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Appendix I: Literature Review Process	Version 3.0

Appendix I:

Literature Review Process

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1. INTRODUCTION

The literature review process is carried out by two different business units at PMP S.A., *i.e.*, Product Safety and Surveillance (PSS) and Scientific and Medical Affairs (SMA).

The PSS Team carries out the literature review to identify potential adverse events and other safety issues reported with the use of *IQOS* System or any product marketed by PMP S.A., excluding conventional cigarettes.

The SMA Team carries out the literature review to identify peer-reviewed publications discussing *IQOS* System or any product marketed by PMP S.A., excluding conventional cigarettes.

2. PRODUCT SAFETY AND SURVEILLANCE REVIEW FOR POTENTIAL SAFETY CASES

In the context of post market surveillance activities, scientific publications are monitored through automatic literature searches with the aim of identifying Adverse Events (AEs) related to *IQOS* System or any product marketed by PMP S.A. excluding conventional cigarettes. Additionally, relevant class products are reviewed (such as heat-not-burn tobacco products not marketed by PMP S.A.).

The searches are set up in EMBASE and PUBMED.

Process

1. Alerts are set up weekly for queries in the aforementioned databases. Search streams are subject to regular review and update to reflect the actual products marketed by PMP S.A. or any regulatory requirements.

Embase: *'iqos' OR 'heat not burn' OR 'tobacco heating system'/exp OR 'tobacco heating system' OR 'heatsticks' OR 'heets' OR 'electronic cigarette'/exp OR 'electronic cigarette' OR 'e-cigarette'/exp OR 'e-cigarette' OR 'e-cig' OR 'teeps' OR 'carbon heated tobacco' OR 'chtp' OR 'ecig' OR 'philip morris international' OR 'philip morris' OR 'electronic nicotine delivery systems'/exp OR 'electronic nicotine delivery systems' OR 'heated tobacco product' OR 'heated tobacco' OR 'kt&g corporation' OR 'kt&g'*

Pubmed: *"electronic nicotine delivery systems"[MeSH Terms] OR ("iqos"[All Fields]) OR ("heat not burn"[All Fields]) OR ("tobacco heating system"[All Fields]) OR ("heatsticks"[All Fields]) OR ("heets"[All Fields]) OR ("electronic cigarette"[All Fields] OR "electronic cigarette e"[All Fields] OR "electronic cigarette e cigarette"[All Fields] OR "electronic cigarette use"[All Fields] OR "electronic cigarettes"[All Fields] OR "electronic cigarettes e"[All Fields] OR "electronic cigarette advertising"[All Fields]*

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Fields] OR "electronic cigarettes e cigarettes"[All Fields])) OR ("teeps"[All Fields])) OR ("carbon heated tobacco"[All Fields])) OR ("chtp"[All Fields])) OR ("ecig"[All Fields])) OR ("philip morris international"[All Fields] OR "philip morris"[All Fields])) OR ("electronic nicotine delivery systems"[All Fields])OR E-cigarette[All Fields]OR e-cig [All Fields]OR "heated tobacco product"[All Fields] OR "heated tobacco" [All Fields]OR "KT&G Corporation" [All Fields] OR "KT&G"[All Fields]

2. A weekly alert is set to send an e-mail even if no new results corresponding to any of the above searches appear. Once the alerts are received, these are reviewed by a PSS designee who looks for articles potentially containing AEs reported with the use of PMP S.A.'s IQOS System or any other product marketed by PMP S.A. (excluding conventional cigarettes). The PSS designee requests the full text versions of any selected articles.
3. Adverse event cases associated with the use of IQOS System or any product marketed by PMP S.A., excluding conventional cigarettes, identified through the literature review are processed as individual cases as per PMI PSS case processing procedures.

3. NON-SAFETY-RELATED LITERATURE RELATED TO IQOS SYSTEM

The SMA Team performs a third-party literature collection in order to identify and sort all articles from peer-reviewed journals related to IQOS System and heat-not-burn products as fast as possible. To identify all published scientific literature related to IQOS System (including all research scientific categories [e.g., aerosol chemistry and physics, non-clinical, clinical and behavioral] and beyond (e.g., policy options, marketing)), alerts in various databases have been set up:

- a) a third-party literature collection is performed on a daily basis and all articles identified are stored in a literature database hosted on a digital platform (owned by RightFind Enterprise). This library, called "SMA_Scientific Literature on SFP", contains scientific and medical articles published in peer-reviewed journals.
- b) the library is updated on a daily basis upon reception of search alerts.
- c) the main sources are Google Scholar, PubMed, Embase, Scopus, SciFinder and RightFind.
- d) The search strings have been optimized for each search engine and are shown below:

- **Google Scholar**

("heated cigarette*") OR ("tobacco heating") OR ("heated tobacco") OR ("tobacco heating system") OR ("heat-not-burn" "tobacco") OR ("IQOS") OR ("HEETS") OR

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("heatsticks ") OR ("heat not burn" "tobacco") OR ("THS" "tobacco") OR ("HNB" "tobacco"); Articles excluding patents.

- **Pubmed**

((eclipse OR accord OR "Heatstick" OR "revo") AND cigarette AND heat* NOT (resin OR column)) OR "tobacco heating"[Title/Abstract] OR "heated cigarette*"[Title/Abstract] OR "electrically heated cigarette*"[Title/Abstract] OR "EHCSS"[Title/Abstract] OR "Electrically Heated Cigarette Smoking System*"[Title/Abstract] OR "heat* tobacco"[Title/Abstract] OR "tobacco heating cigarette*"[Title/Abstract] OR "EHCSS-K3"[Title/Abstract] OR "EHCSS-K6"[Title/Abstract] OR "heated tobacco"[Title/Abstract] OR "tobacco heating system"[Title/Abstract] OR ("heat-not-burn"[Title/Abstract] AND "tobacco"[Title/Abstract]) OR "IQOS"[Title/Abstract] OR "HEETS"[Title/Abstract] OR "heatsticks*"[Title/Abstract] OR ("heat-not-burn"[Title/Abstract] AND "tobacco"[Title/Abstract]) OR ("HNB"[Title/Abstract] AND "tobacco"[Title/Abstract]) OR ("THS"[Title/Abstract] AND "tobacco"[Title/Abstract]) OR ("Lil"[Title/Abstract] AND "tobacco"[Title/Abstract]) OR ("TEEPS"[Title/Abstract] AND "tobacco"[Title/Abstract])) OR ("Modified risk tobacco product*"[Title/Abstract]) OR ("non-cigarette combustible*"[Title/Abstract]) OR ("non combusted" AND cigarette [Title/Abstract]) OR ("Risk continuum "[Title/Abstract] AND "tobacco"[Title/Abstract]) OR ("non-combustible" AND "tobacco"[Title/Abstract])

- **Embase**

ths:ab AND tobacco:ab NOT ('third hand smok*' OR 'thirdhand smok*') OR (tobacco NEAR/2 heat*) OR 'heated tobacco product'/exp OR 'heated tobacco product*' OR 'heated tobacco' OR 'tobacco heating system'/exp OR 'tobacco heating system*' OR 'heat not burn' OR iqos OR heets OR heatstick* OR 'electrically heated cigarette smoking system'/exp OR 'electrically heated cigarette' OR ehcss OR (heat* NEAR/2 cigarette) OR 'modified risk tobacco product'/exp OR 'modified risk tobacco product*' OR (lil NEAR/2 tobacco) OR (teeps NEAR/2 tobacco) OR (hnb:ti,ab,kw AND tobacco:ti,ab,kw) OR 'noncombustible cigarette' OR 'non-cigarette combustible' OR ('risk continuum' AND tobacco)

- **Scopus**

ALL("tobacco W/2 heat*")OR ALL("heated tobacco product") OR ALL("heated tobacco product*") OR ALL("heated tobacco") OR ALL("tobacco heating system") OR ALL("tobacco heating system*") OR ALL("heat not burn") OR ALL(iqos) OR

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ALL(heets) OR ALL(heatstick*) OR ALL("electrically heated cigarette smoking system") OR ALL("electrically heated cigarette") OR ALL(ehcss) OR ALL(heat* W/2 cigarette)OR ALL("modified risk tobacco product") OR ALL("modified risk tobacco product*") OR ALL(lil W/2 tobacco) OR ALL(teepees W/2 tobacco) OR ALL(hnb AND tobacco) OR ALL("noncombustible cigarette") OR ALL("non-cigarette combustible") OR ALL("Risk continuum" AND tobacco) OR ALL(thh AND tobacco) AND NOT ALL("third hand smok*" OR "thirdhand smok*")

- **SciFinder**

"heat not burn" OR "tobacco heating system" OR "modified risk tobacco" OR "electrically heated cigarette" OR "heated tobacco"

- **RightFind**

"heated cigarette" or "tobacco heating" or "heated tobacco" or "tobacco heating system" or ("heat-not-burn" and Tobacco) or IQOS or HEETS or heatsticks or (HNB and Tobacco) or (Lil and Tobacco) or "Modified risk tobacco product" or "primarily heat tobacco"

- **RightFind II**

"noncombustible cigarette" or "non-cigarette combustible" or ("risk continuum" and Tobacco)

4. REPORTING

Any safety reports meeting the definition of an individual case safety report associated with the use of *IQOS* System that were identified in the literature review and processed in the safety database, will be included in the Safety Update Report (SUR). Any publication that contains potential new safety-related information associated with the use of *IQOS* System will be as well presented in the SUR.

All other publications relating to *IQOS* System either sponsored by PMI or by a third party will be summarized and reported annually as part of the reporting obligations in the context of the Premarket Tobacco Product Application (PMTA) and the Modified Risk Tobacco Product (MRTP) marketing orders, respectively.

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Version History

Version	Version Date	Rationale for Modification(s)
1.0	06 August 2020	First version
2.0	24 March 2022	Updated search strings and added new literature databases
3.0	19 April 2024	Updated search strings and literature databases

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