No. 21-13340

IN THE UNITED STATES COURT OF APPEALS
FOR THE ELEVENTH CIRCUIT

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BIDI VAPOR LLC,

*Petitioner*,

v.

U.S. FOOD AND DRUG ADMINISTRATION; JANET WOODCOCK, M.D., in her official capacity as Acting Commissioner of the FDA; and the U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES,

*Respondents.*

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On Petition for Review of a Final Marketing Denial Order Issued by the U.S. Food and Drug Administration Under the Federal Tobacco Control Act

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# PETITIONER BIDI VAPOR LLC'S MOTION FOR A STAY PENDING REVIEW

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**CERTIFICATE OF INTERESTED PERSONS AND CORPORATE DISCLOSURE STATEMENT**

Pursuant to Eleventh Circuit Rule 26.1-1, Petitioner hereby certifies that the following have an interest in the outcome of this petition for review:

Baker & Hostetler LLP (Counsel for Petitioner)

Becerra, Xavier (Secretary, U.S. Department of Health and Human Services)

Berry, Daniel J. (Acting General Counsel, U.S. Department of Health and Human Services)

Chowdhury, Azim (Counsel for Petitioner)

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United States Attorney's Office, Middle District of Florida

United States Department of Health & Human Services (Respondent)

United States Department of Justice

United States Food & Drug Administration (Respondent)

Vicente, Wendy (Senior Counsel, Office of the Chief Counsel, U.S. Food and Drug Administration)

Woodcock, Janet M.D. (Respondent)

Zeller, Mitch (Director, Center for Tobacco Products, U.S. Food and Drug Administration)

Pursuant to Federal Rule of Appellate Procedure 26.1 and Eleventh Circuit Rule 26.1-3, Petitioner certifies that none of the corporate entities listed above are public traded. Further, pursuant to Eleventh Circuit Rule 26.1-C,

Petitioner certifies that this Certificate of Interested Persons is complete and accurate at the time of filing.

*/s/ Eric P. Gotting*
Eric P. Gotting

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## INTRODUCTION

Over a decade ago, Congress struck a balance between ensuring adult smokers have access to tobacco products that are safer than traditional cigarettes while also protecting against underage use. Pub. L. No. 111-31, §§3(4), 3(7). Since then, Electronic Nicotine Delivery Systems ("ENDS"), commonly known as "e-cigarettes," have entered the marketplace, a product the National Academies of Sciences ("NAS") determined presents significantly less health risk than cigarettes.[1] The U.S. Food and Drug Administration ("FDA") agrees. It has repeatedly acknowledged that using e-cigarettes presents far less risk to individuals than cigarettes and switching to ENDS may significantly reduce harm.[2]

Petitioner Bidi Vapor LLC ("Bidi") was founded on this premise. Its mission is providing a safer alternative to smoking in the form of a closed-system device containing flavored e-liquid and providing effective nicotine delivery to the addicted smoker. At the same time, Bidi has gone to great lengths to prevent underage use. It has implemented extensive measures to

[1] NAS, *Public Health Consequences of E-Cigarettes*, at 7, https://tinyurl.com/mupy83j3.

[2] 81 Fed. Reg. 28976, 29035 (May 10, 2016).

ensure minors do not have access to these products. Indeed, research confirms Bidi's customers are primarily older adults who smoke.

Regrettably, recent actions by FDA have jeopardized Bidi's efforts. To keep selling products, Bidi was required to obtain retroactive marketing authorization from FDA. Under the applicable statute, it had to demonstrate these products are "appropriate for the protection of the public health" ("APPH"). Bidi spent over two years and $6.6 million dollars conducting surveys and studies comprising over 285,000 pages to make this showing. However, instead of doing a full scientific review of the application as required by law, FDA denied Bidi marketing authorization based on a mere box-checking exercise. Despite repeatedly instructing manufacturers, and Bidi explicitly, that no specific type of study would be required, FDA abruptly changed course. Without warning, FDA denied Bidi's applications, and over one million others, simply because they did not contain a discrete, long-term study that FDA had never indicated would be required. That study would involve comparing the potential cessation benefits of Bidi's non-tobacco flavored products to a tobacco-flavored product.

FDA's actions here were unlawful. It was arbitrary and capricious under the Administrative Procedure Act ("APA"), as well as *ultra vires*, for FDA not to conduct any scientific review of Bidi's applications. And FDA

violated due process and the APA by failing to provide fair notice of the long-term study requirement. Now Bidi has suffered millions of dollars in lost sales and good will, and will continue to do so, as product is removed from the marketplace. Accordingly, Bidi requests that this Court stay the marketing denial pending judicial review.

## BACKGROUND

### I. Tobacco Control Act And The Deeming Rule

In 2009, Congress enacted the Family Smoking Prevention and Tobacco Control Act ("TCA"), amending the Food, Drug and Cosmetic Act ("FDCA") to give the U.S. Food and Drug Administration ("FDA") authority over "tobacco products." 21 U.S.C. §387, *et seq.* On August 8, 2016, FDA's "Deeming Rule" went into effect, which applied the TCA for the first time to ENDS. 21 U.S.C. §387a(a); 81 Fed. Reg. 28,974 (May 10, 2016).

Consequently, ENDS were immediately subject to numerous TCA provisions, including a requirement that ENDS manufacturers obtain premarket authorization from FDA before selling their products. 21 U.S.C. §387j. A manufacturer must submit a Premarket Tobacco Product Application ("PMTA") which entails a time-consuming and costly process of compiling extensive scientific and technical data that FDA must review before deciding whether to grant marketing authorization.

## II. PMTA Filing Deadlines And Enforcement Discretion

Because the sudden retroactive application of the TCA's premarket requirements to ENDS would abruptly force them off the market, FDA established an enforcement policy permitting existing ENDS to remain on the market until PMTAs were due. The Deeming Rule established an August 8, 2018 deadline, and if a timely PMTA was filed, the product could remain on the market for up to a year pending FDA review. 81 Fed. Reg. at 28,978.

FDA changed the deadline several times in the following years, finally landing on August 8, 2021. A001-2; A003-5. Then, in response to a lawsuit filed by anti-ENDS groups, the federal district court in Maryland shortened the deadline to May 2020, which was extended to September 9, 2020 due to COVID-19. *Am. Academy of Pediatrics, et al. v. FDA*, 8:18-cv-00883-PWG (D. Md.) (Dkt. Nos. 127 & 182). Any ENDS subject to a timely filed PMTA could remain on the market until September 9, 2021 while FDA considered the application. *Id.*

Although FDA anticipated receiving 6,800 PMTAs (A007), applications covering 6.7 *million* products were filed. A009-10. Mitch Zeller, Director, FDA Center for Tobacco Products ("CTP"), stated in a February 2021 post that this overwhelming number would present "challenges" due to the "size, complexity and diversity" of the PMTAs. A032-33.

## III. APPH Standard For PMTAs Requires A Multi-Factor, Multi-Disciplinary Analysis

The TCA requires FDA to conduct a complex, science-based evaluation based on all contents in a PMTA to determine whether a product is "appropriate for the protection of the public health" ("APPH"). The TCA directs FDA to make that determination "with respect to 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." 21 U.S.C. §387j(c)(4) (emphasis added). Accordingly, FDA has repeatedly described APPH as a multi-factored and multi-disciplinary standard.

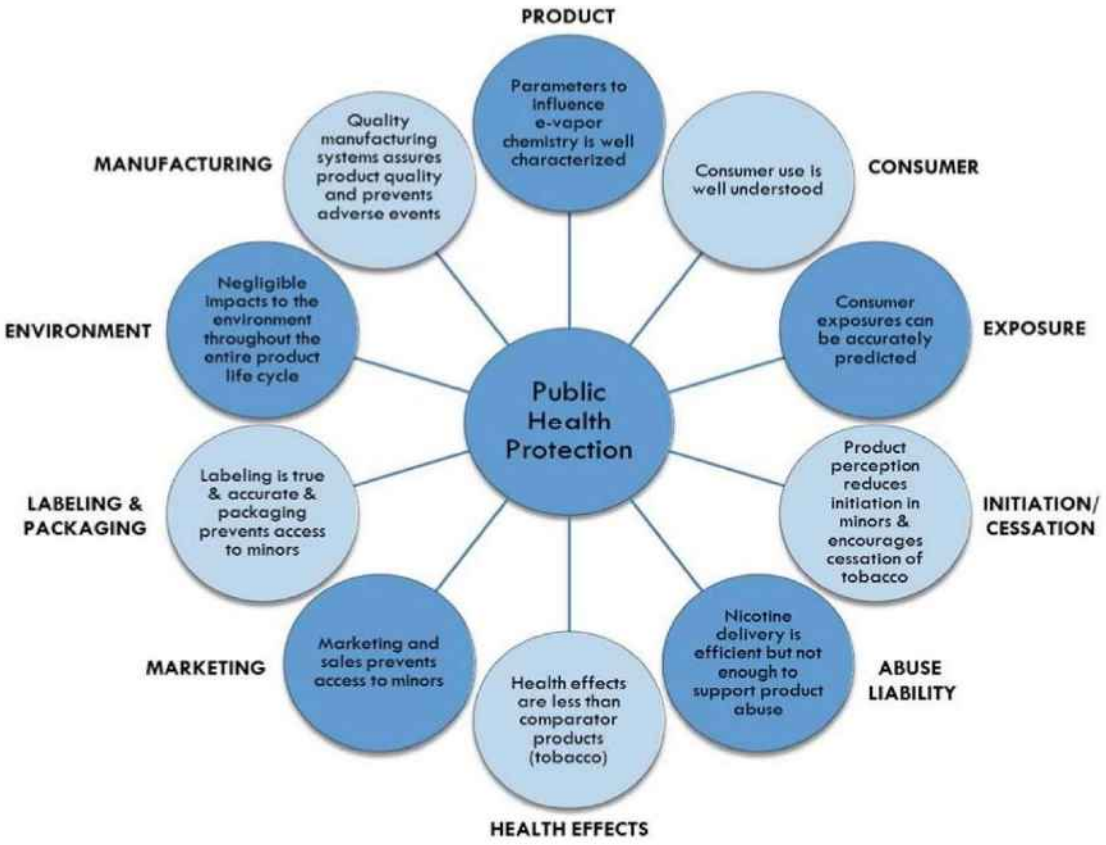
For instance, on October 5, 2021, FDA issued the PMTA Final Rule. 86 Fed. Reg. 55300 (Oct. 5, 2021).[3] FDA noted APPH involves a "complex determination," *id.* at 55335, that FDA "considers many factors," *id.* at 55314, and that FDA does not make a "determination on one static set of requirements," *id*. at 55385. FDA further declined "to assign weight to

[3] The pre-publication version was issued on January 19, 2021 at the end of President Trump's term. The Biden Administration halted publication in the Federal Register so it could review the rule and re-published it in virtually identical form on October 5, 2021.

different types of evidence," *id.,* emphasizing APPH "requires a balancing" of risks and benefits. *Id.* at 55384. FDA also refused "to create a series of criteria" that all products must meet for APPH, stated that an APPH "determination would involve consideration of many factors," and noted it "will be made with respect to…the population as a whole, rather than whether a product meets each item in a series of specific criteria." *Id.* at 55386. Indeed, FDA stated it would determine APPH "based on *all* of the contents of the application." *Id.* at 55320 (emphasis added).

Similarly, in June 2019, FDA issued final PMTA Guidance which also discussed APPH. A011-16. Specifically, FDA said it "weighs all of the potential benefits and risks from information contained in the PMTA" to make an APPH determination. A013. This would include specific restrictions on sale and distribution of a product that would decrease the likelihood of underage use. A013. Furthermore, during an October 2019 public meeting, FDA described reviewing a PMTA as a "[m]ulti-disciplinary approach," and characterized APPH by citing to numerous factors that must be considered (*e.g.*, health risks, marketing plans). A025-27. And Director Zeller noted the "complexity of those applications and the scientific review process" during the *Am. Academy of Pediatrics* litigation when asking the court to set a reasonable PMTA filing deadline. A008.

For the court's convenience, presented below is a diagram depicting the many APPH factors that FDA considers as part of a complete APPH analysis.

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## IV. No Requirement For Long-Term Studies

Before the September 9, 2020 filing deadline, FDA identified what forms of scientific evidence would (and would not) be required in a PMTA to demonstrate APPH. FDA made clear long-term studies would likely not be necessary. In the 2019 PMTA Guidance, FDA stated "in general, FDA does not expect that applicants will need to conduct long-term studies to support an application" and said it considers long term studies to last six months or

longer. A014. Instead, FDA suggested ENDS manufacturers could rely on other sources of information, such as "existing longer duration studies in published literature [on similar products]…and extrapolating from short-term studies." A014. FDA concluded "[a]though randomized clinical trials could address cessation behavior of users of tobacco products, FDA believes this would also be true for observational studies (perception, actual use, or both) examining cessation behaviors." A016.

Likewise, during an October 2018 public meeting, FDA advised that "[n]o specific studies are required for a PMTA; it may be possible to support a marketing order for an ENDS product without conducting new nonclinical or clinical studies given other data sources can support the PMTA." A021-22; *see* A028 (similar 2019 public statement). In fact, in the PMTA Final Rule, FDA again concluded that manufacturers would not be expected to conduct long-term clinical studies (lasting six months or longer). 86 Fed. Reg. 55387. At no time did FDA state, however, that a manufacturer must conduct the specific type of long-term study identified in the MDO, let alone indicate its absence would *automatically* result in marketing authorization denial.

## V. Bidi's PMTAs

The company that eventually became Bidi was founded in 2014 by Niraj Patel. A060. A former smoker who used ENDS to quit cigarettes, Mr. Patel

relied on his degrees in chemistry and pharmacology to develop a recreational, non-combustible alternative for adult smokers. A060. Bidi manufactures and sells 11 flavored, disposable ENDS (called the BIDI® Stick). A065. Mr. Patel turned to disposables because of their advantages over other ENDS types, including safety features and more consistent nicotine delivery needed for adult smokers to effectively move away from cigarettes. A063-65.

Bidi is vehemently opposed to all underage ENDS use and has implemented extensive youth prevention measures. It only distributes products to business partners who employ strict age-restriction protections, requires wholesalers and distributors to implement comprehensive age-verification procedures, does not employ online influencers or brand ambassadors, does not sponsor sporting or music events, does not market using kid-friendly imagery or messaging, and includes extensive age-related warnings on its products. A067-75.

Bidi filed its PMTAs on September 8, 2020 for its 11 BIDI® Sticks containing 285,000 pages of information, including toxicological data, marketing restrictions, and scientific literature reviews. It spent over two years assembling the applications and spent approximately $6.6 million. A083. However, the PMTAs did not include product-specific long-term studies given FDA's repeated representations that such studies would not be required to

demonstrate APPH. In fact, in response to a February 2020 meeting request by Bidi to discuss clinical testing requirements, FDA sent a letter explicitly stating there are no requirements "for applicants to conduct clinical studies or trials to support a PMTA" and there are no "specific requirements for evaluating comparator products." A056-57. Significantly, FDA never mentioned the type of study cited in the MDO. A089.

At FDA's request (due to COVID-19 related delays), Bidi has continued to supplement its applications with information critical to the APPH determination. Specifically, it has filed four amendments containing updated literature reviews, consumer surveys, and product perception and intention behavioral studies. Moreover, Bidi notified FDA that it is also conducting four additional behavioral studies and a clinical pharmacokinetic trial, the results of which will be submitted in the coming weeks. A084-86. Unfortunately, FDA did not wait. The MDO was issued on September 7, 2021. A034-35.

## VI. FDA's "Form" Marketing Denial Order

The MDO was not based on a scientific review of Bidi's PMTAs; rather, it was the product of a literal box-checking exercise that apparently took only a half-day to complete. A040-44. FDA rejected the PMTAs because they did not contain a single, highly-specific study designed to elicit one datapoint – *i.e.*, a randomized controlled trial ("RCT") and/or longitudinal cohort study

comparing the cessation benefits of Bidi's flavored e-liquids to a tobacco-flavored product. A034-35. Within a few hours, FDA staff concluded Bidi's application did not contain such a study and issued the MDO. A034-35; A040-44. Both the MDO and the checklists clearly state FDA did not review any other aspect of Bidi's 285,000-page PMTA. A035; A042.

This holds true even though the technical review document (called a "TPL") supporting the MDO repeatedly states that PMTAs require a full scientific review and that all data must be considered to determine whether a product is APPH. A047 (FDA will conduct a "science-based evaluation" to determine APPH); A048 (FDA required to "balance" benefits and risks of all users and nonusers "as a whole"); A050 (stating applications are evaluated in their "totality," including marketing plans); A049 (stating potential health risks are relevant and must be evaluated on a "case-by-case" basis, and that benefits to adult consumers must be considered using "behavioral" and "pharmacological" studies). In fact, except for FDA's discussion of RCT/longitudinal studies, the MDO and TPL do not mention any other aspect of Bidi's PMTA. Indeed, the TPL appears to be an almost identical, cookie-cutter version of an exemplar TPL published by FDA and issued to

other applicants covering millions of ENDS, thus evincing FDA's across-the-board, perfunctory review of the PMTAs.[4] A010.

Finally, leading up to the MDO, FDA told ENDS manufacturers that it would issue a single "deficiency letter" to an applicant giving the manufacturer a chance to correct any shortcomings in the PMTA. A015. But FDA abandoned that approach as the filing deadline neared, believing that applicants would not be able to conduct an RCT/longitudinal study within a short amount of time. A055.

The MDO concludes Bidi Vapor's products are misbranded and adulterated (*citing* 21 U.S.C. §§387b, 387c) and continued sale may result in civil penalties, seizure, and/or an injunction. A035; *see* 21 U.S.C. §§331, 333.

## LEGAL STANDARD

This Court has discretion to enter a stay of FDA's MDO pending judicial review. *See* 5 U.S.C. §705; 21 U.S.C. §387*l*(b). When considering whether to grant a stay, a court considers four factors: (1) whether petitioner has made a strong showing that it is likely to succeed on the merits; (2) whether petitioner will be irreparably injured absent a stay; (3) whether issuance of the stay will substantially injure the other parties interested in the

[4] FDA, Tobacco Products Marketing Orders: FDA Sample Decision Summary Document, https://www.fda.gov/media/152482/download.

proceeding; and (4) where the public interest lies. *LabMD, Inc. v. Fed. Trade Comm'n*, 678 Fed. App'x 816, 819 (11th Cir. 2016).

## ARGUMENT

### I. Bidi Is Likely To Succeed On The Merits

#### A. FDA's Box-Checking Review Of Bidi's PMTA Was Arbitrary And Capricious

FDA failed to take a "hard look" at Bidi's PMTAs and thus the MDO constitutes arbitrary and capricious decision-making. 5 U.S.C. §706(2)(A); *Sierra Club v. U.S. Army Corps Of Eng'rs*, 295 F.3d 1209, 1216 (11th Cir. 2002). Agency action must be overturned where it failed to rely on factors Congress intended to be evaluated or consider an important aspect of the problem. *Id.*; *Marquez-Martinez v. U.S. Attorney General*, 752 Fed. Appx. 832, 835 (11th Cir. 2018) (same). An "agency cannot ignore evidence that undercuts its judgment; and it may not minimize such evidence without adequate explanation." *Genuine Parts Co. v. EPA*, 890 F.3d 304, 312 (D.C. Cir. 2018); *see Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto Ins. Co.*, 463 U.S. 29, 43 (1983) (agency must examine relevant evidence and articulate a satisfactory explanation).

FDA has consistently stated that APPH determinations will be based on numerous factors rather than turning on a single issue or piece of evidence. Indeed, the TCA says as much. Congress directed FDA to consider the "risks and benefits to the population *as a whole*." 21 U.S.C. §387j(c)(4). This is all-

encompassing language demanding that more than cessation (*see* MDO) be evaluated. Likewise, FDA has described APPH expansively, at various times using terms like "complex," depicting it as a "multi-disciplinary" or "balancing" process, noting FDA must "consider[] many factors," and maintaining APPH is not limited to specific criteria. A033; A012-13; A018; A025-26; A008. As such, FDA instructed ENDS manufacturers to include a wide-range of data and information in their PMTAs that would support marketing authorization, such as aggressive youth prevention measures or evidence of relatively fewer health risks. A030; A023; A027.

But FDA disregarded this approach and instead issued the MDO without reviewing the 285,000 pages of data and other information contained in Bidi's PMTAs. A035; A042-43. Even though the TPL said FDA would conduct a "science-based evaluation," stated it must consider the "totality" of the applications, pledged to "balance" risks and benefits to users and non-users alike, and highlighted "behavioral" and "pharmacological" studies as being highly relevant, no such assessment occurred. A047; A049; A050.

Nowhere did FDA consider whether Bidi's own substantial youth prevention measures could tip the balance in favor of adult access. A067-73. Nor did FDA address survey data and behavioral studies showing BIDI® Sticks are not used by minors, but rather older adult smokers. A068. Also

going unreviewed were Bidi's scientific literature reviews, as well as aerosol and toxicological test results, demonstrating BIDI® Sticks present relatively lower health risks. A083. And FDA disregarded Bidi's PMTA amendments and written reminders that it would soon produce the results of four additional behavioral studies and a pharmacokinetic clinical trial showing that benefits to addicted smokers outweigh any risks of flavored ENDS to youth. A084-88. This hardly constitutes a "hard look"; rather it represents a wholesale failure to consider any submitted evidence relevant to APPH.[5] [6]

Finally, FDA never explains its about-face in the context of Bidi's PMTAs. APPH is clearly a relative concept. Each PMTA will have its strengths and weaknesses. But how each of those elements impacts the others and dictates the quantum of evidence that is needed cannot be known without evaluating an entire application. Indeed, in the TPL, FDA refers to the need for case-by-case analysis. A049-50; *see* 86 Fed. Reg. at 55390 (stating TCA requires "individualized determination"). And FDA further highlights the

[5] FDA also included a BIDI® Stick menthol-flavored product in the MDO after stating in the TPL that such flavors would be reviewed separately. A046; A088. This oversight is the height of arbitrary behavior and indicates that Bidi's materials received no more than a passing glance.

[6] FDA also completely ignored the risks of pulling over one million products off the market that adults, like those smokers who use Bidi products, rely on to move away from cigarettes. A0068; A0008 (FDA expressing concerns about public health implications stemming from a "mass exit" of ENDS).

relative nature of APPH when it says that as "known risks increase, so too does the burden of demonstrating a substantial enough benefit" (the opposite holds true as well). A048-49. But then FDA ignores its own advice.

Without reference to Bidi's PMTAs, FDA argues that experience with *other* PMTAs indicates a discrete type of RCT/longitudinal study is *always* needed. A050. It maintains that research *in general* demonstrates minors are primarily attracted to flavored products and age-prevention measures do not work. A050. FDA never grapples, however, with the specific information and data in Bidi's PMTAs and whether those, *taken as a whole*, might compel a different conclusion. A full scientific review might reveal relatively lower risks for BIDI® Sticks, thus dictating a lower overall burden of proof.

But no matter. FDA appeared more intent on finding a reason to deny PMTAs for non-tobacco flavored ENDS *en masse* rather than on their merits. Indeed, FDA's across-the-board issuance of virtually identical, cookie-cutter MDOs and TPLs belies any claims of reasoned decision-making here.

### B. FDA Failed To Give Fair Notice To Bidi Of The Long-Term Study Requirement

The MDO also violates due process and is arbitrary and capricious as FDA failed to give Bidi fair notice that its PMTAs would be denied if they did not contain the specified RCT/longitudinal study. "A fundamental principle

in our legal system is that [agencies]…must give fair notice of conduct that is…required." *FCC v. Fox Television Stations, Inc.*, 567 U.S. 239, 253 (2012) (citing due process). This principle applies to informal guidance and thus it is arbitrary and capricious for an agency not to state a regulatory interpretation with "ascertainable certainty" prior to the alleged unlawful conduct. *ExxonMobile Pipeline Co. v. U.S. Dep't of Transp.*, 867 F.3d 564, 578 (5th Cir. 2017); *Georgia Pacific Corp. v. OSHRC*, 25 F.3d 999, 1005-06 (11th Cir. 1994) (same). Through regulations and "other [agency] public statements," an entity should be able to discern what conduct is demanded for compliance. *General Elec. Co. v. EPA*, 53 F.3d 1324, 1329 (D.C. Cir. 1995).

FDA failed in this regard. Before the September 2020 filing deadline, in guidance intended to help ENDS manufacturers file complete PMTAs and during public meetings, FDA consistently stated that applicants could rely on scientific literature reviews and behavioral/perception studies to demonstrate APPH. It repeatedly maintained that "no specific studies" would be required to support a PMTA and that any form of long-term studies would likely be unnecessary. A021-22; *see supra*. Even after the MDO was issued, FDA maintained in the PMTA Final Rule that manufacturers would not be expected to conduct long-term studies lasting more than six months. 86 Fed. Reg. at 55387. At no juncture, however, did FDA warn the absence of an

RCT/longitudinal study comparing non-tobacco flavored e-liquids to tobacco-flavored products would be a deal-breaker.

Moreover, FDA's conduct here is particularly egregious given statements it made directly to Bidi. In February 2020, Bidi asked for a meeting with FDA to discuss what clinical studies would be required, including how it should compare its flavored ENDS to other tobacco products. A079-80. FDA declined to meet face-to-face. But in follow-up correspondence, FDA said there are no clinical study/trial requirements and no specific requirements for evaluating comparator products, and then said to "compare the health risks of your tobacco product to both products within the same category and subcategory, as well as products in different categories as appropriate." A057. FDA then referred Bidi to the 2019 PMTA guidance and 2019 public meeting for more information on comparator products, the very sources indicating long-term studies generally would not be needed. *Id.* Significantly, FDA never mentioned the key issue in this matter – *i.e.*, that an MDO would *automatically* issue if the specified long-term studies were not done.

Indeed, FDA's public statements characterize APPH as turning on a full scientific review of numerous factors, not just a single, discrete study. *See supra*. Unsurprisingly, Bidi in good faith embraced FDA's advice and submitted extensive PMTAs containing, among other evidence, the very types

of literature reviews, survey data, and perception/behavioral studies FDA said would support an APPH determination, but now suddenly maintains are completely irrelevant. A082-83; *see Encino Motorcars, LLC v. Navarro*, 136 S. Ct. 2117, 2126 (2016) (arbitrary and capricious not to consider reliance interests engendered by past representations); *Christopher v. SmithKline Beecham Corp.*, 567 U.S. 142, 156-57 (2012) (agencies should not change interpretations in adjudications where regulated entities have acted in "good-faith" reliance on prior statements). Bidi also reasonably assumed based on FDA's assurances that a deficiency letter would be issued if its PMTAs were missing any key information. A053. No deficiency was issued. A085; A090. FDA cannot now penalize Bidi for following years of guidance only to do a 180-degree turn and rely solely on a rudimentary, box-checking exercise.

### C. The MDO Is Ultra Vires

By refusing to conduct a full scientific review of Bidi's PMTAs, FDA also violated the TCA itself. 5 U.S.C. §§706(2)(A), (2)(C), (2)(D). Under the statute, once FDA receives an application, it must do more than a cursory evaluation. The TCA provides that a PMTA shall be denied if "*upon the basis of information submitted* to [FDA]…and any other information before [FDA]" the applicant has not demonstrated APPH. 21 U.S.C. §387j(c)(2) (emphasis added). The statute enumerates numerous forms of evidence that must be in

any PMTA, including data on health risks, ingredient and additive information, manufacturing practices, product samples, labeling specimens, and any other information required by FDA. 21 U.S.C. §387j(b)(1). It also defines APPH in broad terms with respect to "risks and benefits to the population *as a whole*," including "users and nonusers of tobacco products." 21 U.S.C. §387j(c)(2) (emphasis added).

It is clear, therefore, Congress intended that any APPH determination be based on a multi-faceted analysis weighing all data and information in a PMTA. FDA must consider not only underage nonusers and adult users, as the MDO does (although in an extremely narrow context), but also any other population demographics that might be impacted by an ENDS product. Moreover, FDA must gauge not only the relative cessation benefits to adults, which is the MDO's focus, but also all other benefits and risks of a given product, including relative health risks. Indeed, this is consistent with FDA's long-standing interpretation of APPH. Completely absent, however, is any hint Congress expected FDA to abandon all scientific review and instead deny an application (and, in fact, over one million applications) based on nothing more than the mere absence of a single study.

In Bidi's case, FDA formally accepted the PMTAs for scientific review on February 5, 2021. A058. As such, the applications previously cleared

several screening reviews to ensure they complied with various procedural and technical requirements. 21 C.F.R. §1105.10. Significantly, this also means FDA found the applications contained information sufficient to make an APPH determination (*e.g.*, published literature, bridging information, product health risk comparisons, abuse liability data, actual use data, data regarding the impacts of labeling on use behavior, etc.). *See* 21 C.F.R. §1114.27(b) (Final PMTA Rule). At this point, FDA was statutorily obligated to provide a full scientific review. It did not. *League of United Latin Am. Citizens v. Regan*, 996 F.3d 673, 691-96 (9th Cir. 2021) (failure of agency to fully consider citizen petition *ultra vires*).

## II. Bidi Faces Irreparable Harm Without A Stay

Agency orders that impose crippling financial burdens on regulated parties present a paradigmatic irreparable harm. Indeed, complying with regulatory action "later held invalid almost always produces the irreparable harm of nonrecoverable compliance costs." *Thunder Basin Coal Co. v. Reich*, 510 U.S. 200, 220–21 (1994) (Scalia, J., concurring in part and in the judgment). This is so because sovereign immunity precludes the injured party from recovering damages from the offending agency. *See Odebrecht Cont. Inc. v. Sec'y, Fla. Dep't of Transp*. 715 F.3d 1268, 1269 (11th Cir. 2013).

Bidi faces immense financial losses as a result of the MDO. A091-94. All told, Bidi has lost revenues of $57.2 million in returned orders and cancelled consignment as a result of the MDO, and projects to lose tens of millions of dollars more going-forward. *Id*. Further, Bidi must undertake additional controlled studies to support its PMTAs, potentially costing it millions more. A093.

Bidi's financial losses from which no "adequate compensatory or other corrective relief will be available at a later date, in the ordinary course of litigation" are irreparable harm. *Texas v.* EPA, 829 F.3d 405, 434 (5th Cir. 2016) (quoting *Meixchem Specialty Resins, Inc. v. EPA*, 787 F.3d 544, 555 (D.C. Cir. 2015)). And this irreparable harm warrants a stay.

But that's not all. Bidi has lost and will continue to lose customers, partners, and goodwill with its products off the market (A091-94), which this Court acknowledged as a standalone irreparable injury warranting preliminary injunctive relief in *BellSouth Telecommunications, Inc. v. MCI-Metro Access Transmission Services, LLC*, 425 F.3d 964, 970 (11th Cir. 2005). Its products have been deemed illegal and cannot be presently sold. Meanwhile, its most dominant competitors in the ENDS market have inexplicably been spared by FDA. A092. So long as Bidi is unable to sell its products, its partners and customers will turn to its competitors (or, worse yet, to counterfeit BIDI®

Sticks that pose health and safety risks) and a real possibility exists it will not be able to recapture them once FDA's illegal MDO is rescinded.[7] A091-94.

## III. A Stay Does Not Harm FDA And Serves The Public Interest

Issuing a stay pending judicial review of the MDO will harm neither FDA, nor the public interest.

FDA previously saw fit to defer resolution of PMTA's for ENDS products until at least 2022. And any concern expressed by FDA about protecting public health and safety in the abstract is undercut by the continued sale of the tens of thousands of ENDS products that remain on the market pending FDA's review of the relevant PMTAs. *See Smoking Everywhere, Inc. v.*

[7] Bidi recently submitted a request to FDA asking that the MDO be rescinded. On October 21, 2021, FDA sent an email to Bidi indicating that it would not bring any enforcement actions against the company as it reviewed the request. Then, on October 22, 2021, FDA issued an administrative stay pursuant to 21 C.F.R. §10.35 pending resolution of the request. A195. While Bidi appreciates FDA's response, it does not provide the relief sought in this motion. First, FDA does not indicate how long the administrative stay will be in place. As such, it is unclear whether it will remain in effect for the duration of this appeal. Second, FDA's review will not be a full scientific review as required by law; rather, it is extremely limited in scope and only asks whether Bidi's PMTAs, in fact, contain studies/data sufficient to satisfy the requirement set forth in the MDO. Third, given the uncertainty in timing, the administrative stay will not fully address on-going harm as product inventory is still being returned, customers move to other brands, and there is no chance of developing new business. Only a stay pending this Court's review will stem these continuing losses. A094.

*FDA*, 680 F. Supp. 2d 62, 77–78 (D.C. Cir. 2010). FDA cannot plausibly argue it would be harmed by a brief stay pending judicial review.

Indeed, a stay benefits the public interest for at least three reasons. For one, Bidi's products are designed to help, and are singularly successful at helping, adult smokers switch from smoking traditional, combustible cigarettes. FDA has consistently acknowledged such a benefit, generally, which remains an important public-health aim. The longer Bidi's products are off the market, the more likely its customers may revert to traditional, combustible cigarettes. And, as indicated *supra*, Bidi's products do not pose risks to youth; the company has implemented best-practices to minimize the risk their products will not end up in the hands of minors. Second, "competition is vital to the public interest" and the longer Bidi is unable to market its products, the more competition in the ENDS market lessens. *See Boardman v. Pac. Seafood Grp.*, 822 F.3d 1011, 1024 (9th Cir. 2016). And third, the public interest is always served when agencies are required to pay mind to limits on their statutory authority and regulate in accordance with administrative law before taking illegal actions likely to cause irreparable harm.

## CONCLUSION

For the foregoing reasons, this Court should stay the MDO pending judicial review.

/s/ *Eric P. Gotting*
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*Counsel for Petitioner Bidi Vapor, LLC*

## CERTIFICATE OF COMPLIANCE

I hereby certify the foregoing complies with the length limitations of Federal Rule of Appellate Procedure ("Rule") 27(d)(2)(A) because it is 5,130 words, excluding the parts that are exempted under Rule 32(f). It complies with the typeface and type-style requirements of Rule 32(a)(5) and Rule 32(a)(6) because it is printed in 14-point Calisto MT font, a proportionally spaced typeface with serifs.

Dated: October 22, 2021

*/s/ Eric P. Gotting*
Eric P. Gotting

*Counsel for Petitioner Bidi Vapor, LLC*

**CERTIFICATE OF SERVICE**

I hereby certify that on October 22, 2021, a true and correct copy of the foregoing was filed via the Court's CM/ECF system and served via electronic filing upon all counsel of record in this case.

/s/ *Eric P. Gotting*
Eric P. Gotting

*Counsel for Petitioner Bidi Vapor, LLC*

# ADDENDUM

Table of Contents

**FDA NEWS RELEASE**

# FDA announces comprehensive regulatory plan to shift trajectory of tobacco-related disease, death

**For Immediate Release:**

July 27, 2017

Español (/news-events/comunicados-de-prensa/la-fda-anuncia-un-plan-de-control-integral-para-cambiar-la-trayectoria-de-las-enfermedades-y-muertes)

The U.S. Food and Drug Administration today announced a new comprehensive plan for tobacco and nicotine regulation that will serve as a multi-year roadmap to better protect kids and significantly reduce tobacco-related disease and death. The approach places nicotine, and the issue of addiction, at the center of the agency's tobacco regulation efforts. The goal is to ensure that the FDA has the proper scientific and regulatory foundation to efficiently and effectively implement the Family Smoking Prevention and Tobacco Control Act. To make certain that the FDA is striking an appropriate balance between regulation and encouraging development of innovative tobacco products that may be less dangerous than cigarettes, the agency is also providing targeted relief on some timelines described in the May 2016 final rule that extended the FDA's authority to additional tobacco products. The agency will also seek input on critical public health issues such as the role of flavors in tobacco products.

Tobacco use remains the leading cause of preventable disease and death in the United States, causing more than 480,000 deaths every single year. In addition to the devastating human toll caused mainly by cigarette smoking, tobacco also causes substantial financial costs to society, with direct health care and lost productivity costs totaling nearly $300 billion a year. A key piece of the FDA's approach is demonstrating a greater awareness that nicotine – while highly addictive – is delivered through products that represent a continuum of risk and is most harmful when delivered through smoke particles in combustible cigarettes.

"The overwhelming amount of death and disease attributable to tobacco is caused by addiction to cigarettes – the only legal consumer product that, when used as intended, will kill half of all long-term users," said FDA Commissioner Scott Gottlieb, M.D. "Unless we change course, 5.6 million young people alive today will die prematurely later in life from tobacco use. Envisioning a world where cigarettes would no longer create or sustain addiction, and where adults who still need or want nicotine could get it from alternative and less harmful sources, needs to be the cornerstone of our efforts – and we believe it's vital that we pursue this common ground."

The FDA plans to begin a public dialogue about lowering nicotine levels in combustible cigarettes to non-addictive levels through achievable product standards. The agency intends to issue an Advance Notice of Proposed Rulemaking (ANPRM) to seek input on the potential public health benefits and any possible adverse effects of lowering nicotine in cigarettes. Because almost 90 percent of adult smokers started smoking before the age of 18 and nearly 2,500 youth smoke their first cigarette every day in the U.S., lowering nicotine levels could decrease the likelihood that future generations become addicted to cigarettes and allow more currently addicted smokers to quit.

"Because nicotine lives at the core of both the problem and the solution to the question of addiction, addressing the addictive levels of nicotine in combustible cigarettes must be part of the FDA's strategy for addressing the devastating, addiction crisis that is threatening American families," said Commissioner Gottlieb. "Our approach to nicotine must be accompanied by a firm foundation of rules and standards for newly-regulated products. To be successful all of these steps must be done in concert and not in isolation."

The FDA is committed to encouraging innovations that have the potential to make a notable public health difference and inform policies and efforts that will best protect kids and help smokers quit cigarettes. To make this effort successful, the agency intends to extend timelines to submit tobacco product review applications for newly regulated tobacco products that were on the market as of Aug. 8, 2016. This action will afford the agency time to explore clear and meaningful measures to make tobacco products less toxic, appealing and addictive. For example, the FDA intends to develop product standards to protect against known public health risks such as electronic nicotine delivery systems (ENDS) battery issues and concerns about children's exposure to liquid nicotine. It also will provide manufacturers additional time to develop higher quality, more complete applications informed by additional guidance from the agency.

The agency plans to issue this guidance describing a new enforcement policy shortly. Under expected revised timelines, applications for newly-regulated combustible products, such as cigars, pipe tobacco and hookah tobacco, would be submitted by Aug. 8, 2021, and applications for non-combustible products such as ENDS or e-cigarettes would be submitted by Aug. 8, 2022. Additionally, the FDA expects that manufacturers would continue to market products while the agency reviews product applications.

Importantly, the anticipated new enforcement policy will not affect any current requirements for cigarettes and smokeless tobacco, only the newly-regulated tobacco products such as cigars and e-cigarettes. This approach also will not apply to provisions of the final rule for which compliance deadlines already have passed, such as mandatory age and photo-ID checks to prevent illegal sales to minors. It also will not affect future deadlines for other provisions of the rule, including, but not limited to, required warning statements, ingredient listing, health document submissions, harmful and potentially harmful constituent reports, and the removal of modified risk claims, i.e., "light," "low," or "mild," or similar descriptors.

In order to further explore how best to protect public health in the evolving tobacco marketplace, the agency also will seek input from the public on a variety of significant topics, including approaches to regulating kid-appealing flavors in e-cigarettes and cigars. In particular, the FDA intends to issue ANPRMs to: 1) seek public comment on the role that flavors (including menthol) in tobacco products play in attracting youth and may play in helping some smokers switch to potentially less harmful forms of nicotine delivery; and 2) solicit additional comments and scientific data related to the patterns of use and resulting public health impacts from premium cigars, which were included in the FDA's 2016 rule. Additionally, the agency plans to examine actions to increase access and use of FDA-approved medicinal nicotine products, and work with sponsors to consider what steps can be taken under the safety and efficacy standard for products intended to help smokers quit.

"This comprehensive plan and sweeping approach to tobacco and nicotine allows the FDA to apply the powerful tools given by Congress to achieve the most significant public health impact," said Mitch Zeller, J.D., director of the FDA's Center for Tobacco Products. "Public input on these complex issues will help ensure the agency has the proper science-based policies in place to meaningfully reduce the harms caused by tobacco use."

To complement these larger policy considerations, the FDA plans to issue foundational rules to make the product review process more efficient, predictable, and transparent for manufacturers, while upholding the agency's public health mission. Among other things, the FDA intends to issue regulations outlining what information the agency expects to be included in Premarket Tobacco Applications (PMTAs), Modified Risk Tobacco Product (MRTP) applications and reports to demonstrate Substantial Equivalence (SE). The FDA also plans to finalize guidance on how it intends to review PMTAs for ENDS. The agency also will continue efforts to assist industry in complying with federal tobacco regulations through online information, meetings, webinars and guidance documents.

The FDA, an agency within the U.S. Department of Health and Human Services, promotes and protects the public health by, among other things, assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the

# Modifications to Compliance Policy for Certain Deemed Tobacco Products

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## Guidance for Industry

## *DRAFT GUIDANCE*

**This guidance document is being distributed for comment purposes only.**

Comments regarding this draft guidance may be submitted within 30 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Electronic comments may be submitted to http://www.regulations.gov. Alternatively, submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft guidance, contact the Center for Tobacco Products at (Tel) 1-877-CTP-1373 (1-877-287-1373) Monday-Friday, 9 a.m. – 4 p.m. ET.

Additional copies are available online at http://www.fda.gov/TobaccoProducts/Labeling/RulesRegulationsGuidance/default.htm. You may send an e-mail request to SmallBiz.Tobacco@fda.hhs.gov to receive an electronic copy of this guidance. You may send a request for hard copies to U.S. Food and Drug Administration, Center for Tobacco Products, Attn: Office of Small Business Assistance, Document Control Center, Bldg. 71, Rm. G335, 10903 New Hampshire Ave., Silver Spring, MD 20993-2000.

**U.S. Department of Health and Human Services**
**Food and Drug Administration**
**Center for Tobacco Products**

**March 2019**

In May 2017, FDA published a guidance document, *Three-Month Extension of Certain Tobacco Product Compliance Deadlines Related to the Final Deeming Rule*, under which the Agency, as a matter of enforcement discretion, stated its intention not to begin enforcement for an additional three months for all future compliance dates for requirements under the final deeming rule.

In July 2017, FDA announced a new comprehensive plan for tobacco and nicotine regulation that would serve as a multi-year roadmap. In an effort to strike an appropriate balance between regulation and encouraging development of innovative tobacco products that may be less dangerous than cigarettes, the Agency announced that it would be providing targeted relief on some timelines described in the preamble to the final deeming rule. The comprehensive plan was announced, in part, to afford the Agency time to explore clear and meaningful measures outside of premarket review to make tobacco products less toxic, appealing, and addictive.

The Agency's July 2017 announcement also indicated that extended compliance periods would allow time for FDA to set out additional rules and guidances and for industry to develop higher quality applications. We are continuing to pursue such regulations and guidances; however, the recent surge in youth use of ENDS products has caused us to reevaluate our priorities and modify the compliance policy for certain products, as set forth in this guidance. With respect to flavored cigars affected by this revised compliance policy, we note that any tobacco product, including cigars, may utilize the appropriate pathway to market, including the SE pathway or an exemption from SE. Manufacturers may obtain information about the application process from the detailed statutory criteria, as well as published guidances, webinars, and the marketing orders and their accompanying documentation provided by FDA.

In accordance with this comprehensive plan, in August 2017, FDA announced an extension of the period during which it did not intend to initiate enforcement action for premarket review requirements under the final deeming rule ("August 2017 Compliance Policy"). This revised policy stated that the compliance dates for submitting EX REQs, SE Reports, and PMTAs for newly regulated combustible tobacco products (such as most cigars) would be extended to August 8, 2021, and the compliance dates for submitting EX REQs, SE Reports, and PMTAs for newly regulated noncombustible tobacco products (such as most ENDS products) would be extended to August 8, 2022. In addition, FDA revised the compliance policy relating to the period after FDA receipt of EX REQs, SE Reports, and PMTAs for deemed tobacco products that were on the market on August 8, 2016. Under this revised compliance policy, FDA established a continued compliance period pending review of those applications. FDA stated that, under this policy, it intended to continue deferring enforcement until the Agency rendered a decision on an application (i.e., issuance of: a Marketing Order; a No Marketing Order; a Refuse to File; or Refuse to Accept) or the application was withdrawn.

However, in late 2017, FDA started to see a marked increase in complaints about ENDS products. FDA initiated an investigation of these complaints, the majority of which pertained to minors' access to and use of these products. This new information suggested an alarming increase in the use of ENDS products by middle and high school students. In April 2018, FDA

Since September 2018, the Agency has repeatedly publicly discussed[3] the fact that these compliance timelines were under reconsideration and has solicited the view of stakeholders—including manufacturers—at many steps along the way. During that period, FDA has continued to receive information underscoring the problem of youth use of ENDS. Data from the 2018 National Youth Tobacco Survey (NYTS), as described throughout this guidance, has documented a significant increase in youth use of ENDS products and revealed the magnitude of the problem. These data have prompted FDA to revise its compliance policies with respect to the continued marketing of deemed tobacco products that have not obtained premarket authorization, and to call on industry to do more to keep their products out of the hands of minors. FDA's revised compliance policy is informed, in part, by the information received from industry, including information the companies shared during meetings each had with FDA leadership. It is also informed by FDA's understanding that manufacturers have the means to control the distribution and sale of their products to retail customers by, for example, including or requiring terms, conditions, or controls in their contracts with downstream distributors (wholesalers, distributors, importers and/or retailers) to prevent youth access.

In issuing this Guidance, FDA intends to communicate its enforcement priorities so that the public will understand the Agency's most pressing public health concerns regarding these products and manufacturers will be prompted to move up their filing of premarket submission for certain deemed tobacco products. FDA's decision to exercise its enforcement authorities with respect to particular products will be determined on a case-by-case basis, informed by the enforcement priorities described in this Guidance.

## III. DEFINITIONS

For purposes of this guidance, FDA intends to use the following definitions:

*Cigar* means a tobacco product that: (1) is not a cigarette; and (2) is a roll of tobacco wrapped in leaf tobacco or any substance containing tobacco. 21 C.F.R. 1143.1. This includes all types of cigars including little cigars, cigarillos, and other types of cigars.

*Component* or *Part* means any software or assembly of materials intended or reasonably expected: (1) to alter or affect the tobacco product's performance, composition, constituents, or characteristics; or (2) to be used with or for the human consumption of a tobacco product. Component or part excludes anything that is an accessory of a tobacco product. 21 C.F.R. 1100.3, 1143.1. The following is a nonexhaustive list of examples of components or parts of ENDS (including e-cigarettes): e-liquids; atomizers; cartomizers (atomizer plus replaceable e-liquid-filled cartridge or pod); clearomizers; tank systems; flavors; and bottles that contain e-liquids.

[3] *See, e.g.,* Statement from FDA Commissioner Scott Gottlieb, M.D., on proposed new steps to protect youth by preventing access to flavored tobacco products and banning menthol in cigarettes https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm625884.htm; Scudder, L., "Vaping and E-Cigarettes in Kids: An Unprecedented Epidemic," Medscape, January 28, 2019, https://www.medscape.com/viewarticle/908077?faf=1.

**IN THE UNITED STATES DISTRICT COURT**
**FOR THE DISTRICT OF MARYLAND**

| | |
|---|---|
| AMERICAN ACADEMY OF PEDIATRICS, *et al.*,<br><br>Plaintiffs,<br><br>v.<br><br>UNITED STATES FOOD AND DRUG ADMINISTRATION, *et al.*,<br><br>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

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

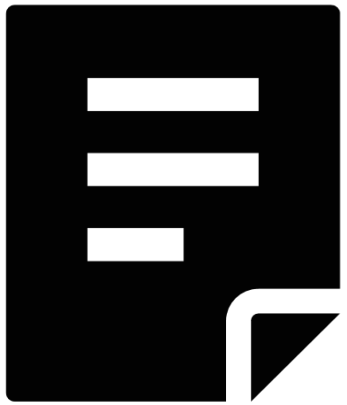
_____

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

FDA

# What You Should Know About FDA Regulation of E-Cigarettes

*Matthew R. Holman, Ph.D.*
*Director*
*Office of Science, CTP*



Received

## 6.7 M PMTAs

for ENDS around Sept 9, 2020

Final Actions

## 6.4 M

**222,000 RTAs**
- All product types
- Missing product-specific EAs

**5.0 M RTFs**
- All product types
- Lack of complete EA for every product
- Lack of complete ingredient list
- Lack of manufacturing information


MDOs

## 1.2 M

**Non-tobacco/non-menthol e-liquids**
Lack randomized controlled trial, longitudinal cohort study, or other product-specific evidence that evaluate product switching or cigarette reduction resulting from use of the new products over time & evaluate these outcomes based on flavor type to enable comparisons between tobacco and other flavors

RTA: Refuse To Accept
RTF: Refuse To File
MDO: Marketing Denial Order
EA: Environmental Assessment

# Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems

## Guidance for Industry

Comments may be submitted at any time for Agency consideration. Electronic comments may be submitted to https://www.regulations.gov. Alternatively, submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852. All comments should be identified with Docket No. FDA-2015-D-2496.

For questions regarding this guidance, contact the Center for Tobacco Products at 1-877-CTP-1373 (1-877-287-1373) Monday - Friday, 9 a.m. – 4 p.m. ET.

Additional copies are available online at https://www.fda.gov/tobacco-products/compliance-enforcement-training/small-business-assistance-tobacco-product-industry. You may send an e-mail request to SmallBiz.Tobacco@fda.hhs.gov to receive an electronic copy of this guidance. You may send a request for hard copies to U.S. Food and Drug Administration, Center for Tobacco Products, Attn: Office of Small Business Assistance, Document Control Center, Bldg. 71, Rm. G335, 10903 New Hampshire Ave., Silver Spring, MD 20993-2000.

**U.S. Department of Health and Human Services**
**Food and Drug Administration**
**Center for Tobacco Products**

**June 2019**

nonclinical information, confirm whether the tobacco product meets applicable product standards under section 907 of the FD&C Act (if any), and confirm that the product can be manufactured according to defined standards outlined in the PMTA. Inspections will also provide important information regarding whether the manufacturing, processing, or packing of the tobacco product conform to tobacco product manufacturing practices, which will be set forth in a future rulemaking.[18]

Under section 910(b)(2) of the FD&C Act, FDA has the discretion, upon your request or on its own initiative, to refer your PMTA to the Tobacco Product Scientific Advisory Committee (TPSAC). FDA Advisory committees are used to obtain independent, expert advice on scientific, technical, and policy matters. TPSAC reviews and evaluates safety, dependence, and health issues relating to tobacco products and provides appropriate advice, information, and recommendations to the Commissioner of Food and Drugs.[19] If you wish to request that FDA refer your PMTA to TPSAC, you should include the request in the cover letter of your initial PMTA submission. If you would like to request that FDA refer your PMTA to TPSAC after your PMTA has been submitted, please contact CTP to discuss this option.

## D. Public Health Considerations for ENDS Products

### *1. Section 910(c)(2)(A) Standard: A Showing That the New Tobacco Product Is Appropriate for the Protection of the Public Health*

Section 910(c)(2)(A) of the FD&C Act requires that FDA deny a PMTA where it finds "there is a lack of a showing that permitting such tobacco product to be marketed would be appropriate for the protection of the public health."[20] FDA's finding of whether there is a showing that permitting a product to be marketed would be appropriate for the protection of the public health (APPH) must be determined with respect to 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.

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[18] FDA intends to issue regulations under section 906(e) of the FD&C Act that will contain the requirements for tobacco product manufacturing practices. At that time, each new PMTA will also be expected to demonstrate that the methods, facilities, or controls used conform to these regulations (section 910(c)(2)(B)).

[19] For more information, please visit the TPSAC website: https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/TobaccoProductsScientificAdvisoryCommittee/default.htm

[20] In addition, the statute provides that FDA shall deny PMTAs under section 910(c)(2) of the FD&C Act where:
(B) the methods used in, or the facilities or controls used for, the manufacture, processing, or packing of such tobacco product do not conform to the requirements of section 906(e);
(C) based on a fair evaluation of all material facts, the proposed labeling is false or misleading in any particular; or
(D) such tobacco product is not shown to conform in all respects to a tobacco product standard in effect under section 907, and there is a lack of adequate information to justify the deviation from such standard.

(Section 910(c)(4) of the FD&C Act.) We provide information in this section to assist applicants in submitting an ENDS PMTA that could support a showing that the marketing of a new tobacco product would be APPH.

Throughout this guidance document, we recommend providing specific information pertaining to different topic areas and scientific disciplines to enable FDA to make a determination of whether your PMTA supports a showing that permitting the marketing of your new tobacco product would be APPH. For example, knowing the full assessment of the toxicological effects of your ENDS (e.g., ingredients, components, use of the product) is important to assess the health effects on users and nonusers under Section 910(b). As such, FDA assesses the toxicology of the product to determine whether product use would have a detrimental effect on users' and nonusers' health. FDA weighs all of the potential benefits and risks from the information contained in the PMTA to make an overall determination of whether the product should be authorized for marketing.

You may propose specific restrictions on sale and distribution that can help support a showing that permitting the marketing of the product would be APPH (e.g., a restriction that decreases the likelihood that those who do not use tobacco products will start using tobacco products). FDA may consider your product in that context and may include your proposed restrictions as mandatory conditions in your marketing order. These restrictions would be in addition to any other restrictions that FDA may require on the sale and distribution of the tobacco product, or any postmarket records and reports FDA may find necessary.

The following sections highlight several broad categories of issues that applicants should consider to help demonstrate that permitting the marketing of their products would be APPH and, consequently, should be authorized for marketing.

2. Valid scientific evidence

The FD&C Act states that the finding of whether permitting the marketing of a product would be APPH will be determined, when appropriate, on the basis of well-controlled investigations[21] (section 910(c)(5)(A)). However, section 910(c)(5)(B) of the FD&C Act also allows the Agency to consider other "valid scientific evidence" if found sufficient to evaluate the tobacco product. Given the relatively new entrance of ENDS on the U.S. market, FDA understands that limited data may exist from scientific studies and analyses.[22] If an application includes, for example, information on other products (e.g., published literature, marketing information) with appropriate bridging studies, FDA intends to review that information to determine whether it is valid scientific evidence sufficient to demonstrate that the marketing of a product would be APPH. Nonclinical studies alone are generally not sufficient to support a determination that permitting the marketing of a tobacco product would be appropriate for the protection of the public health.

[21] Well-controlled investigations are generally those that are designed and conducted in such a way that minimizes or controls for bias, confounding variables, and other factors that may render the results unreliable.
[22] As discussed in section VI.H.2., due to the limited nonclinical or clinical research conducted on specific ENDS products, it is likely that applicants will conduct certain investigations themselves and submit their own research findings as a part of their PMTA.

Nonetheless, in general, FDA does not expect that applicants will need to conduct long-term studies to support an application.[23] As an example for nonclinical assessments, long-term studies such as carcinogenicity bioassays are not expected to be included in an application. For clinical assessments, instead of conducting clinical studies that span months or years to evaluate potential clinical impact, applicants could demonstrate possible long-term health impact by including existing longer duration studies in the public literature with the appropriate bridging information (i.e., why the data used are applicable to the new tobacco product) and extrapolating from short-term studies.[24] In addition, nonclinical in vitro assays that assess the toxicities that are seen following long-term use of tobacco products may be supportive of these clinical assessments. These studies, used as a basis to support a PMTA, should be relevant to the new tobacco product and address, with robust rationale, acute toxicological endpoints or other clinical endpoints that may relate to long-term health impacts. In this context, FDA considers long-term studies to be those studies that are conducted over six months or longer.

FDA recommends that you provide a detailed explanation of how the data and information provided in your PMTA (including the information required by section 910(b)(1) of the FD&C Act) constitute valid scientific information that would support a finding by FDA that marketing your new tobacco product is APPH.

If an applicant has questions about investigations, including alternatives to well-controlled investigations it would like to utilize, we recommend that the applicant meet with FDA to discuss the approach prior to preparing and submitting an application.[25]For additional information regarding alternatives to well-controlled investigations please see section X of this guidance.

3. Comparison Products

As part of FDA's consideration under 910(c)(4) of the FD&C Act of the risks and benefits of the marketing of the new tobacco product to the population as a whole, including users and nonusers of tobacco products, FDA reviews the health risks associated with changes in tobacco product use behavior (e.g., initiation, switching, dual use, cessation) that are likely to occur with the marketing of the new tobacco product. We recommend an applicant compare the health risks of its product to both products within the same category and subcategory, as well as products in different categories as appropriate. It is helpful for FDA to understand applicant's rationale and justification for comparators chosen within the same category or different categories of tobacco products. This comparative health risk data is an important part of the evaluation of the health effects of product switching.

Information about tobacco products in the same category or subcategory is important to FDA's evaluation of a tobacco product's potential effect on public health because current users may switch to other products within the same category. For tobacco products that are within the same category and subcategory, we recommend applicants consider products that consumers are most likely to considered interchangeable between your proposed product and other similar products.

[23] See section X for additional discussion.
[24] See section X of the guidance for more information about alternatives to conducting long-term studies.
[25] See the R&D meetings guidance.

- Managerial oversight and employee training;
- Manufacturing processes and controls for product design, including a hazard analysis that details the correlation of the product design attributes with public health risk, and any mitigations for identified hazards that have been implemented;
- Activities related to identifying and monitoring suppliers and the products supplied (including, for example, purchase controls and materials acceptance activities);
- Validation and verification activities used to ensure that the new tobacco product matches specifications, including any voluntary standards with which your product complies;
- Test methods and procedures conducted before the new tobacco product is released for sale and distribution in the United States, including information on test parameters, such as the concentration of the standard solution, as well as a description of acceptance activities with protocol and acceptance criteria. If the product is manufactured without a solution, you should describe its performance characteristics (e.g., particle size, heating temperature); and
- Handling of complaints, nonconforming products and processes, and corrective and preventive actions.

FDA may request that you submit copies of selected SOPs if needed to enable FDA to more fully understand the methods used in, and the facilities and controls used for, the manufacturing and processing of the new tobacco product.

### *2. Nonclinical and Human Subject Studies*

Section 910(b)(1)(A) of the FD&C Act requires that a PMTA contain "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." FDA interprets the information required under this provision to include not only investigations that support the PMTA, but also any investigations that do not support, or are adverse to, the PMTA. Information on both nonclinical and clinical investigations that must be provided, including, but not limited to, any studies assessing constituents of tobacco, aerosol, toxicology, consumer exposure, consumer use profiles, and consumer risk perception. Furthermore, information on investigations concerning products with novel components, ingredients, additives, or design features that are similar or related to those of the new tobacco product and investigations concerning products that share novel components, ingredients, additives, or design features with the new tobacco product should also be provided so that FDA may adequately assess the product's health risks. To the extent the information is available, you should indicate the source of funding for all studies and provide a statement regarding any potential financial or other conflicts of interest on the part of the investigator(s). Due to the emerging nature of ENDS products within the general tobacco market, FDA acknowledges that there may be limited nonclinical or clinical research conducted on specific ENDS products. Thus, it is likely that applicants will conduct certain investigations themselves and submit their own research findings as a part of their PMTA. However, in general, FDA does not expect that applicants will have to conduct long-term studies to support an application.

i. Consumer perceptions and intentions

Consumer perception evaluations should address how consumers perceive product harms and include consideration of packaging and labeling. These evaluations should also address interest in and intentions to use the product, including among populations of non-users of tobacco products (e.g., vulnerable populations such as youth and young adults). Examples of information that may be considered in this analysis include published reports and data on consumer perceptions of the new tobacco product and its packaging and consumer intentions to use the product, and data you collect on consumer perceptions of the harms of the new tobacco product and of its proposed labeling or advertising and intentions to use the product, including among populations of non-users of tobacco products. If you are collecting data on consumer perceptions or intentions, we recommend evaluating perceptions of the product, both absolute and in comparison to other categories of tobacco products and to quitting all tobacco use. This evaluation should include the use intentions among current ENDS users, nonusers, and other tobacco product users, as well as reasons for use (e.g., complete substitution, use in environments where smoking is not allowed, fun and enjoyment).

ii. Likelihood of initiation and cessation by both users and nonusers of tobacco products

Evaluations of the likelihood of initiation among never-users and former users of tobacco products and cessation among current tobacco users should cover a range of tobacco use behaviors related to your new tobacco product. Examples of information that FDA recommends considering in these evaluations include:

- Published literature or applicant-initiated studies evaluating the effects of the ENDS on users, including effects on initiation, switching behavior, cessation, and dual use; and on nonusers' initiation of the product. Published literature or studies should be of the same or similar ENDS product. Where the ENDS product studied is similar to the new tobacco product, the applicant should explain why making such a comparison is appropriate; and
- Scientific information (e.g., information collected from peer-reviewed literature or data you collect on your product) on the likelihood of tobacco product use by nonusers, specifically youth and young adults, pregnant women, and other vulnerable populations.

Although randomized clinical trials could address cessation behavior of users of tobacco products, FDA believes this would also be true for observational studies (perception, actual use, or both) examining cessation behaviors.[43]

iii. Product use patterns

Evaluation of product use patterns should consider the topography of how individual users consume the product (e.g., the number of puffs, puff duration, puff intensity, duration of use), the

[43] FDA recognizes that some clinical investigations examining cessation may require an investigational new drug application (IND). FDA encourages applicants to contact FDA with questions about whether the IND requirements apply to a particular clinical investigation.

**FOOD AND DRUG ADMINISTRATION**

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**CENTER FOR TOBACCO PRODUCTS**

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**TOBACCO PRODUCT APPLICATION REVIEW PUBLIC MEETING**

**+ + + + +**

**MONDAY**
**OCTOBER 22, 2018**

**+ + + + +**

**The Public Meeting convened at the Hilton Washington DC/Rockville Hotel and Executive Meeting Center, 1750 Rockville Pike, Rockville, Maryland, at 8:30 a.m.**

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submit a new application once, again, they're able to provide all the required statutory and regulatory elements.

If the application is accepted by CTP, it moves to Phase 3, which deals with substantive review and an action by CTP. The substantive review phase is a multidisciplinary approach to review the data submitted by the applicant to determine if such data is sufficient to demonstrate -- sorry -- to demonstrate that authorizing the marketing of the product would be appropriate for the protection of public health as previously described.

During this review phase, CTP may conduct inspections such as of clinical or manufacturing facilities in conjunction with CTP's Office of Compliance and Enforcement. Also of note, an application may be referred to the Tobacco Product Scientific Advisory Committee, otherwise known as TPSAC. If the applicant would like TPSAC -- excuse me -- if the applicant would like CTP to consider referral to TPSAC, they

move into that filing stage. So the end result is the filing letter or the RTF letter. This is a multidisciplinary approach, so you can have anywhere up to 13 disciplines taking a look at various parts of the application for what's required for filing.

Looking through all your documents. Are your studies there? Do you actually have some of the source data? Is there anything missing? So anything that's laid out in filing criteria in 910(b) for your PMTAs and under 911 for your MRTPs is what they're looking at for that RTF. If those items are missing, it would be listed in that letter. If you passed that and received filing, then you're in that substandard review phase.

MS. BELTRE: Great. I would add to that, clearly identify these sections in your application. When we're talking about large submissions such as the MRTPs and PMTAs that we have received, it would help everyone involved in this process if you can clearly identify what

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**TOBACCO PRODUCT APPLICATION REVIEW PUBLIC MEETING**

**+ + + + +**

**TUESDAY**
**OCTOBER 23, 2018**

**+ + + + +**

**The Public Meeting convened at the Hilton Washington DC/Rockville Hotel and Executive Meeting Center, 1750 Rockville Pike, Rockville, Maryland, at 8:30 a.m.**

**This transcript has not been edited or corrected but appears as received from the commercial transcribing service.**

exposures and potential harm are likely anticipated worth evaluating? What is the likely nicotine exposure for the user, and do various flavorings or other ingredients impact nicotine exposure?

This could be a direct chemical interaction, or it could be through a metabolic interaction. Sorry. We have some understanding that factors, such as nicotine concentration, voltage, puffing behavior, impact nicotine exposure. Thus, evaluating such parameters is likely helpful in understanding the range of nicotine exposure.

And recall that when evaluating potential risk of a proposed product, the statute itself requires that applicants show the health risks of the tobacco product, and whether tobacco product presents lower risk than other tobacco products.

Applicants have also asked: what studies are required for a PMTA? There are specific study requirements for a PMTA, and it

may be possible to support a marketing order for an ENDS product, as an example, without conducting new non-clinical or clinical studies, given other data sources can support the PMTA, and provide sufficient information to inform FDA that the product is appropriate for the protection of public health, APPH, and address the other 910(c)(2) issues discussed earlier.

In most situations, it is likely that at least some analytical testing specific to the product would be conducted to support a PMTA. If you have a product currently available on the market, it is possible that research has been done on the product, or your product is similar to other products, which are publicly available and are a subject of research studies, in which case, you may submit the available information, along with bridging information to justify the use of such underlying studies.

If conducting studies, alternatives to the traditional randomized controlled clinical trials, which are typically used for drug

comparing to set of comparator products. And for MRTP, it's even, you know, it's even more complicated.

So I guess the answer is we consider the totality of the HPHCs, and we look at what was given to us, and you know, and we look to see whether the HPHCs provided can cover the, give us an understanding of the relative risk, you know, in the case of PMTA, relative to the market, and the users who are using the products that we think, you know, are using the product. I hope that answers the question.

MS. RUDOLPH: It looks like Kim has some other additional thoughts.

MS. BENSON: Tag team. One other thing that's good to remember when you're looking at the HPHCs is, you know, they don't all have the same target. They don't have the same toxicity.

So just a case in point, if you have a, you know, reduction in an HPHC that causes cancer, and a huge increase in one that causes

**UNITED STATES FOOD AND DRUG ADMINISTRATION**

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**DEEMED TOBACCO PRODUCT APPLICATIONS:**
**A PUBLIC MEETING**

**+ + + + +**

**MONDAY**
**OCTOBER 28, 2019**

**+ + + + +**

**The public meeting met at the FDA White Oak Campus, Great Room, Room 1503, 10903 New Hampshire Avenue, Silver Spring, Maryland, at 8:30 a.m., Anne Radway, Moderator, presiding.**

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information relevant to the subject matter of the application. Other information may be identified during the pre-submission meeting if held, that is specific to the tobacco product.

At the end of the filing phase, similar to the acceptance phase, CTP will issue one of two types of correspondence. If the submitted information is inadequate to continue with substantive review, the applicant will receive a refusal to file letter. In this letter, FDA will include the reasons for the refusal. If refused, the applicant has the option to submit a new application once they are able to meet the filing requirements for a PMTA.

If the application meets the filing requirements for a PMTA seeking a marketing order, CTP will issue a letter to notify the applicant that the application has been filed. If filed by CTP, the PMTA moves into Phase 3, which deals with substantive review and results in an action by CTP.

The substantive review phase is a

multi-disciplinary approach to review the data submitted by the applicant and determine if such data is sufficient to demonstrate that authorizing the marketing of the new product would be appropriate for the protection of public health.

During the substantive review phase, CTP's Office of Science, in conjunction with the Office of Compliance and Enforcement, may conduct inspections of clinical or manufacturing facilities. You will hear more about inspections in a later presentation.

Additionally, CTP may conduct testing of the new product. At this phase, CTP should have received the samples requested in the sample request letter. An application may be referred to the Tobacco Products Scientific Advisory Committee, also known as TPSAC. If the applicant would like CTP to consider referral to TPSAC, they should include this request in the cover letter of their initial submission. Along this request, it would be helpful for the applicant to

useful.

Going back to thinking about the proposed product itself, human factors are important to consider when designing a product. Human factor considerations assess if users will be able to operate their product appropriately by focusing on the interactions between the people and products. Importantly, when considering a new proposed product, FDA seeks to understand the likely impact on human health.

To evaluate the acute and chronic health effects associated with the product or polytobacco product use, the proposed rule out for public comment states that the applicant include studies, other scientific evidence or both that identify biomarkers and health outcome measurements or end points, and provide data to support the impact of the new tobacco product on the health of users and non-users.

This may include health effects associated or related to specific constituents. When designing studies, it is helpful if the

and have changes that are clinically relevant are the most useful. There is not an agreed upon panel of biomarkers established to understand ENDS impact on human health at this time.

Applicants have also asked what studies are required to support a PMTA? It may be possible to support a marketing order for a ENDS product without conducting new, non-clinical or clinical studies given other data sources can support this PMTA. In most situations, it is likely that at least some analytical testing specific to the product would be conducted to support your PMTA.

If conducting studies, alternatives to the traditional randomized, controlled clinical trials, which are typically used for drug development, may be appropriate to support a PMTA. Again, the most useful studies are those that are generalizable to the U.S. population.

If you have a product currently available on the market, it is possible that research has been done on that product or your

**UNITED STATES FOOD AND DRUG ADMINISTRATION**

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**DEEMED TOBACCO PRODUCT APPLICATIONS:**
**A PUBLIC MEETING**

**+ + + + +**

**TUESDAY**
**OCTOBER 29, 2019**

**+ + + + +**

**The public meeting was held at the FDA White Oak Campus, Great Room, Salon A, 10903 New Hampshire Avenue, Silver Spring, Maryland, at 8:30 a.m., Todd Cecil, Moderator, presiding.**

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product evidence that over their lifetime, youth aren't taking up or switching?

DR. MURPHY: I think people are looking at me to answer the question. So what I would say is that we know that youth use of electronic nicotine device systems is very problematic and concerning, right.

So that the, I think what's important is that applicants address how they are going to restrict youth access and youth use. Whether, you know, are there marketing -- what are their marketing plans. What are the age verification plans.

I mean these are some of the kinds of things that you might want to take time to describe in your application to ensure to FDA that your product will not kind of exacerbate the current situation in methods to curb and improve limiting youth access.

MS. TALBERT: I would just add that tobacco product advertising can blend across categories. So in the advertising that you're

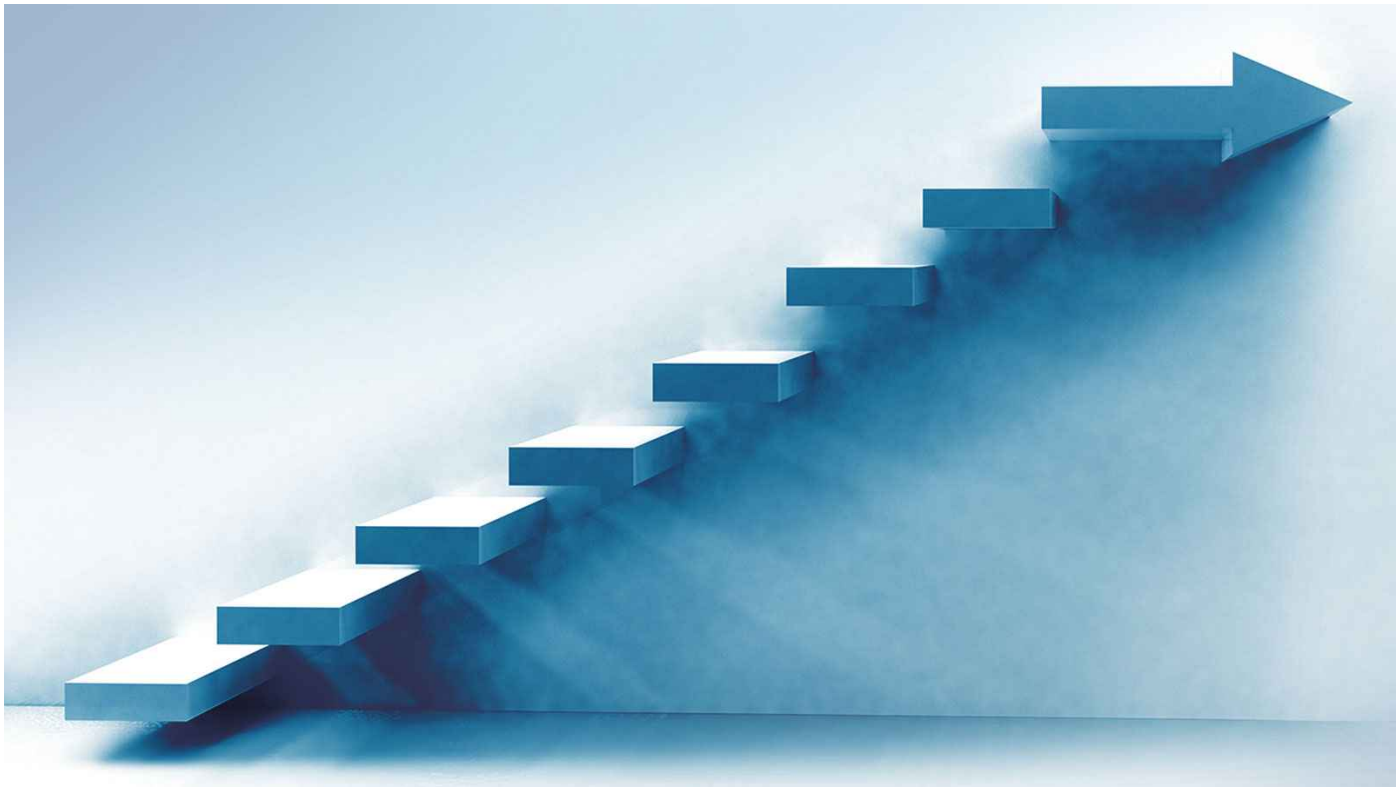
# Perspective: FDA's Progress on Review of Tobacco Product Applications Submitted by the Sept. 9, 2020 Deadline

By Mitch Zeller, Director of the FDA's Center for Tobacco Products (CTP)
February 16, 2021

*Per a court order, premarket applications for many new tobacco products, including e-cigarettes, certain cigars, and hookah products, currently on the market were due to FDA by Sept. 9, 2020. Also consistent with a court order, products for which applications were submitted by the Sept. 9 deadline may remain on the market for up to a year pending FDA review, although they remain subject to FDA enforcement. This piece is a follow-up to our August perspective piece (/tobacco-products/ctp-newsroom/perspective-fdas-preparations-september-9-submission-deadline)and aims to provide an update on the progress we have made on the processing and review of these applications.* [1]

## Background

Following the Sept. 9 premarket application deadline (/tobacco-products/manufacturing/submit-tobacco-product-applications-deemed-tobacco-products) for certain deemed new tobacco products (/tobacco-products/products-guidance-regulations/market-and-distribute-tobacco-product) on the market as of Aug. 8, 2016, FDA's job is to process, review, and take action on a massive number of applications for products that are currently on the market. Premarket review of new tobacco products is a critical part of how we carry out our mission to protect the public—especially kids—from the harms associated with tobacco use.



This undertaking represents a major milestone for tobacco product regulation and for public health as a whole. By implementing the premarket review requirement for new electronic nicotine delivery systems (ENDS) and other "deemed" new tobacco products, such as hookah and pipe tobacco, we are taking steps to transform the marketplace toward one where deemed new tobacco products available for sale will have undergone careful, science-based review and oversight by the FDA. [2]

We have worked for several years to prepare for premarket review of a large number of deemed products. These efforts included improving information technology systems, engaging with stakeholders, significantly increasing hiring, streamlining review procedures, and providing and promoting guidance and resources to inform industry.

As anticipated, we received thousands of tobacco product submissions covering millions of tobacco products, the majority of which came in very close to the Sept. 9 deadline. Furthermore, the submissions varied substantially in number of tobacco products contained in each submission, size, format and organization. However, despite these challenges, due to our preparations and continued engagement with stakeholders, the "intake" of the large number of submissions went smoothly; our IT systems performed as designed and were able to handle both a high number of submissions within a short period of time and extremely large individual submissions. Now, the initial "intake" of submissions is nearly complete, and the acceptance, filing, and substantive review of applications is underway.

In an August perspective piece, (/tobacco-products/ctp-newsroom/perspective-fdas-preparations-september-9-submission-deadline) I pledged that the agency would keep interested stakeholders updated on the agency's progress. We are now at a point in the review of these applications where we can share some updates on our progress.

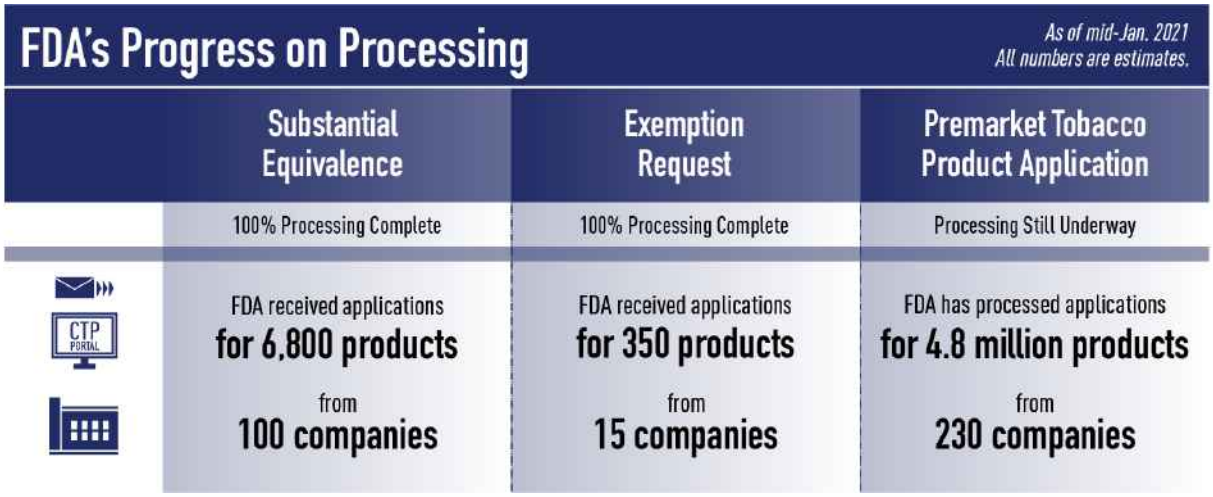
## Processing and Reviewing Applications

**Receipt and Processing of Submissions**

After a firm submits their application(s) to the FDA, the agency goes through a number of Processing steps to properly receive and prepare it for the review process (e.g., acceptance review, filing review, substantive review). This includes physical or electronic "intake" of the submission and determining the type and number of applications contained in the submission. For example, this is when we determine if a submission is a Premarket Tobacco Product Application (PMTA) or Substantial Equivalence (SE) Report and how many individual applications for tobacco products are included within the submission. This is also when FDA ensures that the files are safely viewable by conducting virus scans on hard drive submissions and unzipping any zipped files. Lastly, FDA uploads all the files into internal review systems to prepare them for the next step in the review process.

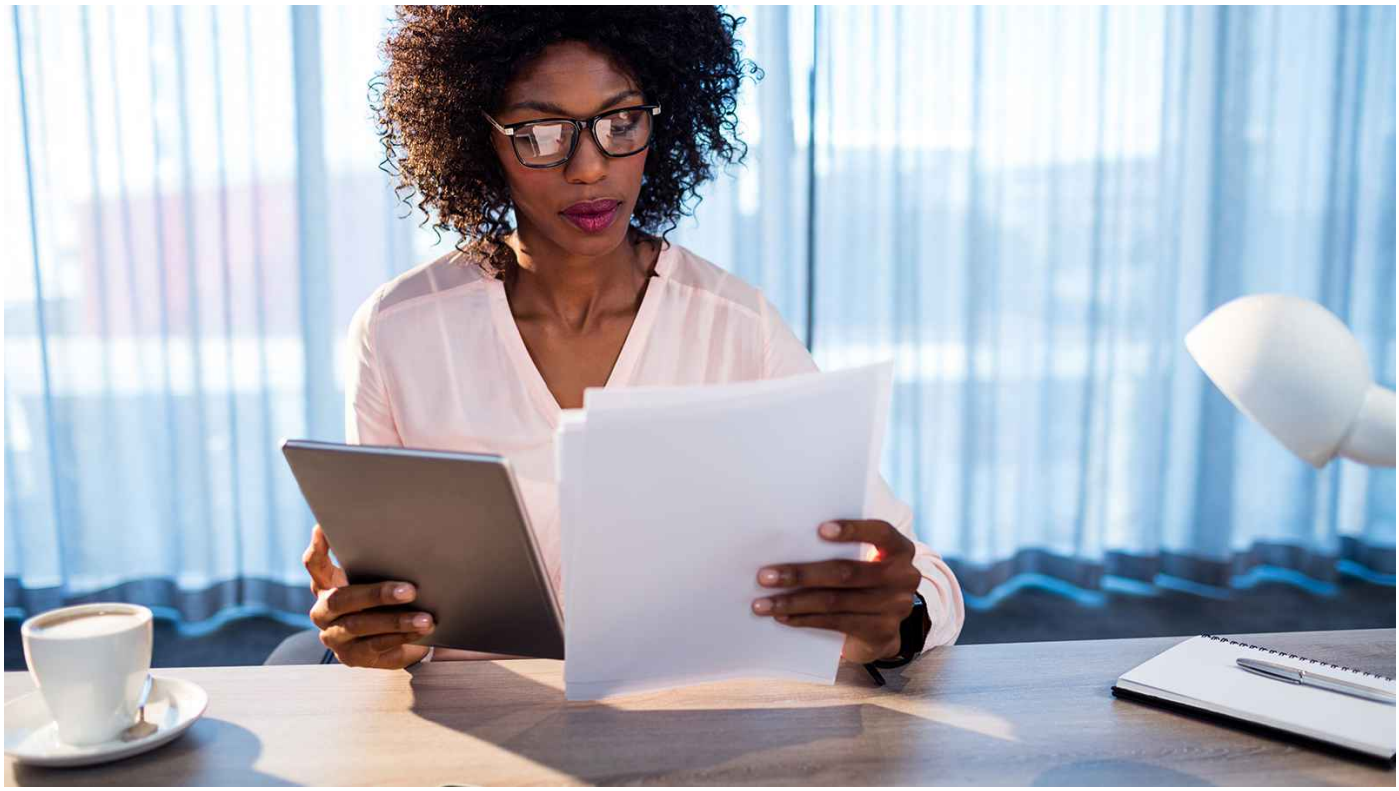
We have seen significant variety in the number of tobacco products included in each submission, so each and every submission package is being carefully assessed. For example, some applicants provided information on one product per submission while other applicants provided information for all of the company's products within one submission. In addition, the submissions arrived in many different formats, including electronic submissions, paper submissions, and mixed media (flash drives, hard drives or CDs, sometimes combined with paper), and varied widely in their organization and presentation of information. We also received several duplicate submissions; for example, companies submitted an electronic version and a paper version of the same application. Lastly, while some firms used a spreadsheet made available by FDA to enable faster processing, most firms used other means to present the information. This impacted our ability to more quickly process the information provided, as it required our staff to manually enter the product information into our systems.

Recently, we completed the Processing step of ALL Exemption from Substantial Equivalence Requests (EX REQ) and ALL Substantial Equivalence (SE) Reports submitted by the Sept. 9 deadline. For the EX REQ pathway, we received applications for about 350 products from about 15 companies. For the SE pathway, we received applications for about 6,800 products from about 100 companies.




For PMTAs, as of mid-January 2021, the agency has completed the Processing step of applications for more than 4.8 million products from over 230 companies. During Processing, FDA found that the PMTAs posed additional challenges due to the size,

complexity and diversity of the submissions; for example, some firms provided separate submissions for each section of the tobacco product application, such as submitting the clinical information separately from product identification and manufacturing information, while others included up to tens of thousands of products within a submission. One firm submitted information on more than 4 million tobacco products within a single submission. The amount of content in each submission also greatly varied, with some applications including up to 2,000,000 files where each file contains multiple pages of content for FDA to review.



Given the high level of public interest in these submissions, we'd hoped to be able to share a list of products submitted under all three pathways at once. However, we have not completed Processing all of the applications submitted through the PMTA pathway. Because we want to provide as much of an update as possible, we are therefore sharing the SE and EX REQ list and providing a PMTA update at this time.

While processing PMTA submissions, the Agency continues to enforce the law. As previously stated in FDA's enforcement priorities (/regulatory-information/search-fda-guidance-documents/enforcement-priorities-electronic-nicotine-delivery-system-ends-and-other-deemed-products-market), after Sept. 9, 2020, FDA is prioritizing enforcement against any ENDS product that continues to be sold and for which the agency did not receive a product application. Additionally, for deemed tobacco products—other than ENDS or "premium cigars"—that do not have premarket authorization, FDA will make enforcement decisions on a case-by-case basis and intends to prioritize enforcement based on the likelihood of youth use or initiation to make the most efficient use of its resources (FDA is currently enjoined from enforcing the premarket requirements for products that meet the definition of "premium cigar" in the court's order).

In January 2021, FDA issued the first set of warning letters (/news-events/press-announcements/fda-warns-firms-remove-unauthorized-e-liquid-products-market-first-letters-issued-manufacturers-did) to firms who have not submitted premarket applications to FDA and are continuing to sell or distribute unauthorized ENDS after Sept. 9, 2020. To date, FDA has sent warning letters to 30 firms who manufacture and operate websites selling electronic nicotine delivery system (ENDS) products, specifically e-liquids, which lack premarket authorization.

We are continuing to process packages submitted by the Sept. 9 deadline and aim to share the final PMTA numbers as soon as possible.

## Acceptance and Filing

Once a submission package is processed, the individual product applications within the submission proceed to the review process.

FDA U.S. FOOD & DRUG ADMINISTRATION

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov

September 07, 2021

**DENIAL**

Bidi Vapor LLC
Attention: Nirajkumar Patel, CEO
4460 Old Dixie High Way
Grant Valkaria, FL 32949

**FDA Submission Tracking Number (STN):** PM0003460, see Appendix A

Dear Mr. Patel:

We are denying a marketing granted order for the products identified in Appendix A. Refer to Appendix B for a list of amendments received in support of your applications.

**Based on our review of your PMTAs[1], we determined that the new products, as described in your applications and specified in Appendix A, lack sufficient evidence to demonstrate that the marketing of these products is appropriate for the protection of the public health (APPH). Therefore, you cannot introduce or deliver for introduction these products into interstate commerce in the United States. Doing so is a prohibited act under section 301(a) of the FD&C Act, the violation of which could result in enforcement action by FDA.**

If you choose to submit new applications for these products, you must fulfill all requirements set forth in section 910(b)(1). You may provide information to fulfill some of these requirements by including an authorization for FDA to cross-reference a Tobacco Product Master File. [2] You may not cross-reference information submitted in the PMTAs subject to this Denial.

Based on review of your PMTA, we identified the following key basis for our determination:

1. All of your PMTAs lack sufficient evidence demonstrating that your flavored ENDS will provide a benefit to adult users that would be adequate to outweigh the risks to youth. In light of the known risks to youth of marketing flavored ENDS, robust and reliable evidence is needed regarding the magnitude of the potential benefit to adult smokers. This evidence could have been provided using a randomized controlled trial and/or longitudinal cohort study that demonstrated the benefit of your flavored ENDS products over an appropriate comparator tobacco-flavored ENDS. Alternatively, FDA would consider other evidence but only if it reliably and robustly evaluated the impact of the new flavored vs. tobacco-flavored products on adult smokers' switching or cigarette reduction over time. We did not find such evidence in your PMTAs. Without this information, FDA concludes that your applications are insufficient to demonstrate that these products would provide an added benefit that is adequate to outweigh

[1] Premarket Tobacco Product Application (PMTA) submitted under section 910 of the Federal Food, Drug, and Cosmetic Act (FD&C Act)

[2] See guidelines at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/tobacco-product-master-files

the risks to youth and, therefore, cannot find that permitting the marketing of your new tobacco products would be appropriate for the protection of the public health.

We cannot find that the marketing of your new tobacco products is APPH. The review concluded that key evidence demonstrating APPH is absent. Therefore, scientific review did not proceed to assess other aspects of the applications. As such, this is not an exhaustive list of all possible deficiencies.

Upon issuance of this order, your products are misbranded under section 903(a)(6) of the FD&C Act and adulterated under section 902(6)(A) of the FD&C Act. Failure to comply with the FD&C Act may result in FDA regulatory action without further notice. These actions may include, but are not limited to, civil money penalties, seizure, and/or injunction.

We encourage you to submit all regulatory correspondence electronically via the CTP Portal[3,4] using eSubmitter.[5] Alternatively, submissions may be mailed to:

Food and Drug Administration
Center for Tobacco Products
Document Control Center (DCC)
Building 71, Room G335
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

The CTP Portal and FDA's Electronic Submission Gateway (ESG) are generally available 24 hours a day, seven days a week; submissions are considered received by DCC on the day of successful upload. Submissions delivered to DCC by courier or physical mail will be considered timely if received during delivery hours on or before the due date[6]; if the due date falls on a weekend or holiday, the delivery must be received on or before the preceding business day. We are unable to accept regulatory submissions by e-mail.

[3] For more information about CTP Portal, see https://www.fda.gov/tobacco-products/manufacturing/submit-documents-ctp-portal
[4] FDA's Electronic Submission Gateway (ESG) is still available as an alternative to the CTP Portal.
[5] For more information about eSubmitter, see https://www.fda.gov/industry/fda-esubmitter
[6] https://www.fda.gov/tobacco-products/about-center-tobacco-products-ctp/contact-ctp

If you have any questions, please contact Antonio Thornton, Regulatory Health Project Manager, at (240) 402-3577 or Antonio.Thornton@fda.hhs.gov.

Sincerely,

Digitally signed by Matthew R. Holman -S
Date: 2021.09.07 13:12:42 -04'00'

Matthew R. Holman, Ph.D.
Director
Office of Science
Center for Tobacco Products

Enclosures **(if provided electronically, the Appendix is not included in physical mail):**

Appendix A – New Tobacco Products Subject of This Letter
Appendix B – Amendments Received for These Applications

**Appendix A[7]**

New Tobacco Products Subject of This Letter

| **Common Attributes** | |
|---|---|
| Submission date | September 8, 2020 |
| Receipt date | September 8, 2020 |
| Applicant | Bidi Vapor LLC |
| Product manufacturer | Bidi Vapor LLC |
| Product category | ENDS (VAPES) |
| Product subcategory | ENDS Component |

[7] Brand/sub-brand or other commercial name used in commercial distribution.

**Appendix B**
Amendments Received for These Applications

| Submission Date | Receipt Date | Applications being amended | Reviewed | Brief Description |
|---|---|---|---|---|
| October 13, 2020 | October 13, 2020 | All | Yes | Technical Update |
| November 23, 2020 | November 23, 2020 | All | Yes | Technical Update |
| November 23, 2020 | November 23, 2020 | All | Yes | Technical Update |
| November 24, 2020 | November 24, 2020 | All | Yes | Technical Update |
| November 24, 2020 | November 24, 2020 | All | Yes | Technical Update |
| November 24, 2020 | November 24, 2020 | All | Yes | Technical Update |
| November 24, 2020 | November 24, 2020 | All | Yes | Technical Update |
| November 24, 2020 | November 24, 2020 | All | Yes | Technical Update |
| November 24, 2020 | November 24, 2020 | All | Yes | Technical Update |
| November 24, 2020 | November 24, 2020 | All | Yes | Technical Update |
| November 24, 2020 | November 24, 2020 | All | Yes | Technical Update |
| November 25, 2020 | November 25, 2020 | All | Yes | Technical Update |
| November 25, 2020 | November 25, 2020 | All | Yes | Technical Update |
| January 6, 2021 | January 6, 2021 | All | Yes | Technical Update |
| March 23, 2021 | March 23, 2021 | All | Yes | Technical Update |
| April 20, 2021 | April 20, 2021 | All | Yes | Technical Update |

| PMTA | PD Number | Product Name | Category | Subcategory | Package Type | Package Quantity | Characterizing Flavor | Additional Properties |
|---|---|---|---|---|---|---|---|---|
| PM0003460 | PD1 | Bidi Stick - Arctic | ENDS(VAPES) | ENDS Component | Plastic box | 1 E-Cigarette | Mint, Menthol | Length: 112.5 mm, Diameter: Not Provided, Nicotine: 60 mg/mL, PG/VG Ratio: 47.99/52.01, E-Liquid Volume: 1.4 mL, Wattage: 1.18 Wh, Battery Capacity: 280 mAh, Width: 15.5 mm, Thickness: 7 mm, Disposable |
| PM0003460 | PD10 | Bidi Stick - Winter | ENDS(VAPES) | ENDS Component | Plastic box | 1 E-Cigarette | Watermelon, Melon, Menthol | Length: 112.5 mm, Diameter: Not Provided, Nicotine: 60 mg/mL, PG/VG Ratio: 48.67/51.33, E-Liquid Volume: 1.4 mL, Wattage: 1.18 Wh, Battery Capacity: 280 mAh, Width: 15.5 mm, Thickness: 7 mm, Disposable |
| PM0003460 | PD11 | Bidi Stick - Zest | ENDS(VAPES) | ENDS Component | Plastic box | 1 E-Cigarette | Melon, Pineapple, Banana | Length: 112.5 mm, Diameter: Not Provided, Nicotine: 60 mg/mL, PG/VG Ratio: 48.67/51.33, E-Liquid Volume: 1.4 mL, Wattage: 1.18 Wh, Battery Capacity: 280 mAh, Width: 15.5 mm, Thickness: 7 mm, Disposable |
| PM0003460 | PD3 | Bidi Stick - Dawn | ENDS(VAPES) | ENDS Component | Plastic box | 1 E-Cigarette | Mint, Ginger, Lemon | Length: 112.5 mm, Diameter: Not Provided, Nicotine: 60 mg/mL, PG/VG Ratio: 48.67/51.33, E-Liquid Volume: 1.4 mL, Wattage: 1.18 Wh, Battery Capacity: 280 mAh, Width: 15.5 mm, Thickness: 7 mm, Disposable |
| PM0003460 | PD4 | Bidi Stick - Gold | ENDS(VAPES) | ENDS Component | Plastic box | 1 E-Cigarette | Fresh Mango | Length: 112.5 mm, Diameter: Not Provided, Nicotine: 60 mg/mL, PG/VG Ratio: 49.14/50.86, E-Liquid Volume: 1.4 mL, Wattage: 1.18 Wh, Battery Capacity: 280 mAh, Width: 15.5 mm, Thickness: 7 mm, Disposable |
| PM0003460 | PD5 | Bidi Stick - Marigold | ENDS(VAPES) | ENDS Component | Plastic box | 1 E-Cigarette | Mango, Menthol | Length: 112.5 mm, Diameter: Not Provided, Nicotine: 60 mg/mL, PG/VG Ratio: 49.14/50.86, E-Liquid Volume: 1.4 mL, Wattage: 1.18 Wh, Battery Capacity: 280 mAh, Width: 15.5 mm, Thickness: 7 mm, Disposable |
| PM0003460 | PD6 | Bidi Stick - Regal | ENDS(VAPES) | ENDS Component | Plastic box | 1 E-Cigarette | Dragonfruit, Strawberry | Length: 112.5 mm, Diameter: Not Provided, Nicotine: 60 mg/mL, PG/VG Ratio: 48.67/51.33, E-Liquid Volume: 1.4 mL, Wattage: 1.18 Wh, Battery Capacity: 280 mAh, Width: 15.5 mm, Thickness: 7 mm, Disposable |
| PM0003460 | PD7 | Bidi Stick - Solar | ENDS(VAPES) | ENDS Component | Plastic box | 1 E-Cigarette | Strawberry, Blueberry | Length: 112.5 mm, Diameter: Not Provided, Nicotine: 60 mg/mL, PG/VG Ratio: 48.67/51.33, E-Liquid Volume: 1.4 mL, Wattage: 1.18 Wh, Battery Capacity: 280 mAh, Width: 15.5 mm, Thickness: 7 mm, Disposable |
| PM0003460 | PD8 | Bidi Stick - Summer | ENDS(VAPES) | ENDS Component | Plastic box | 1 E-Cigarette | Blueberry, Pomegranate | Length: 112.5 mm, Diameter: Not Provided, Nicotine: 60 mg/mL, PG/VG Ratio: 48.67/51.33, E-Liquid Volume: 1.4 mL, Wattage: 1.18 Wh, Battery Capacity: 280 mAh, Width: 15.5 mm, Thickness: 7 mm, Disposable |
| PM0003460 | PD9 | Bidi Stick - Tropic | ENDS(VAPES) | ENDS Component | Plastic box | 1 E-Cigarette | Mango, Apple, Orange | Length: 112.5 mm, Diameter: Not Provided, Nicotine: 60 mg/mL, PG/VG Ratio: 47.99/52.01, E-Liquid Volume: 1.4 mL, Wattage: 1.18 Wh, Battery Capacity: 280 mAh, Width: 15.5 mm, Thickness: 7 mm, Disposable |

FDA U.S. FOOD & DRUG ADMINISTRATION

# Review for Flavored[1] ENDS PMTAs

| New Products Subject of this Review | |
|---|---|
| Submission tracking numbers (STNs) | PM0003460, See Appendix A |
| **Common Attributes** | |
| Submission date | September 8, 2020 |
| Receipt date | September 8, 2020 |
| Applicant | Bidi Vapor LLC |
| Product manufacturer | Bidi Vapor LLC |
| Application type | Standard |
| Product category | ENDS (VAPES) |
| Product subcategory | ENDS Component |
| **Cross-Referenced Submissions** | |
| All STNs | MF0000403, MF0000494, and MF0000498 |

| Amendments | | | |
|---|---|---|---|
| **Amendment STN** | **Primary STN** | **Description** | **FDA Receipt Date** |
| PM0004039 | PM0003460 | Technical Update | October 13, 2020 |
| PM0004276 | PM0003460 | Technical Update | November 23, 2020 |
| PM0004277 | PM0003460 | Technical Update | November 23, 2020 |
| PM0004312 | PM0003460 | Technical Update | November 23, 2020 |
| PM0004295 | PM0003460 | Technical Update | November 23, 2020 |
| PM0004296 | PM0003460 | Technical Update | November 23, 2020 |
| PM0004297 | PM0003460 | Technical Update | November 24, 2020 |
| PM0004298 | PM0003460 | Technical Update | November 24, 2020 |
| PM0004299 | PM0003460 | Technical Update | November 24, 2020 |
| PM0004300 | PM0003460 | Technical Update | November 24, 2020 |
| PM0004313 | PM0003460 | Technical Update | November 25, 2020 |
| PM0004301 | PM0003460 | Technical Update | November 25, 2020 |
| PM0004500 | PM0003460 | Technical Update | January 6, 2021 |
| PM0004612 | PM0003460 | Technical Update | March 23, 2021 |
| PM0004646 | PM0003460 | Technical Update | April 20, 2021 |

[1] Throughout this review, and solely as a matter of shorthand to aid in the drafting of this document, the term *flavored ENDS* refers to any ENDS other than tobacco-flavored and menthol-flavored ENDS.

| Conclusion |
| --- |
| Evidence is absent in PMTAs |

| | |
| --- | --- |
| **Reviewer:** | Colin Cunningham, Ph.D.<br>Pharmacologist<br>Division of Individual Health Science |
| **Concurrence:** | |

**SCOPE OF REVIEW**

This review determines whether the subject PMTAs contain evidence from a randomized controlled trial, longitudinal cohort study, and/or other evidence regarding the impact of the new ENDS on switching or cigarette reduction that could potentially demonstrate the benefit of their flavored ENDS over an appropriate comparator tobacco-flavored ENDS. This review includes a search of the PMTAs to determine whether such evidence is found anywhere within the PMTAs. However, this review does not evaluate whether the evidence, if present, is robust enough to demonstrate that the applicant's flavored ENDS are more beneficial than their tobacco-flavored ENDS. If such evidence is present in the application, the Technical Project Lead will determine if full scientific review is necessary.

**Presence of Evidence for Flavored ENDS Products**

| **Criterion A** | **Present** | | **Absent** |
|---|---|---|---|
| ***Randomized Controlled Trial (RCT) on new product use and smoking behavior*** | ☐ | | ☒ |
| Instructions: To select "Present", all of the following boxes must be checked "Yes": | **Yes** | **No** | **N/A[2]** |
| Was the RCT conducted using new products? | ☐ | ☐ | ☒ |
| Does the RCT include a tobacco-flavored arm and a flavored product arm[3]? | ☐ | ☐ | ☒ |
| Do the outcomes include users' ENDS and smoking behavior to assess switching and/or cigarette reduction (e.g., measures of cigarettes per day, smoking cessation, ENDS use)? | ☐ | ☐ | ☒ |
| Comment(s):<br>N/A | | | |

| **Criterion B** | **Present** | | **Absent** |
|---|---|---|---|
| ***Longitudinal Cohort Study (LCS) on new product use and smoking behavior*** | ☐ | | ☒ |
| Instructions: To select "Present", all of the following boxes must be checked "Yes": | **Yes** | **No** | **N/A[2]** |
| Was the LCS conducted and does it include users of new products who are followed over time? | ☐ | ☐ | ☒ |
| Was use of tobacco-flavored products and other flavored products assessed[3]? | ☐ | ☐ | ☒ |
| Do outcomes include users' ENDS and smoking behavior to assess switching and/or cigarette reduction (e.g., measures of cigarettes per day, smoking cessation, ENDS use)? | ☐ | ☐ | ☒ |
| Comment(s):<br>N/A | | | |

[2] Not applicable, because no such study was present.
[3] Check "yes" if at least one non-tobacco flavored product is compared to a tobacco-flavored product.

| Criterion C |
| --- |
| **Other evidence in the PTMA(s) related to potential benefit to adults**<br><br>N/A |

| STN | PD Number | Product Name | Category | Subcategory | Package Type | Package Quantity | Characterizing Flavor | Additional Property |
|---|---|---|---|---|---|---|---|---|
| PM0003460 | PD1 | Bidi Stick - Arctic | ENDS(VAPES) | ENDS Component | Plastic box | 1 E-Cigarette | Mint, Menthol | Length: 112.5 mm, Diameter: Not Provided, Nicotine: 60 mg/mL, PG/VG Ratio: 47.99/52.01, E-Liquid Volume: 1.4 mL, Wattage: 1.18 Wh, Battery Capacity: 280 mAh, Width: 15.5 mm, Thickness: 7 mm, Disposable |
| PM0003460 | PD10 | Bidi Stick - Winter | ENDS(VAPES) | ENDS Component | Plastic box | 1 E-Cigarette | Watermelon, Melon, Menthol | Length: 112.5 mm, Diameter: Not Provided, Nicotine: 60 mg/mL, PG/VG Ratio: 48.67/51.33, E-Liquid Volume: 1.4 mL, Wattage: 1.18 Wh, Battery Capacity: 280 mAh, Width: 15.5 mm, Thickness: 7 mm, Disposable |
| PM0003460 | PD11 | Bidi Stick - Zest | ENDS(VAPES) | ENDS Component | Plastic box | 1 E-Cigarette | Melon, Pineapple, Banana | Length: 112.5 mm, Diameter: Not Provided, Nicotine: 60 mg/mL, PG/VG Ratio: 48.67/51.33, E-Liquid Volume: 1.4 mL, Wattage: 1.18 Wh, Battery Capacity: 280 mAh, Width: 15.5 mm, Thickness: 7 mm, Disposable |
| PM0003460 | PD3 | Bidi Stick - Dawn | ENDS(VAPES) | ENDS Component | Plastic box | 1 E-Cigarette | Mint, Ginger, Lemon | Length: 112.5 mm, Diameter: Not Provided, Nicotine: 60 mg/mL, PG/VG Ratio: 48.67/51.33, E-Liquid Volume: 1.4 mL, Wattage: 1.18 Wh, Battery Capacity: 280 mAh, Width: 15.5 mm, Thickness: 7 mm, Disposable |
| PM0003460 | PD4 | Bidi Stick - Gold | ENDS(VAPES) | ENDS Component | Plastic box | 1 E-Cigarette | Fresh Mango | Length: 112.5 mm, Diameter: Not Provided, Nicotine: 60 mg/mL, PG/VG Ratio: 49.14/50.86, E-Liquid Volume: 1.4 mL, Wattage: 1.18 Wh, Battery Capacity: 280 mAh, Width: 15.5 mm, Thickness: 7 mm, Disposable |
| PM0003460 | PD5 | Bidi Stick - Marigold | ENDS(VAPES) | ENDS Component | Plastic box | 1 E-Cigarette | Mango, Menthol | Length: 112.5 mm, Diameter: Not Provided, Nicotine: 60 mg/mL, PG/VG Ratio: 49.14/50.86, E-Liquid Volume: 1.4 mL, Wattage: 1.18 Wh, Battery Capacity: 280 mAh, Width: 15.5 mm, Thickness: 7 mm, Disposable |
| PM0003460 | PD6 | Bidi Stick - Regal | ENDS(VAPES) | ENDS Component | Plastic box | 1 E-Cigarette | Dragonfruit, Strawberry | Length: 112.5 mm, Diameter: Not Provided, Nicotine: 60 mg/mL, PG/VG Ratio: 48.67/51.33, E-Liquid Volume: 1.4 mL, Wattage: 1.18 Wh, Battery Capacity: 280 mAh, Width: 15.5 mm, Thickness: 7 mm, Disposable |
| PM0003460 | PD7 | Bidi Stick - Solar | ENDS(VAPES) | ENDS Component | Plastic box | 1 E-Cigarette | Strawberry, Blueberry | Length: 112.5 mm, Diameter: Not Provided, Nicotine: 60 mg/mL, PG/VG Ratio: 48.67/51.33, E-Liquid Volume: 1.4 mL, Wattage: 1.18 Wh, Battery Capacity: 280 mAh, Width: 15.5 mm, Thickness: 7 mm, Disposable |
| PM0003460 | PD8 | Bidi Stick - Summer | ENDS(VAPES) | ENDS Component | Plastic box | 1 E-Cigarette | Blueberry, Pomegranate | Length: 112.5 mm, Diameter: Not Provided, Nicotine: 60 mg/mL, PG/VG Ratio: 48.67/51.33, E-Liquid Volume: 1.4 mL, Wattage: 1.18 Wh, Battery Capacity: 280 mAh, Width: 15.5 mm, Thickness: 7 mm, Disposable |
| PM0003460 | PD9 | Bidi Stick - Tropic | ENDS(VAPES) | ENDS Component | Plastic box | 1 E-Cigarette | Mango, Apple, Orange | Length: 112.5 mm, Diameter: Not Provided, Nicotine: 60 mg/mL, PG/VG Ratio: 47.99/52.01, E-Liquid Volume: 1.4 mL, Wattage: 1.18 Wh, Battery Capacity: 280 mAh, Width: 15.5 mm, Thickness: 7 mm, Disposable |

FDA U.S. FOOD & DRUG ADMINISTRATION

# Technical Project Lead (TPL) Review of PMTAs

| **New Products Subject of this Review**[i] | |
|---|---|
| Submission tracking numbers (STNs) | PM0003460, See Appendix A |
| **Common Attributes** | |
| Submission date | September 8, 2020 |
| Receipt date | September 8, 2020 |
| Applicant | Bidi Vapor LLC |
| Product manufacturer | Bidi Vapor LLC |
| Application type | Standard |
| Product category | ENDS (VAPES) |
| Product subcategory | ENDS Component |
| **Cross-Referenced Submissions** | |
| All STNs | MF0000403, MF0000494, and MF0000498 |
| **Recommendation** | |
| Issue marketing denial orders for the new tobacco products subject of this review. | |

**Technical Project Lead (TPL):**

Lynn C. Hull, Ph.D.
Deputy Director
Division of Individual Health Science

**Signatory Decision:** Concur with TPL recommendation and basis of recommendation

Matthew R. Holman, Ph.D.
Director
Office of Science

[i] Product details, amendments, and dates provided in the Appendix. PMTA means premarket tobacco application. Scientific references are listed at the end of this document and referred to with Arabic numerals; general footnotes are referred to with Roman numerals.

## 1. EXECUTIVE SUMMARY

These applications for flavored ENDS[ii] products lack evidence to demonstrate that permitting the marketing of these products would be appropriate for the protection of the public health (APPH). Given the known and substantial risk of flavored ENDS with respect to youth appeal, uptake, and use, applicants would need reliable and robust evidence of a potential benefit to adult smokers[iii] that could justify that risk. Accordingly, in order to show that a flavored ENDS is APPH, the applicant must show that the benefit to adults switching from or reducing cigarettes outweighs the risk to youth.

Based on existing scientific evidence and our experiences in conducting premarket review employing the APPH standard over the last several years, FDA has determined for these applications that, to effectively demonstrate this benefit in terms of product use behavior, only the strongest types of evidence will be sufficiently reliable and robust — most likely product specific evidence from a randomized controlled trial (RCT)[iv] or longitudinal cohort study, although other types of evidence could be adequate, and will be evaluated on a case-by-case basis.[v,vi] Moreover, tobacco-flavored ENDS may offer the same type of public health benefit as flavored ENDS, i.e., increased switching and/or significant reduction in smoking, but do not pose the same degree of risk of youth uptake. Therefore, to demonstrate the potential benefit to current users, FDA has reviewed these applications for any acceptably strong evidence that the flavored products have an added benefit relative to that of tobacco-flavored ENDS in facilitating smokers completely switching away from or significantly reducing their smoking.

We have reviewed the subject applications to determine whether they contain sufficient evidence of the type described above to demonstrate APPH. Our review determined that the subject PMTAs do not contain evidence from a randomized controlled trial, longitudinal cohort study, or other evidence regarding the impact of the ENDS on switching or cigarette reduction that could potentially demonstrate the benefit of their flavored ENDS over tobacco-flavored ENDS. As a result, the applicant has failed to provide evidence to overcome the risk to youth and show a net population

[ii] The term *flavored ENDS* in this review refers to any ENDS other than tobacco-flavored and menthol-flavored ENDS. Tobacco-flavored ENDS are discussed below. Applications for menthol-flavored ENDS will be addressed separately. When it comes to evaluating the risks and benefits of a marketing authorization, the assessment for menthol ENDS, as compared to other non-tobacco-flavored ENDS, raises unique considerations. The term *flavored ENDS* also includes unflavored "base" e-liquids that are designed to have flavors added to them. This includes e-liquids made for use with open systems as well as closed system ENDS (e.g., cartridges or disposable ENDS) containing e-liquids.

[iii] The standard described in Section 910 requires an accounting of the risks and benefits to the population as a whole, balancing the potential impacts to both current tobacco users and non-users. This review is focused on the risk to youth nonusers as well as the potential benefit to adult smokers as current users, as they are the group through which the potential benefit to public health is most substantial and could overcome the known risk to youth.

[iv] A randomized controlled trial is a clinical investigation or a clinical study in which human subject(s) are prospectively, and randomly assigned to one or more interventions (or no intervention) to evaluate the effect(s) of the intervention(s) on behavioral, biomedical, or health-related outcomes. *Control or controlled* means, with respect to a clinical trial, that data collected on human subjects in the clinical trial will be compared to concurrently collected data or to non-concurrently collected data (*e.g.,* historical controls, including a human subject's own baseline data), as reflected in the pre-specified primary or secondary outcome measures.

[v] A longitudinal cohort study is an observational study in which human subjects from a defined population are examined prospectively over a period of time to assess an outcome or set of outcomes among study groups defined by a common characteristic (e.g., smoking cessation among users of flavored ENDS compared with users of tobacco-flavored ENDS).

[vi] For example, we would consider evidence from another study design if it could reliably and robustly assess behavior change (product switching or cigarette reduction) over time, comparing users of flavored products with those of tobacco-flavored products. In our review of PMTAs for flavored ENDS so far, we have learned that, in the absence of strong evidence generated by directly observing the behavioral impacts of using a flavored product vs. a tobacco-flavored product over time, we are unable to reach a conclusion that the benefit outweighs the clear risks to youth.

the surge in ENDS use among youth and thus prioritized enforcement against certain flavored ENDS products, with the goal of protecting youth from these products. [viii]

After FDA implemented this enforcement policy prioritizing enforcement against a subset of ENDS products known to appeal to youth, there was a meaningful reduction in youth use prevalence. Youth ENDS use peaked in 2019 when these products were widely available. Although several other policy changes and interventions were occurring during this same time period, [ix] it is reasonable to infer that prioritizing enforcement against many flavored products resulting in their removal from the market contributed to the decline in use in 2020. Despite this decline, ENDS remained the most widely used tobacco product among youth, with youth use at levels comparable to what originally led FDA to declare a youth vaping epidemic. Moreover, despite the overall reduction in ENDS youth use observed in 2020, there was simultaneously a substantial rise in youth use of disposable ENDS, products that were largely excluded from the enforcement policy described in the 2020 Enforcement Priorities Guidance because, at that time that policy was developed, those products were the least commonly used device type among high school ENDS users and therefore remained on the market as a flavored option.[3,4]

Section 910(c)(2)(A) of the FD&C Act requires that FDA deny a PMTA where it finds "there is a lack of a showing that permitting such tobacco product to be marketed would be [APPH]." Through the PMTA review process, FDA conducts a science-based evaluation to determine whether marketing of a new tobacco product is APPH. Section 910(c)(4) requires FDA, in making the APPH determination, to consider the risks and benefits to the population as a whole, including users and nonusers of tobacco, and take into account, among other things, the likelihood that those who do not use tobacco products will start using them. FDA's scientific review is not limited to considering only information in a PMTA, but also extends to any other information before the Agency, including the relevant existing scientific literature (See Section 910(c)(2)). As described in greater detail below, in reviewing PMTAs for flavored ENDS, FDA evaluates, among other things, the potential benefit to adult smokers who may transition away from combustible cigarettes to the ENDS product, weighed against the known risks of flavored ENDS to youth.

### 2.3.1. The Risk to Youth of Flavored ENDS Products

As noted, the APPH determination includes an assessment of the risks and benefits to the population as a whole, and for ENDS (as well as many other tobacco products) the application of that standard requires assessing the potential impact of the marketing of a new product on youth use. As a group, youth are considered a vulnerable population for various reasons, including that the majority of tobacco use begins before adulthood[5] and thus youth are at particular risk of tobacco initiation. In fact, use of tobacco products, no matter what type, is almost always started and established during adolescence when the developing brain is most vulnerable to nicotine addiction. Indeed, almost 90 percent of adult daily smokers started smoking by the age of 18.[6] Adolescent tobacco users who initiated tobacco use at earlier ages were more likely than those initiating at older ages to report symptoms of tobacco dependence, putting them at greater risk for maintaining tobacco product use into adulthood.[7] On the other hand, youth and young adults who

[viii] Due to the overwhelming amount of evidence showing a substantial increase in youth use of flavored ENDS products, as well as their demonstrated popularity among youth, in January 2020, FDA finalized a guidance prioritizing enforcement against flavored (other than tobacco or menthol) prefilled pod or cartridge-based e-cigarettes, as well as other categories of unauthorized products.

[ix] The change in ENDS product availability coincided with other events such as the enactment of legislation raising the federal minimum age for sale of tobacco products from 18 to 21 years (Tobacco 21), the outbreak of e-cigarette, or vaping, product-use associated lung injury (EVALI), and public education campaigns which also may have contributed to the decline in ENDS use.

product use to combusted cigarette use has been observed for other non-cigarette products, such as cigars, as well.[58] Although it is challenging to empirically separate causality from shared risk factors among youth combusted cigarette and ENDS users, some studies have found an association between ENDS and subsequent combusted cigarette use while controlling for similar risk profiles.[54]

The precise relationship between youth ENDS use and youth smoking remains undetermined. On the one hand, the prevalence of combusted cigarette smoking in youth has continued to decline,[9,59,60] suggesting that youth use of ENDS has not significantly slowed or impeded that positive public health trajectory. On the other hand, there is a growing body of evidence showing a link between ENDS use and subsequent smoking among youth that raises significant concerns. This evidence also increases concern that over time—and particularly if youth ENDS use were to return to the rates seen in 2019 or worsen--the trend of declining cigarette smoking could slow or even reverse.

#### 2.3.1.5. Other health risks associated with ENDS use

In addition to the risk of tobacco initiation and progression among youth, there is epidemiologic evidence from the cross-sectional[xvi] Behavioral Risk Factor Survey system (BRFSS) suggesting positive associations between ENDS use among those who never smoked and some health outcomes. Two studies found associations between ENDS use and self-reported history of asthma, chronic bronchitis, emphysema, or chronic obstructive pulmonary disease with increased ENDS use (i.e., daily use) relating to increased odds of disease.[61,62] Another found an association between ENDS use and respiratory symptoms in younger adults (ages 18-34) but not in older adults.[63] ENDS use has also resulted in acute harm to individuals through battery explosion-related burns and e-liquid nicotine poisoning.[64-66] Ultimately, as this is still a relatively novel product category, much remains unknown about other potential long-term health risks.

#### 2.3.1.6. Conclusion

The exponential growth in youth ENDS use observed from 2017 to 2019, and the enduring prevalence of youth ENDS use in the U.S. is alarming. Despite a reduction in youth use of ENDS from 2019 to 2020, there were still 3.6 million youth ENDS users in 2020 and the majority used a flavored ENDS product. Youth users are more likely to use flavored ENDS than adult ENDS users. Flavors are associated with ENDS initiation and progression among youth. The full extent of the harms of ENDS use are not yet known, but evidence to date suggests they include permanent effects of nicotine on the developing adolescent brain and the risk of nicotine addiction. Studies indicate an additive effect of e-liquid flavorings on the rewarding and reinforcing effects of nicotine containing e-liquids. Studies also demonstrate that e-liquid flavors affect nicotine exposure. Among youth who use ENDS, there is a risk of progression to other tobacco products with greater health risks including combustible cigarettes. Finally, though long-term health risks are not fully understood, studies suggest an association between never-smoking ENDS users and respiratory and cardiovascular health effects. This evidence demonstrates that flavored ENDS pose a significant risk to youth.

### 2.3.2. Balancing Known Risks to Youth with a Potential Benefit to Adults

Determining whether marketing a new product is APPH includes evaluating the risks and benefits to the population as a whole. This requires FDA to balance, among other things, the negative public health impact for nonusers against the potential positive public health impact for current tobacco users. Accordingly, for marketing of a new product to be found to be APPH, any risks posed by a new product to youth would need to be overcome by a sufficient benefit to adult users, and as the

[xvi] Cross-sectional surveys examine these relationships at a single point in time, and as a result, do not establish causality.

known risks increase, so too does the burden of demonstrating a substantial enough benefit. In the case of a new flavored ENDS product, the risk of youth initiation and use is substantial, given the clearly documented evidence described above. In order for marketing of a new flavored ENDS product to be found APPH, an applicant would have to show that the significant risk to youth could be overcome by likely benefits substantial enough such that the net impact to public health would be positive, taking into account all relevant evidence and circumstances, including whether there are effective limitations on youth access.

#### 2.3.2.1. Potential benefit of new flavored ENDS

Current scientific literature demonstrates that ENDS are generally likely to have fewer and lower concentrations of harmful and potentially harmful constituents (HPHCs) than combustible cigarettes, and biomarker studies demonstrate significantly lower exposure to HPHCs among current exclusive ENDS users than current smokers.[57] However, whether this is true for any particular new ENDS product, and the implications for health risks from a particular product, are considered on a case-by-case basis during the course of FDA's scientific review of a PMTA.

FDA also considers the potential that current cigarette smokers may experience a reduction in health risks if they switch completely to an ENDS, or if they use both products but substantially reduce their cigarette smoking. For a flavored ENDS product, assuming that the evaluation of the product shows the likelihood for lower HPHC exposure, then to demonstrate the likely individual and population benefit, applicants must demonstrate that current smokers are likely to start using the new ENDS product exclusively or predominantly (e.g., dual use with a significant smoking reduction).[64]

#### 2.3.2.2. Behavioral evidence appropriate to demonstrate the potential benefit to smokers

FDA's PMTA review includes an evaluation of any potential benefits of the product for the likely users, such as a possible reduction in health risks. In general, as FDA stated in its guidance for PMTAs for ENDS,[xvii] an assessment of how a new product may be used by current smokers can be derived from a variety of sources. FDA may consider direct behavioral evidence on the specific products under review or indirect evidence derived from studies of behavioral intentions; pharmacological studies of nicotine delivery, abuse liability, and/or use topography; and bridging from studies based on comparable products. Further, in the case of a flavored ENDS product, to demonstrate that the marketing of the new product is APPH, the magnitude of the likely benefit would have to be substantial enough to overcome the significant risk of youth uptake and use posed by the flavored ENDS product.

Section 910(c)(5) of the FD&C Act provides that determining whether marketing of a new tobacco product is APPH shall, when appropriate, be based on "well-controlled investigations, which may include one or more clinical investigations by experts qualified by training and experience to evaluate the tobacco product." FDA believes well-controlled investigations are "appropriate" for demonstrating that permitting the marketing of specific flavored ENDS would be APPH given the significant risks to youth of flavored ENDS. One type of well-controlled investigation that could effectively demonstrate a potential benefit of a flavored ENDS product would be an RCT. In addition, as CTP has previously described,[xviii] another well-controlled investigation that could serve as an alternative to conducting an RCT to demonstrate adequate benefit is a longitudinal cohort study.

[xvii] Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems: Guidance for Industry (p.47); October 2020 Public Meeting on Deemed Tobacco Product Applications

[xviii] Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems: Guidance for Industry (p.47); October 2020 Public Meeting on Deemed Tobacco Product Applications

For flavored ENDS, the known and substantial risk to youth in particular is high. Therefore, to show a net population health benefit, FDA has determined that these applications must demonstrate potential benefits to smokers from marketing such products with robust and reliable evidence – including both robust study design and methods and the strength of the study results. In other words, because the potential benefit to adults is gained through its impact on smoking behavior, FDA is reviewing these applications to determine whether they demonstrate that a benefit of a new product is significant enough to overcome the risk to youth. In particular, FDA's review of these applications has considered the degree of benefit to a flavored ENDS product over a tobacco-flavored variety in facilitating smokers completely switching or significantly reducing their smoking, given the significant increase in risk of youth initiation associated with flavored ENDS compared to tobacco-flavored ENDS. Note that applications with this type of information may still not be APPH: applications containing this evidence would still be evaluated to determine that the totality of the evidence supports a marketing authorization. As it relates to the risk to youth, for example, this assessment includes evaluating the appropriateness of the proposed marketing plan.[xix]

We have been using the APPH standard for several years in reviewing previous PMTAs for non-ENDS products. Our substantive review of PMTAs for ENDS and our completion of numerous scientific reviews over the last 10 months have deepened our understanding of the APPH evaluation with respect to behavior. In these reviews, the expectations for scientific evidence related to potential adult benefit can vary based on demonstrated risk to youth. Although indirect evidence or bridged data from the literature may still be appropriate for many new products, including tobacco-flavored ENDS, robust and direct evidence demonstrating potential benefit has been needed when the known risks are high as with all flavored ENDS products. At the same time, we have learned from experience that, in the absence of strong direct evidence, we are unable to reach a conclusion that the benefit outweighs the clear risks to youth. For instance, applicants who do not conduct their own behavioral studies must rely on, and bridge to, the general ENDS category literature to inform an evaluation of the potential benefit to adult users. To date, that approach has not been sufficient in our evaluation of flavored ENDS PMTAs because, in contrast to the evidence related to youth initiation—which shows clear and consistent patterns of real-world use that support strong conclusions--the evidence regarding the role of flavors in promoting switching among adult smokers is far from conclusive.[xx] In fact, the findings are quite mixed and as a result the literature does not establish that flavors differentially promote switching amongst ENDS users in general. Aside from differences in study design/methods, the heterogeneity of the existing literature is likely due, at least in part, to differences in the products studied. Therefore, given the state of the science on flavored ENDS, and the known risks to youth, FDA has reviewed these applications for any acceptably strong product-specific evidence.

[xix] Limiting youth access and exposure to marketing is a critical aspect of product regulation. It is theoretically possible that significant mitigation efforts could adequately reduce youth access and appeal such that the risk for youth initiation would be reduced. However, to date, none of the ENDS PMTAs that FDA has evaluated have proposed advertising and promotion restrictions that would decrease appeal to youth to a degree significant enough to address and counter-balance the substantial concerns, and supporting evidence, discussed above regarding youth use. Similarly, we are not aware of access restrictions that, to date, have been successful in sufficiently decreasing the ability of youth to obtain and use ENDS. Accordingly, for the sake of efficiency, the evaluation of the marketing plans in applications will not occur at this stage of review, and we have not evaluated any marketing plans submitted with these applications.

[xx] This discrepancy between the literature for youth initiation and adult switching also likely reflects fundamental differences in the two outcomes being assessed—youth initiation and switching among adult smokers—and their determinants. For switching among adult smokers, the behavior change is occurring in the context of nicotine dependence. Thus, the specific product's ability to provide adequate reinforcement and continue to satisfy a smoker's cravings over time, which is a function of the design of the specific product itself, are critical factors in determining likelihood of continued use and the product's ability to promote switching. Whereas for youth initiation, experimentation among naïve or novice users is not driven by these factors.

FDA U.S. FOOD & DRUG ADMINISTRATION

# Technical Project Lead (TPL) Review of PMTAs

| New Products Subject of this Review[i] | |
|---|---|
| Submission tracking number (STNs) | (b) (4) See Appendix A |
| **Common Attributes** | |
| Submission date | September 7, 2020 |
| Receipt date | September 7, 2020 |
| Applicant | (b) (4) |
| Product manufacturer | (b) (4) |
| Application type | Standard |
| Product category | ENDS (VAPES) |
| Product subcategory | ENDS Component |
| **Cross-Referenced Submission** | |
| All new products | None |
| **Recommendation** | |
| Issue marketing denial orders for the new tobacco products subject of this review. | |

**Technical Project Lead (TPL):**

Digitally signed by David B. Portnoy -S
Date: 2021.09.17 10:42:36 -04'00'

David B. Portnoy, Ph.D., M.P.H.
Branch Chief, Social Science Branch 2
Division of Population Health Science

**Signatory Decision:** Concur with TPL recommendation and basis of recommendation

Digitally signed by Matthew R. Holman -S
Date: 2021.09.17 10:59:24 -04'00'

Matthew R. Holman, Ph.D.
Director
Office of Science

[i] Product details, amendments, and dates provided in the Appendix. PMTA means premarket tobacco application. Scientific references (if any) are listed at the end of this document and referred to with Arabic numerals; general footnotes are referred to with Roman numerals.

ANNE RADWAY:
Hello, everyone, thank you for joining us today and welcome, I'm Anne Radway, the Associate Director in the Division of Regulatory Project Management in CTP's Office of Science. I've worked with CTP and the Office of Science for the last nine years. I started as a regulatory health project manager and moved up through many leadership positions and took my current role. As Associate Director, among many other things, I'm responsible for the training and development of the division. One of the main priorities is to prepare the regulatory health project managers to serve as industry liaisons and the regulatory experts and the Office of Science.

ANNE RADWAY:
Prior to joining CTP, I spent several years in the military and as a contractor working with biological select agents. I started my current role as Associate Director in the Division of Regulatory Project Management in October 2019. We are really excited to welcome everyone to the public meeting as we share the latest updates on Deemed product review. During today's meeting, we'll cover a range of topics related to deemed product review, including an overview of the CTP OS planning and preparation for the September 9th deadline. We will highlight our current review progress and current metrics and reporting and also provide information on the public lists of products.

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After the presentation, we will also have time to answer your questions during an open panel discussion with you and representatives from the Office of Science. I encourage you to submit your questions at any time during the meeting by entering your name and your question in the chat box below and then pressing post. You will not see a confirmation, but after pressing post, your question will be successfully submitted to us. Feel free to submit multiple questions as well. Please be aware that we will not take questions that are not related to the topic of this meeting or any questions about individual applications.

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If you have questions about your specific applications, please reach out directly to your assigned regulatory health project manager or email askCTP@fda.hhs.gov. Now, I'd like to start the meeting by introducing Dr Matthew Holman, the director of the Office of Science at the Center for Tobacco Products. Dr Holman has 20 years of experience working as a regulator at FDA, including over 10 years at CTP. During his first six years at CTP, he headed the division of Product Science. In this position, he oversaw evaluation of the composition and design of tobacco products. In addition, he was involved in chemical microbiological and engineering research on tobacco products,

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resulting in numerous publications and peer reviewed scientific journals. He was appointed to his current position as director of the Office of Science in January 2017. In addition to reviewing tobacco product applications, the Office of Science provides scientific support for regulations and guidance, evaluates the knowledge basis for regulatory decisions, and carries out research to fill the gaps in scientific knowledge related to tobacco product regulation. Many thanks to Dr Holman for joining us today. I will now turn it over to Matt to share more information on deemed product review.

Thanks, Cristi. The next question, if there is no long no long term health data about how a product will impact public health, would that product receive a deficiency letter? Matt, do you wanna take this one?

MATTHEW R. HOLMAN:
Sure. Yeah, I would, I think in that scenario, we would like to send a deficiency letter. I mean, I think once we get a substantial scientific review, as we've said a couple of times this afternoon, our intent is to issue a signal deficiency letter. And as I explained with the new language we put in the PMTA deficiency letter, specifically, the intent of those letters is to identify information that we think is necessary to complete our review and make it and make our final determination on whether to issue marketing, brand or marketing denying order. So if there is missing information like no long term health data about the product, we would likely put a deficiency, likely send the deficiency letter,

MATTHEW R. HOLMAN:
and that would certainly be one of the deficiencies. I will reiterate what I believe Todd and maybe even Cristi talked about, which is such data does it, can be public data, it can be public data that. So I guess just to clarify, if if there is no data specific to that, none of this long term data specific to the product that is subject to application that wouldn't necessarily result in the deficiency, because if they did actually give us some public data and they the application clearly explain how that data is applicable to the product subject to the application. If we we agree with that, we would actually send it officially.

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Now, if they submitted some general public health for a long term data and they didn't link it to their didn't adequately link it to their product, then again, that would result in deficiency.

ANNE RADWAY:
OK, next question is for Crystal, CTP's website has frequent updates. Is there a good way to know when those changes are made?

CRYSTAL ALLARD:
There are a couple of different ways to tell when our website's changed, all of our websites have content current as of dates on them up at the top right corner. You can also always sign up for email. It's from CTP, which would give you notifications when ever CTP has something like to share with you. For instance, there are multiple types of email outreach that describe things like regulation, updates, guidances ,enforcement actions, compliance related announcements, etc. and CTP's also on social media, so, for instance, you can follow us on CTP on Twitter @FDATobacco. And if you have any specific questions about content on the websites, you can always email the e-submissions Help Desk or the AskCTP email address.

ANNE RADWAY:
Thank you. OK, we have a follow up for Todd on controls and standards. The question is, we manufacturer NS devices, how do we know what controls and standards to test vapor output against when there is there are no known standard e-liquids.

TODD CECIL:

**Autum:** [00:00:03] Hi, everyone. My name is Autum Brunelle. I hope everyone enjoyed the networking session. It's my honor to introduce our next speaker, Dr. Matt Holman, who is currently director of the Office of Science at the Center for Tobacco Products of the U.S. FDA, a position that he has held since January 2017, before taking on his current position. Dr. Holman served as director of the Division of Product Science within CTP's, Office of Science for six years. In this position, he oversaw evaluation of the composition and design of tobacco products, and he served as technical project lead, which involved reviewing over a thousand SE reports. Over his career he has authored numerous publications regarding tobacco products and peer reviewed scientific journals. Dr. Holman will be speaking on what we should know about FDA regulation of e-cigarettes. Thank you for joining us, Matt.

**Matt Holman:** [00:00:56] Right, thank you, Autum. Happy to be here, thank you very much for the invitation to speak. (resolving technical difficulties) Perfect. So I'm going to talk really about three different things. First, I want to give everyone just a sort of snapshot about where do we stand right now within the PMTA review? I think most, if not all, of you are pretty familiar with that. So I won't spend a ton of time on that part of the presentation. Really, rather, I'll spend more time talking about our APPH determination. So I think all viewers know that under Section nine 10, which is what or premarket tobacco product applications are submitted under, we have to determine if marketing of a new tobacco product is appropriate for the protection of public health or not. And that's what we reviewed APPH if it's found APPH we issue a marketing granted order or shorthand as MGO. If we don't find it, marketing of a new product is appropriate for the protection of public health. And then we issue marketing denial or MDO. So I'll talk to that a little bit more and make sure that folks understand the science and the public health thinking that's gone behind the determinations that we've made to date and that we're currently working on. And then lastly, I think all of you guys probably saw that the PMTA final published this morning in the Federal Register. So I want to just spend a little bit of time walking through some key aspects of that final rule because that will impact PMTAs that are submitted to us going forward.

**Matt Holman:** [00:02:34] So with that, let me start with where do we currently stand with our review of these PMTAs? We got over six and a half million PMTAs for ends products by the court order mandate court mandated date of September 9th of last year. Some of these all came in shortly before or at that date. We were able to take final

deficiency letter under the PMTA path before we go to an order letter. Typically, there are some deficiencies and we would communicate those to the applicant to give the applicant an opportunity to respond and then finish out our scientific review and issue an order letter, whether it be positive or negative. The reason we do skip deficiency letters at times and the reason we did in this case is if there is any major data that is required to find that product or marketing that new product APPH, we would skip the deficiency letter if that data was missing under certain conditions. If we thought the applicant didn't have that data and would need to collect that data and time to collect that data would exceed the time that we would provide in the deficiency letter in order to respond. In other words, there was no way an applicant would respond to the deficiency letter and that time identified by FDA and that deficiency letter.

**Matt Holman:** [00:10:12] We would skip to an order letter and not bother sending the deficiency. So that really is the case here. We didn't think the types of data that we would need by applicants if we skip the deficiency letter. We didn't think the applicant had that data in hand, and it would take a long time to pull longer than the time we grant and the deficient letter to respond. That being said, there is still an opportunity to respond to this through this negative marketing orders that have the deficiency, and I'm going to talk about that in a moment when I talk about the final rule. Let me also say I know another question, another thing I've seen a lot of commentary about by stakeholders is marketing and access restrictions. I've said consistently for quite a while now in all different fora that I think with ends, marketing restrictions, access restrictions are really, I think, an important piece of this puzzle. And I think we'll plan do plan actually to an APPH based determination. In fact, we have for any products that we've issued positive marketing works. We do have restrictions that are identified in those marketing orders. But what we have seen to date is that there are no marketing or access restrictions that are proposed to date, that when we've done our review, we saw were adequate in and of themselves to alleviate our public health concerns, which I'm going to talk about right now.

**Matt Holman:** [00:11:39] So I don't think a lot of this will surprise most of you. We are still very much interested in the consumer risk. We are still very much interested in taking users of tobacco product and moving them from the most harmful to the least harmful. So in my graph here in moving from the left side of the screen to the right side of the screen towards no tobacco use also ensure that we minimize new or non-users

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov

May 8, 2020

**WRITTEN RESPONSE**

Bidi Vapor LLC, USA
Attention: Mr. Nirajkumar Patel, CEO
401 N Wickham Rd, Ste 130
Melbourne, FL 32935

**FDA Submission Tracking Number (STN): TC0005671**

Dear Mr. Patel:

Please refer to the February 27, 2020 Meeting Granted letter where FDA notified you of our decision to provide a written response only in lieu of a face-to-face meeting as indicated in your meeting request.

This letter provides our written response to your February 8, 2020 meeting request related to your planned submission of a PMTA[1] for your electronic nicotine device system (ENDS) product, Bidi Stick.

A copy of our official written response is attached for your information. This meeting request is now closed. Should you decide to request another meeting on this topic, a new meeting request is required.

If you have any questions please contact Antonio Thornton, Regulatory Health Project Manager, at (240) 402-3577 or Antonio.Thornton@fda.hhs.gov.

Sincerely,

Mary E. Kushman -S 2020.05.08 13:14:16 -04'00'

Mary Kushman, Ph.D., M.P.H.
Lead Toxicologist
Division of Nonclinical Science
Office of Science
Center for Tobacco Products

Enclosure:
Appendix A - Written Response

[1] Premarket Tobacco Product Application (PMTA) submitted under section 910 of the Federal Food, Drug, and Cosmetic Act (FD&C Act))

**Additional Comments**

You noted that one of the objectives of your meeting request was to seek clarification on the requirement, type, and category for a comparator product, if any, for a PMTA application. However, you did not include specific questions related to this topic. Section 910(b)(1) of the FD&C Act discusses that a PMTA shall contain "whether such tobacco product presents less risk than other tobacco products." Currently, FDA does not have specific requirements for evaluating comparator products in studies in a PMTA submission. However, FDA recommends you compare the health risks of your tobacco product to both products within the same category and subcategory, as well as products in different categories as appropriate. In your PMTA, it is important to provide a rationale and justification for the comparator products selected for your clinical studies. We refer you to the PMTA ENDS Guidance[4], PMTA NPRM[16], and the 2018 and 2019 CTP Public Meetings[17,18] for more information on comparator products.

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[17] US Food and Drug Administration. Tobacco Product Application Review - A Public Meeting. October 22-23, 2018. *https://www.fda.gov/tobacco-products/ctp-newsroom/tobacco-product-application-review-public-meeting*, content current as of 5/30/2019.

[18] US Food and Drug Administration. Deemed Tobacco Product Applications - A Public Meeting. October 28-29, 2019. https://www.fda.gov/tobacco-products/ctp-newsroom/deemed-tobacco-product-applications-public-meeting-10282019-10292019 , content current as of 12/18/2019.

U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
www.fda.gov

February 05, 2021

**ACCEPTANCE**

Bidi Vapor LLC
Attention: Nirajkumar Patel, CEO
4460 Old Dixie Hwy
Grant Valkaria, FL 32949

**FDA Submission Tracking Number (STN):** PM0003460, see Appendix A

Dear Mr. Patel:

We accept your PMTA[1] for the tobacco product identified in Appendix A. Note that attributes in Appendix A may display converted values.

Your PMTA will move forward in the review process. FDA may request to conduct inspections, which may include manufacturing inspections and clinical and nonclinical research inspections, to verify the information submitted in your PMTA. The results of these inspections may also be used to verify the information submitted in any additional applications that reference the same manufacturing and research information. To ensure that the appropriate records and personnel will be available during the inspections, FDA will notify the point(s) of contact identified prior to the inspection start date.

We will notify you if samples are required for independent testing and verification. If samples are required, you will be notified by letter of the number of samples required and the laboratory address where samples must be received. All requested samples should be received by the laboratory identified in the letter within 14 calendar days of the request.

If you have any questions, please contact Maria Suarez, Regulatory Health Project Manager, at 301-348-1867 or Maria.Suarez@fda.hhs.gov.

Sincerely,

Digitally signed by Laila S. Noory -S
Date: 2021.02.05 11:55:50 -05'00'

Laila Noory, M.P.H., P.M.P.
Lead Regulatory Health Project Manager
Division of Regulatory Project Management
Office of Science
Center for Tobacco Products

**Enclosures (if provided electronically, the Appendix is not included in physical mail):**
Appendix A – New Tobacco Product Subject of This Letter

[1] Premarket Tobacco Product Application (PMTA) submitted under section 910 of the Federal Food, Drug, and Cosmetic Act (FD&C Act)

# AFFIDAVIT OF NIRAJ PATEL

1. My name is Nirajkumar (Niraj) Patel. I am the founder, Chief Executive Officer, and principal owner of Bidi Vapor LLC, which is a privately held Florida limited liability company in the business of manufacturing and selling electronic nicotine delivery systems to adult smokers and tobacco users 21 and over.

2. I have personal knowledge as to the facts alleged herein.

## *Personal Background*

3. I am a U.S. citizen holding a Bachelor of Science Degree in Pharmacy from AISSMS College of Pharmacy in Pune, India, and a Master of Science in Chemistry from the Florida Institute of Technology. I am 38 years old and currently reside in Melbourne, Florida with my wife and two young children.

4. My family in India has been in the tobacco business for three generations. My paternal grandfather was a tobacco farmer and trader. My father followed in my grandfather's footsteps on the farm and worked to expand the business into tobacco blending and processing. As a young boy, I would visit the factory and see the harmful effects tobacco was having on the workers, especially those that had to handle the raw tobacco plants, and were often covered in tobacco dust and waste generated from the processing equipment. Even the workers that did not smoke would often get ill and suffered from inhaling harmful toxins all day from working in the factory.

5. Many members of my family and friends in India smoke cigarettes and use tobacco products, and are facing the health consequences. My maternal grandfather was 70 years old when he died from years of smoking. He was a daily smoker for almost his entire life, and literally died with a cigarette in his hand. My father suffered two heart attacks after years of smoking, but was only able to quit after he began using my company's product, the BIDI® Stick.

6. Despite witnessing these harmful effects from tobacco and smoking cigarettes, I also began smoking cigarettes when I joined the family business at the age of 20.

7. I might have continued down the same path as my father and grandfather, but in 2010 I learned about e-cigarettes and vaping technology. After some research, I became very excited by what this new technology could offer for adult smokers like myself and my father. Not long after, I was able to use an e-cigarette – specifically, a disposable product – to quit my own cigarette smoking habit. My health has improved dramatically since I quit smoking.

8. This inspired me to leave my family's tobacco business, and start my own company developing electronic nicotine delivery system (ENDS) technology. In 2013, I formed Just Chill Products, LLC, and used my background in chemistry and pharmaceutical studies to develop various ENDS products for adult smokers, including flavored e-liquid formulations containing USP-grade tobacco-derived nicotine.

***Background on Disposable ENDS***

9. There are two broad categories of ENDS products: open-systems and closed-systems. Open-system devices utilize a refillable e-liquid tank and large, rechargeable 18650 lithium-ion batteries. These products raise several safety concerns. The larger batteries in these products are often unregulated and are prone to overheating and exploding. Open-systems also require consumers to purchase separately bottled e-liquid to fill the tanks on their own. This means the consumers must directly handle the nicotine e-liquids. Both the Food and Drug Administration (FDA) as well as the Consumer Product Safety Commission (CPSC) have raised serious concerns about the danger this presents to young children and pets who could accidentally come into contact with or ingest flavored e-liquids in unsealed bottles.

10. Closed-system devices include pod/cartridge-based ENDS, as well as disposable ENDS. Pod/cartridge-based ENDS (like the JUUL) use smaller batteries, but are still rechargeable, presenting some potential to overheat. While the pods are prefilled with e-liquid by the manufacturer, they are often easily manipulated, sometimes leak and can be refilled by consumers. Counterfeit pods made by black market entities to fit with authentic products also present major safety and health concerns.

11. While all ENDS products are beneficial for adult cigarette smokers who are unable to quit completely, because of the safety concerns associated with open-systems

and pod/cartridge systems, I focused my research on developing disposable ENDS. Disposable ENDS are completely self-contained single units that use smaller batteries that cannot be recharged. These do not present any overheating concerns or fire hazards. The e-liquid in these devices is also prefilled into a sealed reservoir by the manufacturer, so there is no way for consumers (or children or pets) to ever come into direct contact with the e-liquid. High quality disposables (like the BIDI® Stick) are designed to be tamper-resistant so that the contained e-liquid cannot be contaminated or adulterated. There are also no pods or cartridges that can be lost or misplaced, and no recharging is required.

12. Disposables are also draw activated and provide a much more consistent nicotine delivery than open system devices, which typically have numerous components and parts and various temperature and other settings. Once the e-liquid in a disposable is consumed the product is discarded (or, like BIDI® Sticks, can be recycled).

13. Disposables ENDS are often painted in a negative light because they are user-friendly, which may make them easier for non-smokers and young people to try. However, it is precisely because disposables are easy to use compared to multi-component open-systems and rechargeable pod/cartridge systems that they have the potential to help millions of adult smokers switch to vaping, particularly older Americans. Like me and my father, these consumers are used to simply "lighting up" a cigarette, but are often not interested in the other, more complicated ENDS products.

14. When I was exploring vaping for personal use, I tried many different ENDS products. But it was a first-generation disposable ENDS that was simple and easy enough to finally help me make the switch and stay off cigarettes. It was for all these reasons that I decided to focus on developing disposable ENDS technology for adult smokers.

15. It also subsequently became clear that the path to FDA authorization would be less onerous for a disposable ENDS compared to an open-system ENDS. In May 2016, FDA published its draft Premarket Tobacco Product Application (PMTA) guidance for ENDS along with the Deeming Rule. This was the first agency guidance on the PMTA process specifically for ENDS and summarized FDA's recommendations to meet the "appropriate for the protection of the public health" (APPH) standard. Among other things, the draft PMTA guidance made clear that constituent testing for closed-system ENDS would be much more straightforward compared to open-systems. More specifically, FDA indicated that testing for an open-system device should reflect the range of operating conditions (such as various temperature, voltage, wattage settings) and use patterns (such as use conditions by light users, typical users, and heavy users) within which consumers are likely to use the product, and that testing for those products should be conducted with a reasonable range of available e-liquids. FDA recommended that a closed-system ENDS (like a disposable), on the other hand, need only be tested with the e-liquids with which it is packaged and sold.

***The Tobacco Control Act and FDA's Deeming Rule***

16. By way of background, ENDS products like the BIDI® Stick that contain tobacco-derived nicotine fall within the meaning of a "tobacco product" in the Food, Drug and Cosmetic Act, as amended by the Tobacco Control Act (TCA). When the TCA was enacted it gave FDA immediate authority over certain tobacco product categories: cigarettes, cigarette tobacco, smokeless tobacco and roll-your-own tobacco. It also gave FDA the authority to use its rulemaking powers to "deem" unregulated tobacco products, like ENDS, to be regulated.

17. In May 2016, FDA published its long-awaited "Deeming Rule" which became effective on August 8, 2016. As of that effective date, all ENDS became subject to the TCA's requirements, including the requirement that all new tobacco products be subject to FDA premarket review. Since there are no grandfathered ENDS that were on the market back in February 2007, all ENDS products must retroactively apply for premarket authorization through the Premarket Tobacco Product Application (PMTA) process.

18. In the Deeming Rule, FDA created an enforcement discretion "compliance policy" to allow ENDS like the BIDI® Stick that were already on the market as of the rule's effective date to remain on the market until PMTAs became due. The deadline to submit PMTAs for currently marketed products has changed multiple times over the

years and, after a July 2019 federal district court order, finally landed on September 9, 2020.

***Background on Bidi Vapor and the BIDI® Stick***

19. In 2014, I purchased the patent rights to a disposable ENDS product from a Chinese manufacturer, SMISS Technology Co. Ltd. (SMISS), and contracted with SMISS to begin manufacturing disposable ENDS products prefilled with my own proprietary nicotine e-liquid formulations.

20. The product now known as the BIDI® Stick was first marketed (in all 11 flavors) in the United States under the Just Chill brand, albeit with limited success, prior to the Deeming Rule becoming effective in August 2016. Unlike certain other ENDS manufacturers, we chose not to market our product to young people, use social media, hire models or influencers or advertise our products on mediums that could be accessed or viewed by minors. Rather, we sold our products only to a core group of confirmed adult smokers.

21. I was deeply disturbed by what appeared to be youth-targeting marketing tactics that companies like Juul Labs were engaged in at the time. It became my mission to ensure that my products never got into the hands of minors. My goal has always been to provide quality, fully compliant products for adult smokers, even if that put us at a competitive disadvantage.

22. In early 2019, I formed Bidi Vapor LLC and rebranded all our products under the Bidi name. We rebranded our disposable ENDS device as the BIDI® Stick, and began marketing it widely as a recreational cigarette alternative for adult smokers.

23. Utilizing a high-quality aluminum frame, the tamper-resistant BIDI® Stick contains 1.4 mL of e-liquid made with Class A tobacco-derived nicotine (60 mg/ml or 6% w/v concentration), high-quality ingredients (propylene glycol, glycerin and flavor additives), a 280 mAh cell phone grade recyclable battery that is UL-8139 certified, an innovated sensitivity control system to ensure consistent nicotine delivery, and a heat-resistant medical-grade absorption pad. The BIDI® Sticks have passed multiple tests and obtained numerous global certifications, such as FCC, UL-8139, UL-1642, UL-62133, FCM, CE, ROHS, TPD, as well as REACH certification in Europe.

24. There are eleven (11) BIDI® Stick varieties – nine fruit flavors (Dawn, Gold, Marigold, Regal, Summer, Tropic, Winter, Zest, and Solar), one menthol (Arctic) and one tobacco (Classic). These simple, non-descriptive product names were chosen specifically to comply with FDA's Enforcement Priorities Guidance to ensure that the BIDI® Sticks do not resemble anything remotely "kid-friendly" or appealing to youth. We have several on-going perception and intention studies evaluating these product names and labels as part of our PMTA. See **Exhibit A**.

25. The BIDI® Stick is currently contract manufactured at SMISS's facilities in Shenzhen, China. Bidi Vapor has invested more than $5 million in SMISS's

manufacturing facilities and quality control systems to ensure that the production of the BIDI® Stick is APPH and will meet FDA's good manufacturing practices for tobacco products, which have not yet been published. The BIDI® Stick is produced in an ISO 9001:2015 certified facility that uses manufacturing controls, documented work instructions and standard operating procedures, and a quality management system based on ISO 13485 (2016) and FDA Quality System Regulation (QSR), 21 CFR Part 820. We have also established an unprecedented 1,000-level e-liquid production facility, which far exceeds the cleanliness level of many pharmaceutical production facilities.

26. Separate from Bidi Vapor, I was one of the founding partners of Kaival Brands Innovations Group, Inc., which was formed in March 2020 to focus on the exclusive distribution of the BIDI® Stick. I currently hold titles of Chief Executive Officer, President, Treasurer and Director for Kaival Brands, which was recently listed on NASDAQ.

27. The BIDI® Stick began to experience exponential growth after Kaival Brands took over its U.S. distribution. By the end of the third quarter of 2020 the BIDI® Stick had become one of the leading closed-system disposable ENDS products in the country according to the Nielsen rankings.

***Bidi Vapor's Focus on Youth Access Prevention***

28. Our founding mission is to provide recreational non-combustible cigarette alternatives to adult smokers. We are vehemently opposed to all illegal underage

tobacco use, including ENDS use, by minors (under 21), and have gone to great lengths to ensure that the BIDI® Sticks are not marketed toward or sold to such persons. There is no evidence whatsoever that authentic BIDI® Sticks are being illegally purchased or used by minors. In fact, the cross-sectional survey data and behavioral studies we have conducted as part of our PMTA show that our product is being used by older adults, the vast majority of whom were already smoking cigarettes. See **Exhibit A**.

29. Our opposition to illegal underage use is not just important from a moral and ethical standpoint, but also because FDA made clear starting with its 2016 draft PMTA guidance that marketing restrictions and youth-access prevention measures would be critical to ultimately obtaining PMTA authorization. Specifically, that draft guidance stated that, "to the extent that you propose specific restrictions on sale and distribution that can help support a showing that the marketing of a product is appropriate for the protection of the public health (e.g., a restriction that decreases the likelihood that those who do not use tobacco products will start using tobacco products), FDA may consider your product in that context and may include your proposed restrictions as mandatory conditions in your marketing order."

30. As detailed in our PMTAs, Bidi Vapor does not use social media to market to consumers. We only use certain age-gated accounts such as LinkedIn, Instagram, Facebook, and YouTube for informational purposes. We also do not use social media influencers, brand ambassadors, models or actors. We have never engaged in any

television or radio advertising, and have never sponsored sporting or entertainment events.

31. In fact, we do not market directly to consumers at all, but only to retail and business partners, such as convenience store owners, wholesalers, and distributors. The marketing materials produced for these business customers do not include content that could be perceived as directed towards youth. We have prohibited the use of any marketing and advertising material that could reasonably be perceived to be targeting minors as identified by FDA. This would include any materials that contain aspirational imagery, cartoons, characters/mascots, fruity images, kid-friendly foods, drinks, and other non-ENDS products that are often marketed and/or appealing to youth, or childish or juvenile designs or graphics that might appeal to youth. All of this was in line with FDA's various guidance documents, proposed rules and recommendations for marketing of tobacco products.

32. In 2020, we halted the production of the BIDI® Stick for two months to revise our packaging and labeling to incorporate new product names to better align with FDA's 2020 Enforcement Priorities Guidance. We adopted single-word, non-characterizing and non-descriptive terms to identify the various flavored BIDI® Stick products. In line with FDA's guidance, we decided to use the following non-descriptive terms to identify the products to further distance the BIDI® Stick from potentially resembling kid-friendly foods, drinks, and other non-ENDS products that are often

marketed and/or appealing to youth: Dawn, Gold, Marigold, Regal, Summer, Tropic, Winter, Zest, Solar, Arctic and Classic. As noted, we have several on-going perception and intention studies evaluating these product names and labels as part of our PMTA.

33. In addition, we developed one of the most comprehensive child-resistant packaging and labeling systems among ENDS (and particularly, disposable ENDS) for the BIDI® Stick. The packaging surface area is covered with warnings, instructions, and informational text intended to inform and protect consumers. This includes the FDA required nicotine addiction warnings, state required warnings such as Proposition 65, as well as several additional warnings, icons, and disclaimers alerting consumers that the product is not for underage sale and intended for adult smokers and vapers over 21 only. An authenticity check sticker on the label makes use of advanced anti-counterfeit technology to protect consumers from counterfeit products. Neither the packaging nor labeling contain any images or graphics that would appeal to youth (this is being confirmed through product-specific perception and intention studies, discussed below). An example image of the product packaging is provided in **Exhibit B**.

34. Each BIDI® Stick is also packaged with a product leaflet that contains a full set of warnings, disclaimers, safety information and instructions for use. See **Exhibit C**.

35. To further ensure minors are not able to get access to our products, we voluntarily discontinued our online direct-to-consumer (DTC) sales through our age-gated website, www.bidivapor.com. Although we had previously implemented one of

the most stringent age-verification programs for our online DTC sales, we nevertheless decided to stop all online DTC sales through our website to ensure compliance with the Prevent All Cigarette Trafficking (PACT) Act, and to help address the larger concerns regarding youth access to ENDS.

36. In March 2021, we partnered with GoPuff (www.gopuff.com) as the exclusive online DTC retailer of authentic BIDI® Sticks. But unlike traditional Internet retailers, GoPuff provides an online platform for consumers to purchase products and have them personally delivered from local brick-and-mortar convenience stores, similar to food delivery platforms such as DoorDash and UberEats. With a long history of distribution of 21+ alcoholic beverages, GoPuff has pioneered a stringent compliance program including PACT Act compliance and age-gating processes, including face-to-face ID verification and adult signature on delivery. With these established procedures, GoPuff is one of the most secure online delivery services in the country. No other Internet-based e-commerce platforms are authorized to sell authentic BIDI® Sticks online directly to adult consumers. We continue to pursue online retailers who appear to be selling products with the "Bidi" name illegally, and have sent dozens of cease-and-desist letters and notifications to local authorities.

37. Aside from GoPuff, we are committed to brick-and-mortar retail, which we believe is a stronger age-verification distribution model compared to traditional online retail channels for ENDS. All our wholesalers and direct retailers are required to sign

our Wholesaler & Direct Retailer Agreement which, among other things, requires parties to comply with all applicable regulations and abide by our comprehensive age verification procedures. Our direct retailers are also required to sign a Retailer Pledge that commits them to complying with, among other things, age-verification requirements and adult-focused marketing, as well as participate in our mystery shopper program. If a retailer does not sign our pledge or breaks it, we will stop doing business with them.

38. To help our business partners understand FDA's tobacco retailer requirements, we have produced training videos for our authorized retailers, an example of which can be found here: https://www.youtube.com/watch?v=o-_4MihIJNc.

39. Beyond FDA, Kaival Brands, as the exclusive distributor of the BIDI® Stick, has made great efforts to comply with all applicable state and federal laws regarding the distribution of ENDS, including obtaining all necessary state licenses, complying with all excise tax requirements, and ensuring compliance with the PACT Act, which was extended to cover ENDS at the end of March 2021.

40. Kaival Brands is doing everything required with respect to PACT Act compliance. Specifically, Kaival Brands has retained a team of legal, tax, and accounting experts to advise on state and local tax, licensing, and regulatory matters associated with the distribution of the BIDI® Stick. We ensured that Kaival Brands is appropriately licensed or registered in every state where required, and invested

substantially in excise tax reporting and compliance software to ensure that all appliable taxes are properly calculated and remitted to the appropriate taxing authorities. Kaival Brands also registered with the Bureau of Alcohol, Tobacco, Firearms and Explosives (ATF) and with the states into which it ships, as required. Finally, Kaival Brands implemented processes to ensure timely filing of all required state reporting. We fully support the PACT Act, including the prohibition on using the U.S. Postal Service to deliver ENDS to consumers via the mail, and believe that compliance with the law will further ensure authentic BIDI® Stick products are not getting into the hands of minors.

***Bidi Vapor's Efforts to Increase Enforcement to Protect Youth***

41. We recognize the legitimate public health concerns about the rising use of disposable ENDS by minors, and completely agree that all efforts should be made to remove non-compliant products from the market – particularly those marketed to youth.

42. We have developed a state-of-the-art authentication system to ensure supply chain security and prevent counterfeit, subpar, and potentially dangerous products from getting in the hands of consumers. Counterfeit products made to resemble authentic BIDI® Sticks are often manufactured using substandard materials that can put consumer health and safety at risk, and increase the potential for illegal youth access.

43. Because of the general lack of enforcement, we have shouldered the burden of pursuing wholesalers and retailers dealing with counterfeit, lookalike products. We have sent dozens of cease-and-desist letters to retailers selling counterfeit "Bidi"

products. In December 2020, for example, we announced that a federal judge in the Southern District of New York granted a temporary restraining order and asset freeze against 24 defendants—most based overseas in China—selling counterfeit, illegally labeled "Bidi" products through the wholesale website, DHGate.com. See **Exhibit D**.

44. We have been working hard for over a year to raise awareness and seek enforcement against counterfeit and non-compliant ENDS products by engaging with members of the U.S. Congress, Attorneys General, and federal agencies, including the FDA, the ATF, the Federal Trade Commission, and U.S. Customs and Border Patrol. We have submitted over a dozen tobacco product violation reports to FDA identifying ENDS on the market that appear to be in violation of the Food, Drug and Cosmetic Act, including the TCA's adulteration and misbranding provisions. We have even sued some of our competitors for selling adulterated and misbranded disposable ENDS.

45. On September 2, 2021, just five days before our PMTA marketing denial order was issued, I participated with my team in a voluntary Listening Session with FDA on the disposable ENDS industry. We presented to over thirty (30) Center for Tobacco Product staff and provided insights into the current disposable ENDS market and enforcement considerations, highlighting the many ways our competitors are marketing ENDS products illegally – including by using synthetic nicotine to avoid the PMTA process. We informed FDA about all of Bidi Vapor's youth-access prevention

efforts, marketing restrictions, comprehensive packaging and labeling requirements and offered suggestions for how FDA might curtail the growing black market.

***FDA's Evolving Compliance Policy and Bidi Vapor's Comprehensive PMTAs***

46. When the Deeming Rule became effective in August 2016 the initial PMTA deadline for ENDS already on the market was set for August 2018, although FDA's only guidance on PMTAs for ENDS was still in draft form. We were in the early stages of developing our PMTA strategy when we learned that there were several industry lawsuits challenging the legality of the Deeming Rule as well as the PMTA deadline, none of which ultimately succeeded.

47. In July 2017, then-FDA Commissioner Dr. Scott Gottlieb announced the Agency's "Comprehensive Plan for Tobacco and Nicotine Regulation". As part of that plan, FDA extended the PMTA deadline to August 8, 2022 by way of a final guidance, and separately announced that it would initiate the notice and comment rulemaking process to establish a "foundational" PMTA rule. I vividly recall Commissioner Gottlieb's statement explaining that more time was necessary to ensure FDA would be able to strike the right balance between consumer protection and fostering innovation for potentially less harmful forms of nicotine delivery for adult smokers.

48. In light of these developments, and based on language in the 2016 draft PMTA guidance, we decided not to invest our limited funds into randomized controlled trials or longitudinal cohort studies. The draft PMTA guidance specifically stated that

randomized clinical trials were not necessary to address consumer cessation behavior, but that observational studies (e.g., perception, actual use, or both) were acceptable. The draft guidance also noted that "it may be possible to support a marketing order for an ENDS without conducting new nonclinical or clinical studies" if, for example, there is existing data in the published literature that could be bridged to our products.

49. The draft PMTA guidance also discussed product comparisons for PMTAs. The guidance recommended manufacturers compare their new products to products in the same and different categories. As a comparison example of "within the same category," FDA recommended that an e-liquid be compared to other e-liquids with *similar nicotine content, similar flavors, or other similar ingredients*. There was no mention in the draft guidance (or the subsequent final PMTA guidance) of testing or comparing non-tobacco flavored ENDS to tobacco ENDS to determine if the flavored products might provide an added benefit to adult smokers that would outweigh any potential risks that non-tobacco flavored ENDS might pose to youth. There was certainly nothing in the draft guidance indicating that any such comparison would need to be made through either a randomized controlled trial or longitudinal cohort study.

50. As a small business, the lack of a final guidance and any formal rules made it very difficult to understand how to navigate and invest in the complicated PMTA process. Nevertheless, by early 2018 we began working on our PMTA including, among other things, e-liquid and aerosol testing for potentially harmful chemicals,

toxicological analysis of the ingredients, preparing comprehensive literature reviews, implementing good manufacturing practices, and developing and implementing marketing restrictions and youth-access prevention measures.

51. In March 2018, we learned that several public health groups sued FDA alleging that it could not move the PMTA deadline to August 2022 without going through the formal notice and comment rulemaking process. Just over a year later, in May 2019, the federal judge in that case ruled in favor of the plaintiffs and vacated FDA's final guidance extending the PMTA deadline. A few months later, in July 2019, the judge announced in a remedy order that the court would be setting its own 10-month compliance period, and that all PMTAs for currently marketed products would now be due by May 12, 2020. That date would ultimately be extended slightly to September 9, 2020 due to the COVID-19 pandemic. As you can imagine, all of these shifting dates made it nearly impossible for a small business like ours to establish a PMTA strategy.

52. Pursuant to the court-order, ENDS products subject to timely submitted applications by September 9, 2020 would be permitted to remain on the market during FDA's review for up to one year, or until September 9, 2021. However, FDA was not obligated to make final marketing authorization determinations by that date. Rather, after September 9, 2021, any ENDS product whose PMTA remains under review would be *subject to* FDA enforcement on a case-by-case basis.

53. Suddenly losing almost three years threw our entire PMTA strategy completely off track. We no longer had time to complete many of our planned studies before the application was due in less than a year. We had to pivot and quickly re-focus on what we thought might be the most critical factors to meet the APPH standard.

54. FDA finally released the final PMTA guidance for ENDS in June 2019 and, a few months later in September 2019, published for comment a proposed rule on the PMTA and recordkeeping requirements. FDA also hosted a two-day seminar on the PMTA process in October 2019, which we were able to attend virtually. We reviewed all these materials very closely and hired legal and scientific consultants to confirm what data and information would be required to ensure that our PMTAs would be accepted and filed to enter scientific review. All agreed that neither randomized controlled trials nor longitudinal cohort studies would be necessary.

55. FDA made clear throughout the PMTA final guidance, the proposed rule, and in its public meetings that the APPH standard is complex and requires FDA to assess multiple factors, including marketing restrictions, youth-access prevention measures, and information in the published literature. FDA also described in detail its PMTA review process and the requirements that needed to be met for an application to be filed to enter into the scientific review phase. FDA also made clear that companies with filed PMTAs would receive at least one "deficiency letter" and an opportunity to respond to FDA's questions prior to any marketing denial orders.

56. FDA's final guidance, proposed rule and public statements also made clear that randomized controlled trials and longitudinal cohort studies would not be necessary to meet the APPH standard. FDA staff, including the Deputy Director of the Center for Tobacco Products Office of Science, stated that they were not setting any standards or requirements for product comparisons in PMTAs. Of course, there was no mention in any of these documents, or in any of FDA's presentations, that companies should consider testing or comparing non-tobacco flavored ENDS to tobacco ENDS to determine if the flavored products might provide an added benefit to adult smokers that would outweigh any potential risks that non-tobacco flavored ENDS might pose to youth. There was certainly no mention that this would be the standard that flavored ENDS would have to meet, through either a randomized controlled trial or longitudinal cohort study, for a filed PMTA to get a complete scientific review.

57. As the May 2020 court-ordered PMTA deadline approached, our team worked non-stop to complete our applications. On February 8, 2020, we submitted a request to FDA for a face-to-face meeting to discuss PMTA testing requirements (analytical, nonclinical, and clinical), and to obtain clarification about a specific comparison product to use in our applications. On February 27, 2020, FDA issued us a letter granting the meeting, but stating that only a written response to the questions would be provided.

58. FDA responded to the questions in our meeting request in writing on May 8, 2020. FDA stated that "there are no requirements from FDA for applicants to conduct clinical studies or trials to support a PMTA" and that "FDA does not have specific requirements for evaluating comparator products in studies in a PMTA submission. However, FDA recommends you compare the health risks of your tobacco product to both products within the same category and subcategory, as well as products in different categories as appropriate." FDA then referred us to the PMTA guidance document, the proposed rule and the 2018 and 2019 public meetings for more information on comparator products. FDA's submission tracking number for this meeting response is TC0005671.

59. Again, FDA failed to mention that we would need to compare, through either a randomized controlled trial or longitudinal cohort study, our non-tobacco flavored BIDI® Sticks to our tobacco-flavored (Classic) BIDI® Stick to determine if the flavored products might provide an added benefit to adult smokers that would outweigh any potential risks that non-tobacco flavored ENDS might pose to youth. FDA of course did not mention that this would be the standard that the flavored BIDI® Stick PMTAs would have to meet, even once accepted and filed, to get a complete scientific review.

60. In March 2020 the World Health Organization (WHO) declared COVID-19 a pandemic, and President Trump declared a national emergency. Like the rest of the

world, our lives were thrown into chaos as schools and businesses had to shut down and the country entered quarantine. We of course had to halt all work on our PMTA to protect our employees and their families.

61. Despite the business, logistical, and human challenges that directly resulted from the pandemic, we were able to submit PMTAs covering all eleven BIDI® Stick varieties on September 8, 2020. As the deadline approached, FDA refused to seek any further extensions, but informed companies seeking extensions that it would consider each company's individual circumstances surrounding COVID-19 and other emergencies if applications were submitted on time.

62. At the annual Food and Drug Law Institute (FDLI) tobacco conference in October 2020, CTP Director Mitch Zeller stated that FDA encouraged companies to provide information on any content missing from their application, including how COVID-19 or any other unforeseen circumstances had prevented them from providing the information, and a timeframe for submission of the missing information. We explained in our PMTAs that while not all product-specific studies were completed by the deadline, such additional information would be forthcoming.

63. FDA encouraged companies making progress on timely submitted applications to keep FDA updated. In fact, FDA responded to a Citizen Petition (Docket No. FDA-2020-P-1797) seeking to extend the September 9, 2020 PMTA submission deadline stating:

> The agency intends to take the firm's individual circumstances into account, including concerns related to COVID-19, as it considers applications that are submitted by the deadline. FDA also intends to take into account relevant considerations in deciding whether to initiate enforcement action against a particular product with respect to applicants who have provided the needed information and made substantial progress toward completion as the one-year period for review comes to an end in September 2021.

64. In addition, during the FDA CTP Office of Science June 11, 2021 virtual public meeting, "Deemed Product Review: A Conversation with the Center for Tobacco Products Office of Science," FDA stated that it expects PMTA applicants to continue their efforts to provide information and develop scientific data to support their submissions. The CTP Office of Science personnel noted that they expect applicants to update their timely submitted PMTAs through amendments to ensure that the Agency has all the relevant data to inform its scientific review. CTP staff further confirmed that applicants could expect to receive a single deficiency letter with FDA's questions once their PMTAs are in scientific review. There was absolutely no indication from FDA during this public meeting that – in just a couple of months – flavored ENDS would effectively need to meet a new standard requiring randomized controlled trials/longitudinal cohort studies in order to receive the complete scientific review envisioned by the TCA and in FDA's own rules and guidance.

65. The PMTAs we submitted on September 8, 2020 were comprehensive and scientifically rigorous and included, among other things, *in vitro* toxicity testing, e-liquid and aerosol analysis of harmful and potentially harmful chemicals,

comprehensive literature reviews containing randomized controlled trials, comparisons to other tobacco products, hardware safety and battery certification information, manufacturing and quality control details, independent and validated consumer insight surveys, environmental assessments and stability data, as well as details about our unique BIDI® Cares recycling program, stringent youth-access prevention measures, adult-focused marketing practices, and post-market surveillance strategies. The submitted PMTAs, including the underlying data, spanned over 285,000 pages combined and, including the on-going studies and amendments, has cost over $6.6 million to prepare so far. See **Exhibits A and E**.

66. The aerosol and toxicological data included in our PMTAs, along with the supporting comprehensive scientific literature review, clearly demonstrate that the BIDI® Sticks present substantially lower health risks compared to other tobacco products, including combustible cigarettes and the FDA-authorized IQOS heat-not-burn device.

67. Our PMTAs were officially accepted on February 5, 2021 and filed on February 23, 2021. FDA assigned a single submission tracking number (STN) PM0003460 to all of our PMTAs.

68. Following submission of our applications, we continued to keep FDA updated on the progress of our on-going product-specific studies. As FDA requested, we submitted PMTA amendments on October 13, 2020; March 23, 2021; April 20,

2021; and September 8, 2021, respectively. These amendments updated our PMTAs with data from additional consumer surveys, literature reviews, manufacturing quality system changes, stability studies and, critically, our product perception and intention behavioral studies and clinical trial. See **Exhibits E, F, G, H, I, J and K**.

69. Our product perception and intention behavioral studies were delayed due to COVID-19 but also because FDA did not publish its draft guidance on "Tobacco Products: Principles for Designing and Conducting Tobacco Product Perception and Intention Studies" until October 2020 – more than a month *after* the PMTA deadline had passed. This was FDA's first-ever guidance providing information on how to design and conduct tobacco product perception and intention (TPPI) studies. TPPI studies are studies that can be used to assess, among other things, individuals' perceptions of tobacco products, understanding of tobacco product information, and intentions to use tobacco products. These are critical to demonstrating APPH.

70. In early 2021, we informed FDA that we had initiated product-specific TPPI studies designed to measure product perception and intention (such as likelihood of use, behavioral intentions, human factors, and patterns of use of the BIDI® Sticks), as well as a clinical pharmacokinetic trial designed to measure the abuse liability and dependence potential of the BIDI® Sticks, and the exposure to nicotine during product use compared to combustible cigarettes and JUUL. After nearly a year of diligent effort and substantial progress, these studies are now nearing completion, and final reports

will be submitted to the Agency within the coming weeks. See **Exhibits A, G, H and K**.

71. On June 25, 2021, in light of the fact that we had not received any updates from FDA or any deficiency letters, we sent FDA a formal request for continued enforcement discretion to permit us to continue selling the BIDI® Sticks to our adult customers following the September 9, 2021 court-ordered PMTA review deadline. That letter provided FDA with a comprehensive update on our PMTA studies as well as additional marketing and youth-access restriction measures we had implemented. See **Exhibit I**.

72. On August 21, 2021, I received an email from FDA stating that the non-tobacco flavored BIDI® Sticks were entering scientific review. Given FDA's statements regarding filing in its PMTA guidance and rule, we interpreted this notification to mean that the applications for our non-tobacco flavored BIDI® Sticks were deemed sufficient to receive a complete scientific review.

73. In response to this notification, we again informed FDA that, in addition to the significant data provided in the original September 8, 2020 submissions and subsequent amendments, we have continued to develop product specific scientific evidence to support that the flavored BIDI® Sticks are APPH. We specifically noted that, as identified in our PMTA amendments, we are continuing to develop robust and reliable evidence intended to demonstrate that the potential benefits of the BIDI® Stick

ENDS products for adult combusted cigarette smokers outweigh any risks to youth posed by flavored ENDS. This robust and reliable evidence includes four behavioral studies designed to measure product perception and intention, as well as a clinical pharmacokinetic study designed to measure the abuse liability/dependence potential of the BIDI® Sticks and the exposure to nicotine during product use. See **Exhibits A and J**.

74. As we did in our June 25, 2021 letter, we also expressed our deep concern that any sudden removal from the market of the BIDI® Sticks could have serious potential adverse and unintended public health consequences for the millions of adult consumers who rely on our products as their nicotine source of choice in lieu of combustible cigarettes.

75. This is supported by the studies submitted in our PMTA and amendments which show that the majority of BIDI® Stick users are older and have used cigarettes. These studies, including the recently completed Patterns of Use study, also show that BIDI® Stick, although not marketed for smoking cessation or any therapeutic purpose, has a "quit rate" of over 60%, and that use of our product has led to a significant reduction in the number of daily cigarettes smoked in those consumers who did not quit smoking entirely. See **Exhibit A**.

76. In addition, the recently completed clinical PK study, which will soon be published, demonstrates that the BIDI® Sticks deliver nicotine to adult users

comparably to their usual brand of cigarette and also elicited similar subjective effects. The study concludes that BIDI® Sticks may be a satisfying alternative to cigarettes among current smokers and may support their transitioning away from cigarette smoking. See **Exhibit L**.

77. With respect to the published literature review, we commissioned a highly regarded scientific consulting firm to update the literature review submitted in our original PMTAs to address, among other things, the impact of non-tobacco flavored ENDS on the public health, focusing on abuse liability, initiation, transition, and cessation. That review found several published studies that directly address FDA's concerns raised in the MDO, including the following (see **Exhibit K**):

- Study results suggest that the use of flavored e-cigarettes can facilitate smoking cessation (Glasser et al. (2021));
- Study results indicate that adults who began using non-tobacco flavored ENDS were more likely to quit smoking than those who used tobacco flavored ENDS (Friedman and Xiu (2020));
- Analyses demonstrate that flavor preferences varied depending on the product, and that both tobacco and non-tobacco flavors are important to adult e-cigarette users (Schneller et al. (2020));
- Compared to tobacco flavor users, participants who used sweet flavors at baseline were significantly more likely to quit smoking and that, regarding flavor transitions between baseline and follow-up, there was more movement away from tobacco to any other flavors than to tobacco from other flavors. Overall, study results demonstrate that use of sweet flavored e-cigarettes at baseline were positively associated with smoking cessation at follow-up (Li et al. (2021));
- A recent study shows that a variety of nontobacco flavors, especially fruit, are popular among adult vapers, particularly among those who have quit smoking and are now exclusively vaping. (Gravely et al. (2020)); and

- E-cigarettes most likely to promote cessation will be those that deliver nicotine in a manner that is reliable and consistent with the nicotine delivery profile of a combusted cigarette. (Blank et al. (2020)).

***The "Form" Marketing Denial Orders***

78. Less than three weeks later, on September 8, 2021, I received the marketing denial order (MDO) in the mail. The MDO was dated September 7, 2021. According to the MDO, all the PMTAs for our non-tobacco flavored BIDI® Sticks lack sufficient evidence – in the form of a randomized controlled trial and/or a longitudinal cohort study – demonstrating that the flavored ENDS will provide a benefit to adult users, over an appropriate comparator tobacco ENDS, that would be adequate to outweigh the risks to youth. This was the first time we had ever seen this standard for a flavored ENDS product.

79. The MDO identified all of our non-tobacco flavored products, including the Arctic (menthol) BIDI® Stick, as adulterated and misbranded. The Arctic BIDI® Stick was arbitrarily included in our MDO even though FDA stated in numerous press releases and public statements that it intended to capture only non-tobacco and non-menthol flavored ENDS in the denials. Without waiving any rights to appeal or challenge the legality of the MDO as it applies to our flavored BIDI® Sticks, we submitted a supervisory review request to FDA to confirm that the inclusion of the Arctic BIDI® Stick was a mistake, but have not yet heard back from the agency. See **Exhibit M**.

80. There was no indication in the two-page MDO that FDA had conducted any kind of actual scientific review, much less engaged in the complicated, multi-factor analysis required to assess whether our products are APPH. Rather, it appeared that FDA had only completed a cursory review of our applications to see if they contained a single type of study – a randomized controlled trial or longitudinal cohort study – addressing a particular type of comparison (tobacco flavors vs. non-tobacco flavors) that FDA *never* previously indicated would be required.

81. We are unaware of any discussion in prior FDA rulemaking, guidance, or public statements that this type of analysis was required or that an entire application would depend on this single datapoint. Aside from a brief mention of "risks to youth," the MDO contained no discussion as to why or how FDA concluded that our PMTAs specifically were insufficient to demonstrate that the flavored BIDI® Sticks would provide an added benefit to adults that is adequate to outweigh the risks to youth, even though our applications and the amendments directly addressed these points. FDA also did not explain why it did not actually review any of our submissions, or provide any rationale as to why FDA it did not conduct a complete scientific review.

82. We immediately submitted a Freedom of Information Act (FOIA) request to FDA for all internal review memos and correspondence related to our PMTAs. What we received shocked us. The FOIA materials, including the boilerplate Technical Product Lead (TPL) memo in our PMTA file, confirmed our worst fear: that FDA did not

actually review *any* of our application materials or amendments. Rather, FDA staff literally engaged in a last-minute "check-the-box" analysis of the applications to determine if either a randomized controlled trial or longitudinal cohort study – which the agency had previously made explicitly clear were not required – was included. If not, scientific review did not proceed to assess other aspects of the applications, and the promised deficiency letter would never come.

**Presence of Evidence for Flavored ENDS Products**

| Criterion A | Present | | Absent |
|---|---|---|---|
| ***Randomized Controlled Trial (RCT) on new product use and smoking behavior*** | ☐ | | ☒ |
| Instructions: To select "Present", all of the following boxes must be checked "Yes": | **Yes** | **No** | **N/A[2]** |
| Was the RCT conducted using new products? | ☐ | ☐ | ☒ |
| Does the RCT include a tobacco-flavored arm and a flavored product arm[3]? | ☐ | ☐ | ☒ |
| Do the outcomes include users' ENDS and smoking behavior to assess switching and/or cigarette reduction (e.g., measures of cigarettes per day, smoking cessation, ENDS use)? | ☐ | ☐ | ☒ |
| Comment(s):<br>N/A | | | |

| Criterion B | Present | | Absent |
|---|---|---|---|
| ***Longitudinal Cohort Study (LCS) on new product use and smoking behavior*** | ☐ | | ☒ |
| Instructions: To select "Present", all of the following boxes must be checked "Yes": | **Yes** | **No** | **N/A[2]** |
| Was the LCS conducted and does it include users of new products who are followed over time? | ☐ | ☐ | ☒ |
| Was use of tobacco-flavored products and other flavored products assessed[3]? | ☐ | ☐ | ☒ |
| Do outcomes include users' ENDS and smoking behavior to assess switching and/or cigarette reduction (e.g., measures of cigarettes per day, smoking cessation, ENDS use)? | ☐ | ☐ | ☒ |
| Comment(s):<br>N/A | | | |

***Bidi Vapor Suffered Irreparable Harm as a Result of the MDO***

83. The MDO identified all our non-tobacco flavored products, including the Arctic (menthol) BIDI® Stick, as adulterated and misbranded. Now, 10 out of our 11 products have been rendered illegal, eliminating 98% of our revenue. We have suffered irreparable harm as we have experienced a massive drop in sales, millions of dollars in product that has been returned by our business customers, and wholesalers and retailers who have stopped re-ordering inventory. The financial losses, as well as the loss of market share and customer good will, are immense and insurmountable.

84. To date, we have lost revenues of $57.2 million in returned orders and cancelled consignment sales as a direct result of the MDO. Specifically, Grocery Supply Warehouse, Inc., which services over 25,000 retail locations, has returned BIDI® Stick orders valued at $2.2 million, and Lakshmi Distributor Inc., d/b/a C-Store Master and Circle K Stores, Inc. have cancelled consignment sales valued at $55 million. When consignment orders are canceled, that means that we must come up with the funds to buy back the now unsellable products from our partners, which essentially doubles the amount lost.

85. We are also projecting to lose tens of millions of dollars going forward. By way of example, we are projecting to lose nearly $2.7 million in monthly sales from just three wholesale and retail partners – Murphy USA, Delek and Kocolene – alone. Circle K Stores have also cancelled future orders for all 4,900 store locations around the

country, resulting in lost revenues of approximately $1,203,930 per week, or $62,604,360 per year (based on average volume of 5.2 units per day at $6.75 per unit). Similarly, as a result of the MDO, GPM Investments has cancelled all future BIDI® Stick orders for its 1,800 retail locations, resulting in weekly lost revenues of approximately $705,915, or $36,707,580 per year.

86. The MDO has also massively impacted our ability to acquire new partners, as our company's reputation has now been tarnished. We are now being viewed in the same light as all the non-compliant players and bad actors who either did not bother to submit PMTAs or did not make a good faith effort, or who are simply selling illegal synthetic nicotine products in packaging designed to target kids.

87. Another concern is that while the PMTA for the Classic (tobacco) BIDI® Stick is still pending, we are learning that many of our wholesale and retail partners are unable to sell this product because they have previously signed exclusivity agreements to sell tobacco ENDS with Big Tobacco companies and Juul Labs, preventing us from even being able to market our tobacco BIDI® Stick (as we have already decided not to sell to customers through our website).

88. To provide some context for how immense these losses are for Bidi Vapor and its future potential, keep in mind that it was just nine months ago that the BIDI® Stick was the market share leader in the disposable ENDS category with nearly 37% of the market, according to Nielsen data. The BIDI® Stick had generated over $100 million

in gross sales between March 2020 and January 2021. As expected for a start-up, those numbers had come down in the second and third quarters of 2021 due to market forces and increased regulation, but were projected to go back up when the MDO was issued and essentially killed our ability to generate revenue.

89. Including the costs for the TPPI behavioral studies, our clinical trial, numerous cross-sectional surveys, and the plethora of non-clinical data included in our PMTAs, we have spent over $6.6 million on our applications to date. In addition to expenses directly related to PMTA preparation, we have also invested over $5 million in manufacturing infrastructure and quality control systems at our manufacturing facility in China to ensure compliance with FDA's eventual Tobacco Product Manufacturing Practices. Those are funds we will never be able to get back.

90. As noted, the removal of the flavored BIDI® Sticks will have additional negative consequences for Bidi Vapor, as consumers are already switching to similarly flavored products offered by other brands (which have either not received MDOs or have had their MDOs rescinded or stayed), or to illegal "synthetic" (non-tobacco derived) nicotine disposables that retailers are now reserving shelf space for under the incorrect assumption that these products are exempt from FDA regulation. See *Some Vaping Companies Are Turning to Synthetic Nicotine to Outsmart the FDA*, available at https://time.com/6098897/vaping-companies-synthetic-nicotine/. We already know that many of our wholesale and retail customers are distributing such other products in the

place of the flavored BIDI® Sticks. We have completely lost the good will we worked hard for years to establish with these wholesalers and retailers that we partnered with.

91. A temporary stay of the MDO will not alleviate these irreparable harms. Since we do not sell products directly to consumers but rather to businesses looking to stock their retail shelves and maintain inventory, a short pause will not address our on-going harm, as product inventory is still being returned, customers move to other brands, and there is no chance of developing new business. Only a judicial stay pending review of our appeal will help stem these continuing losses.

* * * *

I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct.

Executed on October 21, 2021

_____

Niraj Patel, CEO
Bidi Vapor LLC

Enclosures to Affidavit (Exhibits A – M):

- Exhibit A – Summary of PMTA Behavioral Studies, Survey and Related Data
- Exhibit B – BIDI® Stick Example Label - Arctic
- Exhibit C – BIDI® Stick Package Insert
- Exhibit D – Bidi Vapor Press Release re Legal Action Against Counterfeits
- Exhibit E – BIDI® Stick PMTA Table of Contents Example
- Exhibit F – First PMTA Amendment Cover Letter, dated October 13, 2020

- Exhibit G – Second PMTA Amendment Cover Letter, dated March 23, 2021
- Exhibit H – Third PMTA Amendment Cover Letter, dated April 20, 2021
- Exhibit I – Letter to FDA re PMTA Update and Extension Request, dated June 25, 2021
- Exhibit J – Correspondence with FDA re PMTA Update, dated August 27, 2021
- Exhibit K – Fourth PMTA Amendment Cover Letter, dated September 8, 2021
- Exhibit L – BIDI® Stick ENDS Abuse Liability and Puffing Topography Assessment - ClinicalTrials.gov
- Exhibit M – 21 CFR § 10.75 Review Request for Arctic BIDI® Stick MDO

# EXHIBIT A

## Bidi Vapor Summary of TPPI Behavioral Studies, Clinical PK Study, Survey and Sales Data to Support PMTAs

### Sales Data

Purchaser Demographic and Sales data from September 2019 to of August 2020 was submitted to FDA.

The consumer status distribution was as follows: 73.98% are accepted, 19% require ID, and 6.71% are denied from purchasing BIDI® Stick.

The percentage of people in each age group with accepted status was as follows: 21-30 years old (46.92%), 31-40 years old (23.54%), 41-50 (17.81%), 51-60 (7.99%), and 61 above (3.73%).

### Pharmacokinetics/Abuse Liability Study

Study to assess BIDI® Stick pharmacokinetics and subjective effects in adult smokers.

Primary Objectives

To determine kinetics of nicotine absorption into the blood of subjects when they smoke a combustible cigarette, use the BIDI® Stick ENDS with varying flavors, or use JUUL ENDS.

To characterize subjective effects after use of the BIDI® Stick ENDS, JUUL ENDS, and a combustible cigarette.

- BIDI® Stick delivered nicotine similarly to a cigarette (90-100%).
- ENDS products and a Heat-not Burn product delivered less nicotine than a cigarette (50-70% respectively).
- BIDI® Stick is as satisfying as a cigarette.
- BIDI® Stick relieves cravings for nicotine like a cigarette.
- Participants liked BIDI® Stick as much as their cigarettes.

| **Bidi Vapor Summary of TPPI Behavioral Studies, Clinical PK Study, Survey and Sales Data to Support PMTAs** |
|---|
| • Data suggest that abuse liability of BIDI® Stick is lower than combustible cigarettes.<br><br>BIDI® Stick offers a far more effective and satisfying nicotine delivery alternative to combustible cigarettes for adult smokers compared to JUUL.<br><br>For adult tobacco users and smokers, BIDI® Stick delivers nicotine more effectively than Vype ePen3, Vuse Solo, myblu, and tobacco heating products including FDA-authorized IQOS.<br><br>https://clinicaltrials.gov/ct2/show/NCT05072925 |
| **National Representative Tobacco Product Perception and Intention (TPPI) Study (n=7700)**<br>Online survey of 4,000 adult never-users of BIDI® Stick 11 flavor profiles. Subjects will be recruited from Ipsos-Insight, LLC's Knowledge Panel®, the largest probability-based online research panel in the United States. The survey will be completed by a national probability sample of approximately 4,000 adults aged 21 years and older in the United States and will consist of approximately 1,000 established current cigarette smokers, 1,000 established former cigarette smokers, 1,000 non-smokers, and an oversample of 1,000 non-smokers aged 21-24years old. Survey questions will address:<br>• Intentions to trial and regularly use BIDI® Stick 11 flavor profiles<br>• Perceptions of the health and addiction risks of using BIDI® Stick 11 flavor profiles<br>• Comprehension of information presented in the label of BIDI® Stick 11 flavor profiles |
| **Patterns of Use Study (n=255)**<br><br>Patterns of Use study that evaluates tobacco/nicotine product (TNP) usage behaviors and reasons for use of BIDI® Sticks within the past 30 days, along with understanding TNP usage prior to vaping. Topics studies will include usage habits, devices used, potential switching and absolute/relative health risks versus other tobacco/nicotine products.<br><br>Among those users of BIDI® Stick who had previously smoked combustible cigarettes, their cigarettes consumption per day dropped from 11.7 prior to their using BIDI® Stick to an average of 5.4 over the past 30 days while using BIDI® Stick. |

| Bidi Vapor Summary of TPPI Behavioral Studies, Clinical PK Study, Survey and Sales Data to Support PMTAs |
|---|
| **Likelihood of Use Study (n=2500)**<br><br>Likelihood of Use study that characterized consumer perceptions of BIDI® Sticks and to assess the likelihood of increased or decreased use of tobacco/nicotine products after becoming aware of BIDI® Sticks among nonusers and users groups, separated by age groups and their usage history of tobacco/nicotine products (TNP). |
| **Electronic Nicotine Product Use Survey (n=195)**<br><br>This survey tackles the electronic nicotine product usage and preferences of each BIDI® Stick user. 195 respondents where asked questions in an online survey around these topics:<br>-Tobacco product usage<br>-Electronic nicotine product usage<br><br>Survey Results Showed: 58.6% (112) of the respondents said the main reason they prefer vape over traditional cigarettes is that it has flavor.<br><br>83.8% (160) of the respondents said they prefer fruity flavors compared to tobacco or menthol. |
| **Bidi Stick Usage and Potential Impact Survey (n=211)**<br><br>This survey tackles the potential impact of the Bidi™ Stick in the user's lifestyle and vaping habits. 211 respondents where asked questions in an online survey around these topics:<br>-Tobacco product usage<br>-BIDI Stick usage<br><br>Survey results showed: 84% (164) of the respondents have used combustible cigarettes. 53.08% (112) of the respondents said they are not smoking anymore. |

| Bidi Vapor Summary of TPPI Behavioral Studies, Clinical PK Study, Survey and Sales Data to Support PMTAs |
|---|
| **Consumer Insight Survey**<br><br>A 15-minute online consumer use survey of consumers aged 21+ who use electronic nicotine delivery systems (ENDS). The survey results from over a thousand respondents were not available as of the date of our timely PMTA submissions but were released afterwards on September 24, 2020.<br><br>The Consumer Insight Survey is designed to assess, among other things, the impact of flavors, access, and nature of usage for our ENDS.<br><br>The Bidi brand appeals primarily to adult-only converts and dual users, less so to new singular users.<br><br>More than three-quarters of converts (76%) and dual users (77%) report the nicotine level in ENDS products helped/helps them reduce combusted cigarette usage<br><br>59% of respondents pointed to flavors as the top reasons for using vape products.<br><br>42% dual users said that flavored products help them reduce cigarette use.<br><br>Overall, the consumer insight survey showed reduction or cessation of traditional cigarette usage. Additionally, the results show that flavors play a key role helping adult cigarette smokers transition to ENDS products. |
| **Disposable Vape User Insights Study**<br><br>In December 2020, Bidi received results from a Disposable Vape User Insights study conducted by Technomic, Inc. (“Technomic”).<br><br>The research provides valuable consumer insights around disposable ENDS relative to other products, as well as user perspectives on the BIDI® Stick brand. The study incorporated recommendations from the FDA’s draft TPPI guidance, including the inclusion of cognitive interview questions in the soft launch and development of measures to avoid bias. |

# EXHIBIT B

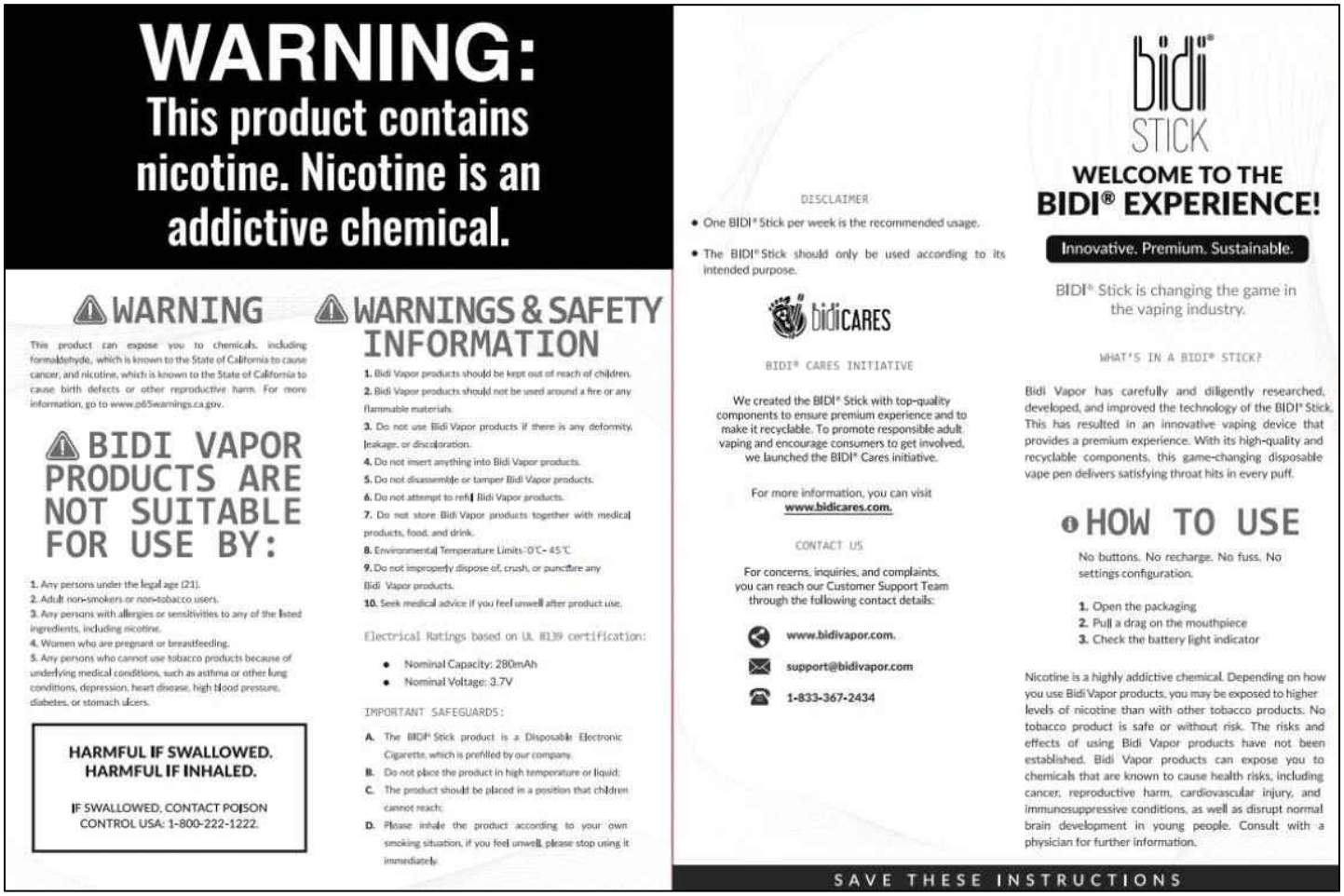
**Exhibit B**

**BIDI® Stick Packaging Example**

# EXHIBIT C

**Exhibit C**

**BIDI® Stick Package Insert**



# WARNING:
## This product contains nicotine. Nicotine is an addictive chemical.

### ⚠ WARNING

This product can expose you to chemicals, including formaldehyde, which is known to the State of California to cause cancer, and nicotine, which is known to the State of California to cause birth defects or other reproductive harm. For more information, go to www.p65warnings.ca.gov.

### ⚠ BIDI VAPOR PRODUCTS ARE NOT SUITABLE FOR USE BY:

1. Any persons under the legal age (21).
2. Adult non-smokers or non-tobacco users.
3. Any persons with allergies or sensitivities to any of the listed ingredients, including nicotine.
4. Women who are pregnant or breastfeeding.
5. Any persons who cannot use tobacco products because of underlying medical conditions, such as asthma or other lung conditions, depression, heart disease, high blood pressure, diabetes, or stomach ulcers.

**HARMFUL IF SWALLOWED.**
**HARMFUL IF INHALED.**

IF SWALLOWED, CONTACT POISON CONTROL USA: 1-800-222-1222.

### ⚠ WARNINGS & SAFETY INFORMATION

1. Bidi Vapor products should be kept out of reach of children.
2. Bidi Vapor products should not be used around a fire or any flammable materials.
3. Do not use Bidi Vapor products if there is any deformity, leakage, or discoloration.
4. Do not insert anything into Bidi Vapor products.
5. Do not disassemble or tamper Bidi Vapor products.
6. Do not attempt to refill Bidi Vapor products.
7. Do not store Bidi Vapor products together with medical products, food, and drink.
8. Environmental Temperature Limits: 0°C- 45°C.
9. Do not improperly dispose of, crush, or puncture any Bidi Vapor products.
10. Seek medical advice if you feel unwell after product use.

Electrical Ratings based on UL 8139 certification:

- Nominal Capacity: 280mAh
- Nominal Voltage: 3.7V

IMPORTANT SAFEGUARDS:

A. The BIDI® Stick product is a Disposable Electronic Cigarette, which is prefilled by our company.
B. Do not place the product in high temperature or liquid.
C. The product should be placed in a position that children cannot reach.
D. Please inhale the product according to your own smoking situation, if you feel unwell, please stop using it immediately.

DISCLAIMER

- One BIDI® Stick per week is the recommended usage.
- The BIDI® Stick should only be used according to its intended purpose.

bidiCARES

BIDI® CARES INITIATIVE

We created the BIDI® Stick with top-quality components to ensure premium experience and to make it recyclable. To promote responsible adult vaping and encourage consumers to get involved, we launched the BIDI® Cares initiative.

For more information, you can visit **www.bidicares.com.**

CONTACT US

For concerns, inquiries, and complaints, you can reach our Customer Support Team through the following contact details:

**www.bidivapor.com.**
**support@bidivapor.com**
**1-833-367-2434**

bidi® STICK

## WELCOME TO THE BIDI® EXPERIENCE!

**Innovative. Premium. Sustainable.**

BIDI® Stick is changing the game in the vaping industry.

WHAT'S IN A BIDI® STICK?

Bidi Vapor has carefully and diligently researched, developed, and improved the technology of the BIDI® Stick. This has resulted in an innovative vaping device that provides a premium experience. With its high-quality and recyclable components, this game-changing disposable vape pen delivers satisfying throat hits in every puff.

### HOW TO USE

No buttons. No recharge. No fuss. No settings configuration.

1. Open the packaging
2. Pull a drag on the mouthpiece
3. Check the battery light indicator

Nicotine is a highly addictive chemical. Depending on how you use Bidi Vapor products, you may be exposed to higher levels of nicotine than with other tobacco products. No tobacco product is safe or without risk. The risks and effects of using Bidi Vapor products have not been established. Bidi Vapor products can expose you to chemicals that are known to cause health risks, including cancer, reproductive harm, cardiovascular injury, and immunosuppressive conditions, as well as disrupt normal brain development in young people. Consult with a physician for further information.

**SAVE THESE INSTRUCTIONS**

# EXHIBIT D

# Bidi Vapor Takes Legal Action Against Counterfeit Sales

Premium e-cigarette maker files federal lawsuit against China-based online wholesalers

NEWS PROVIDED BY
**Bidi Vapor, LLC →**
Dec 31, 2020, 11:23 ET

MELBOURNE, Fla., Dec. 31, 2020 /PRNewswire/ -- Bidi Vapor, LLC, the manufacturer of a premium vape pen called Bidi® Stick, announced that on December 11, 2020, a federal judge in the Southern District of New York granted a temporary restraining order and asset freeze against 24 defendants—most based overseas in China—selling counterfeit Bidi-branded products through the wholesale website, DHGate.com.

The federal lawsuit is a part of Bidi Vapor's comprehensive, anti-counterfeit program designed to combat the sale of counterfeit and infringing products. Through the robust program, the company aims to help create a more responsible marketplace consisting of high-quality, authentic products.

**"The manufacture and sale of counterfeit goods hurts all responsible suppliers of quality products."**

Tweet this

"The manufacture and sale of counterfeit goods hurts all responsible suppliers of quality products," said Niraj Patel, president and CEO of Bidi Vapor, Melbourne, Fla. "It's a shame that independent manufacturers like Bidi Vapor have to shoulder the burden of pursuing

wholesalers and retailers dealing in these illegal products, but our goal is to provide high-quality, electronic nicotine-delivery systems (ENDS) to adult consumers who are 21 and older."

In September 2020, Bidi Vapor submitted a robust Premarket Tobacco Application (PMTA) to the U.S. Food and Drug Administration (FDA). The PMTA process will allow the FDA to review ENDS from individual manufacturers to potentially authorize continued marketing in the United States, officials said.

Bidi Vapor's application included details about its e-liquid ingredients, device components and manufacturing processes, as well as scientific research into product use among consumers. The submission runs over 285,000 pages—one of the largest submissions compiled across all e-cigarette manufacturers—and supports the public need to provide options to adult smokers of combustible cigarettes, officials said.

At Bidi Vapor, innovation is key to our mission, with the Bidi® Stick promoting environmental sustainability while providing a unique vaping experience to adult smokers. Contributing to a smoke-free world for our future generations is in Bidi Vapor's DNA.

**Forward-Looking Statements**

This press release includes statements that constitute "forward-looking statements" within the meaning of federal securities laws, which are statements other than historical facts that frequently use words such as "anticipate," "believe," "continue," "could," "estimate," "expect," "forecast," "intend," "may," "plan," "position," "should," "strategy," "target," "will," and similar words. All forward-looking statements speak only as of the date of this press release. Although we believe that the plans, intentions, and expectations reflected in or suggested by the forward-looking statements are reasonable, there is no assurance that these plans, intentions, or expectations will be achieved. Therefore, actual outcomes and results could materially differ from what is expressed, implied, or forecasted in such statements.

This release contains certain forward-looking statements that are based on current plans and expectations and are subject to various risks and uncertainties. Our business may be influenced by many factors that are difficult to predict, involve uncertainties that may

materially affect results, and are often beyond our control. Factors that could cause or contribute to such differences include, but are not limited to, factors detailed by us in our public filings with the Securities and Exchange Commission.

All forward-looking statements included in this press release are expressly qualified in their entirety by such cautionary statements. Except as required under the federal securities laws and the rules and regulations of the Securities and Exchange Commission, we do not have any intention or obligation to update publicly any forward-looking statements, whether as a result of new information, future events, or otherwise.

**WARNING:** This product can expose you to chemicals including formaldehyde, which is known to the state of California to cause cancer, and nicotine, which is known to the state of California to cause birth defects or other reproductive harm. For more information, go to www.p65warnings.ca.gov.

Nicotine is a highly addictive chemical. Depending on how you use Bidi Vapor products, you may be exposed to higher levels of nicotine than with other tobacco products. No tobacco product is safe or without risk. The risks and effects of using Bidi Vapor products have not been established. Bidi Vapor products can expose you to chemicals that are known to cause health risks, including cancer, reproductive harm, cardiovascular injury, and immunosuppressive conditions, as well as disrupt normal brain development in young people. Consult with a physician for further information.

**Additional Warnings:**

1. Bidi Vapor products should be kept out of reach of children.
2. Bidi Vapor products should not be used around a fire or any flammable materials.
3. Do not use Bidi Vapor products if there is any deformity, leakage, or discoloration.
4. Do not insert anything into Bidi Vapor products.
5. Do not disassemble or tamper Bidi Vapor products.
6. Do not attempt to refill Bidi Vapor products.

**Bidi Vapor products are not suitable for use by:**

1. Any persons under the legal age (21)

2. Adult non-smokers or non-tobacco users
3. Any persons with allergies or sensitivities to any of the listed ingredients, including nicotine
4. Women who are pregnant or breastfeeding
5. Any persons who cannot use tobacco products because of underlying medical conditions, such as asthma or other lung conditions, depression, heart disease, high blood pressure, diabetes, or stomach ulcers.

SOURCE Bidi Vapor, LLC

# EXHIBIT E

# BIDI VAPOR LLC

# Premarket Tobacco Product Application (PMTA) for

# Completely Self-Contained Disposable

# BIDI™ STICK - ARCTIC

# (Formerly Known as BIDI™Stick–MINT FREEZE)

## Nicotine Levels – 60 mg/mL

## E-Liquid Volume: 1.4 mL/unit

## Submission Date: September 8, 2020

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## LIST OF TABLES

# LIST OF FIGURES

# EXHIBIT F

*BIDI VAPOR LLC*

**PMTA Amendment**
Center for Tobacco Products
October 13, 2020

**Niraj Patel**
**+1(321)223-3101**
**raj@bidivapor.com**

**CONTAINS CONFIDENTIAL BUSINESS INFORMATION**

October 13, 2020
**Via CTP Portal**

**PMTA Amendment**

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Tobacco Products
Office of Science
Document Control Center
Building 71, Room G335
10903 New Hampshire Avenue
Silver Spring, Maryland 20993-0002

Re: **Bidi Vapor LLC; Amendment to Premarket Tobacco Product Applications for Bidi Stick E-Cigarette Products; FDA Submission Tracking Numbers (STNs): PM0000XXX - XX**

To Whom It May Concern:

On September 8, 2020, Bidi Vapor LLC ("Bidi") timely submitted eleven (11) Premarket Tobacco Product Applications (PMTAs) for Bidi Stick e-cigarette products to FDA, and is currently awaiting FDA acceptance and filing confirmation of these PMTAs. Please find below a list of products that are the subject of these applications:

1. Bidi Blazing Vibes
2. Icy Mango Bidi Vapor
3. Bidi Berry Blast
4. Bidi Lush Ice
5. Bidi Champion Ice
6. Bidi Classic Tobacco
7. Bidi Fruity Mango
8. Bidi Jungle Juice
9. Dragon Venom
10. Kick Start
11. Mint Freeze

In these original PMTA submissions, we made FDA aware that our business continues to face numerous challenges in preparing the timely PMTA submissions due to the COVID-19 pandemic. While the information contained in the original submissions meet the statutory requirements for application acceptance and filing as set forth in Section 910 of Federal Food, Drug, and Cosmetic Act (FDCA), as well as FDA's guidance and proposed rules, we have now completed an additional study, a Consumer Insight Survey, that we believe will

**PMTA Amendment**
Center for Tobacco Products
October 13, 2020

help the agency assess the potential public health appropriateness of flavored electronic nicotine delivery systems (ENDS) such as the Bidi Sticks. The purpose of this PMTA Amendment is to update all of the above-referenced Bidi Stick PMTAs with the Consumer Insight Survey results and data analysis to support the original PMTA submissions.

With respect to the survey, Bidi worked with third-party research provider Technomics, Inc. to develop and deploy a 15-minute online consumer use survey of consumers aged 21+ who use electronic nicotine delivery systems (ENDS). The survey results from over a thousand respondents were not available as of the date of our timely PMTA submissions, but were released afterwards on September 24, 2020. The Consumer Insight Survey is designed to assess, among other things, the impact of flavors, access, and nature of usage for our ENDS. As indicated in the enclosed Consumer Insight Survey Summary and data, we believe the survey's overall results showed that ENDS significantly reduce or cease traditional cigarette usage, and support that flavors play a key role in helping to transition adult existing tobacco users to ENDS products. We believe these data further support that our Bidi Stick e-cigarette products are appropriate for the protection of the public health as recreational alternatives to combustible cigarettes for adult smokers.

This PMTA Amendment submission contains trade secret and confidential commercial information that Bidi considers to be proprietary and highly sensitive, and which is protected from disclosure under FDCA §§ 301(j) and 906(c) (21 USC §§ 331(j) and 387f(c)), the Trade Secrets Act (18 USC § 1905), the Freedom of Information Act (FOIA) (5 USC § 552), and FDA's implementing regulations, 21 CFR Part 20. If FDA receives a request for these records and tentatively determines that any portion of these submissions is disclosable, Bidi requests that FDA provide notice and an opportunity for Bidi to object to any disclosure in accordance with 21 CFR §§ 20.47 and 20.61. Bidi reserves all legal rights to protect against public disclosure of its trade secret and confidential commercial information and to seek legal recourse against anyone who discloses such information without legal authorization.

Should you have any questions regarding the enclosed submission, please do not hesitate to contact the undersigned with any questions, preferably by telephone or e-mail so that we may respond as soon as possible.

Respectfully submitted,

Niraj Patel
Chief Executive Officer
Bidi Vapor LLC

Enclosures

# EXHIBIT G

**Niraj Patel, CEO**
**(321) 223-3101**
**raj@bidivapor.com**

**PMTA Second Amendment**

CONTAINS CONFIDENTIAL BUSINESS INFORMATION

March 23, 2021

**Via CTP Portal**

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Tobacco Products
Office of Science
Document Control Center
Building 71, Room G335
10903 New Hampshire Avenue
Silver Spring, Maryland 20993-0002

**RE**: **Bidi Vapor, LLC; Second Amendment to Premarket Tobacco Product Applications for BIDI® Stick ENDS; FDA Submission Tracking Number (STN): PM0003460**

To Whom It May Concern:

On September 8, 2020, Bidi Vapor LLC (Bidi) timely submitted eleven (11) Premarket Tobacco Product Applications (PMTAs) for BIDI® Stick electronic nicotine delivery systems (ENDS) products to FDA. Please find below a list of BIDI® Stick products that are the subject of these applications, which have been accepted and filed by the Agency:

1. **Tropic** (Formerly Blazing Vibe)
2. **Marigold** (Formerly Icy Mango)
3. **Solar** (Formerly Berry Blast)
4. **Winter** (Formerly Lush Ice)
5. **Dawn** (Formerly Champion Juice)
6. **Classic** (Formerly Classic Tobacco)
7. **Gold** (Formerly Fruity Mango)
8. **Zest** (Formerly Jungle Juice)
9. **Regal** (Formerly Dragon Venom)
10. **Summer** (Formerly Kick Start)
11. **Arctic** (Formerly Mint Freeze)

In these original PMTA submissions, Bidi made FDA aware that our business continues to face numerous challenges in preparing PMTAs due to the COVID-19 pandemic. While the information contained in the original submissions meet the statutory requirements for application acceptance, filing and appropriate for the protection of the public health ("APPH") determination as set forth in Section 910 of Federal Food, Drug, and Cosmetic Act (FDCA), as well as FDA's guidance and proposed rules, we are continuing to make substantial progress on further studies and updates to our quality

management system to support our PMTAs and assist FDA in establishing that these products are APPH.

On October 13, 2020, we submitted an amendment to the PMTAs that provides an additional study ("Consumer Insight Survey") that was designed to assess, among other things, the impact of flavors, access, and nature of usage for flavored ENDS products such as the BIDI® Sticks. The purpose of the first PMTA Amendment was to update the above-referenced BIDI® Stick PMTAs with the Consumer Insight Survey results and data analysis to support the original PMTA submissions. Now, we have received additional study results that we wish to incorporate into our PMTAs with this Second Amendment. Bidi also seeks to notify FDA of additional work in progress with respect to these applications, as well as its efforts to combat underage use and ensure availability of quality, consistent products to adult consumers.

Specifically, Bidi seeks to inform FDA of the following important updates: (1) Bidi's decision to discontinue online direct-to-consumer sales through its website to further combat access to minors; (2) new consumer insight study results specific to disposable ENDS; (3) forthcoming FDA meeting request to discuss product-specific Tobacco Product Perception and Intention Studies (TPPI) studies and abuse liability assessment; (4) achievement of UL 8139 battery certification; (5) update on status of pending BIDI® Stick flavor quantitative analysis; (6) status of stability testing; (7) summary of recent quality management system improvement efforts; and (8) status of environmental local permits. We discuss these further below. The specific PMTA modules and sections that are being amended with this Amendment are specified below.

## I. Termination of Direct-to-Consumer Online Sales Through Bidi Website (Update PMTA Section 2.4.2)

To further curb underage access to vaping devices, and consistent with Bidi's desire to go above and beyond regulatory requirements to ensure its products are APPH, Bidi has discontinued its online direct-to-consumer ("DTC") sales of the BIDI® Stick product through its website as of February 22, 2021. While Bidi Vapor believes its online age verification program for DTC sales was one of the most stringent programs in the industry, Bidi hopes that its decision to halt online DTC sales through www.bidivapor.com will set an example for the industry and help address the larger concerns regarding underage access to vaping devices. The decision also reinforces Bidi's commitment to brick-and-mortar retail, which Bidi believes to be a stronger age-verification distribution model than online sales. This is particularly true when considering that, throughout the ongoing COVID-19 pandemic, minors are switching to online sources for products, which are less likely to enforce strict, age-verification processes. Bidi goes above and beyond and requires its brick-and-mortar partners to sign a Retailer Pledge and has produced training videos for all authorized retailers of Bidi Vapor products. Bidi also has a mystery shopper program to better ensure retailer compliance with its age-verification policies.

To further ensure supply chain security and prevent counterfeit, subpar, and potentially dangerous products from getting in the hands of consumers, Bidi has partnered with goPuff as the exclusive, online DTC marketer for all of Bidi Vapor's products. With a long history of distribution of 21+ alcoholic beverages, goPuff has pioneered a very stringent and dynamic compliance program (including Prevent All Cigarette Trafficking (PACT) Act compliance) and age-gating process, which

Bidi Vapor endorses. In fact, with its commitment to protecting minors and stringent procedural implementations, goPuff is one of the fastest growing and most secure online delivery services in the country with face-to-face ID verification on delivery.

Bidi has updated its Marketing Plan to reflect this recent change to discontinue online DTC sales through www.bidivapor.com and to update FDA on various corporate initiatives related to the BidiCares (recycling) Program and authentication efforts, among other things. See attached updated Marketing Plan for the BIDI® Stick (Attachment 1). Bidi would like to amend Section 2.4.2 of its PMTAs with these additional marketing information and restrictions.

## II. New Technomic Disposable Vape User Insights Study (Update PMTA Section 1.2.9)

In December 2020, Bidi received results from a Disposable Vape User Insights study conducted by Technomic, Inc. ("Technomic"). The research provides valuable consumer insights around disposable ENDS relative to other products, as well as user perspectives on the BIDI® Stick brand. The study incorporated recommendations from the FDA's draft TPPI guidance[1], including the inclusion of cognitive interview questions in the soft launch and development of measures to avoid bias.

Bidi commissioned this consumer research to better understand consumer decision drivers, attitudes, usage and perspectives relative to the available product types, as well as to better understand the disposable user, including the BIDI® Stick user. Specifically, the study sought to gain understanding about, among other things, ENDS product type selection decision drivers (including user knowledge of various product types, prioritized attributes, and user demographic profiles by product type), brand awareness, perceptions, usage of BIDI® Stick products relative to other ***disposable*** ENDS, Bidi user demographics, and perspectives on underage use, counterfeit products, flavored product restrictions, as well as other market dynamics.

Technomic conducted secondary research and developed a quantitative survey for this assessment. As part of the secondary research, Technomic gathered and analyzed all relevant published materials, including trade publications, available market research, and Technomic nonproprietary studies. For the quantitative survey, Technomic developed a custom, online structured survey fielded to a sample of 1,000 consumers ages 21+ who use electronic/vape products and an oversample of 500 users in Alabama, Georgia, and Tennessee. Consistent with FDA's draft TPPI guidance, an initial 100-respondent soft launch of the survey was performed to collect cognitive interview data. The survey covered three user groups, consisting of converts, dual users, and new singular users. Key findings from the survey include:

- BIDI® Stick is used in conjunction with combusted cigarettes by the largest share of users (46%), indicating the brand may be utilized as a smoking cessation tool.

- Disposable ENDS are the least likely to be used as a consumer's primary ENDS device.

[1] U.S. Food & Drug Admin., Draft Guidance for Industry: Tobacco Products: Principles for Designing and Conducting Tobacco Product Perception and Intention Studies (October 2020) (available at https://www.fda.gov/media/143322/download) (hereafter, "draft TPPI guidance").

- Almost a quarter (23%) of dual users using a nicotine concentration of 6% report that it helps them use fewer conventional cigarettes.

- Bidi awareness and usage is the lowest among all brands listed.

- Bidi outperforms others for non-counterfeit authentication methods, adult-only positioning, customer service, and device recyclability

Please see attached Disposable Vape User Insights Study final report for details around these and other significant findings from the assessment, along with the data files (**Attachment 2**). Bidi would like to amend Section 1.2.9 of its PMTAs with these additional data.

## III. Forthcoming Product-Specific TPPI Studies and Abuse Liability Assessment and FDA Meeting Request (Update PMTA Sections 4.3 and 4.4)

Bidi seeks to notify FDA of forthcoming, product-specific study data. As stated in our PMTAs, due to the pandemic and associated challenges, Bidi was unable to secure laboratory and research organizations to complete certain TPPI and abuse liability studies in advance of FDA's September 9, 2020 PMTA deadline.

Bidi has engaged research firms to complete TPPI studies (that would measure, among other things, likelihood of use, behavioral intentions, human factors, and patterns of use), along with a separate abuse liability assessment. Together, we believe these studies will address critical PMTA elements to support the submission and APPH marketing standard. Consistent with the draft FDA TPPI guidance, the TPPI studies will involve development of a detailed protocol that will discuss research methods, strengths and limitations, data quality procedures, power and sample size, study sample size justification, and representativeness. TPPI study objectives will address, among other things, dual use, consumer perceptions and intentions, likelihood of use, behavioral intentions, labeling comprehension, product use patterns, and actual use. Based on our discussions with the research firms to date, these studies are expected to be completed by Q3/Q4 2021. Bidi will provide these data to FDA as they become available.

A separate abuse liability assessment will be conducted in light of the fact that BIDI® Sticks are marketed exclusively with a higher nicotine content (6%) intended to appeal to and satisfy current combusted cigarette smokers, and to get seasoned smokers to transition over to exclusive use of the BIDI® Stick. The abuse liability study will be designed to measure the addictiveness, abuse, and misuse potential of the new product and the exposure to nicotine during product use. Bidi has made considerable progress in securing laboratory availability and expects to have study completed around the October - November 2021 timeframe. These data will be provided to FDA once they become available. Bidi would like to amend Sections 4.3 and 4.4 of its PMTAs with these additional studies.

The fact that the BIDI® Stick is a completely self-contained disposable further supports this conclusion that marketing of the BIDI® Stick is APPH because these non-cartridge-based ENDS products are designed to appeal to seasoned adult smokers. The BIDI® Stick is engineered for a precisely calculated dose and consistent delivery with a sensitivity control system, packaged in a child-

resistant container with a simple yet sophisticated design, and manufactured with medical-grade recyclable components and a reusable, certified battery that recently obtained UL-8139 certification. The BIDI® Stick is intended to provide adults with a premium vaping experience and a satisfying recreational alternative to combusted cigarettes, but is not intended for any therapeutic use (including smoking cessation). Each of the BIDI® Stick disposable ENDS devices contains 1.4 ml e-liquid containing tobacco-derived nicotine with 6% w/v concentration (60 mg/ml). The BIDI® Stick is not offered in a lower or introductory nicotine level because the product is targeted to seasoned adult smokers, and not intended for smokers who recently began smoking or to non-users (especially minors). By offering this concentration exclusively, and no lower, introductory nicotine levels below 6%, Bidi intends to deliver a satisfaction similar to combusted cigarettes, and eventually curb seasoned adult smokers' cravings and dual-use of combusted cigarettes. We believe our product specific TPPI and abuse liability studies will provide sufficient data to support the PMTAs and that marketing of the BIDI® Stick is APPH.

Bidi will be submitting an FDA meeting request to further discuss these studies and their impact on the applications and FDA's compliance policy. Our expectation is that Bidi's continued efforts to improve its timely-submitted PMTAs during the pandemic demonstrate substantial progress on its applications as detailed in this amendment (and as will be described further in our forthcoming meeting request and future amendments), and will be given due consideration by FDA as part of the Bidi PMTAs' scientific review process. Bidi's objective is to give FDA sufficient notice and time to plan for the receipt of what we believe to be a major amendment critical to the BIDI® Stick's APPH determination. **Bidi hopes that FDA will consider all of these efforts when determining whether to allow the continued marketing of its products following the September 9, 2021 FDA review deadline.**

## IV. UL 8139 Battery Certification to Support PMTA "Human Factors" Analysis and Product Description/Manufacturing (Update PMTA Sections 2.6.3.2.11 and 3.1.5.1)

FDA and the U.S. Consumer Product Safety Commission (CPSC) have long held concerns with respect to battery safety in ENDS. For instance, the CPSC recently warned consumers about purchasing or using individual, loose 18650 lithium-ion battery cells without protection circuits due to possible fire risk. The concerns include, for example, exposed metal positive and negative terminals that can short-circuit when coming in contact with metal objects (*e.g.*, keys or loose change in a pocket). Once shorted, loose cells can overheat and experience thermal runaway, igniting the cell's internal materials and forcibly expelling burning contents, resulting in fires, explosions, serious injuries and even death.

Bidi is pleased to inform FDA that, effective October 2020, Bidi achieved the UL 8139 Standard for Safety for Electrical Systems of Electronic Cigarettes and Vaping Devices certification, which is intended to mitigate potential battery-related risks associated with battery-operated ENDS products. Bidi believes this certification stands as a testament to Bidi's commitment to delivering quality, consistent products to consumers. The BIDI® Stick's 280 mAH lithium ion battery has met rigorous safety standards and demonstrated compliance with various analyses (*e.g.*, water ingress, drop test, crush test, accidental activation test, *etc*.) required for the voluntary UL certification. *See* UL Notice of Completion and Authorization to Apply the UL Mark, File E514030 (**Attachment 3**). Accordingly, Bidi would like to amend Module 3, Section 3.1.5.1 of its PMTAs to reflect this new UL 8139 certification. We believe Bidi's UL certification addresses FDA's and CPSC's concerns with battery safety to ensure the

aforementioned safety concerns are not an issue, further supporting that marketing of the BIDI® Stick to adult consumers is APPH.[2]

To accommodate increased demand, Bidi has had to incorporate additional battery suppliers that can comply with the UL 8139 certification requirements. To meet this need, Bidi added the following, additional battery suppliers: DongGuan Golden CEL Battery Co., Ltd, HuiZhou Kaiyesheng Energy Co., Ltd., and Guangdong Miyear Technology Co., Ltd.

Bidi also believes the UL 8139 certification and associated lithium battery quality acceptance testing, including fire and explosion risk mitigation efforts, support Bidi's human factor analysis in the PMTAs. Generally, human factors involves a multidisciplinary approach. Human factors is a process to design products that people can use correctly. The battery testing resulting in issuance of the certificate is key to Bidi's human factors evaluation to identify risks associated with "real world" use of the BIDI® Stick and demonstrate that potential risks associated with use for both users and nonusers have been mitigated. Risk management is an important tool for determining and controlling unintended hazards, and risk management is a continuous process that includes postmarket monitoring for unanticipated user injuries or harm.

The UL battery certification mitigates human errors and risks based on a user-friendly interface. Accordingly, Bidi would like to amend the Human Factors Analysis section of its PMTAs (Section 2.6.3.2.11) to include this information.

## V. Updated Product Packaging to reflect UL 8139 Battery Certification (Update PMTA Section 1.9)

Bidi has updated its BIDI® Stick product packaging to reflect the new UL certification by using the authorized UL logo. *See* Updated BIDI® Stick Labeling (**Attachment 4**). Accordingly, Bidi would like to update section 1.9 of its PMTAs to reflect the updated product packaging.

## VI. Quality Management System Update (Update PMTA Sections 2.3 and 3.5)

Bidi strives to have its products meet the highest possible standards (*see*, *e.g.*, ROHS, FCC, and CE certifications). As provided in its PMTAs, Bidi's contract manufacturer Smiss Technology Co., Ltd. has been certified with quality management system ISO9001:2015, quality management system for medical instruments ISO13485:2016, enterprise intellectual property management system GB/T29490, and GMP system. To further its commitment to producing high-quality ENDS products, Bidi has performed a global assessment of its contract manufacturer's standard operating procedures (SOPs) and is in the process of updating its quality management system (QMS). Bidi will be undertaking various activities in the near future in furtherance of this goal, including conducting a comprehensive virtual

[2] FDA's compliance policy provides that FDA does not intend to enforce violations of the premarket review requirements against battery-operated tobacco products that were on the market as of August 8, 2016 and that are then modified only to the extent necessary to comply with UL 8139.[2] Bidi has made such modifications in compliance with this policy. *See* U.S. Food & Drug Admin., Guidance for Industry: Compliance Policy for Limited Modifications to Certain Marketed Tobacco Products (November 2019) (available at https://www.fda.gov/media/133009/download).

audit, revising SOPs, and implementing robust processes. Bidi has engaged the regulatory consulting firm EAS Consulting Group, LLC to assist with these quality control efforts. Bidi would like to amend section 3.5 of its PMTAs to revise the description of its quality controls and will provide detailed information once available.

## VII. Status of BIDI® Stick Flavor Quantitative Analysis (Update PMTA Section 3.2.2.6)

In Module 3, Section 3.2.2.6 of its PMTAs, Bidi stated that it would perform additional quantitative flavor analysis on its various product formulations. Bidi informed FDA that method development and validation for flavor analysis was ongoing and likely to submitted to FDA by November 2020. Due to delays associated with the pandemic, the analysis is now expected to be completed by April 2021. Once these data are available, we will forward to FDA for the purposes of amending this section of our application.

## VIII. Status of Stability Testing (Update PMTA Section 3.3.3.2)

As provided in Section 3.3.3.2 of its PMTAs, Bidi conducted real time stability testing for pH, boiling point, specific gravity, viscosity, water activity at condition of 25±2 ºC and 60%±5% RH for total duration of 24 months. The study consisted of four time points: 0 time, 6 months, 12 months and 24 months for both the e-liquid and the finished BIDI® Stick product. The 6-month ambient stability testing results were scheduled for February 9, 2021. The report is pending, and results will be provided to FDA as soon as they are available via another PMTA amendment.

## IX. Updated Environment Assessment Information (Update PMTA Section 7.1)

Bidi provided an EA for every product variation in its PMTAs. In those EAs, Bidi stated that Smiss Technology Co. Ltd. was in the process of obtaining local permits, and was working with the local government to get such permits in place. The final EA license is expected to be issued at the end of March. See attached China Environmental Assessment Process timeline (**Attachment 5**).

* * * *

This PMTA Amendment submission contains trade secret and confidential commercial information that Bidi considers to be proprietary and highly sensitive, and which is protected from disclosure under FDCA §§ 301(j) and 906(c) (21 USC §§ 331(j) and 387f(c)), the Trade Secrets Act (18 USC § 1905), the Freedom of Information Act (FOIA) (5 USC § 552), and FDA's implementing regulations, 21 CFR Part 20. If FDA receives a request for these records and tentatively determines that any portion of these submissions is disclosable, Bidi requests that FDA provide notice and an opportunity for Bidi to object to any disclosure in accordance with 21 CFR §§ 20.47 and 20.61. Bidi reserves all legal rights to protect against public disclosure of its trade secret and confidential commercial information and to seek legal recourse against anyone who discloses such information without legal authorization.

Bidi appreciates the FDA's careful consideration of this Second Amendment to its BIDI® Stick PMTAs and looks forward to working with the Agency to secure an order under FDCA § 910. We trust that the information enclosed herein provides sufficient information for the Agency to conclude that the marketing of the BIDI® Stick is appropriate for the protection of the public health.

Should you have any questions regarding the enclosed submission, please do not hesitate to contact the undersigned with any questions, preferably by telephone or e-mail so that we may respond as soon as possible.

Respectfully submitted,

Niraj Patel
Chief Executive Officer
Bidi Vapor, LLC

**Enclosures (Attachments 1-5):**

Attachment 1 – Marketing Plan for the BIDI® Stick

Attachment 2 – Technomic Disposable Vape User Insights Study Final Report and Data Files

Attachment 3 – UL Notice of Completion and Authorization to Apply the UL Mark, File E514030

Attachment 4 – Updated BIDI® Stick Labeling

Attachment 5 – China Environmental Assessment Process timeline

# EXHIBIT H

**Niraj Patel, CEO**
**(321) 223-3101**
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April 20, 2021

**PMTA Third Amendment: PM0003460**

**Via CTP Portal**

**CONTAINS CONFIDENTIAL BUSINESS INFORMATION**

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Tobacco Products
Office of Science
Document Control Center
Building 71, Room G335
10903 New Hampshire Avenue
Silver Spring, Maryland 20993-0002

**RE**: **Bidi Vapor, LLC; Third Amendment to Premarket Tobacco Product Applications for BIDI® Stick ENDS; FDA Submission Tracking Number (STN): PM0003460**

To Whom It May Concern:

On September 8, 2020, Bidi Vapor, LLC (Bidi) timely submitted eleven (11) Premarket Tobacco Product Applications (PMTAs) for BIDI® Stick electronic nicotine delivery systems (ENDS) products to FDA. Please find below a list of BIDI® Stick products that are the subject of these applications, which have been accepted and filed by the Agency (STN PM0003460):

1. **Tropic** (Formerly Blazing Vibe)
2. **Marigold** (Formerly Icy Mango)
3. **Solar** (Formerly Berry Blast)
4. **Winter** (Formerly Lush Ice)
5. **Dawn** (Formerly Champion Juice)
6. **Classic** (Formerly Classic Tobacco)
7. **Gold** (Formerly Fruity Mango)
8. **Zest** (Formerly Jungle Juice)
9. **Regal** (Formerly Dragon Venom)
10. **Summer** (Formerly Kick Start)
11. **Arctic** (Formerly Mint Freeze)

In these original PMTA submissions, Bidi made FDA aware that our business continues to face numerous challenges in preparing PMTAs due to the COVID-19 pandemic. While the information contained in the original submissions meet the statutory requirements for application acceptance, filing and appropriate for the protection of the public health ("APPH") determination as set forth in Section 910 of Federal Food, Drug, and Cosmetic Act (FDCA), as well as FDA's guidance and proposed rules, we are continuing to make substantial progress on further studies and updates to our quality management system to support our PMTAs and assist FDA in establishing that these products are APPH.

By way of background, on October 13, 2020, we submitted an amendment to the PMTAs that provides an additional study ("Consumer Insight Survey") that was designed to assess, among other things, the impact of flavors, access, and nature of usage for flavored ENDS products such as the BIDI® Sticks. The purpose of the first PMTA Amendment was to update the above-referenced BIDI® Stick PMTAs with the Consumer Insight Survey results and data analysis to support the original PMTA submissions.

On March 23, 2021, Bidi submitted a second amendment to the PMTAs that informed FDA of the following important updates: (1) Bidi's decision to discontinue online direct-to-consumer sales through its website to further combat access to minors; (2) new consumer insight study results specific to disposable ENDS; **(3) a forthcoming FDA meeting request to discuss product-specific Tobacco Product Perception and Intention Studies (TPPI) studies and Abuse Liability Assessment;** (4) achievement of UL 8139 battery certification; (5) update on status of pending BIDI® Stick flavor quantitative analysis; (6) status of stability testing; (7) summary of recent quality management system improvement efforts; and (8) status of environmental local permits. The purpose of the second PMTA Amendment was to provide additional study results to FDA, and to notify the Agency of additional work in progress with respect to these applications, as well as Bidi's efforts to combat underage use and ensure availability of quality, consistent products to adult consumers.

Now, Bidi is submitting this third PMTA Amendment to provide FDA additional information about its progress on the product-specific TPPI studies and Abuse Liability Assessment (third point highlighted above). As mentioned in our most recent PMTA Amendment, Bidi's objective is to give FDA sufficient notice and time to plan for the receipt of what we believe to be a major amendment critical to the BIDI® Stick's APPH determination. We believe our product-specific TPPI and abuse liability studies will provide sufficient data to support the PMTAs and that marketing of the BIDI® Stick is APPH for adult tobacco users. Bidi is providing FDA with the enclosed timelines and protocols for these studies as noted below. Our expectation is that Bidi's continued efforts to improve its timely-submitted PMTAs during the pandemic demonstrate substantial progress on its applications as detailed in this amendment (and as will be described further in our forthcoming meeting request to FDA and future amendments), and will be given due consideration by FDA during its scientific review of our applications.

## I. Progress of Product-Specific TPPI Studies and Abuse Liability Assessment (Update PMTA Sections 4.3 and 4.4)

Bidi seeks to update FDA on the progress of its product-specific study data critical to the BIDI® Stick's APPH determination. As stated in our PMTAs, due to the pandemic and associated challenges, Bidi was unable to secure laboratory and research organizations to complete TPPI and abuse liability studies in advance of FDA's September 9, 2020 PMTA deadline. Bidi has since been working diligently to engage research firms to complete TPPI studies (that would measure, among other things, likelihood of use, behavioral intentions, and patterns of use), along with an abuse liability assessment. Together, we believe these studies will address important PMTA elements to support the submission and APPH marketing standard.

### a. TPPI Studies: Likelihood of Use and Patterns of Use Studies

More specifically, Bidi has engaged Kantar Health, LLC to conduct two quantitative TPPI studies for its BIDI® Stick product: Likelihood of Use (LOU) and Patterns of Use (POU) studies. Both studies are designed as self-report surveys and have received approval from the Sterling Institutional Review Board (IRB). Consistent with the draft FDA TPPI guidance,[1] these TPPI studies involve development of detailed protocols that discuss research methods, strengths and limitations, data quality procedures, power and sample size, study sample size justification, and representativeness. The TPPI study objectives will address, among other things, dual use, consumer perceptions and intentions, likelihood of use, behavioral intentions, labeling comprehension, product use patterns, and actual use.

**i. Likelihood of Use Study**

Specifically, the objective of the LOU study, which received IRB approval on April 5, 2021, is to characterize consumer perceptions of the BIDI® Stick and determine how product labeling impacts various cohorts of adult consumers' perceptions of health risk of BIDI® Stick products and consumers' subsequent intentions. Consistent with FDA's PMTA Guidance and the PMTA Final Rule, the studies seek to understand the impact of the BIDI® Stick on a subject's likelihood of changing their usage behavior. Special attention will be given to dual usage with combusted cigarettes and how the product is perceived relative to other ENDS products in the marketplace to inform FDA's scientific review. *See* Protocol for Observational Study BV-2021-02F: Likelihood of Use Study for BIDI® Stick (**Attachment 1**). The LOU study is set to commence in mid-May and fieldwork is scheduled to be completed by end of June 2021. The final report is expected by the end of September 2021. *See* Kantar Health, LLC Bidi Vapor Likelihood of Use Study and Patterns of Use Study Timelines (**Attachment 2**). Bidi will provide these data to FDA in a future PMTA amendment as soon as possible after the study has been completed.[2]

**ii. Patterns of Use Study**

The objective of the POU study, which received IRB approval on April 13, 2021, is to understand among BIDI® Stick users the patterns of use, with emphasis on usage habits, devices used, potential for dual use and switching, and absolute/relative risks versus other tobacco and nicotine products, as well as BIDI® Stick flavors used and any impact of flavors on interest and usage of the product. *See* Protocol for Observational Study BV 2021-01: BIDI® Stick Patterns of Use Study (Attachment 3). The POU study is set to commence in late April 2021 and fieldwork is scheduled to be completed by first week of June 2021. The final report is expected by the end of August 2021. *See* Kantar Health, LLC Bidi Vapor Likelihood of Use Study and Patterns of Use Study Timelines (Attachment 2). Thus, both TPPI studies are expected to be completed by Q3/Q4 2021. Bidi will provide these data to FDA in a future PMTA amendment as soon as possible after the study has been completed.

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[1] U.S. Food & Drug Admin., Draft Guidance for Industry, Tobacco Products: Principles for Designing and Conducting Tobacco Product Perception and Intention Studies (October 2020) (available at https://www.fda.gov/media/143322/download).

[2] Bidi is in the process of submitting an FDA Meeting Request to discuss extension of time on the market for the duration of FDA's scientific review of its PMTAs beyond September 9, 2021.

**b. Abuse Liability Assessment**

In addition, a separate abuse liability assessment will be conducted in light of the fact that BIDI® Sticks are marketed exclusively with a higher nicotine content (6%) intended to appeal to and satisfy current adult combusted cigarette smokers, and to get seasoned adult smokers to transition over to exclusive use of the BIDI® Stick. The abuse liability study will be designed to measure the dependence potential of the new product and the exposure to nicotine during product use. Specifically, the study is intended to determine kinetics of nicotine absorption into the blood of subjects when they smoke a combustible cigarette, use the BIDI® Stick ENDS with varying flavors and nicotine concentrations, or use JUUL® pod-based ENDS, in each study arm. The study will also characterize subjective effects (such as product liking, satisfaction, and intent to use again) after use of the BIDI® Stick ENDS, JUUL® pod-based ENDS, and a combustible cigarette. *See* Protocol Study No. BIDI-PK-01: Abuse liability and puffing topography assessments of the BIDI® Stick electronic nicotine delivery system (ENDS) in comparison to a combustible cigarette and JUUL® pod-based ENDS (**Attachment 4**).

Bidi is working with the regulatory consultant firm McKinney Regulatory Science Advisors, LLC on the abuse liability assessment. The study will be conducted at MTZ Clinical Research Sp. z o.o. in Warszawa, Poland. The abuse liability study will be carried out in accordance with the protocol, the ethical principles set forth in the Declaration of Helsinki, GCP, and the ICH harmonized tripartite guideline regarding GCP (E6 Consolidated Guidance, April 1996). The study is currently in review with the Warsaw District Medical Chamber Ethics Committee (EC) or Institutional Review Board (IRB), and the study will not commence until the IRB has approved the protocol or a modification thereof. Assuming that IRB approval is obtained by mid-May, the study is expected to begin in June 2021 and the final report is expected by end of September. *See* McKinney RSA, LLC BIDI-PK-01 Study Overview (**Attachment 5**). Bidi will provide these data to FDA in a future PMTA amendment as soon as possible after the study has been completed.

## II. Conclusion

Bidi would like to amend Sections 4.3 and 4.4 of its PMTAs with the enclosed information on these additional studies. Our expectation is that Bidi's continued efforts to improve its timely-submitted PMTAs during the pandemic demonstrate substantial progress on its applications as detailed in this amendment (and as will be described further in our forthcoming meeting request and future amendments), and will be given due consideration by FDA as part of the Bidi PMTAs' scientific review process. Bidi's objective is to give FDA sufficient notice and time to plan for the receipt of what we believe to be a major amendment critical to the BIDI® Stick's APPH determination. **Bidi hopes that FDA will consider all of these efforts when determining whether to allow the continued marketing of its products following the September 9, 2021 FDA review deadline.**

* * * *

This PMTA Amendment submission contains trade secret and confidential commercial information that Bidi considers to be proprietary and highly sensitive, and which is protected from disclosure under FDCA §§ 301(j) and 906(c) (21 USC §§ 331(j) and 387f(c)), the Trade Secrets Act (18 USC § 1905), the Freedom of Information Act (FOIA) (5 USC § 552), and FDA's implementing

regulations, 21 CFR Part 20. If FDA receives a request for these records and tentatively determines that any portion of this submission is disclosable, Bidi requests that FDA provide notice and an opportunity for Bidi to object to any disclosure in accordance with 21 CFR §§ 20.47 and 20.61. Bidi reserves all legal rights to protect against public disclosure of its trade secret and confidential commercial information and to seek legal recourse against anyone who discloses such information without legal authorization.

Bidi appreciates the FDA's careful consideration of this Second Amendment to its BIDI® Stick PMTAs and looks forward to working with the Agency to secure an order under FDCA § 910. We trust that the information enclosed herein provides sufficient information for the Agency to conclude that the marketing of the BIDI® Stick is appropriate for the protection of the public health.

Should you have any questions regarding the enclosed submission, please do not hesitate to contact the undersigned with any questions, preferably by telephone or e-mail so that we may respond as soon as possible.

Respectfully submitted,

Niraj Patel
Chief Executive Officer
Bidi Vapor, LLC

**Enclosures (Attachments 1-5):**

Attachment 1 – Protocol for Observational Study BV 2021-02F: Likelihood of Use Study for BIDI® Stick

Attachment 2 – Kantar Health, LLC Bidi Vapor Likelihood of Use Study and Patterns of Use Study Timelines

Attachment 3 – Protocol for Observational Study BV 2021-01: BIDI® Stick Patterns of Use Study

Attachment 4a – Protocol Study No. BIDI-PK-01: Abuse liability and puffing topography assessments of the BIDI® Stick electronic nicotine delivery system (ENDS) in comparison to a combustible cigarette and JUUL® pod-based ENDS

Attachment 4b - Protocol Study No. BIDI-PK-01 PI Signature

Attachment 5 – McKinney RSA, LLC BIDI-PK-01 Study Overview

# EXHIBIT I

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**CONTAINS CONFIDENTIAL BUSINESS INFORMATION**

**Re: Bidi Vapor, LLC; Request for Continued Enforcement Discretion to Remain on the Market After September 9, 2021; PMTA STN PM0003460**

Dear Director Simoneau:

On behalf of our client, Bidi Vapor, LLC ("Bidi Vapor" or the "Company"), we respectfully request the U.S. Food and Drug Administration ("FDA" or the "Agency") Center for Tobacco Products ("CTP") Office of Compliance and Enforcement ("OCE") continue to exercise enforcement discretion and allow the Company's BIDI® Stick electronic nicotine delivery system ("ENDS") products to remain on the market following the September 9, 2021 court-ordered Premarket Tobacco Product Application ("PMTA") review deadline. Specifically, we request the OCE permit the continued marketing of all eleven (11) BIDI® Stick products for the duration of the Agency's scientific review (*i.e.*, until FDA reaches a final marketing authorization determination) of the Company's timely submitted, accepted and filed PMTAs (STN PM0003460)[1].

[1] The following BIDI® Stick products are being reviewed under PM0003460:

As detailed below, despite the ongoing impact of the COVID-19 pandemic, Bidi Vapor has continued to make substantial progress on its PMTAs and has, among other things, several clinical and behavioral studies in progress that will assist FDA in determining whether the BIDI® Sticks are appropriate for the protection of the public health ("APPH"). Furthermore, any sudden removal from the market of the BIDI® Stick, which is the fastest-growing closed-system disposable (non-cartridge based) ENDS in the United States – *before* an APPH determination is made – could be detrimental to the public health. Such an action would deprive the Company's dedicated adult (21+) consumers an alternative to combusted cigarettes. Based on data provided in the PMTAs and currently being developed, many of these adult consumers smoked cigarettes before switching to the BIDI® Stick.

## I. Bidi Vapor Continues to Make Substantial Progress on its PMTAs

In response to an industry Citizen Petition (Docket No. FDA-2020-P-1797) seeking to extend the September 9, 2020 PMTA submission deadline for certain ENDS manufacturers, FDA stated in pertinent part (emphasis added):

> The agency intends to take the firm's individual circumstances into account, including concerns related to COVID-19, as it considers applications that are submitted by the deadline. FDA also intends to take into account relevant considerations in deciding whether to initiate enforcement action against a particular product with respect to applicants **who have provided the needed information and made substantial progress toward completion** as the one-year period for review comes to an end in September 2021."[2]

In addition, during the FDA CTP Office of Science June 11, 2021 webinar on Deemed Products, FDA stated that it expects PMTA applicants to continue their efforts to provide information and develop scientific data to support their submissions. Office of

1. Tropic (formerly Blazing Vibe)
2. Marigold (formerly Icy Mango)
3. Solar (formerly Berry Blast)
4. Winter (formerly Lush Ice)
5. Dawn (formerly Champion Juice)
6. Classic (formerly Classic Tobacco)
7. Gold (formerly Fruity Mango)
8. Zest (formerly Jungle Juice)
9. Regal (formerly Dragon Venom)
10. Summer (formerly Kick Start)
11. Arctic (formerly Mint Freeze)

[2] *See* Letter from U.S. Food & Drug Admin., Ctr. for Tobacco Prod., to Azim Chowdhury Re: Response to Citizen Petition Docket No. FDA-2020-P-1797 (Feb. 12, 2021), *available at*: https://www.regulations.gov/document/FDA-2020-P-1797-9319.

Science personnel noted that FDA expects applicants to update their timely submitted PMTAs through amendments to ensure that the Agency has all the relevant data to inform its scientific review.

In this regard, while no deficiency letters have been received for any of the BIDI® Stick PMTAs to date, Bidi Vapor has continued to make substantial progress on its applications to ensure completion, despite continuing to face numerous COVID-19 related business and logistical challenges. As described in detail in its PMTA amendments submitted on October 13, 2020, March 23, 2021, and April 20, 2021, respectively, Bidi Vapor has continued to:

- Develop analytical, toxicological, and stability data on its products;
- Update its comprehensive literature review on disposable ENDS;
- Assess the impact of flavors, product access and usage through consumer insight surveys;
- Evaluate product perception and intention by conducting behavioral studies designed to measure, among other things, likelihood of use, behavioral intentions, human factors, and patterns of use of the BIDI® Sticks;
- Assess abuse liability potential through a clinical pharmacokinetic study designed to measure the dependence potential of the BIDI® Sticks and the exposure to nicotine during product use (compared to combusted cigarettes and JUUL); and
- Update its battery certifications (UL 8139), environmental assessments, quality systems and manufacturing controls.

As it completes its ongoing clinical, behavioral and analytical studies in the coming months, and makes updates to its post-market surveillance strategies, Bidi Vapor expects to continue submitting all relevant data and information to FDA via additional PMTA amendments.[3]

Accordingly, as FDA has stated, when deciding whether or not it should continue to extend enforcement discretion to the BIDI® Stick ENDS after September 9, 2021, the Agency should take into account that Bidi Vapor has continued to make substantial progress on its PMTAs to develop and provide FDA information necessary to inform the Agency's review and APPH determination.

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[3] The Company expects to have the behavioral and abuse liability studies completed around October - November 2021 timeframe, at which time the data will be provided to FDA as soon as possible. *See* Bidi Vapor PMTA PM0003460 Amendments *submitted on* March 23, 2021, and April 20, 2021.

## II. Removal of the BIDI® Sticks from the Market Before an APPH Determination is Made Could Be Detrimental to the Public Health

Bidi Vapor's founding mission is to provide recreational non-combusted cigarette alternatives to adult smokers. The Company is vehemently opposed to all illegal underage tobacco use, including ENDS use, by minors (under 21), and has gone to great lengths to ensure that its products are not marketed toward or sold to such persons. Bidi Vapor recognizes the legitimate public health concerns about the rising use of disposable ENDS by minors, and completely agrees that all efforts should be made to remove non-compliant products from the market – particularly those marketed to youth.[4] Unlike many disposable ENDS currently on the market, the BIDI® Stick was first introduced prior to August 8, 2016, and is marketed responsibly toward adult consumers. Indeed, as provided in its PMTAs, it is Bidi Vapor's adult consumers who have propelled the BIDI® Stick to the top of the Nielsen rankings for disposable ENDS.[5]

Bidi Vapor is committed to fully complying with all applicable laws and regulations and has gone above and beyond regulatory requirements to implement strict marketing restrictions and youth access prevention measures.[6] These efforts should give FDA comfort that the continued marketing of the BIDI® Sticks during PMTA review period will not

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[4] *See* Potential Tobacco Product Violations Report, submitted to OCE on June 25, 2021, regarding several currently marketed disposable ENDS products. Further, on March 15, 2021, Bidi Vapor filed a lawsuit in the U.S. District Court for the Northern District of Illinois, Eastern Division against VAPERZ LLC, OEM Partners and VAPERZ ENTERPRISE LLC, the distributors of the MNGO Stick ENDS. The lawsuit challenges, among other things, packaging and labeling practices of the MNGO Stick and contends that the defendants failed to comply with FDA requirements, including numerous violations of the Food, Drug and Cosmetic Act and false advertising claims (including misbranding due to inaccurate nicotine content on the labeling). *See Bidi Vapor, LLC v. Vaperz LLC*, No. 21 C 1430, 2021 U.S. Dist. LEXIS 111843 (N.D. Ill. June 15, 2021).

[5] *See* Press Release, Kaival Brands Innovations Grp., Inc., *Kaival Brands Becomes Second Largest ENDS Offering in U.S.; Expands Disposable E-Cig Market Share to 24.2%* (Dec. 22, 2020), *available at*: https://www.prnewswire.com/news-releases/kaival-brands-becomes-second-largest-ends-offering-in-us-expands-disposable-e-cig-market-share-to-24-2-301197212.html. Kaival Brands Innovations Group, Inc. is the exclusive global distributor of products manufactured by Bidi Vapor.

[6] *See BIDI® Youth Access Prevention Program*, BIDI® VAPOR, https://bidivapor.com/bidi-youth-access-prevention-program/.

contribute to youth use of ENDS. A few of the measures Bidi Vapor has implemented to protect minors include the following:

- In Fall 2020, Bidi Vapor prioritized compliance over business objectives by halting production of the BIDI® Sticks for two months in order to revise its packaging and labeling to incorporate new product names to better align with FDA's Enforcement Priorities Guidance[7]. Specifically, Bidi Vapor took the initiative of adopting single-word, non-characterizing terms to identify its BIDI® Stick products (*e.g.*, Tropic, Marigold, Solar, Winter, Dawn, Classic, Gold, Zest, Regal, Summer and Arctic). In line with FDA's guidance, the Company's intent was that these non-descriptive terms would further distance the BIDI® Sticks from resembling kid-friendly foods, drinks, and other non-ENDS products that are often marketed and/or appealing to youth.[8]

- The BIDI® Stick has one of the most comprehensive labeling systems among ENDS (and particularly, disposable ENDS), with much of the viable packaging surface area covered with warnings, instructions, and product information text intended to inform and protect consumers. Bidi Vapor complies with FDA packaging and labeling requirements, including 21 C.F.R. § 1143.3 compliant nicotine addictiveness warnings placed in a prominent location on all labeling, packaging, and advertisements. The BIDI® Stick also features tamper-resistant packaging and several adult-use only (21+) and underage sale prohibited warnings. Bidi Vapor also makes use of several warning icons and provides a batch code and expiration date. An authenticity check sticker features an advanced anti-fake technology to protect consumers from counterfeit products. A "right-to-know" warning is present in compliance with California Proposition 65 requirements. The BIDI® Stick even includes a comprehensive product leaflet with warnings and instructions for reference after the consumer discards the product packaging.

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[7] *See* U.S. FOOD & DRUG ADMIN., CTR. FOR TOBACCO PROD., ENFORCEMENT PRIORITIES FOR ELECTRONIC NICOTINE DELIVERY SYSTEMS (ENDS) AND OTHER DEEMED PRODUCTS ON THE MARKET WITHOUT PREMARKET AUTHORIZATION (REVISED): GUIDANCE FOR INDUSTRY (Apr. 2020), *available at*: https://www.fda.gov/media/133880/download.

[8] Per FDA's guidance, this includes, for example, labeling and/or advertising that results in a tobacco product resembling juice boxes, candy, or kid-friendly cereal, and products marketed with youth-appealing cartoon or animated characters, such as those that depict or resemble popular children's characters.

- In February 2021, Bidi Vapor discontinued its online direct-to-consumer ("DTC") sales of the BIDI® Stick (all flavors) through its age-restricted website (www.bidivapor.com). While the Company believes its online age verification program for DTC sales was one of the most stringent programs in the industry, Bidi Vapor hopes that its decision to halt all online DTC sales through its website will set an example for the industry and help address the larger concerns regarding youth access to ENDS.

- In March 2021, the Company partnered with GoPuff (www.gopuff.com) as the exclusive online DTC retailer of authentic Bidi Vapor products. Unlike national Internet retailers of ENDS, GoPuff provides an online platform for consumers to purchase products and have them personally delivered from local facilities (similar to food delivery platforms such as DoorDash and Postmates). With a long history of distribution of 21+ alcoholic beverages, GoPuff has pioneered a stringent compliance program including Prevent All Cigarette Trafficking (PACT) Act compliance and age-gating processes, including face-to-face ID verification and adult signature on delivery. With these established procedures, GoPuff is one of the most secure online delivery services in the country. No other Internet-based e-commerce platforms are authorized to sell authentic BIDI® Sticks online directly to adult consumers.[9]

- Aside from GoPuff, Bidi Vapor is committed to brick-and-mortar retail, which the Company believes is a stronger age-verification distribution model compared to traditional online retail channels for ENDS. Bidi Vapor's wholesalers and direct retailers are required to sign the Company's Wholesaler & Direct Retailer Agreement which, among other things, requires parties to comply with all applicable regulations and abide by Bidi Vapor's comprehensive age verification procedures.[10] Direct retailers are further required to sign a Retailer Pledge that commits them to complying with, among other things, age-verification requirements and adult-focused marketing, as well as participating in the

[9] Other Internet retailers and e-commerce platforms that purport to sell BIDI® Sticks online DTC are not authorized to do so and, in fact, are marketing counterfeit products designed to resemble authentic BIDI® Sticks and that make improper use of the BIDI® trademarks.

[10] *See Wholesaler & Direct Retailer Agreement*, BIDI® VAPOR, *available at*: https://bidivapor.com/wholesaler-and-direct-retailer-agreement/.

Company's mystery shopper program.[11] Failure to comply with the agreement and/or pledge carries immediate, material consequences, including order cancellation and revocation of product distribution rights. To help its business partners understand FDA's tobacco retailer guidance, Bidi Vapor has produced training videos for its authorized retailers.

- As detailed in its PMTAs, Bidi Vapor does **not** (1) use social media to market to consumers (but only uses certain age-gated platforms such as LinkedIn, Instagram, Facebook, and YouTube for informational purposes)[12]; (2) use social media influencers, brand ambassadors, models or actors; (3) engage in any television or radio advertising; or (4) sponsor sporting or entertainment events.[13] In fact, the Company does not market directly to consumers at all, but only to retail and business partners (e.g., convenience store owners and distributors). The marketing materials produced for these businesses does not include content that may be perceived as directed towards youth, as Bidi Vapor prohibits any such material that could reasonably be perceived to be targeting minors as identified by FDA (e.g., aspirational imagery, cartoons, characters/mascots, fruity images, kid-friendly foods, drinks, and other non-ENDS products that are often marketed and/or appealing to youth, or childish or juvenile designs or graphics that might appeal to youth).[14]

- Bidi Vapor uses a state-of-the-art authentication system to ensure supply chain security and prevent counterfeit, subpar, and potentially dangerous products from getting in the hands of consumers. Counterfeit products made to resemble authentic

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[11] *See* BIDI® VAPOR RETAILER PLEDGE TERMS, *available at*: https://wholesale.bidivapor.com/wp-content/uploads/2020/05/Retailer-Pledge-.pdf; *see also* BIDI® Stick, *BIDI® Retailer Pledge US*, YOUTUBE (Dec. 10, 2020), https://www.youtube.com/watch?v=SVUKzzXv2yY.

[12] Bidi Vapor does not authorize any third-party social media accounts to advertise the BIDI® Stick or make use of the BIDI® trademarks. To the extent that such accounts appear to use BIDI® Sticks on their platforms, these products are likely counterfeit products designed to resemble authentic BIDI® Sticks and that make improper use of the BIDI® trademarks.

[13] *See* BIDI® Stick, *Bidi Vapor's Responsible Advertising Efforts*, YOUTUBE (May 26, 2021), https://www.youtube.com/watch?v=iNuHo8hn0x0.

[14] *See* U.S. FOOD & DRUG ADMIN., THE PUBLIC HEALTH RATIONALE FOR RECOMMENDED RESTRICTIONS ON NEW TOBACCO PRODUCT LABELING, ADVERTISING, MARKETING, AND PROMOTION (Apr. 29, 2019), *available at*: https://www.fda.gov/media/124174/download.

BIDI® Sticks are often manufactured using substandard materials that can put consumer health and safety at risk.[15] The authentication measures are also intended to safeguard against procurement by minors.[16]

- Bidi Vapor has engaged in various initiatives to demonstrate responsible corporate citizenship and product stewardship. For example, the BIDI® Cares recycling program is the Company's sustainable recycling and proper electronic waste disposal initiative – the first of its kind for the ENDS industry.[17]

Finally, Bidi Vapor believes postmarket surveillance ("PMS") is an important tool to ensure that the marketing of new tobacco products, once authorized, will continue to be APPH – particularly taking into account initiation among non-users and youth. Bidi Vapor's proposed PMS program consists of a combination of passive and active surveillance activities that are designed to monitor the effects of the BIDI® Sticks on individual and population health, and to allow for identification and collection of unexpected experiences related to the BIDI® Stick as it actually performs on the market. As new data come in from the Company's intention and perception studies, Bidi Vapor plans on updating its PMS program and will provide this to FDA via a PMTA amendment when complete.

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[15] *See* BIDI® Stick, *BIDI® US: Anti-Fake Packaging – Real vs Fake*, YOUTUBE (Jan. 21, 2021), https://www.youtube.com/watch?v=j2FC-PZtGZ4.

[16] Bidi Vapor believes that the manufacture and sale of counterfeit products designed to resemble authentic BIDI® Sticks and that make improper use of the BIDI® trademarks hurt responsible suppliers of authentic products and are dangerous for consumers. The Company has shouldered the burden of pursuing wholesalers and retailers dealing with counterfeit BIDI® Sticks. In December 2020, the Company announced that a federal judge in the Southern District of New York granted a temporary restraining order and asset freeze against 24 defendants—most based overseas in China—selling counterfeit, illegally labeled "Bidi" products through the wholesale website, DHGate.com. *See* Press Release, Bidi Vapor, *Bidi Vapor Takes Legal Action Against Counterfeit Sales*, *available at*: https://www.prnewswire.com/news-releases/bidi-vapor-takes-legal-action-against-counterfeit-sales-301199706.html.

[17] *See* Bidi Cares, www.bidicares.com (last visited Jun. 24, 2021); *see also* QRx Digital, *BIDI® Youth Access Prevention Program + BIDI® Cares Recycling Program*, YOUTUBE (Jan. 21, 2021), https://www.youtube.com/watch?v=8L2WgB52bXg.

## III. Request for Continued Enforcement Discretion While FDA Reviews the BIDI® Stick PMTAs

In light of these significant measures to prevent youth use of its products, as well as the reality that millions of adults prefer to use BIDI® Sticks as their nicotine source of choice, there are serious potential adverse and unintended public health consequences if these products are removed from the market and current adult consumers are suddenly deprived of their preferred ENDS after September 9, 2021. For example, there is significant risk that current adult BIDI® Stick consumers may revert to combusted cigarettes, or may start using counterfeits or other illegal, subpar products that may pose health and safety risks.[18] More importantly, a sudden market removal would be tantamount to a "no marketing order" without providing FDA the opportunity to review all the information and data necessary for an APPH determination. It would also result in significant interruptions and delays leading to loss of real-time market data that can continue to provide valuable information about who is using the BIDI® Sticks, how they are using it, and why. This real-world data is needed to inform Bidi Vapor's PMS strategy and FDA's APPH determination.

Our expectation is that Bidi Vapor's continued efforts to improve its timely-submitted PMTAs during the pandemic demonstrate substantial progress on its applications as detailed in the Company's amendments (and as will be described further in forthcoming amendments), and will be given due consideration by FDA as part of the PMTA scientific review process. Bidi Vapor hopes that FDA will consider these efforts, as well as the potential adverse consequences of an immediate market removal, when determining whether to allow the continued marketing of the BIDI® Sticks following the September 9, 2021 review deadline.

**For the reasons explained above, Bidi Vapor respectfully requests that FDA provide written confirmation that it will continue to exercise enforcement discretion for all eleven (11) currently marketed varieties of the BIDI® Stick ENDS (subject to PMTA STN PM0003460) to permit their continued marketing for the duration of FDA's scientific review until the Agency reaches a final marketing authorization determination.**

* * * *

[18] *See* Stacey A. McKenna, *Banning Flavored E-Cigarettes Could have Unintended Consequences*, R STREET POLICY STUDY NO. 222 (Mar. 2021), *available at*: https://www.rstreet.org/wp-content/uploads/2021/03/Updated-Final-No.-222-.pdf.

Please note that this letter contains trade secret, proprietary and confidential business information, which, in accordance with the Agency's public information regulations under 21 C.F.R. Part 20, should not be disclosed to the public or any third-party. If the Agency plans to release information contained in this letter, we request that you notify us first, in accordance with FDA's regulations, so that we may exercise our right of appeal.

Of course, should you require any additional information, please do not hesitate to let us know. Bidi Vapor would also be glad to meet with FDA to discuss any of these issues. We look forward to your reply.

Respectfully submitted,

Azim Chowdhury

cc:

Mitchell Zeller, JD, Director, CTP (Mitchell.Zeller@fda.hhs.gov)
Matthew Holman, Ph.D., Director, CTP Office of Science (Matthew.Holman@fda.hhs.gov)
Nathan Hurley, Ombudsman, CTP (CTPOmbudsman@fda.hhs.gov)
Nirajkumar Patel, CEO, Bidi Vapor, LLC (raj@bidivapor.com)

# EXHIBIT J

**Van-Tull, LieAnn T.**

| | |
|---|---|
| **From:** | Chowdhury, Azim |
| **Sent:** | Friday, August 27, 2021 11:00 AM |
| **To:** | Samuel.Motto@fda.hhs.gov; Antonio.Thornton@fda.hhs.gov |
| **Cc:** | Zeller, Mitchell; J. D. Ann Simoneau (Ann.Simoneau@fda.hhs.gov); Matthew.Holman@fda.hhs.gov; ctpcompliance@fda.hhs.gov; CTPOmbudsman@fda.hhs.gov; 'bidi Vapor' |
| **Subject:** | RE: Notification of Scientific Review (Bidi Vapor; PMTA STN PM0003460) |
| **Attachments:** | Bidi Vapor Request for Continued Case-By-Case Discretion - OCE.pdf |

Dear Mr. Motto and Mr. Thornton,

On behalf of our client, Bidi Vapor LLC, thank you for your email from August 20, 2021 informing the company that the PMTAs for its non-tobacco flavored ENDS have now entered scientific review. As described in detail in the company's PMTA amendments (STN PM0003460) submitted on October 13, 2020, March 23, 2021, and April 20, 2021, while no deficiency letters have been received for any of the BIDI® Stick PMTAs to date, Bidi Vapor has continued to make substantial progress on its applications to ensure completion, despite continuing to face numerous COVID-19 related business and logistical challenges. In addition to the significant data provided in the original September 8, 2020 submissions, Bidi Vapor has continued to develop product specific scientific evidence to support that its flavored ENDS are appropriate for the protection of the public health (APPH). Specifically, Bidi Vapor is continuing to develop robust and reliable evidence intended to demonstrate that the potential benefits of the BIDI® Stick ENDS products for adult combusted cigarette smokers outweigh any risks to youth posed by flavored ENDS. This includes four behavioral studies designed to measure product perception and intention (e.g., likelihood of use, behavioral intentions, human factors, and patterns of use of the BIDI® Sticks), as well as a clinical pharmacokinetic study designed to measure the abuse liability/dependence potential of the BIDI® Sticks and the exposure to nicotine during product use (compared to combusted cigarettes and JUUL). In addition, as we have informed FDA on several occasions, since submitting its PMTAs, Bidi Vapor has continued to:

- Develop analytical, toxicological, and stability data on our products;
- Update the comprehensive literature review to include analysis of most recent published studies on consumer behavior and perception;
- Assess the impact of flavors, product access and usage through consumer insight surveys; and
- Update its battery certifications (UL 8139), environmental assessments, quality systems and manufacturing controls.

As the company completes its ongoing clinical, behavioral and analytical studies, Bidi Vapor expects to continue submitting all relevant data and information to FDA via additional PMTA amendments as soon as they are available.

On June 25, 2021, Bidi Vapor submitted a request to CTP Office of Compliance and Enforcement (OCE) to permit the continued marketing of all eleven (11) BIDI® Stick products for the duration of the Agency's scientific review (*i.e.,* until FDA reaches a final marketing authorization determination) of the Company's timely submitted, accepted, and filed PMTAs. We have attached this letter herein for easy reference. Bidi Vapor is still awaiting feedback from OCE regarding this request.

Further to its request for continued marketing as provided in the attached letter and various PMTA amendments, Bidi Vapor requests confirmation that FDA will permit its products to remain on the market past September 9, 2021. We understand this will be assessed on a case-by-case basis. We believe Bidi Vapor qualifies for this case-by-case discretion, given its significant measures to prevent youth use of its products as detailed in its PMTA and subsequent amendments. Further, since millions of adults prefer to use BIDI® Sticks as their nicotine source of choice, there are serious potential

adverse and unintended public health consequences if these products are removed from the market and current adult consumers are suddenly deprived of their preferred ENDS after September 9, 2021. For example, there is significant risk that current adult BIDI® Stick consumers may revert to combusted cigarettes, or may start using counterfeits or other illegal, subpar products that can pose significant health and safety risks. Bidi Vapor wants FDA to have the opportunity to review all the information and data necessary for an APPH determination, and we are concerned that abrupt market removal would result in significant interruptions and delays leading to loss of real-time market data that can continue to provide valuable information about who is using the BIDI® Sticks, how they are using it, and why. This real-world data is needed to inform Bidi Vapor's post-market surveillance strategy as well as FDA's APPH determination.

Many thanks in advance for your attention and timely consideration of our request. As we quickly approach September 9, Bidi Vapor anxiously awaits FDA's guidance and confirmation of its ability to continue marketing its products pending FDA's PMTA review. Please feel free to reach me at any time if you would like to discuss or have any questions.

Best regards,
Azim

Keller & Heckman

khlaw.com
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*Serving Business through Law and Science®*

**Azim Chowdhury**
Partner

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Keller and Heckman LLP | 1001 G Street NW, Suite 500 West | Washington, DC 20001

Washington, DC Brussels San Francisco Shanghai

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**From:** "Motto, Samuel" <Samuel.Motto@fda.hhs.gov>
**Date:** August 20, 2021 at 11:32:02 AM EDT
**To:** raj@bidivapor.com
**Cc:** "Motto, Samuel" <Samuel.Motto@fda.hhs.gov>, "Thornton, Antonio" <Antonio.Thornton@fda.hhs.gov>
**Subject: Notification of Scientific Review**

Good morning Mr. Patel,

This email is to inform you that your non-tobacco flavored ENDS products have entered scientific review. Please refer to your acceptance letter that identify these products.

This email does not communicate an intention to defer enforcement of the premarket authorization requirements for your products beyond September 9, 2021. Additionally, we remind you that all regulated tobacco products, including the new tobacco products that are the subject of this correspondence, are subject to the requirements of Chapter IX of the FD&C Act and related regulations. It is your responsibility to ensure the tobacco products that are the subject of this correspondence comply with all applicable statutory and regulatory requirements, including any that may be forthcoming.

If you have any questions, please contact POC, Antonio Thornton, Regulatory Health Project Manager, at (240) 402-3577 or Antonio.Thornton@fda.hhs.gov.

Sincerely,

-Sam

***Samuel Motto, Ph.D., MPH., MT(ASCP)***
**LCDR, U.S. Public Health Service Commissioned Corps**
***Regulatory Health Project Manager***
**Center for Tobacco Products**
**Office of Science**
**U.S. Food and Drug Administration**

**Tel: 240-402-5887** | Samuel.motto@fda.hhs.gov


# EXHIBIT K

September 8, 2021

**Niraj Patel, CEO**
**(321) 223-3101**
**raj@bidivapor**

**Via CTP Portal**

**PMTA Fourth Amendment: PM0003460**

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Tobacco Products
Office of Science
Document Control Center
Building 71, Room G335
10903 New Hampshire Avenue
Silver Spring, Maryland 20993-0002

CONTAINS CONFIDENTIAL
BUSINESS INFORMATION

**RE**: **Bidi Vapor LLC; Fourth Amendment to Premarket Tobacco Product Applications for BIDI® Stick ENDS; FDA Submission Tracking Number (STN): PM0003460**

## I. Background

On September 8, 2020, Bidi Vapor LLC ("Bidi Vapor" or the "Company") timely submitted to the U.S. Food and Drug Administration ("FDA" or the "Agency") eleven (11) Premarket Tobacco Product Applications ("PMTAs") for the following BIDI® Stick electronic nicotine delivery system ("ENDS") products, identified by Submission Tracking Number ("STN") PM0003460:

1. **Tropic** (Formerly Blazing Vibe)
2. **Marigold** (Formerly Icy Mango)
3. **Solar** (Formerly Berry Blast)
4. **Winter** (Formerly Lush Ice)
5. **Dawn** (Formerly Champion Juice)
6. **Classic** (Formerly Classic Tobacco)
7. **Gold** (Formerly Fruity Mango)
8. **Zest** (Formerly Jungle Juice)
9. **Regal** (Formerly Dragon Venom)
10. **Summer** (Formerly Kick Start)
11. **Arctic** (Formerly Mint Freeze)

The PMTAs for these products have been accepted and filed by the Agency. On August 24, 2021, Bidi Vapor received an e-mail notification from FDA stating that the PMTAs for our non-tobacco flavored ENDS have now entered scientific review.[1] This email notification did not specify the products to which the notification of scientific review applies, but referred to our PMTA acceptance letter. For the purposes of this Amendment, Bidi Vapor hereinafter refers to all of its non-tobacco flavored BIDI® Stick ENDS (i.e., other than the Classic BIDI® Stick) as

1 See e-mail dated August 24, 2021 from Dr. Samuel Motto (Samuel.motto@fda.hhs.gov) to Niraj Patel (raj@bidivapor.com).

the "Non-Tobacco BIDI® Sticks," but notes that four of these products (e.g., the Arctic, Winter, and Marigold and Dawn BIDI® Sticks) contain menthol as a characterizing flavor. The remaining Non-Tobacco BIDI® Sticks (e.g., Tropic, Solar, Gold, Zest, Regal and Summer BIDI® Sticks) contain other non-menthol characterizing flavors.

In our original PMTA submissions, Bidi Vapor made FDA aware that our business continues to face numerous challenges in preparing PMTAs due to the COVID-19 pandemic. While we put forth our best efforts and diligence in the original submissions, as FDA has recommended on numerous occasions, we have been working hard to make substantial progress on additional studies and updates to youth access restriction measures, as well as our quality management system to support our PMTAs and inform FDA in making its appropriate for the protection of the public health ("APPH") determination. We have provided these data and updated information generated from our on-going work and studies in three PMTA amendments submitted on October 13, 2020, March 23, 2021 and April 20, 2021.

This submission contains our **fourth** PMTA amendment, the purpose of which is to inform FDA of Bidi Vapor's additional, recently commenced Actual Use ("AU") and tobacco product perception and intention ("TPPI") studies which are intended to assess, among other things, whether our Non-Tobacco BIDI® Sticks provide an "added benefit" for adult combusted cigarette smokers compared to the tobacco-flavored Classic BIDI® Stick, and that such benefit outweighs any potential risk that the Non-Tobacco BIDI® Sticks may pose to youth.[2] We also use this opportunity to provide FDA with an update on the status of our additional, ongoing studies that Bidi Vapor provided to FDA in previous amendments, as well as our updated literature review.

## II. Role of Non-Tobacco BIDI® Sticks for Adult Combusted Cigarette Smokers

In addition to the comprehensive literature review (Module 2 Section 2.9), the original PMTA submissions contain product-specific evidence regarding the role of Non-Tobacco BIDI® Sticks for adult combusted cigarette smokers. This includes, but is not limited to, surveys of Bidi Vapor's customer base and surveys commissioned by Technomic, Inc.

2 See FDA Press Release, FDA Denies Marketing Applications for About 55,000 Flavored E-Cigarette Products for Failing to Provide Evidence They Appropriately Protect Public Health, available at: https://www.fda.gov/news-events/press-announcements/fda-denies-marketing-applications-about-55000-flavored-e-cigarette-products-failing-provide-evidence (quoting CTP Director Mitch Zeller, "[c]ompanies who want to continue to market their flavored ENDS products must have robust and reliable evidence showing that their products' potential benefit for adult smokers outweighs the significant known risk to youth.").

Leading up to the expedited, court-ordered September 9, 2020, PMTA submission deadline[3], and in light of the on-going challenges brought about by the COVID-19 public health emergency and absence of FDA guidance on tobacco product perception and behavioral studies, Bidi Vapor was still able to conduct the surveys of our adult customers provided in Module 5 Section 5.3 of the PMTAs. As encouraged by FDA on numerous occasions, Bidi Vapor has continued to make substantial progress on its submission, and continue product-specific testing, such as our stability, leachability, flavor analyses and additional consumer insight surveys since our original PMTA submissions.

At the end of October 2020, almost two months after the original September 9, 2020 deadline, FDA issued draft guidance to industry that provided direction on designing and conducting TPPI studies.[4] Bidi Vapor swiftly took action following release of this guidance (which is still in draft form) and immediately began working with the limited available research organizations and firms proficient in this area, to design and conduct behavioral studies that would measure the perception and appeal of BIDI® Sticks, including the Non-Tobacco BIDI® Sticks, on current and never users. These behavioral studies are intended to, among other things, further assess the role of Non-Tobacco BIDI® Stick ENDS products in combusted cigarette switching and cessation for adult smokers. These ongoing studies include four studies evaluating BIDI® Stick consumer perceptions and intentions (*e.g.*, likelihood of use, patterns of use/actual use). Around that time, Bidi Vapor also, on its own initiative (i.e., without waiting for any FDA deficiency or other Agency communication), commissioned a separate clinical pharmacokinetic ("PK") study that is designed to measure the abuse liability and dependence potential of the BIDI® Sticks, as well as the levels of exposure to nicotine during product use (compared to combusted cigarettes and JUUL). Because of our swift, voluntary action, Bidi Vapor is pleased to report to FDA that we have recently completed this PK study and have preliminary findings available for FDA's review. Together, we hope that all of these studies (i.e., both the recently completed and currently on-going studies) will provide robust and reliable product-specific scientific evidence on the BIDI® Sticks to inform FDA's APPH determination. These studies are also intended to specifically address whether the public health impact of the Non-Tobacco BIDI® Sticks for adult combusted

[3] *See American Academy of Pediatrics v. Food and Drug Administration*, No. 8:18-cv-883 (PWG), (D. Md. Apr. 22, 2020), ECF #182.

[4] Bidi Vapor initiated TPPI studies following the publication of FDA's October 2020 draft guidance. *See* U.S. Food & Drug Admin., Draft Guidance for Industry: Tobacco Products: Principles for Designing and Conducting Tobacco Product Perception and Intention Studies (October 2020) (available at https://www.fda.gov/media/143322/download) (hereafter, "draft TPPI guidance").

cigarette smokers outweighs any risks to youth posed by the flavored products, in light of the Company's extensive youth-access prevention measures.[5]

In addition to these product-specific studies, Bidi Vapor commissioned Cardno ChemRisk to update its literature review (**Attachment 2**) to address, among other things, the impact of non-tobacco flavored ENDS on the public health, focusing on abuse liability, initiation, transition, and cessation. The summary of the review is enclosed herein (**Attachment 2**), but we highlight the following findings with respect to flavored ENDS products and smoking cessation:

- Study results suggest that the use of flavored e-cigarettes can facilitate smoking cessation (Glasser et al. (2021));
- Study results indicate that adults who began using non-tobacco flavored ENDS were more likely to quit smoking than those who used tobacco flavored ENDS (Friedman and Xiu (2020));
- Analyses demonstrate that flavor preferences varied depending on the product, and that both tobacco and non-tobacco flavors are important to adult e-cigarette users (Schneller et al. (2020));
- Compared to tobacco flavor users, participants who used sweet flavors at baseline were significantly more likely to quit smoking and that, regarding flavor transitions between baseline and follow-up, there was more movement away from tobacco to any other flavors than to tobacco from other flavors. Overall, study results demonstrate that use of sweet flavored e-cigarettes at baseline were positively associated with smoking cessation at follow-up (Li et al. (2021));
- A recent study shows that a variety of nontobacco flavors, especially fruit, are popular among adult vapers, particularly among those who have quit smoking and are now exclusively vaping. (Gravely et al. (2020)).
- E-cigarettes most likely to promote cessation will be those that deliver nicotine in a manner that is reliable and consistent with the nicotine delivery profile of a combusted cigarette. (Blank et al. (2020))

[5] See **Attachment 1**, Bidi Vapor's June 25, 2021 letter to the CTP Office of Compliance and Enforcement (OCE) requesting enforcement discretion to continue marketing the BIDI® Sticks for the duration of the Agency's PMTA review. The letter describes the Company's ongoing efforts to market its products strictly to adult tobacco users 21 and over and to ensure youth-access prevention.

Furthermore, based on preliminary PK data and the importance of nicotine delivery enabling ENDS to act as a substitute for combusted cigarettes,[6] we believe that the BIDI® Sticks are going to exceed comparable ENDS products (e.g., JUUL, Myblu, and Vuse Solo) and an FDA authorized tobacco product (e.g., IQOS) in converting smokers to noncombustible tobacco products. Our preliminary PK data indicate that the BIDI® Sticks deliver nicotine like a combusted cigarette and produces positive subjective effects. These data suggest, similar to published literature, that the tobacco-flavored Classic BIDI® Stick and the Non-Tobacco BIDI® Sticks are likely to be used by existing smokers as a satisfying alternative to smoking combusted cigarettes.

We provide an update to the ongoing studies and literature review below.

## III. Update on PK/Abuse Liability Study (Amend PMTA Module 5 Section 5.2)

McKinney Regulatory Science Advisors, LLC working with whatIF Consulting LTD (Dr. Ian Fearon), executed an assessment of abuse liability (incorporating nicotine PK and subjective effects measures) and puffing topography in users of BIDI® Stick in comparison to a similar e-vapor product (JUUL) and combusted cigarettes.

This study was conducted in full compliance with International Council for Harmonization Good Clinical Practice (ICH-GCP). In a randomized, crossover manner, study subjects either smoked a combusted cigarette of their usual brand, used a BIDI® Stick, or used JUUL, by taking 10 puffs 30-seconds apart (defined use). Before, during and after this use session, venous blood samples were collected for plasma nicotine analysis and various questionnaires were administered (urge to smoke, product liking, intent to use again, and a Product Evaluation Scale) to gain subjective effects information. Both PK and subjective effects data will facilitate a robust examination of the abuse liability of BIDI® Stick relative to combusted cigarettes and a comparator e-vapor product (JUUL).

Two hours after the start of the product use session, a further 1-hour ad libitum product use session was initiated. During this session, puffing topography data were collected and a single blood sample was taken at the end of the session for plasma nicotine analysis.

[6] "However, for many individual addicted cigarette smokers, the potential for ENDS to act as a substitute for cigarettes, thereby encouraging smokers to seek to switch completely away from combustible cigarettes, may be dependent, in part, upon the product having acceptability and abuse liability more comparable to a cigarette." (*See* January 2020 FDA Enforcement Priorities Guidance)

Our preliminary analysis of the plasma nicotine data shows that use of the BIDI® Stick under defined use conditions delivered nicotine in a manner comparable to combusted cigarettes. Thus, mean $C_{max}$ values for all BIDI® Stick products were not significantly different to that from a combusted cigarette. Furthermore, preliminary analysis of the subjective effects data showed that satisfaction and liking when using all BIDI® Stick products were similar to satisfaction and liking seen when subjects smoked their usual brand of combusted cigarettes. Significantly, the preliminary data suggest that use of BIDI® Stick was just as effective as combusted cigarettes in reducing smoking urges.

Our conclusion based on these preliminary analyses is that the BIDI® Stick delivers nicotine in a manner comparable to combusted cigarettes while producing positive subjective effects and reducing urges to smoke. These data suggest that BIDI® Stick is likely to be used by existing adult smokers as a satisfying alternative to smoking combusted cigarettes.

## IV. Update on Kantar Health TPPI Studies on BIDI® Stick: Likelihood of Use and Patterns of Use (Amend PMTA Module 5 Section 5.3 and Module 6 Section 6.2.1)

Bidi Vapor engaged Kantar Health, LLC ("Kantar") to conduct two quantitative tobacco product perception and intention ("TPPI") studies for its BIDI® Stick product: Likelihood of Use ("LOU") and Patterns of Use ("POU") studies. Both studies were designed as self-report surveys and have received approval from the Sterling Institutional Review Board ("IRB"). Consistent with the draft FDA TPPI guidance,[7] these TPPI studies involve development of detailed protocols (**Attachments 3 and 5**) that discuss research methods, strengths and limitations, data quality procedures, power and sample size, study sample size justification, and representativeness. The TPPI study objectives address, among other things, perceptions and intentions, likelihood of use, label comprehension and product use patterns, including dual use.

### a. BIDI® Stick Likelihood of Use Study

The BIDI® Stick LOU study was administered between May 17 and August 13, 2021 to BIDI® Stick nonusers using a web-based survey (**Attachment 4**) to participants age 21 years and older to assess tobacco use behavior, perceptions, and intentions (Table 1). All study participants were exposed to the BIDI® Stick product description and package label, and provided a picture of

[7] U.S. Food & Drug Admin., Draft Guidance for Industry, Tobacco Products: Principles for Designing and Conducting Tobacco Product Perception and Intention Studies (October 2020) (available at https://www.fda.gov/media/143322/download).

the product and a schematic of the label for the top, bottom, and side of the package for one variety of the BIDI® Stick. The package label included the description of contents, strength, flavor, and the nicotine warning statement. Additionally, participants were shown the front of the packaging (as the other parts of the packaging do not vary) for each of the other 10 flavors of BIDI® Stick.

**Table 1 BIDI® Stick LOU Study Cohort Summary**

| Cohort |
|---|
| 1) Never tobacco/nicotine users |
| 2) Former tobacco/nicotine users from legal age and older |
| 3) Current cigarette smokers with intention to quit |
| 4) Current cigarette smokers without intention to quit |
| 5) Current ENDS users |
| 6) Oversampling young adults (21 to 24 years) |

Future intention to try BIDI® Stick flavors was asked of all participants. Future intention to try was assessed post-exposure to the BIDI® Stick product description and package label via an 11-point Juster Scale. This item was asked for all 11 currently available flavors of BIDI® Stick:

- Solar (Strawberry + Blueberry)
- Tropic (Mango + Apple + Orange)
- Dawn (Mint + Ginger + Lemon)
- Regal (Dragon Fruit + Strawberry)
- Gold (Mango)
- Marigold (Mango + Menthol)
- Winter (Watermelon + Melon + Menthol)
- Arctic (Mint + Menthol)
- Zest (Melon + Pineapple + Banana)
- Summer (Blueberry + Pomegranate)
- Classic (Tobacco Leaf)

Future intention to use BIDI® Stick fairly regularly was also asked for similar flavors. These future intention results will be compared for the Non-Tobacco BIDI® Sticks versus the

Classic BIDI® Stick to highlight any differences in interest due to flavors among Tobacco and/or Nicotine Product ("TNP")[8] study cohorts and young adults versus older adults.

The relevant stated hypotheses are:

1. "After exposure to the BIDI® Stick product description and packaging, the likelihood to try BIDI® Stick among non-users (never and former) of TNP will not differ by flavors."

2. "After exposure to the BIDI® Stick product description and packaging, the association between the likelihood to try BIDI® Stick and flavors of BIDI® Stick will not differ between non-users age 21-24 (never and former) and non-users age 25 or above (never and former)."

Reasons for interest in using BIDI® Stick was measured where respondents were given a list of potential reasons and could select as many reasons as possible that apply to them. This question will only be answered by people who indicate greater than or equal to "4" interest in trying BIDI® Stick. Response options include:

- To help me reduce my combustible cigarette smoking
- To completely replace my combustible cigarette smoking
- To help me quit smoking combustible cigarettes
- It is a more appealing option that my current ENDS
- It is a less harmful option than my current ENDS
- Less harmful to my health than combustible cigarettes
- Less harmful to my health than other tobacco products, excluding combustible cigarettes
- Comes in flavors I like
- Comes in one nicotine strength
- None of the above

The responses will provide information on the importance of flavors for users with an interest in using BIDI® Stick.

[8] TNP is defined in the protocol as combustible cigarettes, electronic nicotine delivery systems (ENDS) other than BIDI® Stick (ENDS are also known as e-cigs, electronic cigarettes, vaping devices, vape pens and/or e-liquids), smokeless tobacco products (moist snuff, chewing tobacco, snus), nicotine pouches (tobacco-free pouch, placed in the mouth), cigars, cigarillos, filtered cigars filled with tobacco, pipe tobacco, hookah or water pipe tobacco and aids to help stop smoking (e.g., Nicorette, Nicoderm CQ).

### b. BIDI® Stick Patterns of Use Study

The BIDI® Stick POU surveyed BIDI® Stick users, specifically those who had used BIDI® Sticks every day or some days within the 30 days prior to taking the survey. The study utilized a retrospective, self-reported, cross-sectional design to measure recalled TNP usage and perceived TNP health risks among current users of BIDI® Stick. Surveys (**Attachment 5**) were completed between May 3 and August 17, 2021.

Kantar recruited potential respondents via email invitation, directly from Bidi Vapor's consumer databases. Bidi Vapor's consumer databases are comprised of people who have either purchased a product directly from Bidi Vapor (via e-commerce prior to the Company halting direct-to-consumer online sales) or are enrolled in the BIDI® Cares product recycling program. Bidi Vapor's consumer databases retain names of people who have opted out of receiving email communication from the Company. Those consumers were not invited to participate in this research study. In addition to the study email invitation, BIDI® Stick users who are enrolled in the BIDI® Cares product recycling program and opted-in for contact information were contacted via telephone, utilizing a verbal script approved in advance by the Sterling Institutional Review Board.

In addition to recruiting participants directly from the Company's consumer databases, participants were also recruited from high volume retail stores where BIDI® Stick is sold. Purchasers of BIDI® Stick were provided a postcard inviting them to participate in the study. Age of respondents recruited from stores will have been age verified to be 21 years of age or older via personal ID provided in store.

The POU survey questions on flavors included an assessment of:

- BIDI® Stick flavors currently used
- BIDI® Stick flavor used most often
- Importance of flavor in the decision to start using BIDI® Stick.

This information will show the importance of flavors in the use of BIDI® Stick among TNP users who switch from combusted cigarettes.

In addition to these questions on flavor, both studies included a series of questions regarding past use and current use of other TNPs and evaluation of absolute and relative health risks of BIDI® Stick versus other TNPs for several conditions.

### c. Current Status of LOU and POU Studies

The studies are currently undergoing data quality control checks, with development of Descriptive Tables to begin soon according to the approved Statistical Analysis Plan. Preliminary information is anticipated to be available in mid-October 2021 with technical regulatory reports available in late November 2021.

## V. Additional Nationally Representative TPPI and Actual Use Studies Assessing, Among Other Things, the Role and Added Benefit of the Non-Tobacco BIDI® Sticks for Adult Combusted Cigarette Smokers in Terms of Adult Switching/Cigarette Reduction

McKinney Regulatory Science Advisors, LLC, working with Russell Burnett Research and Consultancy Ltd ("RBRC"), was commissioned to design, conduct and report two additional quantitative research studies: (i) Perceptions and Behavioral Intentions (PBI) Study of the BIDI® Stick ENDS; and (ii) Patterns of Use of the BIDI® Stick ENDS and Transitions in Cigarette Smoking Status in a Convenience Sample of BIDI® Stick Ever-Users. Together, these two studies will collect data that address, among other important research questions, the likelihood that adult current combusted cigarette smokers would partially or completely replace combusted cigarettes with one of Non-Tobacco BIDI® Sticks or the Classic BIDI® Stick. These studies will also allow, if applicable, bridging to published behavioral studies.[9] The current expected timeline for reporting of these studies is Q1 of 2022 for end of data collection and preliminary data analysis, and Q2 of 2022 for submission of the final report to FDA.

### a. Study 1: Perceptions and Behavioral Intentions (PBI) Study of the BIDI® Stick ENDS ('the PBI Study')

- The PBI Study is a cross-sectional, internet-based survey study of risk perceptions and behavioral intentions in relation to the BIDI® Stick ENDS in 11 flavor profiles among large, U.S. nationally representative samples of adult current combusted cigarette smokers, former smokers, and non-smokers of combusted cigarettes.
- Subjects in this study will be adults aged 21 years and older who are living in the United States and are enrolled either as a panelist in Ipsos-Insight LLC's proprietary KnowledgePanel® – the largest probability-based online research panel in the United States that is designed to be representative of the non-institutionalized U.S. population aged 18 years and older – or as a panelist in a non-probability internet research panel to which Ipsos has access.

[9] Citation to Juul AJHB Special Issue, available at: https://ajhb.org/wp-content/uploads/2021/04/AJHB_JUUL_Special_Issue.pdf.

- Approximately 7,700 subjects will be recruited to this study, comprised of approximately 2,200 current smokers, 2,200 former smokers, 2,200 non-smokers, and an oversample of 1,100 young adult (aged 21-24 years) non-smokers.
- This study will form part of Bidi Vapor's program of research on the potential population health impact of the BIDI® Stick ENDS by obtaining quantitative data that characterize:
    1. Intentions to try, purchase to try, and regularly use the BIDI® Stick ENDS in each of the 11 flavor profiles among legal age adult current smokers, former smokers, and non-smokers.
    2. Current smokers' intentions to use the BIDI® Stick ENDS (in each of the 11 flavor profiles) in addition to combusted cigarettes (i.e., dual use) or as a partial or complete replacement for combusted cigarettes (i.e., product switching).
    3. Adults' conditional and unconditional perceptions of the absolute and comparative health and addiction risks associated with different tobacco product use behaviors, including starting to use the BIDI® Stick ENDS in addition to, in place of, and instead of combusted cigarettes.
    4. Adults' understanding of the nicotine warning statement and legal purchasing age information that is communicated on the packaging container of the BIDI® Stick ENDS.
- Draft (i.e., non-final) versions of the PBI study protocol and questionnaire are attached as **Attachments 7** and **8**.

**b. Study 2: Patterns of Use of the BIDI® Stick ENDS and Transitions in Cigarette Smoking Status in a Convenience Sample of BIDI® Stick Ever-Users ("the Actual Use Study")**

- The Actual Use Study is a cross-sectional, internet-based survey study that will aim to characterize patterns of use of BIDI® Sticks in a convenience sample of legal age adult ever-purchasers of BIDI® Sticks, and describe transitions in these individuals' combusted cigarette smoking status since initiation of use of BIDI® Sticks.
- Subjects in this study will be adults aged 21 years and older in the United States who have ever purchased a BIDI® Stick (target n = 500). Subjects will be recruited from customer databases that are maintained by or accessible to Bidi Vapor.
- This study will obtain quantitative data that characterize:
    1. Consumers' combusted cigarette smoking status at the time of their first purchase of a BIDI® Stick for their own personal use.
    2. Consumers' reasons for first purchasing a BIDI® Stick for their own personal use.
    3. Consumers' reasons for continuing/discontinuing use of a BIDI® Stick.
    4. Patterns of use of BIDI® Sticks in each flavor profile, including volume, duration, frequency and intensity of consumption.

5. Distributions of BIDI® Stick ever-users across key demographic and socioeconomic variables.
6. The prevalence of transitions into and out of combusted cigarette smoking that are attributed by consumers to their use of BIDI® Sticks.

## VI. Comprehensive Literature Review: Update to PMTA Module 2 Section 2.9

Bidi Vapor recently commissioned Cardno ChemRisk to update its existing literature review and state-of-science report (see Module 2 Section 2.9) specifically on the impact of non-tobacco flavored ENDS on patterns and features of ENDS abuse liability, initiation, transitions, and cessation. This updated review starts where the last review left off and covers the relevant science published between July 1, 2019 and April 28, 2021. This is our most up-to-date literature review, and demonstrates some shifts in the appeal, preference, and use of flavored ENDS across age groups. See **Exhibit B**.

**In short, the majority of all age groups reported that flavors, and particularly non-tobacco favors, are an important reason for using ENDS**. Regarding prevalence of flavored ENDS use, initial conclusions on youth and young adults remained consistent when considering the updated literature. Specifically, non-tobacco flavored ENDS are appealing to youth, although the prevalence of flavored ENDS use has remained relatively stable or even declined in recent years. Additionally, other factors associated with ENDS use among youth and young adults besides flavors should be considered, such as use of other tobacco products and substances (e.g., alcohol, marijuana, prescription drugs), psychological factors (e.g., internalizing and externalizing problems), and social factors (e.g., use of products by friends and family). Adult appeal to flavored ENDS has evolved in the most recent years, with an increasingly greater number of adults reporting use of non-tobacco flavored ENDS.

Moreover, a review of the recently published literature on flavored ENDS demonstrated that the availability of these products, especially non-tobacco flavored ENDS, is becoming increasingly important for adult smokers who are looking for an alternative nicotine product to reduce or quit smoking combusted cigarettes. **As discussed above,** among other things, this updated literature review noted the following findings in the literature on flavored ENDS products and smoking cessation:

- Study results suggest that the use of flavored e-cigarettes can facilitate smoking cessation (Glasser et al. (2021));

- Study results indicate that adults who began using non-tobacco flavored ENDS were more likely to quit smoking than those who used tobacco flavored ENDS (Friedman and Xiu (2020));
- Analyses demonstrate that flavor preferences varied depending on the product, and that both tobacco and non-tobacco flavors are important to adult e-cigarette users (Schneller et al. (2020));
- Compared to tobacco flavor users, participants who used sweet flavors at baseline were significantly more likely to quit smoking and that, regarding flavor transitions between baseline and follow-up, there was more movement away from tobacco to any other flavors than to tobacco from other flavors. Overall, study results demonstrate that use of sweet flavored e-cigarettes at baseline were positively associated with smoking cessation at follow-up (Li et al. (2021));
- A recent study shows that a variety of nontobacco flavors, especially fruit, are popular among adult vapers, particularly among those who have quit smoking and are now exclusively vaping. (Gravely et al. (2020)).
- E-cigarettes most likely to promote cessation will be those that deliver nicotine in a manner that is reliable and consistent with the nicotine delivery profile of a combusted cigarette. (Blank et al. (2020))

## VII. Continued Youth Access Prevention Efforts

Bidi Vapor continuously goes above and beyond regulatory requirements to employ rigorous youth-access prevention measures. These efforts are detailed in the Company's recent correspondence with the CTP OCE, (**Attachment 1**). Bidi Vapor also addressed its various industry-leading efforts in a Listening Session with the Agency on September 2, 2021.

## VIII. Conclusion

Bidi Vapor would like to amend Module 2 Section 2.9, Module 5 Sections 5.2 and 5.3, and Module 6 Section 6.2.1 of its PMTAs with the information contained herein. Our expectation is that Bidi Vapor's continued efforts to improve its timely-submitted PMTAs during the pandemic demonstrate substantial progress on its applications as detailed in this amendment (and as will be described further in our forthcoming meeting request and future amendments), and will be given due consideration by FDA as part of the Company's PMTAs' scientific review process. As we complete our ongoing clinical, behavioral and analytical studies, Bidi Vapor expects to continue submitting all relevant data and information to FDA via additional PMTA amendments as soon as these data become available.

* * * *

This PMTA amendment submission contains trade secret and confidential commercial information that Bidi Vapor considers to be proprietary and highly sensitive, and which is protected from disclosure under FDCA §§ 301(j) and 906(c) (21 USC §§ 331(j) and 387f(c)), the Trade Secrets Act (18 USC § 1905), the Freedom of Information Act (FOIA) (5 USC § 552), and FDA's implementing regulations, 21 CFR Part 20. If FDA receives a request for these records and tentatively determines that any portion of this submission is disclosable, Bidi Vapor requests that FDA provide notice and an opportunity for Bidi Vapor to object to any disclosure in accordance with 21 CFR §§ 20.47 and 20.61. Bidi Vapor reserves all legal rights to protect against public disclosure of its trade secret and confidential commercial information and to seek legal recourse against anyone who discloses such information without legal authorization.

We appreciate FDA's careful consideration of this fourth PMTA amendment PM0003460 and look forward to working with the Agency to secure a marketing authorization order under FDCA § 910. We trust that the information enclosed herein provides sufficient information for the Agency to conclude that the marketing of the BIDI® Stick, both the non-tobacco flavored and tobacco-flavored products, is APPH.

Should you have any questions regarding the enclosed submission, please do not hesitate to contact the undersigned with any questions, preferably by telephone or e-mail so that we may respond as soon as possible.

Respectfully submitted,

Niraj Patel
Chief Executive Officer
Bidi Vapor LLC

## IX. Enclosures (Attachments 1-8)

**Attachment 1** – Bidi Vapor's June 25, 2021 Letter to the CTP Office of Compliance and Enforcement Requesting Case-By-Case Discretion and Continued Marketing Pending PMTA Review

**Attachment 2** – Cardno ChemRisk Updated Literature Review – ENDS & E-Liquid Updated State of the Science – Behavioral Endpoints (August 25, 2021)

**Attachment 3** – BIDI® Stick LOU Study Protocol

**Attachment 4** – BIDI® Stick LOU Study Survey

**Attachment 5** – BIDI® Stick POU Study Protocol

**Attachment 6** – BIDI® Stick POU Study Survey

**Attachment 7** – PBI Study of the BIDI® Stick ENDS Draft Protocol

**Attachment 8** – PBI Study of the BIDI® Stick ENDS Draft Questionnaire

# EXHIBIT L

## COVID-19 Information

Public health information (CDC)

Research information (NIH)

SARS-CoV-2 data (NCBI)

Prevention and treatment information (HHS)

Español

NIH U.S. National Library of Medicine

ClinicalTrials.gov

# BIDI Stick ENDS Abuse Liability and Puffing Topography Assessment



ClinicalTrials.gov Identifier: NCT05072925

Recruitment Status : Completed
First Posted : October 11, 2021
Last Update Posted : October 11, 2021

**Sponsor:**
BIDI Vapor

**Information provided by (Responsible Party):**
BIDI Vapor

Study Details | Tabular View | No Results Posted | Disclaimer | How to Read a Study Record

**Tracking Information**

**First Submitted Date** ICMJE

September 26, 2021

**First Posted Date** ICMJE

October 11, 2021

**Last Update Posted Date**

October 11, 2021

**Actual Study Start Date** ICMJE

July 7, 2021

**Actual Primary Completion Date**

July 23, 2021 (Final data collection date for primary outcome measure)

**Current Primary Outcome Measures** ICMJE
**(submitted: October 6, 2021)**

- Baseline-adjusted plasma nicotine Cmax0-120 [ Time Frame: 0-120 minutes ]

  Maximum baseline-adjusted plasma concentration of nicotine from time zero to 120 minutes after the start of product use
- Baseline-adjusted plasma nicotine Tmax0-120 [ Time Frame: 0-120 minutes ]

  Baseline-adjusted plasma nicotine Tmax following defined product use
- Baseline-adjusted plasma nicotine AUC0-120 [ Time Frame: 0-120 minutes ]

  Baseline-adjusted area under the plasma nicotine concentration-versus-time curve from time zero to 120 minutes after the start of product use
- Baseline-adjusted plasma nicotine Cmax0-180 [ Time Frame: 0-180 minutes ]

  Maximum baseline-adjusted plasma concentration of nicotine from time zero to 180 minutes after the start of product use
- Baseline-adjusted plasma nicotine Tmax0-180 [ Time Frame: 0-180 minutes ]

  Baseline-adjusted plasma nicotine Tmax following both defined and ad libitum product use
- Baseline-adjusted plasma nicotine AUC0-180 [ Time Frame: 0-180 minutes ]

  Baseline-adjusted area under the plasma nicotine concentration-versus-time curve from time zero to 180 minutes after the start of product use
- Product liking [ Time Frame: 180 minutes ]

Visual analog scale product liking assessment; scale from 0 to 100 with higher scores representing stronger liking.

- Intent to Use Product Again [ Time Frame: 180 minutes ]

  Visual analog scale intent to use product again assessment; scale from 0 to 100 with higher scores representing stronger intent to use the product again.

- Urge to Smoke [ Time Frame: 0-180 minutes ]

  Visual analog scale urge to smoke assessment; scale from 0 to 100 with higher scores representing stronger urge to smoke.

- Product Evaluation Scale [ Time Frame: 180 minutes ]

  Subjective effects assessment using Product Evaluation Scale, which included 21 items with responses recorded on a scale of 1 to 7 ranging from 'Not at all' to 'Extremely'.

- Mass change [ Time Frame: 0-5 minutes and 120-180 minutes ]

  Mass change in grams of ENDS products during use sessions

**Original Primary Outcome Measures** ICMJE

*Same as current*

**Change History**

No Changes Posted

**Current Secondary Outcome Measures** ICMJE
**(submitted: October 6, 2021)**

- Puff duration [ Time Frame: 120-180 minutes ]

  Puff duration from puffing topography measurements

- Puff volume [ Time Frame: 120-180 minutes ]

  Puff volume from puffing topography measurements

- Peak puff flow rate [ Time Frame: 120-180 minutes ]

  Peak puff flow rate from puffing topography measurements

- Average puff flow rate [ Time Frame: 120-180 minutes ]

  Average puff flow rate from puffing topography measurements

- Inter-puff interval [ Time Frame: 120-180 minutes ]

  Time between puffs from puffing topography measurements

**Original Secondary Outcome Measures** ICMJE

*Same as current*

**Current Other Pre-specified Outcome Measures**
**(submitted: October 6, 2021)**

- Heart rate [ Time Frame: 0-180 minutes ]

  Heart rate measurements made to assess safety
- Blood pressure [ Time Frame: 0-180 minutes ]

  Blood pressure measurements made to assess safety
- Adverse events [ Time Frame: From screening through study completion, an average of 1 month ]

  Adverse event reporting

**Original Other Pre-specified Outcome Measures**

*Same as current*

## Descriptive Information

**Brief Title** ICMJE

BIDI Stick ENDS Abuse Liability and Puffing Topography Assessment

**Official Title** ICMJE

Abuse Liability and Puffing Topography Assessments of the BIDI Stick Electronic Nicotine Delivery System (ENDS) in Comparison to a Combustible Cigarette and JUUL Pod-Based ENDS

**Brief Summary**

This study assessed the abuse liability (measured by assessing how much nicotine enters the body when the BIDI Stick is used, and how this makes users feel) and puffing topography (puff characteristics like volume and duration) of the BIDI Stick ENDS, a type of electronic cigarette.

**Detailed Description**

This is a part-randomized, open label abuse liability assessment (ALA) and puffing topography study of nicotine-containing products carried out in 18 healthy adult volunteers who smoke combustible cigarettes.

Subjects will attend the study site 8 times (Visits 2-9) during the main study for ALA and puff topography assessments. Prior to each visit, subjects will be required to refrain from using any nicotine-containing products for a period of at least 12 hours before study product use.

At Visit 2, the subjects will smoke their usual brand cigarette during 2 use sessions. In the first session, subjects will smoke a single combustible cigarette of their usual brand by taking 10 puffs, 30 seconds apart.

Blood samples will be obtained for plasma nicotine analysis, and blood pressure and heart rate will be recorded. Subjects will be asked to complete subjective effects questionnaires at various points either before, during, or after product use.

In the second session, which will begin immediately after the last blood draw following the first session and after all questionnaires have been completed, subjects will be allowed to take ad libitum puffs on their usual brand cigarette for a period of 60 minutes (1 hour). In a randomly-selected subset of 8 subjects, during this ad libitum puffing session puffing topography measurements will be made with a CReSS Pocket device. Subjects may smoke as many cigarettes as they like. In all subjects, a blood sample for nicotine PK analysis will be drawn at the end of the session. Blood pressure and heart rate will be recorded at this time. Subjective effects questionnaires will also be completed at specified timepoints.

At Visits 3-9, the subjects will use their randomly-assigned ENDS product during 2 use sessions. These use sessions, and the assessments made, will be the same as at visit 2. Prior to visit 3-9, subjects will be provided with a supply of their randomly-assigned product to use at home before their next visit (familiarization). This familiarization period should last a minimum of 2 and a maximum of 5 days.

**Study Type** ICMJE

Interventional

**Study Phase** ICMJE

Not Applicable

**Study Design** ICMJE

Allocation: Randomized
Intervention Model: Crossover Assignment
Masking: None (Open Label)
Primary Purpose: Basic Science

**Condition** ICMJE

- E-cigarette Use
- Cigarette Smoking

**Intervention** ICMJE

Other: Tobacco products

Products will be used under defined (10 puffs, 30 seconds apart) and ad libitum puffing conditions

**Study Arms** ICMJE

- Active Comparator: Combustible Cigarette

The usual brand of combustible cigarette smoked by study subjects, with a minimum Federal Trade Commission tar yield of 8mg

Intervention: Other: Tobacco products

- Experimental: BIDI Stick ENDS Arctic flavor

  BIDI Stick ENDS containing 6% nicotine and Arctic flavor

  Intervention: Other: Tobacco products

- Experimental: BIDI Stick ENDS Classic flavor

  BIDI Stick ENDS containing 6% nicotine and Classic flavor

  Intervention: Other: Tobacco products

- Experimental: BIDI Stick ENDS Zest flavor

  BIDI Stick ENDS containing 6% nicotine and Zest flavor

  Intervention: Other: Tobacco products

- Experimental: BIDI Stick ENDS Regal flavour

  BIDI Stick ENDS containing 6% nicotine and Regal flavor

  Intervention: Other: Tobacco products

- Experimental: BIDI Stick ENDS Winter flavour

  BIDI Stick ENDS containing 6% nicotine and Winter flavor

  Intervention: Other: Tobacco products

- Experimental: BIDI Stick ENDS Solar flavor

  BIDI Stick ENDS containing 6% nicotine and Solar flavor

  Intervention: Other: Tobacco products

- Active Comparator: JUUL ENDS Virginia Tobacco flavor

  JUUL ENDS containing 5% nicotine and Virginia Tobacco flavor

  Intervention: Other: Tobacco products

**Publications ***

*Not Provided*

*** Includes publications given by the data provider as well as publications identified by ClinicalTrials.gov Identifier (NCT Number) in Medline.**

## Recruitment Information

**Recruitment Status** ICMJE

Completed

**Actual Enrollment** ICMJE
**(submitted: October 6, 2021)**

18

**Original Actual Enrollment** ICMJE

*Same as current*

**Actual Study Completion Date** ICMJE

July 23, 2021

**Actual Primary Completion Date**

July 23, 2021 (Final data collection date for primary outcome measure)

**Eligibility Criteria** ICMJE

Inclusion Criteria:

1. Healthy males or females within the ages of 21 to 65 years, inclusive.
2. Subjects will have a body mass index (BMI) of 18.5 to 35.0 kg/m2, inclusive, and a body weight exceeding 52 kg (males) or 45 kg (females).
3. Subjects must be current smokers (≥10 per day) of factory-made, high tar (10mg) combustible cigarettes (eCO >10 ppm at screening) for at least one continuous year before Visit 1 and may be occasional or dual users of e-cigarettes.
4. Urine cotinine >200 ng/mL.
5. Subject demonstrates understanding of the study and willingness/consent to participate as evidenced by voluntary written informed consent and has received a signed and dated copy of the consent form.
6. Subject understands and is willing, able, and likely to comply with all the study procedures and restrictions.
7. Subject is in good general health in the opinion of the investigator, with no clinically significant and relevant abnormalities of medical history (e.g., uncontrolled hypertension, recent myocardial infarction or unstable angina, history of seizures or recent stomach ulcer).
8. Subject has a seated systolic blood pressure ≤160 mmHg, diastolic blood pressure ≤95 mmHg, and heart rate ≤100 bpm.
9. Females of childbearing potential are, in the opinion of the investigator, practicing a reliable method of contraception.

Exclusion Criteria:

1. Subjects who, in the judgment of the study physician, have recent or active COVID 19 infection, as evidenced by the following:

   a. Endorsement of symptoms that could indicate COVID-19 during screening (Section 13.1) and/or
   b. Body temperature ≥38.0°C and/or
   c. Laboratory test results suggestive of active or recent exposure to SARS-CoV-2 (Section 9.4).
2. Laboratory serology results positive for HBsAg, hepatitis C virus (HCV) antibody, (HIV) type 1 or 2.
3. Subjects who have participated in another clinical study within 30 days of Visit 1 or who have previously participated in this study.
4. Subjects who have an acute illness (e.g., upper respiratory tract infection, viral infection) requiring treatment in the 4 weeks prior to Visit 1, or an active respiratory infection at time of the Screening Visit.
5. Subject has a clinically significant abnormal finding on the physical examination, medical history, vital signs, ECG, lung x-ray or clinical laboratory results that could interfere with, or for which use of the study products might interfere with, the conduct of the study, or that would, in the opinion of the investigator, pose an unacceptable risk to the subject in this study.
6. Subjects who have used any nicotine or tobacco product other than e-cigarettes or factory-made combustible cigarettes in the 14 days prior to the Visit 1.
7. Subjects who are self-reported or observed (during the trial session at Visit 2) non inhalers during ENDS/cigarette use.
8. Subjects who have used any prescription or over-the-counter (OTC) smoking cessation treatments, including, but not limited to any form of nicotine replacement therapy (NRT), varenicline, cytisine, or bupropion within 30 days prior to Visit 1.
9. Is planning to quit smoking during the study or postponing a quit attempt in order to participate in the study.
10. Subjects who have used prescription or OTC bronchodilator medication (e.g., inhaled or oral β adrenergic agonists, anticholinergics, glucocorticoids, cromones, or theophylline) to treat a chronic condition within the 12 months prior to Visit 1 or have a history of lung disease.
11. Subjects who have received any medications or substances that interfere with the cyclooxygenase pathway within 14 days prior to Visit 1 or are known to be strong inducers or inhibitors of cytochrome P450 (CYP) enzymes within 14 days or 5 half lives of the drug (whichever is longer) prior to Visit 1.
12. Women who are pregnant or who have a positive urine pregnancy test.
13. Women who are breast-feeding.
14. Subject has a history or diagnosis of adult asthma, COPD (including emphysema and chronic bronchitis), or use of an inhaler within the past 3 months.
15. Subject has been hospitalized in the 28 days prior to the Visit 1.
16. Subject has a history of schizophrenia, psychosis, or bipolar disorder.

17. Subject provides a positive drugs of abuse urine test at Visit 1. Tested drugs will include cocaine, amphetamines, methamphetamines, opiates (morphine, heroin), barbiturates, and benzodiazepine.
18. Subject has a self-reported use of more than 21 drinks per week. A drink is defined as 25 ml of spirits (e.g., whisky, vodka), 250 ml of beer, or 75 ml of wine.
19. Subjects who have lost or donated more than 450 mL of blood within the 2 months preceding the first product use.
20. Subject is an employee of the sponsor or the study site, or members of their immediate family.
21. In the opinion of the investigator, the subject should not participate in this study.
22. A history of allergy/oversensitivity to the ingredients of the study products.

**Sex/Gender** ICMJE

**Sexes Eligible for Study:**
All

**Ages** ICMJE

21 Years to 65 Years (Adult, Older Adult)

**Accepts Healthy Volunteers** ICMJE

Yes

**Contacts** ICMJE

*Contact information is only displayed when the study is recruiting subjects*

**Listed Location Countries** ICMJE

Poland

**Removed Location Countries**

## Administrative Information

**NCT Number** ICMJE

NCT05072925

**Other Study ID Numbers** ICMJE

BIDI-PK-01

**Has Data Monitoring Committee**

No

**U.S. FDA-regulated Product**

**Studies a U.S. FDA-regulated Drug Product:**

No

**Studies a U.S. FDA-regulated Device Product:**

No

**IPD Sharing Statement** ICMJE

**Plan to Share IPD:**

No

**Responsible Party**

BIDI Vapor

**Study Sponsor** ICMJE

BIDI Vapor

**Collaborators** ICMJE

*Not Provided*

**Investigators** ICMJE

**Principal Investigator:**

Anna O Popko, MD

MTZ Clinical Research Sp z.o.o.

**PRS Account**

BIDI Vapor

**Verification Date**

October 2021

ICMJE **Data element required by the International Committee of Medical Journal Editors and the World Health Organization ICTRP**

# EXHIBIT M

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**Azim Chowdhury**
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September 21, 2021

**VIA CTP Portal**

Mitch Zeller, J.D.
Director - Center for Tobacco Products
U.S. Food and Drug Administration
Document Control Center
Building 71, Room G335
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
E-mail: Mitchell.Zeller@fda.hhs.gov

**CONTAINS CONFIDENTIAL AND PRIVILEGED BUSINESS INFORMATION**

**REQUEST FOR SUPERVISORY REVIEW UNDER 21 C.F.R. § 10.75**

**Re: Bidi Vapor LLC; 21 C.F.R. § 10.75 Request for Supervisory Review of Arctic (Menthol) BIDI® Stick (PD1) Inclusion in Marketing Denial Order for Flavored ENDS Subject to PMTA STN PM0003460**

Dear Mr. Zeller:

On September 7, 2021, our client Bidi Vapor LLC (Bidi Vapor or the Company) received a Marketing Denial Order (MDO) in response to its filed Premarket Tobacco Product Applications (PMTA) identified by STN PM0003460. *See* **Exhibit A**. The MDO was intended to cover all non-tobacco and non-menthol flavored BIDI® Stick electronic nicotine delivery systems (ENDS), but also appears to have inadvertently captured the Company's Arctic BIDI® Stick, which has a menthol characterizing flavor.[1] Pursuant to 21 C.F.R. § 10.75 and the Family Smoking Prevention and Tobacco Control Act (TCA), on behalf of Bidi Vapor, we respectfully request supervisory review of the MDO specifically as it relates to the inclusion of the Arctic BIDI® Stick (PD1) along with the Company's non-tobacco and non-menthol flavored ENDS.[2]

[1] The Arctic BIDI® Stick is identified as product number "PD1" of PMTA PM0003460.

[2] This request should in no way be construed as a waiver of any other potential challenges to the MDO on different or separate grounds. Bidi Vapor reserves the right to seek review of or otherwise appeal or challenge the legality of the MDO as it applies to all the Company's flavored ENDS.

Based on the language in the MDO and numerous FDA public statements and press releases, we understand that the MDO was intended to apply only to the Company's non-tobacco and non-menthol flavored BIDI® Sticks (*e.g.*, the Dawn, Gold, Marigold, Regal, Summer, Tropic, Winter, Zest and Solar BIDI® Sticks, identified as PD3 to PD11, respectively, of PM0003460). Specifically, the MDO alleges, in pertinent part, that the PMTAs lack sufficient evidence demonstrating that the *flavored* products will provide a benefit to adult users that would be adequate to outweigh the known risks to youth of marketing *flavored* ENDS. Moreover, the FDA news release announcing the first MDOs for flavored ENDS (*see* **Exhibit B)** provides, in relevant part (emphasis added)[3]:

> The scientific review of menthol ENDS, as compared to other non-tobacco-flavored ENDS products, raises unique considerations. Although ***menthol-flavored ENDS are not included in the decisions described above***, the FDA notes that its reviews will similarly examine whether the evidence in the application demonstrates a benefit to existing adult users that outweighs the known youth use of such products.

FDA has also emphasized its position that tobacco and menthol ENDS are not intended to be covered by the MDOs in several e-mails announcing additional marketing denials, stating, "[c]ompanies receiving these MDOs may have submitted premarket applications for other products (such as ENDS devices, tobacco-flavored ENDS, or menthol-flavored ENDS), and those products, if still pending, ***remain under review at FDA***."[4] Emphasis added. *See* **Exhibit C**.

However, despite clearly intending to cover only non-tobacco and non-menthol flavored BIDI® Sticks, the MDO also lists the Arctic BIDI® Stick in its Appendix A. It is possible that FDA may have misunderstood the characterizing flavor of this product to be a flavor other than menthol because of the "Arctic" (or previous "Mint Freeze") branding, or because the packaging previously described the product as having a "menthol + mint" flavor. As Bidi Vapor clarified in amendments to the Company's PMTA and related Tobacco Product Master File (TPMF) MF0000498, the Arctic BIDI® Stick has a menthol characterizing flavor. In fact, the Arctic

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[3] U.S. Food & Drug Admin., FDA News Release: *FDA Denies Marketing Applications for About 55,000 Flavored E-Cigarette Products for Failing to Provide Evidence They Appropriately Protect Public Health* (August 26, 2021) (available at https://www.fda.gov/news-events/press-announcements/fda-denies-marketing-applications-about-55000-flavored-e-cigarette-products-failing-provide-evidence). (Exhibit B)

[4] U.S. Food & Drug Admin., FDA CTP News E-mail, dated September 17, 2021, *FDA Denies Marketing Applications for Over 1 Million Flavored E-Cigarette Products* (Exhibit C).

BIDI® Stick only contains menthol oil and menthol crystals as flavoring agents.[5] Furthermore, the packaging has now been updated to clarify that the Arctic BIDI® Stick is a menthol product. *See* **Exhibit D**, which contains the Company's September 16, 2021, PMTA amendment and supporting documents. As such, we believe that CTP inadvertently included the Arctic BIDI® Stick in the list of Bidi Vapor ENDS identified in Appendix A of the MDO, and that CTP did not intend for the MDO to apply to that product.

**Accordingly, because it has a menthol characterizing flavor, we respectfully request that FDA provide written clarification that the Arctic BIDI® Stick is not subject to Bidi Vapor's MDO, and that the filed PMTA (PM0003460-PD1) for this product remains in scientific review.**

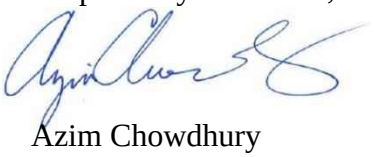
This request for supervisory review contains trade secret and confidential commercial information that Bidi Vapor considers to be proprietary and highly sensitive, and which is protected from disclosure under the Food, Drug and Cosmetic Act (FDCA) §§ 301(j) and 906(c) (21 USC §§ 331(j) and 387f(c)), the Trade Secrets Act (18 USC § 1905), the Freedom of Information Act (FOIA) (5 USC § 552), and FDA's implementing regulations, 21 CFR Part 20. If FDA receives a request for these records and tentatively determines that any portion of this submission is disclosable, Bidi Vapor requests that FDA provide notice and an opportunity for Bidi Vapor to object to any disclosure in accordance with 21 CFR §§ 20.47 and 20.61. Bidi Vapor reserves all legal rights to protect against public disclosure of its trade secret and confidential commercial information and to seek legal recourse against anyone who discloses such information without legal authorization.

* * * *

[5] Since menthol oil is extracted from the leaves of peppermint, the supplier refers to this ingredient as "mint oil," which may have been another source of confusion.

We appreciate FDA's careful consideration of this supervisory review request. Should you have any questions regarding the enclosed submission, please do not hesitate to contact the undersigned with any questions, preferably by telephone or e-mail so that we may respond as soon as possible.

Respectfully submitted,



Azim Chowdhury

Enclosures:

- **Exhibit A** – Bidi Vapor's September 7, 2021 Marketing Denial Order for Flavored BIDI® Stick ENDS
- **Exhibit B** - FDA News Release, *FDA Denies Marketing Applications for About 55,000 Flavored E-Cigarette Products for Failing to Provide Evidence They Appropriately Protect Public Health* (August 26, 2021)
- **Exhibit C** - FDA CTP News E-mail *FDA Denies Marketing Applications for Over 1 Million Flavored E-Cigarette Products* (September 17, 2021)
- **Exhibit D** – Bidi Vapor's PMTA PM0003460 – PD1 Amendment Clarifying the Arctic BIDI® Stick is a Menthol ENDS (September 16, 2021)

cc:

Niraj Patel, CEO, Bidi Vapor LLC, raj@bidivapor.com
Matthew R. Holman, CTP, Office of Science, Director, Matthew.Holman@fda.hhs.gov
Cristi Stark, Director, Division of Regulatory Project Management at Office of Science, Cristi.Stark@fda.hhs.gov
Nathan Hurley, CTP Ombudsman, CTPOmbudsman@fda.hhs.gov
Tobacco-Small Business, smallbiz.tobacco@fda.hhs.gov

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service

Food and Drug Administration
Silver Spring, MD 20993-0002

October 22, 2021

BY E-MAIL

Bidi Vapor LLC
Attention: Nirajkumar Patel, CEO
4460 Old Dixie Highway
Grant Valkaria, FL 32949

Re: September 7, 2021 marketing denial order related to certain products under Premarket Tobacco Product Application ("PMTA") PM0003460; *Bidi Vapor LLC v. FDA*, 21-13340 (11th Cir.)

Dear Mr. Patel:

Pursuant to 21 C.F.R. § 10.75, FDA's Center for Tobacco Products ("CTP") has concluded that it will review the marketing denial order it issued to Bidi Vapor LLC related to certain products outlined in Appendix A thereto (related to PMTA PM0003460). CTP is undertaking this review, in part, to assess whether Bidi Vapor LLC's PMTA contains studies and/or data that are similar to a PMTA with a marketing denial order that CTP recently rescinded. Pursuant to 21 C.F.R. § 10.35(a), and in consultation with CTP, I am staying Bidi Vapor LLC's marketing denial order pending this review. I have determined that a stay is in the public interest to help reduce public confusion about the status of the marketing denial order during this review. Neither this stay of the marketing denial order nor CTP's review of the marketing denial order constitute authorization to market, sell, or ship the products outlined in Appendix A.

Accordingly, the marketing denial order issued to Bidi Vapor LLC, dated September 7, 2021, related to certain products outlined in Appendix A thereto (related to PMTA PM0003460), is hereby stayed pending FDA's review.

Lauren Roth -S Digitally signed by Lauren Roth -S
Date: 2021.10.22 15:50:12 -04'00'

Lauren Roth
Associate Commissioner for Policy
Office of the Commissioner
U.S. Food and Drug Administration

cc: Azim Chowdhury, Keller & Heckman LLP (by email)
Eric P. Gotting, Keller & Heckman LLP (by email)
Maureen Berard Soles, Baker & Hostetler LLP (by email)