FDA U.S. FOOD & DRUG ADMINISTRATION

Technical Project Lead (TPL) Review of PMTA

New Product Subject to this Review[1]	
STN[2]	PM0004691.PD1
Common Attributes	
Submission date	May 25, 2021
Receipt date	May 25, 2021
Applicant	Philip Morris Products S.A.
Product manufacturer	Philip Morris Products S.A.
Application type	Supplemental
Product category	Heated Tobacco Product (HTP)
Product subcategory	HTP Consumable
Cross-Referenced Submissions	
All STNs	PM0000424, PM0000479, MR0000059
Supporting FDA Memoranda Relied Upon in this Review	
All STNs	None
Recommendation	
Issue marketing granted order for the new tobacco product subject to this review.	

Technical Project Lead (TPL): /S/

Todd L. Cecil, Ph.D.
Deputy Director for Regulatory Management
Office of Science

Signatory Decision: Concur with TPL recommendation and basis of recommendation

/S/

Benjamin Apelberg, Ph.D.
Director (Acting)
Office of Science

[1] Product details, amendments, and dates provided in the Appendix. PMTA means premarket tobacco application(s).
[2] Submission tracking numbers

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1. EXECUTIVE SUMMARY

On December 14, 2020, FDA received a supplemental Premarket Tobacco Product Application (sPMTA) for Marlboro Amber HeatSticks (PM0004691.PD1). The applicant referenced the PMTAs for the Marlboro HeatSticks (PM0000424) and for the IQOS 2.4 Holder and Charger (PM0000479). The products subject to the previous PMTAs were granted marketing authorization April 30, 2019 (hereafter, referred to as "the authorized products").

Scientific review of the application found that the comparisons between the new product and the authorized products are appropriate. The applicant has provided adequate information on the manufacturing process and product quality controls that will help ensure that the new product is manufactured consistently and will meet the applicant's specifications. The aerosols from the new product have been evaluated and found to be comparable to that from use of the authorized products.

The new product is not marketed in the U.S.; however, the applicant has provided user information from the international marketing experience with the new product as well as consumer reports, complaint, published literature and product safety information. There were no new safety concerns or unexpected adverse experiences identified. Currently, there is no evidence the user population for the new product will be different from the population who use the authorized products. Although the marketing information provided is not U.S. data, current use patterns available for the authorized products within the U.S. have not raised concerns regarding product use in youth and young adults. Given the product similarities, there is currently no available evidence of increased risk for youth initiation and use for the new product as compared to the authorized products.

The similarities in the product designs of the new and authorized products make it unlikely there are new concerns related to health effects, product quality, human factors, or product misuse for the new product as compared to the authorized products. As the new and authorized products have similar operating procedures, use similar tobacco sources, and produce comparable aerosols, FDA currently has no reason to believe the new product will result in different nicotine exposure, use patterns, user populations, or abuse liability.

The Agency determined that the environmental impacts of simultaneously marketing the authorized and the new products do not represent a significant environmental impact from the proposed and alternative actions.

In conclusion, none of the grounds specified in Section 910(c)(2) of the FD&C Act apply. Specifically, I find the following:

1. Permitting the marketing of the product is appropriate for the protection of the public health (APPH), as described in Section 910(c)(4) of the FD&C Act (subject to the labeling and advertising changes described below);
2. The methods used in, and the facilities or controls used for, the manufacture, processing, and packing of the product do not fail to conform to the requirements in Section 906(e) of the FD&C Act;
3. Based on a fair evaluation of all material facts, the proposed labeling is not false or misleading in any particular; and
4. The product does not fail to conform to a tobacco product standard in effect under Section 907 of the FD&C Act.

I recommend FDA grant marketing authorization for PM0004691.PD1.

FDA has examined the environmental effects of finding the new product APPH and made a Finding of No Significant Impact (FONSI).

2. BACKGROUND

2.1. NEW PRODUCTS

The applicant submitted information for the new product listed on the cover page and with more detail in the Appendix.

2.2. REGULATORY ACTIVITY

On May 25, 2021, FDA received an sPMTA from Philip Morris Products S.A. FDA issued an Acceptance letter to the applicant on June 1, 2021. FDA issued a Filing letter to the applicant on June 7, 2021. FDA issued a Deficiency letter to the applicant on August 19, 2021.

Refer to the Appendix, Table 3, for a complete list of amendments received by FDA.

2.3. SCOPE OF REVIEW

This review captures all compliance and scientific reviews completed for the new product subject of this review.

Table 1. Disciplines reviewed

Discipline	Cycle 1		Cycle 2	
	Reviewer(s)	Review Date	Reviewer(s)	Review Date
Regulatory	Donna Cheung	6/1/2021	Not assigned	N/A
Engineering	Mary Searing	8/18/2021	Not assigned	N/A
Chemistry	Delauren McCauley	8/19/2021	Delauren McCauley	12/15/2021
Medical	Lester (Jao) Lacorte	7/14/2021	Not assigned	N/A
Environmental Science	Bria Martin	8/18/2021	Bria Martin	4/25/2022

Table 2. Consultations

Discipline or Office	Cycle 1		Cycle 2	
	Reviewer(s)	Review Date	Reviewer(s)	Review Date
Medical	Susan Rudy	6/22/2021	Susan Rudy	12/9/2021
	Lester (Jao) Lacorte	7/14/2021		

3. SCIENTIFIC REVIEW

3.1. COMPARISON PRODUCTS

3.1.1. Discipline key findings

The following discussion is based on key findings provided in the discipline reviews.

- Product Comparison
  - The new product is a line extension of, and is being compared to, the currently authorized tobacco product (PM0000424)
- Ingredient comparison
  - The tobacco blend of the new product is identical to the authorized products.
  - The new product contains only minor ingredient modifications when compared to the authorized products.

3.1.2. Synthesis

The applicant provided a complete description of the new tobacco product and provided a comparison of the product to the authorized tobacco product (PM0000424). The comparison product data are appropriate and sufficient to determine the relative risks associated with this new tobacco product with respect to the previously authorized tobacco product. The applicant has demonstrated that using the new product is comparable to use of the authorized product when used with the authorized device (PM0000479).

3.2. PRODUCT CHARACTERIZATION

3.2.1. Discipline key findings

The following discussion is based on key findings provided in the discipline reviews.

3.2.1.1. Product design and composition

- The tobacco blend of the new product is identical to the authorized product.
- The applicant made minor ingredient modifications resulting in similar or lower total ingredient quantities that are unlikely to result in changes to HPHCs in the aerosol.
- The packaging is identical in the new and authorized products with the exception of the inner liner paper made from white paper in the new product compared to the metalized/coated paper in the authorized product. Because the inner liner paper does not contain ingredients that may effect the performance of the new product or transfer any constituent that may increase the users exposure to HPHCs, the change in inner liner paper is acceptable.

3.2.1.2. Manufacturing

- The applicant stated that the new product is manufactured in the same facilities (i.e., PMP S.A. (Switzerland) and Philip Morris Manufacturing and Technology Bologna S.p.A. (Italy)) as the authorized product.
- The manufacturing processing steps for the new product are identical to those of the authorized product with the exception of the (b)(4) (b)(4) The change in (b)(4) results in (b)(4)
  The manufacturing information submitted by the applicant is adequate.

3.2.1.3. Product stability

The applicant stated that they maintained the same principles of process controls and quality assurance in the new product as the authorized product. The new product has an identical tobacco blend and similar design, formulation, and container closure system as the authorized product.

3.2.1.4. Product test data

- The applicant provided minor ingredient component changes in the new product which are expected to generate lower mainstream aerosol yields (e.g., tar, nicotine, carbon monoxide, PAHs, phenols, aldehydes, and ketones) compared to the authorized product. The data were considered acceptable.

3.2.2. Synthesis

As TPL, I agree with the reviewers' conclusions that this sPMTA contains sufficient information to characterize the product design and adequate processes and controls to help ensure that the new products meet the manufacturer's specifications.

3.3. TOXICANT EXPOSURE

3.3.1. Discipline key findings

There were no specific data related to product toxicity included in the applications. Because the tobacco blend and materials that come into contact with the emitted aerosol in the new product are identical to the authorized product, and the new product is a line extension of an authorized product it is reasonable for the toxicant exposure to translate to the new product.

3.3.2. Synthesis

The changes to the new products are limited to components that are not affected by the development and filtering of the aerosol. HPHCs in the aerosol of the new product, as reported in the environmental assessment, are comparable to that of the authorized product and the changes described by the applicant do not demonstrate a different exposure risk than the authorized product.

3.4. ABUSE LIABILITY

3.4.1. Discipline key findings

There were no specific data related to nicotine pharmacokinetics, withdrawal, craving, or subjective effects included in this application. Because the tobacco blend and materials that come into contact with the emitted aerosol of the new product are identical to the authorized product, and the new product is a line extension of an authorized product it is reasonable for the nicotine exposure, use patterns, user populations, or abuse liability to translate to the new product.

3.4.2. Synthesis

There are no new data specifically related to abuse liability in this sPMTA. The new product operates in a similar manner and uses the same IQOS device as the previously authorized products. The ingredient difference in the new product has been evaluated and found to be comparable to that of the authorized product. As the new product has a similar flavor profile, operating procedures, use similar tobacco sources, and produce comparable aerosols, FDA has no reason to believe the new product will result in different nicotine exposure, use patterns, user populations, or abuse liability.

3.5. USER POPULATIONS

3.5.1. Discipline key findings

There were no specific data related to current tobacco users, tobacco non-users, vulnerable populations, mitigation strategies or labeling and advertising included in this application. Because the new product is a line extension of an authorized product it is reasonable for the current tobacco users, tobacco non-users, vulnerable populations, mitigation strategies or labeling and advertising to translate to the new product.

3.5.1.1. Labeling and advertising

The application included full copies of all the proposed product labeling, including color variations.

3.5.2. Synthesis

While the applicant did not provide specific data related to current tobacco users, tobacco non-users, vulnerable populations, mitigation strategies or labeling and advertising for the new products, they did provide user information from the international marketing experience with the new product as well as consumer reports, complaint, published literature and product safety information. There were no new safety concerns or unexpected adverse experiences identified. Currently, there is no evidence the user population for the new product will be different from the population who use the authorized products. Although the marketing information provided is not U.S. data, current use patterns available for the authorized products within the U.S. have not raised concerns regarding product use in youth and young adults. Given the product similarities, there is currently no available evidence of increased risk for youth initiation and use for the new product as compared to the authorized products. FDA has no reason to believe that the marketing and use patterns for the new products will be significantly different from the authorized product. I recommend that the postmarket restrictions imposed on the authorized products would also be imposed on the new products; these restrictions will reduce the likelihood of acquisition of the new products by consumers below legal age. Additionally, I recommend that any MGO letter encourage the applicant to take additional steps to limit youth exposure to print and point-of-sale advertising, including, for example, limiting advertising to print publications where 85% or more of the readership is 21 years of age or older and/or selecting publications that do not over-index for youth, requiring advertising to be placed inside the store, and placing product displays near other age-restricted products and away from toys and candy.

Similar to the authorized products, I recommend that any MGO letter state the removal of the warning “SURGEON GENERAL’S WARNING: Cigarette Smoke Contains Carbon Monoxide.” from the required warnings to be displayed on the product package labels and advertisements under FCLAA. Based on a fair evaluation of all material facts, the warning is misleading with respect to these products which, although categorized as cigarettes, do not produce carbon monoxide above environmental levels and do not increase CO-related health risks.

3.6. HEALTH EFFECTS

3.6.1. Discipline key findings

The applicant references the clinical and observational studies provided in the application for the authorized HeatSticks product (PM0000424). There were no specific data related to addiction, short- and long-term health effects, or likelihood and effects of product misuse included in the application. Because the new product is a line extension of an authorized product it is reasonable for the addiction, short- and long-term health effects and likelihood of product misuse to translate to these new products.

3.6.1.1. BIMO inspection findings

No inspections were conducted.

3.6.1.2. Adverse experiences

The applicant did not report any adverse experiences over what was previously reported under the post market experience for PM0000424 and PM0000479. FDA also performed a search for any reported adverse experiences and found none directly related to the authorized product.

3.6.2. Synthesis

The similarities in the product designs of the new and authorized products make it unlikely that there are new concerns related to health effects, product quality, human factors, or product misuse for the new product. To that point, similar to the authorized product, the new products do not present signals of cytotoxicity .

3.7. POPULATION AND PUBLIC HEALTH

3.7.1. Discipline key findings

There were no specific data related to population or public health studies included in this sPMTA. Because the new product is a line extension of an authorized product it is reasonable for the specific data related to population or public health studies to translate to the new product.

3.7.2. Synthesis

As the product design, characteristics, and tobacco source are similar, and the aerosol produced from the new product is comparable to that produced from the authorized product, there is no reason to believe the impact on population health will be different for the new product compared to the authorized product. Similarly, there is no evidence the user population for the new product will be different from the population who use the authorized product. Given the product similarities, there is currently no evidence of increased risk for youth initiation and use for the new product as compared to the authorized product.

3.8. STATUTORY REQUIREMENTS

3.8.1. Public health conclusion

Based on the findings and evaluations discussed in Sections 3.1-3.7, permitting marketing of the Marlboro Amber HeatSticks (PM0004691.PD1) as described by the applicant for use with

the authorized IQOS device is determined to be appropriate for the protection of the public health.

3.8.2. Tobacco product manufacturing practices

The methods used in, and the facilities or controls used for, the manufacture, processing, and packing of these products do not fail to conform to the requirements in Section 906(e) of the FD&C Act. The sPMTA contains sufficient information to characterize the product design and adequate processes and controls to help ensure that the product meets the manufacturer's specifications.

3.8.3. Labeling

The proposed product labeling is not false or misleading.

3.8.4. Product standards

There are no applicable product standards for this sPMTA.

4. ENVIRONMENTAL DECISION

4.1. DISCIPLINE FINDINGS

The environmental science review concluded that the provided information is adequate.

4.2. ENVIRONMENTAL CONCLUSION

A finding of no significant impact (FONSI) was signed by Luis G. Valerio, Jr., Ph.D., ATS on October 24, 2022. The FONSI was supported by an environmental assessment prepared by FDA on October 19, 2022.

5. CONCLUSION AND RECOMMENDATION

Based on our review of the sPMTA, I find that permitting the marketing of the new product is appropriate for the protection of the public health. Periodic reporting is required on an annual basis. Due to the similarity between the new product and the authorized products, the marketing restrictions applied to PM0000424 will also be applied to this product, with an update in frequency to annual reporting (see Appendix D).

FDA has examined the environmental effects of finding the new product APPH and made a Finding of No Significant Impact (FONSI).

Marketing granted orders should be issued for the new product subject of this review, as identified on the cover page of this review.

6. APPENDIX

Appendix A. New products

Common Attributes	
Submission date	May 25, 2021
Receipt date	May 25, 2021
Applicant	Philip Morris Products S.A.
Product manufacturer	Philip Morris Products S.A.
Product category	Heated Tobacco Product[3]
Product subcategory	HTP Consumable
Attributes[4,5]	**New Product**
STN	**PM0004691**
Static Product ID	PD1
Product name	Marlboro Amber HeatSticks[6]
Package type	Box
Package quantity	20 HeatSticks
Characterizing flavor	Tobacco[7]
Nicotine Source	Tobacco
Diameter	7.42 mm
Length	45 mm
Ventilation	Not Applicable
Additional property	Source of energy: Electric (rechargeable battery)

Table 3. Amendments received

Submission Date	Receipt Date	Amendment	Applications being amended	Reviewed	Brief Description
Oct 13, 2021	Oct 13, 2021	PM0005103	All[8]	Yes	Response to Aug 19, 2021 Deficiency Letter
Feb 25, 2022	Feb 25, 2022	PM0005188	All[8]	No. Amendment withdrawn	Additional information to original submission
Apr 20, 2022	Apr 20, 2022	PM0005255	All[8]	Yes	Withdrawal of amendment PM0005188

[3] The IQOS products meet the definition of cigarette in section 900(3) of the FD&C Act and components and parts in 21 CFR 1100.3 and 1141.3. Cigarettes and their components and parts must comply with the applicable provisions of the FD&C Act and regulations. For purposes of scientific review, the product category and subcategory have been revised.
[4] We interpret package type to mean container closure system and package quantity to mean product quantity within the container closure system, unless otherwise identified.
[5] Effective April 14, 2022, FDA's authority to regulate tobacco products was extended to include tobacco products containing nicotine from any source. As such, nicotine source is considered a required property for unique identification. https://www.congress.gov/bill/117th-congress/house-bill/2471
[6] Brand/sub-brand or other commercial name used in commercial distribution.
[7] The characterizing flavor previously identified as "None" has been updated in FDA records to "Tobacco" to accurately reflect that the product provides a tobacco characterizing flavor from the filler. As such, this product does not have any change in characterizing flavor.
[8] This amendment applies to all STNs subject of this review.

6.1. MARKETING GRANTED ORDER APPENDICES

Based on experience gained to date on postmarket review of PMTAs, as well as review of postmarket reports for the IQOS brand, I recommend updates to requirements under sections 910(c)(1)(B) and 910(f) of the FD&C Act. As such, the following appendices should be attached and applied to all IQOS products that have received marketing authorization.

6.1.1. Appendix B: Postmarket Recordkeeping and Retention

Under section 910(f) of the FD&C Act, this order requires that you establish and maintain the records listed below. At any time during the retention period described in this order, FDA may request that you provide any of the documents described below. In addition, under section 704 of the FD&C Act, FDA may inspect your establishment(s) and request to inspect any record(s) described below.

The following records must be retained according to the retention periods described below. These records must be legible, in English, and available for inspection and copying by officers or employees duly designated by the Secretary, upon request.

Record	Description	Retention Period
Prior PMTAs	Each PMTA submitted prior to marketing orders	4 years from the date that FDA issues the marketing order
Postmarket reports	Postmarket reports, including periodic and adverse experience reports as described in this order	4 years from the date the report was submitted to FDA or until FDA inspects the records, whichever occurs sooner
Correspondence with FDA	Correspondence with FDA pertaining to each authorized product	4 years from the date of distribution of the last batch of each product subject to this order
Study data	Nonclinical or clinical study documentation including: • Source data; • Study protocols (including statistical analysis plan) and amendments showing the dates and reasons for each protocol revision; • Institutional Review Board (IRB) or Independent Ethics Committee (IEC) approvals; • Informed consent forms; • Correspondence with study monitors/investigators/contract research organizations/sponsors/IRB/IEC; • Investigator financial disclosure statements; • Progress reports; • Monitoring reports; • Adverse experience reports; • Case report forms/subject diaries/medical records/laboratory reports; • Subject data line listings/observations records; • Test article accountability records; • Study results/protocol summaries/study reports; and • Certifications and amendments to certifications	4 years from the date of the order or 4 years from the conclusion of the study, whichever occurs later
Manufacturing records	Records pertaining to the manufacture, in process and release testing, production process (including any changes to the process, facility, or controls), packaging, storage, and stability monitoring and testing (including protocol and results) Records and reports of all manufacturing deviations, investigations, and corrective and preventive actions including, but not limited to, those deviations associated with processing, testing, packing, labeling, storage, holding and distribution; and any deviation that may affect the characteristics of each final product	4 years from the date of distribution of each batch of each product subject to this order

Record	Description	Retention Period
Sales and/or distribution records	A list of distributors and retailers of the products, including brick-and-mortar and digital[9] (including internet/online and mobile) Any available information (not to include personally identifiable information) about product purchasers, such as purchasers' demographics (e.g., age, gender, race/ethnicity, geographic region) and previous or current use of other tobacco products (i.e., dual use) With respect to individuals under the federal minimum age of sale of tobacco products, policies and procedures regarding restrictions on access to the products, including purchaser age and identity verification processes	4 years from the date of distribution of each batch of each product subject to this order
Complaints	Records pertaining to any and all complaints associated with the tobacco product that is the subject of this order; such records may also include your analysis of those complaints	4 years from the date of distribution of each batch of each product subject to this order
Health hazard analysis	Health hazard analyses, if performed voluntarily or directed by FDA	4 years from the date of distribution of each batch of each product subject to this order
Labeling	Specimens of all labeling (including all labeling variations, such as those reflecting different required warnings), labels, inserts/onserts, instructions, and other accompanying information	4 years from the date of initial dissemination to the public
Advertising, marketing and promotional materials and plans	Copies of all advertising, marketing, and/or promotional materials published, disseminated to consumers, or for use in engaging or communicating with consumers Copies of all advertising and marketing plans including strategic creative briefs and paid media plans, by channel and by product, and the details, dollar amount(s) and flighting of such plans, by channel and by product, including any: • Use of competent and reliable data sources, methodologies, and technologies to establish, maintain, and monitor highly targeted advertising and marketing plans and media buys, including a list of all data sources used to target advertising and marketing plans and media buys; • Targeting of specific group(s) by age-range(s), including young adults, ages 21-24, and other demographic or psychographic	4 years from the date of initial dissemination to the public or implementation

[9] For the purposes of this order, here and throughout the document, "digital" includes internet/online and mobile.

Record	Description	Retention Period
	characteristics that reflect your intended audience(s), including the source(s) of such data; • With respect to individuals under the federal minimum age of sale of tobacco products, actions taken to restrict access to the products and limit exposure to the products' labeling, advertising, marketing, and/or promotion; • Use of owned, earned, shared, or paid media to create labeling for, advertise, market, and/or promote the products; • Use of partners, influencers, bloggers, or brand ambassadors to create labeling for, advertise, market, and/or promote the products; • Consumer engagements – whether conducted by you, on your behalf, or at your direction -including events at which the products will be demonstrated and how access will be restricted to individuals at or above the federal minimum age of sale of tobacco products; or • Use of public relations or other communications outreach to create labeling for, advertise, market, and/or promote the products Copies of all records pertaining to media tracking and optimization, by channel, by product, and by audience demographics (e.g., age, gender, race/ethnicity, geographic region), and all post-launch delivery-verification reports submitted to you from an accredited source, by channel, by product, and by audience demographics Policies and procedures for real-time digital media monitoring to identify, correct, and prevent delivery of advertising impressions to individuals under the federal minimum age of sale of tobacco products, including documentation of such monitoring activities and implementation of corrective and preventive measures	
Formative consumer research	Copies of any formative research studies conducted among any audiences, in the formation of the labeling, advertising, marketing, and/or promotional materials, including qualitative and quantitative research studies used to determine message	4 years after the studies are completed

Record	Description	Retention Period
	effectiveness, consumer knowledge, attitudes, beliefs, intentions, and behaviors toward using the products, and including copies of the stimuli used in testing	
Consumer evaluation research	Copies of any consumer evaluation research studies conducted among any audiences to determine the effectiveness of the labeling, advertising, marketing, and/or promotional materials and any shifts in consumer knowledge, attitudes, beliefs, intentions, and behaviors toward using the products, and including copies of the stimuli used in testing	4 years after the studies are completed
Contractual agreements	Copies of any contractual agreements regarding the creation or dissemination of the products' labeling, advertising, marketing, and/or promotional materials, including, for example, in print media, online or through digital platforms (e.g., social media and mobile applications), such as influencers, bloggers, and ambassadors, on your behalf, or at your direction	4 years from the date of the contract or until the contract expires, whichever is later

6.1.2. Appendix C: Postmarket Reporting

I. Annual Reporting

Under section 910(f) of the FD&C Act, these orders require that you submit the following postmarket reports to FDA on an annual basis, beginning twelve months from the date of the order to help FDA determine whether continued marketing of each new tobacco products are appropriate for the protection of public health or whether there is or may be other grounds for withdrawing or temporarily suspending such order. For each 12-month reporting period, the report must include:

1. A single submission with a cover letter that includes the following subject line: **ANNUAL REPORT for PM0004691.PD1 .** The cover letter should include the STN(s) and corresponding tobacco product name(s), applicant name, date of report, reporting period, and marketing status outside the United States;

2. All final printed labeling (including all variations, such as those reflecting different required warnings) not previously submitted (e.g., if previously submitted under section 905(i) or previously submitted at the last reporting period and no changes were made, please list the date and manner of submission), including the date the labeling was first disseminated and the date when the labeling was discontinued, and a description of all changes to the labeling. The labeling must include all the panels and be presented in the actual size and color with legible text. The labeling must include labels, inserts/onserts, instructions, and any other accompanying information or materials for the products;

3. All final full-color advertising, marketing, and/or promotional materials, published, disseminated to consumers, or for use in engaging or communicating with

consumers not previously submitted (e.g., if previously submitted under 905(i) or previously submitted at the last reporting period and no changes were made, please list the date and manner of submission), along with the original date such materials were first disseminated and the date they were discontinued, and a description of all changes to the materials. The materials must be legible, include all panels where applicable (e.g., print ads, point of sale signs) and reflect the actual size and colors used. For any materials that would not fit on an 8.5" x 11" piece of paper, you may resize and submit electronic versions of such materials in a format that FDA can review and with sufficient resolution to allow FDA to read lettering clearly. If resizing the advertisement does not allow for text to be read easily, the complete text must be provided separately and clearly referenced. Digital media, such as videos and animations must be submitted in a format that FDA is able to open and review;

4. A description of each change made to the manufacturing, facilities, or controls during the reporting period, including:
    a. A comparison of each change to what was described in the PMTAs;
    b. The rationale for making each change and, if any, a listing of any associated changes; and
    c. The basis for concluding that each change does not result in a new tobacco product that is outside the scope of the marketing granted order.

5. A summary of any stability monitoring, and testing of the products, including the monitoring and testing protocol(s) (including batch/lot sampling) and results;

6. A complete list of ongoing and completed studies about the tobacco products conducted by, or on your behalf, that have not been previously reported;

7. Full reports of information published or known to you, or which should be reasonably known to you, concerning scientific investigations and literature about the tobacco products that have not been previously reported, as well as significant findings from publications not previously reported;

8. A summary and analysis of all serious and unexpected adverse experiences associated with the tobacco products that have been reported to you or that you are aware of, accompanied by a statement of any changes to the overall risk associated with the tobacco products, and a summary of any changes in the health risks, including the nature and frequency of the adverse experience, and potential risk factors;

9. A summary of sales and distribution of the tobacco products for the reporting period, to the extent that you collect or receive such data, including:
    a. Total U.S. sales reported in dollars, units, and volume with breakdowns by U.S. census region, major retail markets, and channels in which the products are sold;
    b. The Universal Product Code that corresponds to the products identified in the PMTA; and
    c. Demographic characteristics of products purchasers, such as age, gender, race/ethnicity, geographic region, and tobacco use status;

10. A summary of the implementation and effectiveness of your policies and procedures regarding verification of the age and identity of purchasers of the products;

11. A summary of the implementation and effectiveness of your policies and procedures regarding restrictions on access to the products for individuals under the federal minimum age of sale of tobacco products;

12. A summary of all formative consumer research studies conducted– whether by you, on your behalf, or at your direction -among any audiences, in the formation of new labeling, advertising, marketing, and/or promotional materials, not previously submitted, including qualitative and quantitative research studies used to determine message effectiveness, consumer knowledge, attitudes, beliefs, intentions and behaviors toward using the products, and including the findings or these studies and copies of the stimuli used in testing;

13. A summary of all consumer evaluation research studies conducted – whether by you, on your behalf, or at your direction - among any audiences, not previously submitted, to determine the effectiveness of labeling, advertising, marketing, and/or promotional materials and shifts in consumer knowledge, attitudes, beliefs, intentions, and behaviors toward using the products, and including the findings of these studies and copies of the stimuli used in testing;

14. A summary of the creation and dissemination of the products' labeling, advertising, marketing, and/or promotional materials – whether conducted by you, on your behalf, or at your direction – including a list of all entities involved and a description of their involvement, including a description of contractual agreements with such entities;

15. A description of the implementation of all advertising and marketing plans – whether conducted by you, on your behalf, or at your direction - not previously submitted, including strategic creative briefs and paid media plans by channel and by product, and the details, dollar amount(s) and flighting of such plans, by channel and by product, including a description of any:
    a. Use of competent and reliable data sources, methodologies, and technologies to establish, maintain, and monitor highly targeted advertising and marketing plans and media buys, including a list of all data sources used to target advertising and marketing plans and media buys;
    b. Targeting of specific group(s) by age-range(s), including young adults, ages 21-24, and other demographic or psychographic characteristics that reflect the intended audience(s), including the source(s) of such data;
    c. With respect to individuals under the federal minimum age of sale of tobacco products, actions taken to restrict access to the products and limit

exposure to the products' labeling, advertising, marketing, and/or promotion;

d. Use of owned, earned, shared, or paid media to create labeling for, advertise, market, and/or promote the products;
e. Use of partners, influencers, bloggers, and/or brand ambassadors to create labeling for, advertise, market, and/or promote the products;
f. Consumer engagements – whether conducted by you, on your behalf, or at your direction – including events at which the products were demonstrated and how access was restricted to individuals at or above the federal minimum age of sale of tobacco products; or
g. Use of public-relations or other communications outreach to create labeling for, advertise, market, and/or promote the products; including the original date such plans were first used and the date they were discontinued, and a description of all changes to such plans since the last periodic report, by channel and by product;

16. A summary of media tracking and optimization, by channel, by product, and by audience demographics (e.g., age, gender, race/ethnicity, geographic region), including a summary of real-time digital media monitoring to identify, correct, and prevent delivery of advertising impressions to individuals under the federal minimum age of sale of tobacco products, and including a summary of implementation of any corrective and preventive measures, not previously submitted;

17. An analysis of the actual delivery of advertising impressions, by channel, by product, and by audience demographics (e.g., age, gender, race/ethnicity, geographic location), including a breakout by age-group (i.e., adults, ages 25+; young adults, ages 18-24; and youth, ages 12-17 and ages 11 and under), not previously submitted. This analysis must be verified against post-launch delivery-verification reports submitted to you from an accredited source; and

18. An overall assessment of how the marketing of the tobacco products continues to be appropriate for the protection of public health.

The products subject to these marketing granted orders are subject to withdrawal or temporary suspension as described in section 910(d) of the FD&C Act. Grounds that FDA will consider for withdrawal under section 910(d) of the FD&C Act include scenarios in which FDA finds that the continued marketing of the product is no longer APPH. These scenarios may include, but are not limited to, certain changes in product use behaviors that were not expected in FDA's assessment of the PMTA (e.g., increases in the percentage or number of youth and young adults who report use of your products, fewer users of potentially more harmful products switching to your products than anticipated), changes in FDA's understanding of the net effects of your products on the population as a whole, or new scientific evidence that demonstrates that the products present a greater risk to health than FDA understood during the review process.

II. Serious and Unexpected Adverse Experiences Reporting and Reporting of Certain Manufacturing Deviations

Under section 910(f) of the FD&C Act, these orders require that you report to the FDA all adverse experiences that are both serious and unexpected and your analysis of the association between the adverse experience and each new tobacco product **within 15 calendar days** after the report is received by you. These experiences may become known to you through any source including a customer complaint, request, or suggestion made as a result of an adverse experience, a manufacturing deviation analysis, tobacco product defect, or failure reported to you; or identified in the literature or media. Your information should be submitted with a cover letter that includes the following subject line: **SERIOUS UNEXPECTED ADVERSE EXPERIENCE REPORT for PM0004691.PD1**.

For purposes of reporting under these orders, serious adverse experience means an adverse experience that results in any of the following outcomes:

- Death;
- A life-threatening condition or illness;
- Inpatient hospitalization or prolongation of existing hospitalization;
- A persistent or significant incapacity or substantial disruption in the ability to conduct normal life functions;
- A congenital anomaly/birth defect; or
- Any other adverse experience that, based upon appropriate medical judgment, may jeopardize the health of a person and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

For purposes of reporting under these orders, unexpected adverse experience means an adverse experience occurring in one or more persons in which the nature, severity, or frequency of the experience is not consistent with:

- The known or foreseeable risks of adverse experiences associated with the use or exposure to each tobacco product as described in the PMTA and other relevant sources of information, such as postmarket reports and studies;
- The expected natural progression of any underlying disease, disorder, or condition of the persons(s) experiencing the adverse experience and the person's predisposing risk factor profile for the adverse experience; or
- The results of nonclinical laboratory studies.

For products that have been distributed, if a manufacturing deviation occurs that you determine presents a reasonable probability that the tobacco product contains a manufacturing or other defect not ordinarily contained in tobacco products on the market that would cause serious, adverse health consequences or death you are required to report the deviation to FDA within 15 calendar days of identification.

III. Notifications

Under sections 910(c)(1)(B) and 910(f) of the FD&C Act, these orders also require that, as of the authorization date of your marketing granted orders, you submit the following notifications of your marketing plans and materials to FDA. This requirement to submit the

product's labeling, advertising, marketing, and promotional materials and plans in advance of their use is not for pre-approval – that is, FDA is not requiring that it review and approve such materials or plans before they may be used. Rather, such advance notification will provide FDA timely access to such materials and plans and, if needed, allow FDA to provide advisory comments, including any concerns about their possible impact on youth appeal and tobacco use initiation. You may begin disseminating the materials 30 days after providing notification to FDA.

This notification must be received by FDA **at least 30 days** prior to dissemination, which includes but is not limited to the publication, dissemination to consumers, or use in engaging or communicating with consumers of such materials. The duration of these notification requirements is as follows:

- For a period of six months starting with the initial dissemination of the materials, provide notification of all labeling, advertising, marketing, and promotion.

Each 30-day notification must include:

1. A single submission with a cover letter that includes the following subject line: **30-DAY NOTIFICATION for PM0004691.PD1**. The cover letter should include the STN(s) and corresponding tobacco product name(s), applicant name, date of notification, and planned dissemination date;

2. Full-color copies of all such labeling, advertising, marketing, and promotional materials for the products. The materials must be legible, include all panels where applicable (e.g., print ads, point of sale signs) and reflect the actual size and colors used. For any materials that would not fit on an 8.5" x 11" piece of paper, you may resize and submit electronic versions of such materials in a format that FDA can review and with sufficient resolution to allow FDA to read all lettering clearly. If resizing the advertisement does not allow for text to be read easily, the complete text must be provided separately and clearly referenced; and

3. All advertising and marketing plans, including strategic creative briefs and paid media plans, by channel and by product, and the details, dollar amount(s) and flighting of such plans, by channel and by product, including any plans to:
    a. Use competent and reliable data sources, methodologies, and technologies to establish, maintain, and monitor highly targeted advertising and marketing plans and media buys, including a list of all data sources used to target advertising and marketing plans and media buys;
    b. Targeting specific group(s) by age-range(s), including young adults, ages 21-24, and other demographic or psychographic characteristics that reflect your intended audience, including the source(s) of such data;
    c. With respect to individuals below the federal minimum age of sale of tobacco products, actions taken to restrict access and exposure to the products' labeling, advertising, marketing, and/or promotion;
    d. Use owned, earned, shared, or paid media to create labeling for, advertise, market, and/or promote the products;
    e. Use partners, influencers, bloggers, or brand ambassadors to create labeling for, advertise, market, and/or promote the products;

f. Conduct consumer engagements – whether by you, on your behalf, or at your direction – including events at which the products will be demonstrated and how access will be restricted to individuals at or above the federal minimum age of sale of tobacco products; or
g. Use public-relations or other communications outreach to create labeling for, advertise, market, and/or promote the products.

6.1.3. Appendix D: Marketing Requirements[10]

Under section 910(c)(1)(B) of the FD&C Act, these orders require you to:

- Include the warning statement: "WARNING: This product contains nicotine. Nicotine is an addictive chemical." on the package labels of all HeatSticks packs and of all kits containing HeatSticks packs as well as in all advertisements for such products and kits[11]. Specifically, the warning statement must appear directly on the package and must be clearly visible underneath any cellophane or other clear wrapping as follows:
    - Be located in a conspicuous and prominent place on the two principal display panels of the package and the warning area must comprise at least 30 percent of each of the principal display panels;
    - Be printed in at least 12-point font size and the warning statement must occupy the greatest possible proportion of the warning area set aside for the required text;
    - Be printed in conspicuous and legible Helvetic bold or Arial bold type (or other sans serif fonts) and in black text on a white background or white text on a black background in a manner that contrasts by typography, layout, or color, with all other printed material on the package;
    - Be capitalized and punctuated as indicated in this order; and
    - Be centered in the warning area in which the text is required to be printed and positioned such that the text of the warning statement and the other information on the principal display panel have the same orientation.
- For print advertisements and other advertisements with a visual component (including, for example, advertisements on signs, shelf-talkers, websites, mobile applications, and e-mail), the warning statement must appear in the upper portion of the area of the advertisement within the trim area as follows:
    - Occupy at least 20 percent of the area of the advertisement;

[10] When the final rule for cigarette health warnings goes into effect, FDA will reevaluate the conditions of marketing with respect to warnings for the products subject to this order
[11] This warning must appear on each package and each advertisement, in addition to the rotating Surgeon General warnings required under FCLAA (except the carbon monoxide warning, which is to be removed from the rotation of the Surgeon General warnings as described in this order).

- Appear in at least 12-point font size and the warning statement must occupy the greatest possible proportion of the warning area set aside for the required text;
- Appear in conspicuous and legible Helvetica bold or Arial bold type (or other similar sans serif fonts) and in black text on a white background or white text on a black background in a manner that contrasts by typography, layout, or color, with all other material on the advertisement;
- Be capitalized and punctuated as indicated in this order;
- Be centered in the warning area in which the text is required to appear and positioned such that the text of the warning statement and the other textual information in the advertisement have the same orientation; and
- Be surrounded by a rectangular border that is the same color as the text of the warning statement and that is not less than 3 millimeters (mm) or more than 4 mm.

- Removal of the warning: "SURGEON GENERAL'S WARNING: Cigarette Smoke Contains Carbon Monoxide." from the required warnings to be displayed on the product package labels and advertisements under the Federal Cigarette, Labeling and Advertising Act (FCLAA).
- As a reminder, under section 4 of FCLAA (15 U.S.C. 1333), you must submit a warning plan to the United States Federal Trade Commission (FTC).

Under section 910(c)(1)(B) of the FD&C Act, this order also requires you to:

- For any **digital sales** – whether conducted by you, on your behalf, or at your direction – establish, maintain, and monitor use of independent age- and identity-verification service(s) that compare customer information against independent, competent, and reliable data sources, such as public records, to prevent the sale of the products to individuals who are under the federal minimum age of sale of tobacco products.
- For any of the products' labeling, advertising, marketing, and/or promotion appearing in your **owned digital properties** (e.g., your company-owned, consumer-directed, product-branded website(s) and/or mobile applications) – whether conducted by you, on your behalf, or at your direction – establish, maintain, and monitor use of independent age- and identity-verification service(s) that compare customer information against independent, competent, and reliable data sources, such as public records, at the first point of access to such properties, to restrict access to such labeling, advertising, marketing, and/or promotion to only individuals who are at or above the federal minimum age of sale of tobacco products.
- For any of the products' labeling, advertising, marketing, and/or promotion appearing in any **shared digital properties** (e.g., your product-branded social media accounts, pages and associated content; content promoting your products on your behalf disseminated through another entity's social media accounts) – whether conducted by you, on your behalf, or at your direction – establish, maintain, and

monitor use of the available site-, platform- and content- (e.g., post, video) specific age-restriction controls (e.g., age-restrict an entire product-branded account and all associated content disseminated through such account; ensure age-restriction of a specific video disseminated by an influencer promoting the products on your behalf through the influencer's account), at the first point of access to such properties, to restrict access to such labeling, advertising, marketing, and/or such promotion to only individuals who are at or above the federal minimum age of sale of tobacco products.

- For any of the products' labeling, advertising, marketing, and/or promotion appearing in **paid digital media** (e.g., paid digital banner advertisements for the products running on another company's website; paid advertising for the products running in social media; paid distribution of influencer content; paid advertising in streaming/Over-The-Top video programming; paid advertising in streaming/internet radio content) – whether conducted by you, on your behalf, or at your direction:
    - Establish, maintain, and monitor use of competent and reliable data sources, methodologies, and technologies to precisely target delivery of such labeling, advertising, marketing, and/or promotion to only individuals who are or above the federal minimum age of sale of tobacco products. Such targeting must use only first- and/or second-party age-verified data, where:
        - "First-party" age-verified data is data owned by you (e.g., your customer registration data collected via site traffic to your company-owned website; data you use in direct marketing to your adult smoking customers) that you have age-verified through independent, competent, and reliable data sources; and
        - "Second-party" age-verified data is first-party data owned and age-verified by another competent and reliable entity (e.g., another company's first-party user registration data) to which you have access. Such data must be age-verified by the second party.
        - "First-party" and "second-party" data does not include data obtained from data aggregators who categorize consumers based on trackable activities and inferred interests (e.g., internet search terms, video interactions, browsing history, purchasing behaviors) to create demographic and psychographic profiles marketers may use to enhance audience targeting. Such data is not considered age-verified and can only be used in combination with first- and/or second-party age-verified data.
- Establish, maintain, and monitor use of competent and reliable data sources, methodologies, and technologies (e.g., using an embedded tracking pixel in all digital advertising) – whether conducted by you, on your behalf, or at your direction – to **track and measure actual delivery of all advertising impressions**, by channel, by product, and by audience demographics (e.g., age, gender, race/ethnicity, geographic region). Such monitoring requires real-time digital media tracking, and identifying, correcting, and preventing delivery of advertising impressions to individuals under the federal minimum age of sale of tobacco products. Such

monitoring also requires post-launch delivery verification reports for other paid media be submitted to you or entities working on your behalf or at your direction from an accredited source.

- For any use of **partners, influencers, bloggers, and/or brand ambassadors** to create labeling for, advertise, market, and/or promote the products – whether conducted by you, on your behalf, or at your direction – disclose to consumers or viewers, via the use of statements such as "sponsored by [firm name]" in such labeling, advertising, marketing, and/or promotional materials, any relationships between you and entities that create labeling for, advertise, market, and/or promote the products, on your behalf, or at your direction.