PHILIP MORRIS
PRODUCTS S.A.

April 26, 2018

Food and Drug Administration
Center for Tobacco Products
Document Control Center
Building 71, Room G335
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Submitted via ESG

Re: MR0000059-MR0000061 and PM0000424-PM0000426 - "P1 Characterization" Study

Dear Sir or Madam,

As previously communicated by PMP S.A. in response to the FDA advice/information request of August 4, 2017 and clarification letter of February 2, 2018 we are hereby submitting the "P1 Characterization" study. The purpose of the study is to provide a comprehensive chemical characterization of all THS aerosol constituents (of concentration ≥ 100 ng/stick) beyond those already identified as being higher in abundance than 3R4F reference cigarette smoke using non-targeted differential screening (NTDS).

The "P1 Characterization" study is accompanied by a document summarizing the THS Aerosol Chemistry data and information submitted to date, including all additional studies referenced below.

In addition and as an official update we are providing the Agency with the following documents:

- Analysis comprising the FDA's full list of HPHCs for THS aerosol compared to 3R4F reference cigarette smoke performed by Labstat International ULC.
- Review of a study from the University of California [Davis et al., 2018], which we found as part of our literature review process. The authors of the study claimed that formaldehyde cyanohydrin is released from the PLA filter of the *HeatStick* upon heating. This claim, however, is purely based on mass spectra matching with the spectral library of the National Institute of Standard and Technology (NIST), and was however not confirmed using a reference standard.

  PMI has replicated the work of Davis et al using gas chromatography with high resolution mass spectrometry and by comparing the results with purchased analytical grade formaldehyde cyanohydrin as a reference standard. While the chromatographic separation

was demonstrated to be congruent with the work of Davis et al, it was demonstrated unambiguously, through the comparison with a reference standard, that the PLA filter does not emit formaldehyde cyanohydrin, and that the compound identification proposed was incorrect. Instead, PMI showed, based on chromatographic data and literature report that the corresponding peak is likely to be meso-lactide, which results from the cyclisation of 2 lactic acid molecules. The PMI's verification report [Polylactic Acid Analysis Response to Davis et al.] is appended to this letter.

We also acknowledge the receipt of the Advice/Information Request dated April 23, 2018 and confirm that responses to the questions and requested additional data for the Non-Targeted Differential Screening Analysis (NTDS) will be provided within the timeframe specified by the Agency.

We are aware of the importance of the full evidence package characterizing THS aerosol for the Agency's review of our MRTP Applications. Therefore, PMI is proposing a face-to-face listening session to present the overall Aerosol Characterization data as well as the results of "P1 Characterization" study to the Agency. We will make our team available at the convenience of the Agency or, should the Agency prefer, we are willing to present the data and answer any questions that the Agency may have in a telephone conference.

This response/amendment contains confidential commercial and/or trade secret information. Protection of this information from public disclosure is hereby claimed under the applicable provisions of United States law. We request the agency to provide pre-disclosure notification and follow the procedures in 21 C.F.R. §20.61(e) before publicly disclosing any information contained in this amendment.

We remain available for any further information that is required.

Sincerely,

Malgorzata Wronowska, PhD
Director Regulatory and Scientific Affairs
Philip Morris Products S.A.

Jeffrey Walker, M.D.
US Agent for PMP S.A.
CEO, Teton Regulatory Sciences

Enclosures : Appendix A