APPENDIX A3.3-5

P1 THS 2.2 STABILITY STUDY PROTOCOL MONITORING

Confidentiality Statement

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Table of Contents

1 Introduction 2
2 Sample Management 2
3 Storage Conditions 3
4 Stability Parameters and Methods 3
4.1 Chemical and Physical Characterization 3
5 Testing Frequency 4
6 Data Evaluation 5
7 Data Presentation 5
8 Responsibilities 5
9 References 5
10 Revision History for Stability Protocol 5
11 Signatures 6

1 Introduction

This document describes the conditions for the Tobacco Heating System (THS) 2.2 version (Platform 1) monitoring stability study and the tests planned for each time point, with the objective to demonstrate the quality and compliance of the THS 2.2 with the specifications, (b) (4) . This study is intended to (b) (4)

(b) (4)

This THS 2.2 monitoring stability study monitors (b) (4)

2 Sample Management

The samples required for the Stability study are delivered by the manufacturing site directly to the QC Unit after manufacturing, and afterwards placed in the climatic chambers in PMI R&D Neuchâtel Product testing laboratories by the Test Item Management (TIM) team.

The samples will be stored in the climatic chambers in polypropylene wrapped bundles of 10 packs. The packs are polypropylene wrapped packs consisted of two collation, each collation containing 10 Tobacco Sticks.

At each time point the dedicated number of samples will be removed from the climatic chambers for chemical, physical and visual inspection.

(b) (4)

3 Storage Conditions

Table 1– Stability Storage Conditions

(b) (4)

4 Stability Parameters and Methods

4.1 Chemical and Physical Characterization

The following chemical mainstream aerosol parameters that will be followed during the stability study are listed in Table 2 and 3. (b) (4)
(b) (4) .

Table 2 - List of Parameter Measured in the Mainstream Aerosol for the THS 2.2 Stability Study

(b) (4)

(b) (4)

Generation of the aerosol will be performed using the Health Canada (HC) smoking regimen:

- Laboratory temperature: 22 ± 2°C

- Laboratory relative humidity: 60 ± 5%
- Puff volume: 55 mL
- Puff duration: 2.0 s
- Puff interval: 30 s
- Number of puffs: 12

(b) (4)

Table 3 - List of Physical Parameters Measured for the THS 2.2 Stability Study

(b) (4)

(b) (4)

5 Testing Frequency

(b) (4)

Table 4 - Testing Matrix

(b) (4)

6 Data Evaluation

The data evaluation will be performed with the verification of the 95% confidence interval for the average against the specifications.

7 Data Presentation

The raw data will be archived and can be audited upon request.

The analysis of the stability results will be performed at each time point and a report issued at the end of the study.

8 Responsibilities

It is the responsibility of the Stability Studies Coordinator to ensure that the stability protocol is followed under the defined rules. It is also his (her) responsibility to schedule the analysis at each time point as well as preparing at each time point the stability results tables. He (she) must also verify that the stability conditions in the stability chambers were met. It is also the responsibility of the Stability Studies Coordinator to evaluate at each time point the generated data in order to identify any OOS values and trigger the subsequent actions.

9 References

International Conference for Harmonization ICH Q1A R2: Q1A(R2) Stability Testing of New Drug Substances and Products

ISO 3402:1999 Tobacco and Tobacco Products -- Atmosphere for Conditioning and Testing

WHO Stability Testing of Active Pharmaceutical Ingredients and Finished Pharmaceutical Products

10 Revision History for Stability Protocol

Version Nr	Description of change (including reason for change)	Justification
2.0	1. (b) (4). 2. [redacted]. 3. (b) (4) [redacted]. 4. Updated signatures list and added roles.	Update protocol.
2.0_SV	1. General revision for submission purposes.	Update of protocol.

11 Signatures

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