FDA U.S. FOOD & DRUG ADMINISTRATION

Technical Project Lead (TPL) Review of PMTAs

New Products Subject to this Review[1]	
STNs[2]	PM0004337.PD1 - PM0004337.PD2
Common Attributes	
Submission date	December 11, 2020
Receipt date	December 14, 2020
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, (b) (4) , MR0000059
Supporting FDA Memoranda Relied Upon in this Review	
All STNs	Addendum to February 24, 2017, Equivalence Testing for SE Evaluations Memo (April 16, 2019).
Recommendation	
Issue marketing granted orders for the new tobacco products 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

TABLE OF CONTENTS

LIST OF TABLES

1. EXECUTIVE SUMMARY

On December 14, 2020, FDA received supplemental Premarket Tobaco Product Applications (sPMTAs) for Marlboro Sienna and Bronze HeatSticks (PM0004337.PD1 and PM0004337.PD2, respectively). The applicant referenced the PMTAs for the Marlboro HeatSticks (PM0000424) 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 applications found that the comparisons between the new products and the authorized products and combusted reference cigarettes are appropriate. The applicant has provided adequate information on the manufacturing process and product quality controls that will help ensure that the new products are manufactured consistently and will meet the applicant's specifications. The aerosols from the new products have been evaluated and found to be comparable to that from use of the authorized products. Both the Marlboro Sienna and Bronze HeatSticks were additionally found to have substantially lower HPHC exposure potential than combusted cigarettes.

The new products are not marketed in the U.S.; however, the applicant has provided user information from the international marketing experience with new products 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 products 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 products 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 products 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 products 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 products 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 products do 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 PM0004337.PD1 – PM0004337.PD2.

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

2. BACKGROUND

2.1. NEW PRODUCTS

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

2.2. REGULATORY ACTIVITY

On December 14, 2020, FDA received two sPMTAs from Philip Morris Products S.A. FDA issued an Acceptance letter to the applicant on May 25, 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 products subject to this review.

Table 1. Disciplines reviewed

Discipline	Cycle 1		Cycle 2	
	Reviewer(s)	Review Date	Reviewer(s)	Review Date
Regulatory	Donna Cheung	5/25/2021	Not Assigned	N/A
Engineering	Mary Searing	8/18/2021	Mary Searing	12/15/2021
Chemistry	Delauren McCauley	8/19/2021	Delauren McCauley	12/15/2021
Toxicology	Not assigned	N/A	Chad Brocker	4/25/2022
Behavioral and Clinical Pharmacology	Katie Hartka	8/18/2021	Not assigned	N/A
Epidemiology	Apostolos Alexandridis & Gabriella Anic	8/18/2021	Not assigned	N/A
Social science	Samantha Stanley	8/18/2021	Not assigned	N/A
Environmental science	Dilip Venugopal	8/18/2021	Dilip Venugopal	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.

- Design Comparison
  - The new products are line extensions of, and are being compared to, the currently authorized tobacco product (PM0000424). No other comparison products were provided with respect to the product design.
- Ingredient comparison
  - The tobacco blends in the new products are comparable to the authorized product (PM0000424), ↑1% (1.9 mg/HeatStick).
  - The applicant made minor ingredient modifications resulting in similar or lower total ingredient quantities.
  - 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 products 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 products or transfer any constituent that may increase the users exposure to HPHCs, the change in inner liner paper is acceptable.
- Analytical Comparison
  - The authorized product's nicotine content (0.98 – 1.50 mg/HeatStick) is similar to Marlboro Sienna and Bronze HeatSticks nicotine content (1.11 – 1.73 mg/HeatStick and 0.93 – 1.73 mg/HeatStick, respectively).
  - The applicant provided HPHC yields for analytes identified in the PMI-58 study and FDA 18+6 study for the new and authorized products, and also provided Non-Targeted Differential Screening (NTDS) of aerosol yields generated in the new and authorized products.
  - Most aerosol yields for the new and authorized products are analytically equivalent, except for the following where yields in the new products were analytically nonequivalent and higher than the authorized products: acetone (↑20% -23%, 6.1-7.0 µg/HeatStick), and mercury (↑48-64%, 0.66-0.88 ng/HeatStick). In addition, compared to the authorized products, there were analytically nonequivalent and higher yields in PM0004337.PD1: TSNAs (i.e., NAB, NAT, NNN) (↑22-33%, 0.51-3.3 ng/HeatStick), acetamide

(↑24%, 0.7 µg/HeatStick), propylene oxide (↑47%, 4.2 ng/HeatStick), isoprene (↑35%, 0.53 µg/HeatStick), and pyrene (↑25%, 1.1 ng/HeatStick).

- The applicant measured mainstream smoke HPHCs of Kentucky reference cigarettes 3R4F and 1R6F. HPHC aerosol yields from the new products are greatly reduced compared to combusted cigarettes, and many of the known HPHCs found in 3R4F cigarette smoke are very low or undetectable in the new products' aerosols.

3.1.2. Synthesis

The applicant provided a complete description of the new tobacco products and provided a comparison of these products to the authorized tobacco product (PM0000424) and to reference cigarettes (3R4F and 1R6F). The application includes data demonstrating that the new products produce similar HPHCs and amounts to the authorized HeatSticks when measured using the same device. The applicant states that certain HPHCs are present in increased amounts in the new products relative to the authorized product. However, each of the increases result in HPHC exposure that is substantially lower than the HPHC exposure reported for the reference cigarettes. The reference cigarettes are neither intended to be used in clinical trials nor are they appropriate for market usage as they contain no flavorings typical in modern cigarette products. Nonetheless, these reference cigarettes were formulated to represent a typical American blend cigarette and are appropriate for comparison of the new products and combusted cigarette constituents. The comparison products data are appropriate and sufficient to determine the relative risks associated with these new tobacco products with respect to the previously authorized tobacco product and typical cigarette products. The applicant has demonstrated that using the new products is comparable to use of the authorized product (PM0000424) 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 two new products have a different (b) (4) and tobacco flavoring compared to the authorized product. In comparison to the authorized product, the (b) (4) formulation (b) (4) of the new products had (b) (4) (b) (4). The applicant stated that the change was to (b) (4) The applicant claims that the changes to (b) (4) do not adversely affect the operation of the new products, and this was supported with data comparing the performance, pH and nicotine. Further, the changes to the formulation are small and are unlikely to result in a change to the content or amount of HPHCs in the aerosol.
- The amount of the (b) (4) in the mouthpiece filter is increased in the new products compared to the authorized product. The applicant claims that the change is made in order to (b) (4) in the aerosol. This claim was verified through the measurement of (b) (4) in the new and

authorized products. The data provided indicates a 35-36% decrease in the (b) (4) content in the aerosol. Therefore, the change in the (b) (4) in the mouthpiece is unlikely to result in an increase in HPHCs in the aerosol and may result in a decreased level of phenol.

- The overall product weight of each of the two new products is reduced approximately 2% compared to the authorized product. This is primarily due to (1) (b) (4) and (2) (b) (4)
- Aerosol droplet size distribution results indicate the upper bound average of the new products are within the respirable range.
- The applicant made minor ingredient modifications resulting in lower or similar total ingredient quantities.

3.2.1.2. Manufacturing

- The applicant demonstrates that the new products can be manufactured in a manner consistent with the authorized product.
- The applicant states that the new products are 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 (b) (4) and ingredient differences result in a small change in potential nicotine content in the aerosol of the new products, however the average yields are still within the acceptance ranges of the authorized product. All batch release results obtained were within specifications and the product performance specifications are identical in the new and authorized products.

3.2.1.3. Product stability

- The applicant stated that product stability information is not included for the new products due to similar design, formulation and container closure system compared to the authorized product. The manufacturer proposes to set a Best Used Before Date (BUBD) of (b) (4) after the production date for the new products, similar to the authorized product.

3.2.1.4. Product test data

- The batch release testing results provided by the applicant fall within the acceptable criteria for both new products.
- The applicant provided two studies to characterize the contents and amount of chemical constituents in the aerosol of the new products, authorized products, and combusted cigarettes. The applicant named them the FDA 18+6 and the PMI-58. They claim that the FDA 18+6 study included the HPHCs typically found in heated tobacco products and the PMI-58 captured 58 constituents that include the FDA HPHCs and other aerosol constituents. The applicant also provided the results of a non-targeted screening that they claim is intended to identify any additional constituents not currently included in the FDA HPHC list.

- Aerosol HPHC data from the PMI-58 study indicated that aerosol HPHC yields for the new products were generally lower or similar to HPHC yields in the authorized products.
- Aerosol HPHC data from the FDA 18+6 study indicated that aerosol HPHC yields for the new products were lower than the mainstream smoke HPHC yields for the 1R6F reference cigarette.
- Non-Targeted Differential Screening: The applicant stated that the NTDS identified 12 aerosol constituents in the new products that were not in the authorized products or in the HPHC list. Of these 5 were probable or possible carcinogens. Of these 5 constituents, only one, (b) (4) , was indicated to increase relative to the authorized product. The levels of (b) (4) and other constituents in the aerosol were low and are unlikely to contribute to exposure concerns.

3.2.2. Synthesis

As TPL, I agree with the engineering, chemistry, and toxicology conclusions that these sPMTAs contain 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

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

3.3.1.1. Toxicity (Tox)

- Evaluation of NTDS study indicates that the new product aerosols contain 5 probable or possible carcinogenic chemicals that are present in higher levels than the authorized product or 1R6F[3] cigarette comparison products. Of these 5 constituents, only one, (b) (4) , was indicated to increase relative to the authorized product. These probable or possible carcinogenic chemicals are present at low levels in the new products. When balanced against the significant decreases in the total number of HPHCs and total HPHC yields found in combusted cigarettes the increase in coumarone is small and does not represent a significantly increased risk when considered in the totality of constituent changes.
- The new products' aerosol contains an increased amount of a few HPHCs relative to the authorized product using a modified Canadian Intense smoking regimen. However, these HPHCs are markedly decreased in comparison to the 3R4F reference cigarette under the same smoking regimen. Glycerol is increased in the new products' aerosols compared to the 3R4F reference cigarette, but this increase is also offset by decreases in several known carcinogens and respiratory toxicants (i.e., acetaldehyde; ammonia, benzene, benzo[a]pyrene, 1,3-butadiene, formaldehyde,

[3] The reference cigarette products 3R4F and 1R6F are both representative of typical marketed products. The 3R4F reference cigarette is no longer available (beginning in 2018). The HPHC yields of these two products are not the same, but are similar enough for the comparison of the new and authorized tobacco products. The application includes several studies, each collected alongside a reference product. Some constituent values are compared to 1R6F and others against 3R4F and are appropriately noted herein reported. While not interchangeable, the results of both reference products are suitable for the evaluation of chemical and toxicological risks.

isoprene, mercury, toluene, TSNAs, and other constituents) when compared to the 3R4F reference cigarette.

- Given the magnitude and statistical significance of the decreases in HPHC number and HPHC yields in the new products' aerosols compared to 3R4F reference cigarette, the data on HPHCs and their associated yields for new products are acceptable.

3.3.2. Synthesis

The sPMTAs contain sufficient information to characterize the toxicant exposure. The applicant provided measurements of tested HPHCs and a screen of constituents in the product aerosol for new products, authorized products, and in the smoke for combusted reference cigarettes. Some HPHCs increased in the new products, when compared to the 1R6F combusted cigarettes. When these constituents were compared to the authorized product, only one increased relative to the authorized products. The absolute increase in this one constituent was small and does not represent an exposure risk when considered in the totality of constituent changes. Further, the toxicant exposure of the new products is low relative to combusted cigarettes. In consideration of a similar level of toxicant exposure compared to the authorized products and when comparing the new products to combusted cigarettes, the significant decreases in the total number of HPHCs observed and total yields of HPHCs observed in the new products, the changes described by the applicant do not demonstrate a different toxicant exposure risk than the authorized products.

3.4. ABUSE LIABILITY

3.4.1. Discipline key findings

No new clinical data regarding abuse liability of the new products was submitted; however, the applicant submitted nicotine yield data to bridge the new products and cross-referenced clinical data submitted with the authorized products. Cross-referenced clinical data suggested that in current adult smokers, nicotine exposure and reduction in craving or withdrawal of the authorized products was similar to combusted cigarettes. Data from the authorized products can be bridged to the new products, thus the abuse liability profile of the new products is expected to be similar to combusted cigarettes.

3.4.2. Synthesis

There are no new data specifically related to abuse liability in these sPMTAs. However, the applicant submitted nicotine yield data to bridge the new products and cross-referenced clinical data submitted with the authorized products. The bridging data is sufficient to allow the application of the findings of the authorized products to the new products. Further, the applicant stated that the new products have a similar flavor profile, operating procedures, use similar tobacco sources, and produce comparable aerosols. Based on the bridging data and underlying clinical data from the authorized product, FDA has no reason to believe the new products will result in different nicotine exposure, use patterns, user populations, or abuse liability.

3.5. USER POPULATIONS

3.5.1. Discipline key findings

The target population of the new products is current adult smokers. The applicant provided bridging data between the new and authorized products that is sufficient to allow the application of the clinical studies submitted for the authorized products to the new products. These studies provide sufficient evidence to inform use behavior of the new products in current adult smokers. Dual use of the new products with combusted cigarettes is likely to occur based on use behavior associated with the authorized products. Observational data suggest that dual use of the new products with combusted cigarettes may occur less frequently than with the authorized products. The nicotine exposure of the new products is predicted to be similar to combusted cigarettes; therefore, current adult smokers who initiate use of the new products may completely switch to the new products. The rate of complete switching to the new products from combusted cigarettes is unknown; however, observational data indicate a similar or higher rate compared to the authorized products. The authorized products were associated with higher nicotine exposures than nicotine nasal spray (NNS)/nicotine replacement therapy (NRT) gum, and these findings can be bridged to the new products. These findings suggest there is a higher likelihood of use of the new products compared to NNS/NRT gum in smokers who are interested in quitting tobacco products. Based on the abuse liability of the authorized products, the new products are predicted to have a similar risk of progression to regular use in non-tobacco users (including youth) as combusted cigarettes. No clinical studies were provided in this supplemental PMTA, nor with the authorized products addressing use of the new products among vulnerable populations. The impact of the new products on abuse liability and product use behavior in vulnerable populations other than youth is unknown.

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 sufficient bridging data to allow the application of appropriate data from the authorized product to the new products. Further, 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. 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 following discussion is based on key findings provided in the discipline reviews. The applicant references the clinical and observational studies provided for the authorized product. There were no specific data related to addiction, short- and long-term health effects, or likelihood and effects of product misuse included in the applications. Because these products are line extensions 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. Toxicology

The applicant provided neutral red uptake (NRU) cytotoxicity assay data comparing the new products and authorized product. The cytotoxicity of the new products and authorized product were statistically equivalent. Therefore, NRU data from the new products are acceptable.

3.6.1.2. BIMO inspection findings

No inspections were recommended or conducted.

3.6.1.3. 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 products.

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 products. 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 these sPMTAs. Because these products are line extensions of an authorized product it is reasonable for the specific data related to population or public health studies to translate to these new products.

3.7.2. Synthesis

As the product design, characteristics, and tobacco source are similar, and the aerosols produced from the new products are comparable to that produced from the authorized product and substantially lower than combusted cigarettes, there is no reason to believe the impact on population health will be different for the new products compared to the authorized product. Similarly, there is no evidence the user population for new products 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 products as compared to 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 Sienna and Bronze HeatSticks (PM0004337.PD1 and PM0004337.PD2, respectively) 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 sPMTAs contain 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 these sPMTAs.

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 April 25, 2022. The FONSI was supported by an environmental assessment prepared by FDA on April 25, 2022.

5. CONCLUSION AND RECOMMENDATION

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

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

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

6. APPENDIX

Appendix A. New products

Common Attributes	
Submission date	December 11, 2020
Receipt date	December 14, 2020
Applicant	Philip Morris Products S.A.
Product manufacturer	Philip Morris Products S.A.
Product category	Heated Tobacco Product (HTP)[4]
Product subcategory	HTP Consumable
Attributes[5,6]	**New Product**
STN	**PM0004337**
Static Product ID	PD1
Product name	Marlboro Sienna HeatSticks[7]
Package type	Box
Package quantity	20 HeatSticks
Characterizing flavor	Tobacco[8]
Nicotine Source	Tobacco
Diameter	7.42 mm
Length	45 mm
Ventilation	Not Applicable
Additional property	Source of energy: Electric (rechargeable battery)
STN	**PM0004337**
Static Product ID	PD2
Product name	Marlboro Bronze HeatSticks[7]
Package type	Box
Package quantity	20 HeatSticks
Characterizing flavor	Tobacco[8]
Nicotine Source	Tobacco
Diameter	7.42 mm
Length	45 mm
Ventilation	Not Applicable
Additional property	Source of energy: Electric (rechargeable battery)

[4] The IQOS products meet the definitions 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.

[5] We interpret package type to mean container closure system and package quantity to mean product quantity within the container closure system, unless otherwise identified.

[6] 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

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

[8] 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.

Table 3. Amendment received

Submission Date	Receipt Date	Amendment	Applications being amended	Reviewed	Brief Description
Oct 13, 2021	Oct 13, 2021	PM0005102	All[9]	Yes	Response to Aug 19, 2021 Deficiency Letter

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;	4 years from the date of the order or 4 years from the conclusion of the study, whichever occurs later

[9] This amendment applies to all STNs subject to this review.

Record	Description	Retention Period
	• 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	
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
Sales and/or distribution records	A list of distributors and retailers of the products, including brick-and-mortar and digital[10] (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	4 years from the date of distribution of each

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

Record	Description	Retention Period
	subject of this order; such records may also include your analysis of those complaints	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 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	4 years from the date of initial dissemination to the public or implementation

Record	Description	Retention Period
	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 effectiveness, 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
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 PM0004337.PD1 - PM0004337.PD2.** 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 PM0004337.PD1 – PM0004337.PD2**.

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 PM0004337.PD1 - PM0004337.PD2**. 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[11]

Under section 910(c)(1)(B) of the FD&C Act, and in accordance with section 202(a) of the Family Smoking Prevention and Tobacco Control 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.[12] 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;
    - 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

[11] 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.
[12] 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).

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.