ANNUAL REPORT FOR PM0000424-PM0000426, PM0000479 and PM0000634 and MR0000059-MR0000061 and MR0000133

FDA STN No.	PM0000424 - MR0000059[1] PM0000425 - MR0000060 PM0000426 - MR0000061 PM0000479 - MR0000133 PM0000634[2]
Tobacco Product Name	*Marlboro* Amber *HeatSticks* *Marlboro* Green Menthol *HeatSticks* *Marlboro* Blue Menthol *HeatSticks* *IQOS* System Holder and Charger *IQOS* 3 System Holder and Charger
Tobacco Product Category	Cigarette
Tobacco Product Sub-category	Non-Combusted
Applicant	Philip Morris Products S.A. (PMP S.A.)
Date of Report	April 29, 2022
Reporting Period	March 1, 2021 to February 28, 2022

[1] Exposure Modification Orders for the *IQOS* System Holder and Charger and three variants of *Marlboro HeatSticks* require that manufacturing information is submitted together with Annual Report for PMTAs.

[2] On March 11, 2022, FDA has issued Modified Risk Granted Order for Exposure Modification order (MR0000192) for *IQOS 3* System Holder and Charger; no data are reported on this product as the MRGO was issued outside of the reporting period for the 2022 PMSS Report.

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FOREWORD

On September 29, 2021 the United States International Trade Commission (ITC) issued a Cease-and-Desist Order (CDO) that prohibited the importation, marketing, sale and distribution of *IQOS* devices and *Marlboro HeatSticks.*[3] As a result of the CDO, PM USA stopped marketing and selling all *IQOS* devices and *Marlboro HeatSticks* by November 28, 2021 at all third-party retail stores, PM USA owned stores and the getIQOS.com website. Therefore, at the end of November 2021, *IQOS* holders and chargers and *HeatSticks* were not available for purchase.

As a result of this cessation of marketing and sales, this periodic report will not show sales data beyond November 28, 2021. This cessation of sales also has a corresponding impact on data on product purchasers, as there have been no product purchasers since November 28, 2021. Lastly, as per our correspondence with CTP on January 14, 2022,[4] this CDO will impact the plans for Post-Market Surveillance and Studies.

Also as a result of the CDO, PM USA ceased all *IQOS* device and *Marlboro HeatSticks* marketing and advertising as of November 28, 2021. This cessation of marketing and advertising will impact reporting data related to advertising impressions, dollar amounts and flighting of paid media plans, and other advertising and marketing metrics which are required as part of this annual report. Except where otherwise noted, a lack of data for a given marketing channel or time period is not a reflection of an error in the report, but rather the data accurately reflecting the lack of marketing and advertising activity in that marketing channel and/or during that time period.

CTP will be kept informed of updates on this situation going forward.

1 EXECUTIVE SUMMARY

On April 30, 2019 the U.S. Food and Drug Administration (FDA) issued a Marketing Order (MO) authorizing the marketing of the *IQOS* System Holder and Charger with three variants of *Marlboro HeatSticks*,[5] determining that such marketing was appropriate for the protection of the public health (APPH). The following year, on December 7, 2020, the FDA granted authorization to market the *IQOS* 3 System Holder and Charger with the

[3] Certain Tobacco Heating Articles and Components Thereof, 337-TA-1199 U.S. International Trade Commission (September 29, 2021).

[4] Adjustment to the Postmarket Surveillance and Studies (PMSS) Plan forMR0000059 - MR000061 and MR0000133, January 14, 2022

[5] *Marlboro* Amber *HeatSticks* were formerly *Marlboro Heatsticks*
Marlboro Green Menthol *HeatSticks* were formerly *Marlboro* Smooth Menthol *Heatsticks*
Marlboro Blue Menthol *HeatSticks* were formerly *Marlboro* Fresh Menthol *Heatsticks*

issuance of a Marketing Granted Order.[6] Altria Client Services LLC (ALCS)[7] and an ALCS affiliate have been licensed to distribute and sell these products in the U.S. The ALCS affiliate that distributes and sells the product in the U.S. is Philip Morris USA Inc. (PM USA).[8]

The MOs established restrictions and postmarket requirements. In accordance with the MOs, Philip Morris Products S.A. (PMP S.A.)[9] is required to report regularly to FDA certain product and marketing information.

In accordance with Section 910(c)(4) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), FDA may grant a MO when sufficient evidence shows that permitting a product to be marketed would be APPH. Whether a tobacco product is APPH is determined with respect to the risks and benefits to the population as a whole, including users and nonusers of the tobacco product, and taking into account:

(A) the increased or decreased likelihood that existing users of tobacco products will stop using such products; and

(B) the increased or decreased likelihood that those who do not use tobacco products will start using such products.

Under section 910(f) of the FD&C Act, the MOs require that PMP S.A. submit to FDA postmarket periodic reports that include a summary of how the marketing of the tobacco products continues to be APPH. The MOs require submission of reports on a quarterly and annual basis.

This is the third Annual Report for the *IQOS* System Holder and Charger with three variants of *Marlboro HeatSticks*, and the second Annual Report for the *IQOS* 3 System Holder and Charger, covering the time period between March 1, 2021 and February 28, 2022. The report provides summaries of required information and records for the *IQOS* System Holder and Charger (PM0000479), the *IQOS* 3 System Holder and Charger (PM0000634) and three variants of *Marlboro HeatSticks* (PM0000424 – PM0000426). Detailed discussion

[6] We refer to both the April 30, 2019 Marketing Order and the December 7, 2020 Marketing Granted Order collectively as the Marketing Orders, MOs, or MO.

[7] Altria Client Services LLC (ALCS) is a wholly-owned subsidiary of Altria Group, Inc. ALCS provides certain services to the Altria family of companies.

[8] PMP S.A.'s parent, Philip Morris International Management (PMI), has entered into an agreement with ALCS by which ALCS and its affiliates, including PM USA, are licensed to sell *IQOS* in the United States.

[9] We refer to Philip Morris International ("PMI") in some sections of this annual report. For clarity and ease of review, all of the following entities are included within the term "PMI": (1) Philip Morris International Inc., the general entity; (2) Philip Morris Products S.A. (PMP S.A.), the PMTA MO holder, manufacturer and the legal entity responsible for clinical trials and post marketing studies and surveillance, (3) Philip Morris International Management S.A., the legal entity responsible for market research and management services, (4) Philip Morris International Research Laboratories Pte. Ltd. responsible for pre-clinical in vivo studies, and (5) Philip Morris Manufacturing & Technology Bologna S.p.A. responsible for the manufacture of Tobacco Sticks.

concerning respective reporting obligations, as specified in Appendix B and C to the MOs, is provided later in this report (Sections 1 – 18 with corresponding Annexes).

The evidence supplied with this Annual Report confirms that the marketing of the authorized tobacco products continues to be APPH because:

- PMP S.A.-sponsored studies, as well as findings reported in publications by PMP S.A and independent researchers not previously reported to the FDA show that IQOS is reaching its intended audience, adult cigarette smokers. Moreover, studies show that *IQOS* use is low among non-users (never or former) of tobacco products, including youth;
- There were no serious and unexpected adverse experiences (SAEs) reported by consumers in the U.S. during the reporting period. The analysis of all reported adverse experiences (AEs) for the tobacco products confirms that there were no changes to risk information related to the products including the nature of AEs and their frequency;
- The summary of the U.S. sales and distribution reports indicates that the market performance of *IQOS* is in-line with expectations, and the company's policies and procedures regarding restrictions on youth access to the products are effective;
- Changes to the manufacturing process, facilities, and/or controls during the reporting period did not result in any modification of the tobacco products (including a change in design, any component, any part, or any constituent, including a smoke or aerosol constituent, or in the content, delivery, or form of nicotine, or any other additive or ingredient);
- None of the reported manufacturing deviations (including deviations associated with processing, testing, packing, labeling, storage, holding, and distribution) affect the characteristics of the products;
- Labeling, advertising, marketing and promotional materials and plans comply with marketing restrictions of the MOs. Materials and plans were shared with the FDA in advance of their use on an ongoing basis through the 30-Day Notifications.

Considering the above, PMP S.A. concludes that the grounds for the marketing authorization for the *IQOS* System Holder and Charger (PM0000479), *IQOS* 3 System Holder and Charger (PM0000634) and three variants of *Marlboro HeatSticks* (PM0000424 – PM0000426) have not changed. The risks and benefits to the population as a whole, including users and nonusers of the tobacco products, have not changed after the products were introduced on the U.S. market, and therefore the continued marketing of those products remains APPH.

2 SUMMARY OF SCIENTIFIC STUDIES AND PUBLICATIONS

The Summary of Scientific Studies and Publications provides an overview of PMP S.A. scientific studies that are either completed or ongoing as well as significant findings from scientific publications by PMP S.A. or other tobacco and nicotine-containing product manufacturers, and independent researchers.

2.1 Ongoing and summary of completed studies

A status report of on-going and completed scientific studies performed by PMP S.A. and not previously submitted to the Agency is provided in Annex 1. This includes completed scientific studies reported as ongoing in the most recent annual report (or from March 1, 2021) until February 28, 2022.

2.2 Significant findings on publications not previously reported

Significant findings from scientific publications are presented by scientific area in Annex 2-1 for the period from March 1, 2021 to February 28, 2022.

Throughout this section, we reference publications that are related to the *IQOS* THS generally. PMP S.A. sells modified versions of the *IQOS* System Holder and Charger and additional variants of *HeatSticks* in markets outside of the U.S. The publications in this section may be related to versions of the *IQOS* System Holder and Charger and *HeatSticks* other than the Authorized Products, as PMP S.A. believes it is important to provide this information because those other versions are designed to have the same principles of operation and performance as the Authorized Products.

The publications included in our literature summary in Annex 2-1 encompass various scientific fields including:

- Aerosol chemistry and physics, including data on product properties related to non-combustion, emissions of harmful and potentially harmful constituent (HPHCs), non-targeted analysis of the emissions from the product, indoor air quality and secondhand exposure;
- Standard and systems toxicology including *in-vitro* toxicology testing, *in-vivo* inhalation studies, and animal models of disease;
- Clinical studies on exposure reduction to HPHCs, effect on biomarkers of potential harm (BoPH) and early markers of disease risk;
- Observational studies on trends related to the potential impact of the product on health care utilization due to smoking-associated diseases;
- Both perception/behavioral and post-market studies, primarily outside the U.S., to assess the impact of the *IQOS* Tobacco Heating System on product use trajectories, impact on former and never smokers, impact on cessation, product acceptability and the impact of marketing approaches;

- Population health impact modeling.

The complete list of publications is available in Annex 2-2.

3 ADVERSE EXPERIENCES (AES) REPORTED TO PMP S.A.

A summary of global AEs reported to PMP S.A. is presented in the Safety Update Report (SUR) and provided as Annex 3 of this report. The SUR, which has the same format and data collection procedure as previous SURs submitted to FDA, provides a comprehensive and critical analysis of the safety profile of all *IQOS* THS device versions and HeatSticks variants sold worldwide. The data presented in the SUR cover the period from January 1, 2021 to December 31, 2021, as well as the period from the first market launch worldwide (November 4, 2014) through December 31, 2021. The SUR also includes an appendix that is specific to reported AEs in the U.S.

In the U.S., a total of (b) (4) non-serious AEs potentially associated with the Authorized Products' use[10] were received from unsolicited sources during the reporting period.

The most frequently reported (>5%) non-serious clinical AEs in the U.S. were Cough (7.03%), Nausea (6.25%), Oropharyngeal pain (6.25%), and Headache (6.25%). The events of Cough, Nausea, Oropharyngeal pain, and Headache are known class effect AEs associated with the use of nicotine-containing products.

There were no serious AEs (SAEs) reported by U.S. consumers during the reporting period.

In total, there were (b) (4) non-serious AEs received from unsolicited sources in the U.S. since distribution of the Authorized Products began. No SAEs were received from the U.S during this period.

Overall, the analysis of the data from the U.S. market did not reveal any unexpected AEs nor new or increased risks in consumers who switched to the Authorized Products. The AEs reported by U.S. consumers are consistent with those reported outside the U.S.

Of note, none of the spontaneous reports received by PMP S.A. during the reporting period were medically confirmed, as they were received from consumers and not healthcare professionals. For most of the reports received, information regarding the AEs and their circumstances was limited. PMP S.A. performs information follow-up attempts if the reporter has provided consent to be contacted back, and only in countries where specific local laws governing the collection of personal data permit such activities.

The evaluation of new information and the cumulative analysis did not demonstrate any changes in the safety profile of the THS. PMP S.A. will continue to meticulously collect and

[10] The majority of the spontaneous reports received by PMI are not medically confirmed, i.e. they were reported directly by the consumers and not by the health care professionals

evaluate all new safety information in order to maintain adequate supervision of the safety of THS products and their impact on public health.

4 SALES AND DISTRIBUTION

Sales and distribution of one of the Authorized Products was addressed in the periodic Quarterly Reports dated: July 30, 2021, October 29, 2021, and January 28, 2022.

In addition to and concurrent with the submission of this Annual Report, a periodic Quarterly Report dated April 29, 2022 was submitted. Annex 4 contains the previously submitted quarterly reports.

The above-referenced reports represent only *IQOS* 3 data because *IQOS* and *HeatSticks* data were no longer required in quarterly reports after the two-year requirement period set forth in the Market Order. Full year 2021 volume and sales data for all Authorized Products are included in the Post Market Surveillance and Studies (PMSS) sales and distribution the 2022 PMSS Report.

5 DATA ON PRODUCT PURCHASERS

During the Annual Reporting Period, PM USA collected data on product purchasers from three sources: registration, consumer panels, and the Adult Tobacco Consumer Tracking Study (ATCT).

Data on product purchasers were included in the periodic Quarterly Reports dated: July 30, 2021, October 29, 2021, and January 28, 2022. In addition, concurrent with the submission of this Annual Report, we provided a periodic Quarterly Report dated April 29, 2022.

Data were included in the Quarterly Reports on all authorized products (*IQOS* 3, *IQOS* (2.4), and *HeatSticks)* from two of the three sources: consumer panels and the ATCT. PM USA included both the *IQOS* 3 and the *IQOS* (2.4) device in the consumer panel and ATCT data to provide a more comprehensive data set even though the MOs no longer require *IQOS* (2.4) inclusion in quarterly reporting. Data from the third source, registration, is provided for both IQOS 3 and IQOS (2.4) for the Annual Reporting Period.

Annex 5 contains the previously submitted quarterly reports and the *IQOS* 3 and *IQOS* (2.4) registration data for the Annual Reporting Period.

6 SUMMARY OF IMPLEMENTED POLICIES AND PROCEDURES REGARDING VERIFICATION OF THE AGE AND IDENTITY OF PURCHASERS

A summary of the implemented policies and procedures regarding age verification and identity of purchasers during the Reporting Period is provided in Annex 6 of this report.

PM USA's policies and controls require that all *IQOS* devices and *Marlboro HeatSticks* transactions are age and identity verified to confirm purchasers are 21 years of age or older.

Current policies and controls are working as expected and PM USA is not aware of any sales of the Authorized Products to consumers under the age of 21 through any of PM USA's owned channels or through third-party retail sales channels.

7 SUMMARY OF IMPLEMENTED POLICIES AND PROCEDURES REGARDING RESTRICTIONS ON YOUTH ACCESS TO THE PRODUCTS

A summary of the implemented policies and procedures regarding restrictions on youth access to the authorized products during the Reporting Period is provided in Annex 7 of this report.

PM USA's policies and procedures regarding the age and identity of purchasers contain requirements to restrict youth access to the Authorized Products. These policies and procedures require all purchasers to be 21 years of age or older. Current policies and controls are working as expected and PM USA is not aware of any sales of the Authorized Products to any consumers under the age of 21 through any of PM USA's owned channels or through third-party retail sales channels.

8 CHANGES TO THE MANUFACTURING, FACILITIES OR CONTROLS

A summary of changes made to the manufacturing, facilities or controls during the reporting period is provided in Annex 8-1 of this report.

The summary contains a description of each change together with:

a. a comparison of each change to what was described in the PMTAs/MRTPAs;

b. the rationale for making each change.

As described in the original PMTAs/MRTPAs, PMP S.A. uses a Change Management Process (CMP) to ensure that all proposed changes are assessed for their potential impact on product performance, safety, and quality before implementation.

The CMP is a robust safeguard ensuring that commercialized *HeatSticks* and *IQOS* System Holder and Charger are comparable to the earlier versions of these products on which PMP S.A. has performed initial testing. This is a critical requirement for assuring that the scientific assessment and data from studies conducted on the investigational tobacco products are representative and equally applicable to commercialized products.

As required by MOs and Exposure Modification Orders, this annual report contains a list of changes to the manufacturing process, facilities and/or controls. These changes did not result in any modification (including a change in design, any component, any part, or any constituent, including a smoke or aerosol constituent, or in the content, delivery, or form of nicotine, or any other additive or ingredient) of the Authorized Products. Changes which could be expected to materially affect any characteristics (materials, ingredients, design, composition, heating source, or other features) were not implemented.

A certification that the reported changes did not result in any modification of the tobacco product together with the basis for concluding that these changes did not result in any modification to the final product is provided in Annex 8-2.

This annual report contains information collected in the time period from March 1, 2021 to February 28, 2022. These changes were managed according to the PMP S.A's processes for change management as part of a continuous improvement plan to address product quality and none of these changes were deemed to impact product performance. In addition no significant environmental impacts or risks associated with the postmarket changes were identified and they do not alter the overall conclusions of the previous EIAs and no additional environmental protection measures, mitigation measures, or alternative actions are necessary to address environmental impacts.

9 MANUFACTURING DEVIATIONS

A summary of all manufacturing deviations, investigations, and corrective and preventive actions, including, but not limited to, those associated with processing, testing, packing, labeling, storage, holding and distribution during the reporting period March 1, 2021 through February 28, 2022, is provided in Annex 9 of this report as required by Marketing Orders and Exposure Modification Orders.

Only manufacturing deviations for the Authorized Products that were released for sale are reported.

As part of the PMP S.A deviation management program, a risk assessment was performed for products manufactured with any major deviation. The products identified as being manufactured with a deviation potentially affecting product characteristics were not released to the market and therefore have not been included in this report.

For the purpose of this risk assessment, PMP S.A. defined product characteristics broadly as:

- Bill of Materials (BoM) including software (product composition),
- Packaging materials, if they can impact the products performance,
- Product configuration, describing how the components are assembled,
- Product specifications (release, stability and performance specifications),
- Critical Quality Attributes (CQAs).

None of the reported manufacturing deviations was considered to affect the characteristics of the final product.

10 SUMMARY OF STABILITY MONITORING AND TESTING

The 24-month stability studies were provided in 2021 Annual Report, and concluded that no changes were observed that could affect the product's potential health risks for consumers.

Therefore, no further stability monitoring and testing of authorized *HeatSticks* were performed during the reporting period March 1, 2021 through February 28, 2022.

11 LABELING CHANGES

A description of all labeling changes within the reporting period March 1, 2021 to February 28, 2022, is provided in Annex 11. The description includes the date the labeling was first disseminated and the date when the labeling was discontinued, with cross-reference to the full color final printed labeling previously submitted in a 30-Day Notifications.

12 ADVERTISING NOT PREVIOUSLY SUBMITTED

Final full-color copies of all advertising for the Authorized Products that have not been previously submitted are provided in Annex 12.

PM USA submitted twenty-four 30-Day Notifications during the Reporting Period with labeling, advertising, marketing, and promotional materials. Those materials previously submitted are not included in this Annex, but 48 assets that were not previously submitted are included. These assets represent updated versions of previously submitted assets. Information regarding the original date the advertisements were first disseminated and the date the advertisements were discontinued, as well as a description of changes to the materials is also provided in this Annex.

13 CONSUMER RESEARCH STUDIES CONDUCTED IN THE FORMATION OF NEW LABELING, ADVERTISING, MARKETING, AND/OR PROMOTIONAL MATERIALS

PM USA conducted consumer research studies during this reporting period that were not classified as formative or evaluative when conducted. Most of the studies have elements that could be reasonably viewed as formative and evaluative based on the definitions provided in the Marketing Orders. Therefore, rather than attempt to categorize summaries of the research studies by placement into a particular annex, we have provided a summary of all consumer research studies that are responsive to the Marketing Orders in Annex 14.

14 CONSUMER EVALUATION RESEARCH STUDIES CONDUCTED TO DETERMINE THE EFFECTIVENESS OF LABELING, ADVERTISING, MARKETING AND/OR PROMOTIONAL MATERIALS

A total of nine adult consumer research studies were completed during the Reporting Period.

These studies provided learning and insights on the adult smokers' 21 years of age or older (AS 21+) journey towards full conversion to *IQOS* and the effectiveness of marketing communications in advancing AS 21+ to successful conversion to *IQOS*. The studies were meant to guide enhancements to the *IQOS* commercialization plan and its goal of maximizing conversion from combustible cigarettes to *IQOS*. The studies provided learnings on:

- Conventional cigarette adult smokers' openness to non-combustible tobacco alternatives;
- barriers to switching from conventional cigarettes and switching behavior over time;
- awareness and understanding levels of *IQOS*; and
- effectiveness and enhancement opportunities of marketing communications and programs, including digital media.

We have provided summaries of these consumer research studies in Annex 14.

15 CREATION AND DISSEMINATION OF THE PRODUCTS' LABELING, ADVERTISING, AND/OR PROMOTIONAL MATERIALS

A summary of the creation and dissemination of the products' labeling, advertising, marketing, and/or promotional materials, including a list and description of all entities involved and their activities, is provided in Annex 15 of this report.

During the Reporting Period, PM USA engaged with adult smokers 21+ through company-owned retail, email, direct mail, print advertisements, digital paid media, social media branded pages, point of sale at third party retailers, brochures, guides, face-to-face interactions, and company-owned websites. PM USA worked with (b) (4) entities to create and disseminate marketing materials.

16 DESCRIPTION OF THE IMPLEMENTATION OF ALL ADVERTISING AND MARKETING PLANS

A description of the implementation of all advertising and marketing plans, including strategic creative briefs and paid media plans, is provided in Annex 16 of this report.

During the Reporting Period, PM USA engaged with adult smokers 21+ through company-owned retail, email, direct mail, print advertisements, digital paid media, social media branded pages, point of sale at third-party retailers, brochures, guides, face-to-face interactions, and company-owned websites. Advertising and marketing plans focused on creating awareness and converting adult smokers 21+ to *IQOS*.

17 ANALYSIS OF THE ACTUAL DELIVERY OF ADVERTISING IMPRESSIONS

An analysis of the actual delivery of advertising impressions, by channel, by product, and by audience demographics was included in the periodic Quarterly Reports submitted on July 30, 2021, October 29, 2021, and January 28, 2022.

In addition, concurrent with the submission of this Annual Report, we submitted a periodic Quarterly Report dated April 29, 2022. The periodic quarterly reports containing an analysis of the actual delivery of advertising impressions are referenced in Annex 17.

We do not differentiate the reporting of advertising impressions of marketing assets based on device type. Therefore, in many cases both device types (*IQOS* and *IQOS* 3) are present across a marketing channel. For this reason, the marketing data shared within these quarterly reports will represent total impressions from all *IQOS*, *IQOS* 3, and *HeatSticks* related assets.

18 SUMMARY OF MEDIA TRACKING AND OPTIMIZATION

A summary of media tracking and optimization, by channel, by product, and by audience demographics is referenced in the periodic Quarterly Reports submitted on July 30, 2021, October 29, 2021, and January 28, 2022.

In addition, concurrent with the submission of this Annual Report, a periodic Quarterly Report dated April 29, 2022 has been submitted that contains summary information. The periodic quarterly reports containing a summary of media tracking and optimization are referenced in Annex 18 of this report.