PMI RESEARCH & DEVELOPMENT

Active Product Surveillance
P1-SUR-03-US

Study Type: Comprehensive Literature Review

Product: *iQOS* with HeatSticks

Country: United States

Sponsor: Philip Morris Products S.A.
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PROTOCOL CONCEPT

Background

Philip Morris Products S.A. (PMP S.A.) is developing novel tobacco and nicotine containing tobacco products with the potential to reduce harm or the risk of tobacco-related disease associated with smoking conventional cigarettes. In accordance with the United States Food and Drug Administration (FDA), PMP S.A. must demonstrate that "the product, as it is actually used by consumers, will:

- Significantly reduce harm and the risk of tobacco-related disease to individual tobacco users; and
- Benefit the health of the population as a whole taking into account both users of tobacco products and persons who do not currently use tobacco products." (FDA 2012)

To assess the product-specific content published in scientific and medical journals, PMP S.A. is developing the process and infrastructure to conduct and assess the literature as part of a Post-Market Assessment Program for *iQOS* with *HeatSticks*. The literature can be a significant source of information for the monitoring of the safety profile and of the risk benefit balance of *iQOS* with *HeatSticks*, particularly in relation to the detection of new safety signals.

Objectives

The objective of the comprehensive literature review is to identify sources of *iQOS* information related to the safety of *iQOS* with *HeatSticks* (e.g., studies, case reports).

Databases and Search Engines for Literature Search

- Health and Medical: Pubmed
- Research and Toxicology: Embase
- General and Citations: Scopus

Additional Sources of Literature

- Google Scholar
- References from identified articles

Eligibility Criteria

Inclusion Criteria:

- Published in English
- Populations where *iQOS* with *HeatSticks* is available
- *iQOS* with *HeatSticks* users, non-users exposed to *iQOS* with *HeatSticks*
- Observational or clinical studies
- Case reports or case series
- Includes data relevant to *iQOS* with *HeatSticks* exposure

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Search Strategy
The full search details including the list of all queries and Medical Subject Headings (MeSH) terms are defined in the coding manual. The concepts that will be searched for are:

- Product: *iQOS*, *HeatStick*(s), Tobacco Heating System, heated tobacco, tobacco stick, Reduced Risk Product, Modified Risk Tobacco Product, electronic heated tobacco, Philip Morris, Marlboro, nicotine, dual use, heat not burn
- Health Events: adverse events, allergy, hypersensitivity, injury, overdose, carcinogen, mutagen, teratogen, toxic, cytotoxic, reaction, pregnancy, safety, monitoring, surveillance, tolerance, risk

Data Extraction Process
The general process of performing the literature search will be:

- Running each search query in each database or search engine
- Screening of publication titles and abstracts for content
- Retrieval of selected full text articles
- Evaluate the article against the inclusion and exclusion criteria
- Assess articles for overlap
- Review references to identify additional potential articles

In general terms, the literature searches will be limited to publications in English and focus on markets where *iQOS* with *HeatSticks* is available commercially or as an investigational product. More details on these specific searches including the search queries, dates when these were performed, etc.

Population
The literature is focused on *iQOS* with *HeatSticks* related use and health events within countries were *iQOS* is available. The population of interest is *iQOS* with *HeatSticks* users and non-users exposed to *iQOS* with *HeatSticks*.

Data Extract Timelines
The literature will be searched and reviewed monthly, however searches may be performed more frequently, if needed.

Analysis
Adverse events (related to *iQOS*) identified in the literature review will be submitted to the safety databases and follow the process of coding and assessment defined for the passive safety surveillance process (e.g., MedDRA coding) (Appendix A8.1).

Reporting
The adverse events identified through the literature search will be included in the safety databases and reported in the *iQOS* Annual Safety Report. The adverse events will be summarized together with the adverse events collected from other sources and will not be reported within the context of the literature search as the denominator from this data are not appropriate for presenting or interpreting safety.

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Standards

- Good pharmacovigilance practices (GVP) related to medical literature monitoring will be followed to the extent defined in the PMP S.A. processes, including the identification of adverse events.

ABBREVIATIONS	
FDA	Food and Drug Administration
GVP	Good Pharmacovigilance Practices
PMP S.A.	Philip Morris Products, SA
MedDRA	Medical Dictionary for Regulatory Activities
MeSH	Medical Subject Headings

REFERENCES	
[1]	FDA (Food and Drug Administration), Guidance for industry - Modified risk tobacco product applications - Draft Guidance. 2012. (FDA 2012)

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