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Annex 2: MRTP Use and Health Risk - Toxicology

FDA STNs	Tobacco Product Names
MR0000059	<i>Marlboro Amber HeatSticks</i>
MR0000060	<i>Marlboro Green Menthol HeatSticks</i>
MR0000061	<i>Marlboro Blue Menthol HeatSticks</i>
MR0000133	<i>IQOS</i> System Holder and Charger
MR0000192	<i>IQOS 3</i> System Holder and Charger
Tobacco Product Category	HTP
Tobacco Product Sub-category	open HTP and HTP consumable
Applicant	Philip Morris Products S.A. (PMP S.A.)
Date of Report	April 28, 2024
Reporting Period	March 1, 2023, to February 29, 2024

Confidentiality Statement

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1 OVERVIEW

As part of the initial product characterization of the *IQOS* System, non-targeted differential screening (NTDS) analyses of the aerosol generated from *Marlboro* Amber *HeatSticks* (MR0000059), *Marlboro* Green Menthol *HeatSticks* (MR0000060), and *Marlboro* Blue Menthol *HeatSticks* (MR0000061) with the *IQOS* System Holder and Charger (MR0000133)¹ were performed to identify compounds which were potentially new, or significantly increased in *IQOS* aerosol relative to 3R4F cigarette smoke. Identification of potential genotoxic and carcinogenic hazards related to the Authorized Products was included in the post-market requirements of the Modified Risks Granted Orders (MRGOs). A hazard identification protocol was developed to determine the genotoxic and carcinogenic potential of both inhaled tobacco product constituents and their potentially reactive and toxic metabolites.

The study is divided in three phases:

- Phase 1 - to determine the genotoxicity and/or carcinogenicity potential of the 80 chemicals identified as potentially new, or significantly increased in *IQOS* aerosol relative to 3R4F smoke in the previous NTDS analyses. Results were reported in the 2022 Annual Report.
- Phase 2 - to determine the potential metabolites of the 80 chemicals relevant to humans. Results were reported in the 2023 Annual Report.
- Phase 3 - to determine the genotoxicity and/or carcinogenicity potential of the relevant metabolites.

Phase 3 of the project is on-going, assessment is completed. We are currently reviewing the data, and the study report is being under preparation. We will submit the report immediately upon its completion.

¹ We refer to the July 07, 2020, and March 11, 2022 Modified Risk Granted Orders for *IQOS* System Holder and Charger, *Marlboro* *HeatSticks* products collectively as Authorized Products.

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