Appendix H:

PMP S.A.'s Post Market Safety Surveillance System for *IQOS* System, as applicable for the United States

Product Safety Surveillance Team

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1. ABBREVIATIONS

AE	Adverse Experience
FU	Follow Up
ICSR	Individual Case Safety Report
PMP S.A.	Philip Morris Products S.A.
PSS	Product Safety Surveillance
RA	Regulatory Affairs
SAE	Serious Adverse Experience
SPI	Summary of Product Information
eSRF	Electronic Safety Reporting Form
SUR	Safety Update Report
SUSAR	Suspected Unexpected Serious Adverse Reaction
US	United States

2. PMP S.A. *IQOS* SYSTEM POST-MARKET SAFETY SURVEILLANCE

Philip Morris Products S.A. (PMP S.A.) develops, assesses, and commercializes the *IQOS* System, which is distributed in the United States (U.S.). The *IQOS* System consists of a tobacco heating device commercialized under the brand name *IQOS* Originals, which is to be used with non-combusted tobacco sticks commercialized as *HEETS*.

Since the *IQOS* System was commercialized worldwide, PMP S.A. has continuously monitored the products' safety profile to ensure that potentially new or different health risks associated with the use of the *IQOS* System are identified in a timely manner and managed efficiently.

The purpose of this document is to describe the activities, roles, and responsibilities of the relevant stakeholders involved in the *IQOS* System post-market safety surveillance activities that PMP S.A. has in place in the U.S. for the commercialized products.

The PMP S.A. Product Safety Surveillance (PSS) team executes the following activities relating to the *IQOS* System in the U.S.:

- Safety data collection,
- Case triage, including duplicate and validity checks as well as (medical) case evaluation,
- Timely transmission of Individual Case Safety Reports (ICSR), including follow-up cases, to Regulatory Affairs (RA) for submission to the FDA,
- Signal detection and management,
- Communication about changes to the risk profile of the *IQOS* System to health authorities and consumers, and
- Preparation of annual Safety Update Reports (SUR) for submission to the FDA.

PMP S.A. uses a robust quality management system through which it defines the organizational structure, responsibilities, procedures, processes, and resources of the product safety surveillance activities.

3. PROCESS DESCRIPTION

Process	Action	Responsible stakeholder/s
Collection	**Report of Adverse Experience/s (AE) to local call centre** Local Call center collect spontaneously reported Adverse Experience/s (AE), including AE from PMP S.A consumer research and PMP S.A post-market studies, or PMP S.A - websites or social media. A reporter who experienced or becomes aware of an AE associated with the use of the *IQOS* System can report it by calling the call center number available on the consumable product package. The local call center agents are trained to recognize and handle AE complaints and have the necessary knowledge of local legal obligations regarding consumer data protection and confidentiality. An electronic Safety Reporting Form (eSRF) is used to capture case information reported directly to the local call center or streamlined to it (PMP S.A sponsored websites and social media). If the call center is closed, the caller is requested to leave a message. The local call center agent will then return the call on the next business day. The local call center agent asks for the reporter's consent to provide additional medical information. If consent is not given, only the mandatory questions marked with "(*)" in the eSRF are completed by the agent. If consent is given, all questions on the eSRF are asked. The reporter is also asked the consent to be called back if additional information is needed for medical assessment purposes. The contact details of each caller are registered immediately when the call is received at the call center.	Local Call center

	Using the eSRF, the local call center sends to the safety database all AE complaints immediately or by end of the same business day.	
	AEs identified through scientific literature screening A weekly screening of scientific literature in online literature databases (PubMed and Embase) is performed by the PSS Team to identify AE reports associated to *IQOS* System. The search details are defined in the Appendix I: Literature Review Process. Any AE report identified during the literature screening is processed and added to the safety database.	PSS Team
	Identification of AE in non-sponsored social media Non- sponsored websites and social media are routinely screened with a defined list of keywords for the identification of AE complaints. The identified valid cases are processed and stored in the safety database.	PSS Team
	Case reports from poison centers According with the agreement that PMP S.A. has put in place with the America's Poison Centers when a safety case involving *IQOS* is reported to a Poison Control Center, the safety information is forwarded to the safety database. The cases received are processed and stored in the safety database.	Poison Center/PSS Team
Case Processing and Expedited Reporting	**SRF receipt and processing** Upon receipt of an eSRF the case may undergo translation, depending on the reported language and several processing steps. The PSS case processing team performs a validity assessment and duplicate check to ensure that the safety cases fulfil minimal criteria for a valid case and have not already been received. If the case is valid and not a duplicate of a pre-existing case, the case is processed.	PSS case processing team, Local Call Centre, Regulatory Team

	Clarification information If the initial information received requires a clarification the PSS case processing team sends a request to the local call center team. The local call center reviews the clarification information request and provides feedback via safety database online query form. The PSS case processing team reviews the clarification input and updates the case in the safety database, as appropriate. **Seriousness assessment** An AE is considered serious if it results in any of the following: death, is life-threatening, leads to an inpatient hospitalization or a prolongation of existing hospitalization, leads to a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or results in a congenital anomaly/birth defect. Any other AE which, based on qualified medical judgment, may jeopardize the health of a person, and may require medical or surgical intervention to prevent one of the outcomes above is also categorized as serious. If the AE is assessed as non-serious the case processing is finalized and the case is then closed/archived. **Expectedness assessment** An AE is considered expected if it is either a known nicotine class-effect or a known risk of the *IQOS* System as described in the respective Summary of Product Information (SPI) document. The SPI serves as the reference safety information for the *IQOS S*ystem. The expectedness of individual AEs for each case is determined by the PSS case processing team and documented in the safety database.	

	Medical Review of Serious Adverse Experiences (SAEs) All cases that include at least one SAE is medically reviewed. The case medical review is performed within the safety database. A determination is also performed as to whether case follow-up is required. **Follow-up for medical assessment** If additional information is required and if the reporter provided consent to be contacted back, a list of questions is prepared by the PSS Team and a follow-up (FU) request is sent to local call centre via safety database online queries. A revised version of the case is created which includes the FU information. The case re-enters the case processing workflow. If FU is not needed or if the reporter did not provide consent to be contacted back, the case processing is finalized, and the case is closed/archived. **Expedited Reporting** Safety cases which include a Suspected Unexpected Serious Adverse Reaction (SUSAR) must be reported within fifteen (15) calendar days to the FDA. For the expedited reporting of SUSARs, the PSS case processing team generates and sends the Individual Case Safety Report (ICSR) to Regulatory Team by Day-12. Regulatory Team submits the ICSR to the FDA via the safety reporting portal by Day-15. The successful submission is confirmed, and the FDA proof of submission is forwarded to the PSS Team. The PSS case processing incorporates the FDA proof of submission into the case in the safety database.	
Signal Management	Signal detection is performed by the PSS Team through the medical review of individual safety cases and aggregated safety data obtained from various data sources.	PSS medical safety team

	All newly identified potential safety signals are escalated and validated within the Product Safety Management Board (PSMB). If the signal is refuted by the PSMB, the signal is closed. In all other cases, it is classified as an open signal. For each open signal, the PSMB assesses if there is enough evidence to validate it. If the open signal is not validated, it is monitored closely during periodic review of aggregated safety data until the signal can be either closed or validated by PSMB.	
Risk Communication	Signals validated by the PSMB are considered new identified risks and are communicated to internal and external stakeholders (*e.g.*, to Regulatory Team for submission). In the event of a new identified risk, the PSS medical safety team updates the Safety Product Information (SPI) and contributes to the update of safety related material addressed to consumers (*e.g.*, safety warnings and instructions). An annual Safety Update Report (SUR) is prepared by the PSS medical safety team to allow a summary of safety concerns (number of AEs collected for each Identified and Potential risk associated with the use of the *IQOS* System) specific to the SUR reporting period. Upon finalization of the SUR, PSS medical safety team sends it to Regulatory Team for submission to FDA.	PSS medical safety team

Version History

Version	Version Date	Rationale for Modification(s)
1.0	06 August 2020	First version
2.0	24 March 2022	Update of AEs collection and case processing
3.0	22 March 2024	Update of information related to Altria Client Services (ALCS) removal as per updated commercial strategy