTP's Center Director, Brian King, a doctoral level scientist, conferred with OS and members of OCD about menthol-flavored ENDS and the Logic menthol-flavored ENDS PMTA.

As explained more fully in the OS memo, OS shared its views as held at that time with Dr. King and engaged in an open discussion on topics that included the general body of literature regarding menthol cigarette smokers and menthol-flavored ENDS use, Logic's clinical studies, risks to youth, and potential postmarketing requirements. After that meeting, the OCD Senior Science Advisor conveyed that Dr. King's position was the same as the previously held OCD position, articulating in particular that, in light of the risk to youth and the lack of robust evidence of actual differential use of menthol-flavored ENDS to quit or significantly reduce cigarettes per day, the approach to menthol-flavored ENDS should be the same as with other flavored ENDS with respect to the evidence of adult benefit. Subsequently, and upon its own initiative, OS reassessed OCD's approach and came to the conclusion that it was scientifically reasonable.

In reaching this conclusion, CTP leadership, supported by FDA leadership, has tried to maintain a balanced, appropriate, and science-driven focus. Among the views that CTP leadership considered are whether its evaluation of ENDS products places too much emphasis on the risks to youth from ENDS use, is not adequately bearing in mind the dangers from conventional smoking, and is pursuing the elimination of youth ENDS use without adequate regard to the impact on potential benefits to adult smokers.[3] CTP's review process has taken into account the magnitude and rigor of the data related to youth ENDS use, how CTP should consider these data in the context of available data related to complete cessation or significant reduction in cigarette smoking among adults, and the critical need to weigh evidence among both youth and adults in deciding whether to grant or deny marketing authorization under the statute. CTP leadership takes the view that a finding that marketing of a product is "appropriate for the protection of the public health" could be reached in spite of some amount of risk to youth, but only where the likely benefit to existing adult users would outweigh that risk. CTP leadership also recognizes that, consistent with the explicit goals of the TCA and extensive science on

[3] Another viewpoint that CTP considered was a concern that CTP's approach to evaluating ENDS applications will result in the removal of all ENDS from the U.S. market except for tobacco-flavored ENDS. This concern is based on an assumption that no applicant would ever submit evidence sufficient to support authorization of a non-tobacco flavored ENDS product, for example by conducting studies designed to assess the benefit of the applicant's non-tobacco-flavored ENDS over that of a tobacco-flavored ENDS and obtaining results that show such benefit.

the unique risks of tobacco use for youth, preventing youth initiation and subsequent tobacco product use must be a key consideration in the implementation of the law.

In the context of menthol-flavored ENDS, although there are published data showing that menthol combustible cigarette smokers indicate a preference for menthol-flavored ENDS products when asked about product appeal/preference, nationally representative data have not demonstrated that menthol combustible cigarette smokers are more likely to actually use menthol-flavored ENDS over tobacco-flavored ENDS to completely quit combustible cigarettes or significantly reduce their cigarette use. Studies that evaluate actual product use and behaviors in a real-world setting are more difficult to conduct, but current OS and OCD leadership agree that such data are much more robust evidence of potential benefit to adult smokers and that conducting such studies is feasible. In contrast, scientific evidence on the role of flavors in youth use of ENDS is significantly more rigorous and robust than the preference data concerning menthol combustible cigarette smokers: the evidence on flavors and youth ENDS use involves nationally representative and appropriately weighted populations and reports on actual use and behavior over time, and it reflects consistent patterns across the literature. In light of this evidence of risk to youth, FDA has reasonably concluded that robust evidence of benefit is required to overcome the risk to youth and show that authorizing the marketing of a menthol-flavored ENDS would be appropriate for the protection of the public health.

In light of these in-depth deliberations, OCD also asked CTP's Ombuds to provide an opportunity for OS staff who had direct involvement in menthol-flavored ENDS reviews to be heard regarding the Center's approach on menthol-flavored ENDS products. The CTP Ombuds Team invited the staff to share feedback, identify concerns, or offer insight related to the scientific review process, background, and direction relevant to menthol-flavored ENDS reviews in a voluntary, confidential, and non-pressured environment. Participants were informed the CTP Ombuds Team would provide a briefing to OS SL and OCD SL without identifying the staff who provided comments. The primary theme from these discussions, which the Ombuds Team shared with OCD SL and OS SL, was a desire for more transparency and communication by Center and OS leadership with OS staff.

Dr. King subsequently met with OS staff involved with menthol-flavored ENDS decisions in late September 2022 to provide additional clarity around the basis for the Center's approach on menthol-flavored ENDS products, including an explanation of the scientific analysis underlying the framework adopted. Dr. King also assured the staff that they will continue to be able to raise and resolve scientific disputes through established Center-wide policies. Although concerns were shared informally with the Ombuds Team, to date, neither the Ombuds Team nor the OCD SL has received a formal complaint or any requests for scientific dispute resolution related to this matter.

Throughout the decision-making process for ENDS applications, including for menthol-flavored ENDS products, CTP has followed the same general processes and procedures that have been followed for other regulatory decisions. The applications at issue involved complex questions of science, law, policy, and process that were matters of first impression. It was therefore appropriate for the discussions of these questions within CTP to include different supervisory levels within OS and CTP leadership, including OCD, before any application decisions were finalized. While the analysis and framework were deliberated, it was also appropriate that interim memos did not prematurely state final conclusions.

Differing scientific opinions are not unexpected within FDA, and FDA's regulations recognize that there will be differences of opinion in the course of regulatory decision-making. Discussions of such differences can lead to a more comprehensive consideration of all of the issues before the Agency reaches its ultimate conclusion, as has occurred here for menthol-flavored ENDS.