EXPERIMENTAL PROTOCOL

DROPLET SIZE DISTRIBUTION FROM P1 THS 2.2 AND MENTHOL TEST ITEMS USING A VALIDATED PIXE CASCADE IMPACTOR

Program Name	Product Development
Project Name	J-1002RDA0016
Covered Time Period	January-March 2016
Category of Experimental Work	Clinical and Regulatory Support
Document Author	Pascal Pratte
Document Owner	Catherine Goujon

TABLE OF CONTENTS

1 APPROVAL AND VERIFICATION 3
2 ABSTRACT 3
3 INTRODUCTION 3
4 RESEARCH QUESTION 4
5 PLAN 4
5.1 Approach 4
5.2 Experiment 4
5.3 Design 4
5.4 Samples 4
5.5 Instruments and Materials 5
5.6 Procedure 5
5.7 Data Processing 6
5.8 Respirability acceptance criteria based on aerosol measured MMAD and GSD 6
6 EXPERIMENTAL REPORT 8
7 CONCLUSIONS 8
8 REFERENCES 8
9 REVISION HISTORY 9
10 ABBREVIATIONS 9

TABLE OF TABLES

Table 1: Test item description 5
Table 2: MMAD and GSD upper limit values for which the aerosol is respirable (assuming lognormal distribution) 7

1 APPROVAL AND VERIFICATION

Name	Justification	Date / Signature
Pratte, Pascal	approved by author, Manager Aerosol Physics	06 June 2016 Pascal Pratte
Goujon, Catherine	approved by owner, Manager Analytical Development and Applications	06 JUNE 2016
Moores, Shelley	verified by Quality Assurance, Manager QA Assessment & Quality Systems	06-June-2016 S. Moores
Miller, Beate	approved by Sponsor, Manager Regulatory Affairs	06 June 2016 B. Miller

2 ABSTRACT

The current document describes the measurement of Droplet Size Distribution (DSD) for P1 THS 2.2 and menthol test. The objective is to evaluate the aerosol Mass Median Aerodynamic Diameter (MMAD) parameter obtained for three different batches of THS 2.2 DORADO I MINT VINNY and confirm that the resulting aerosol size is comprised in the respirable range (Particulate Matter below 2.5 µm, named PM2.5).

3 INTRODUCTION

The Droplet Size Distribution (DSD) influences the deposition pattern in the respiratory tract of inhaled aerosols. This assay is used to determine the DSD of the aerosol generated from P1 THS 2.2 device using menthol test items (see Table 1). This assay is based on the use of a cascade impactor to gravimetrically determine the DSD. This instrument was chosen due to its large DSD size range (60nm – 16µm).

4 RESEARCH QUESTION

Is the DSD in the respirable range for P1 device using menthol test items (THS 2.2 Dorado I Vinny Low)?

5 PLAN

5.1 Approach

The experimental approach is described in details in the work instruction named "Droplet Size Determination using the PIXE Cascade Impactor."

5.2 Experiment

Experiments are planned to be performed by the Analytical Laboratory Team on week 11 or 12 in 2016.

5.3 Design

At the beginning of each experimental day, a suitability test will be performed to verify that the PIXE cascade impactor is functioning in a correct manner. To this end, a 3R4F cigarette monitor is going to be used using the Health Canada regimen. The weight of the impaction plates, before and after the experiment, will be recorded in a validated form. On this form, the pass criterion for the suitability test is met when the mass fraction for plate 2 is comprised between 0.70 and 1.00. When a suitability test passes on a specific day, the PIXE cascade impactor is disassembled and cleaned. Subsequently, the plates are weighed, reassembled and the PIXE cascade impactor connected to a Programmable Dual Syringe Pump (PDSP). The aerosol generation will be performed under Health Canada regimen and the resulting loaded plates weighed upon aerosol collection. The mass of the plates, prior and after the aerosol collection, will be recorded on a dedicated form.

5.4 Samples

Prior conducting the aerosol generation experiment, samples will be conditioned according to ISO conditions for both 3R4F and P1 menthol test items. Ten replicates will be performed for three distinct batches over three different days. The laboratory condition set during the aerosol generation will be maintained at 22°C ± 2°C and 60% ± 5%

relative humidity. The aerosol will be generated under Health Canada smoking regimen (Health Canada, T-115, 1999).

Table 1: Test item description

Product/ test item	Consumable Batch number	Manufacturing date	Additional information
THS 2.2 Dorado I Vinny Low	B-25900 / 41.2381531	21 Dec 2015	10 replicates per batch
	B-25901 / 41.2374718	22 Dec 2015	
	B-25902 / 41.2379112	16 Dec 2015	

5.5 Instruments and Materials

Measurements and analyses will be performed based on the working instruction named "Droplet Size Determination using the PIXE Cascade Impactor."

5.6 Procedure

In a first step, before conducting the experiments according to Table 1, pre-experiments will be performed to determine the overloading threshold (maximum number of puffs collected without overloading the PIXE cascade impactor). The test items will be connected to the inlet of the PDSP and the aerosol generation started. The first 5 puffs are going to be exhausted to the waste. Iteratively, an increasing number of puffs will be collected in the PIXE cascade impactor. The PIXE cascade impactor will be dismantled while visual inspection is used to determine whether the PIXE cascade impactor is overloaded. An overloaded impaction plate is recognized when aerosol particle/droplet has not only been precipitated on the impaction plate and also on the nozzle of the impactor segment located directly above the respective impaction plate. If at least one impactor plate is overloaded, the pre-experiment is repeated by reducing the number of collected puff by one in an iterative manner. In the case the impactor is not overloaded, the pre-experiment is repeated with one additional puff in an iterative manner. This means that the procedure is repeated until the maximum number of puffs is reached without overloading the PIXE cascade impactor.

After identifying the maximum number of puffs collected without overloading, PIXE impactor tests will be performed according to Table 1. The weight of each impaction plate prior aerosol collection will be measured and recorded. The PIXE cascade impactor is assembled and connected to the PDSP. The test item are connected and the aerosol generation starts. The first 5 puffs are exhausted to the waste while puffs 6 and onwards are selected according to the result of the overloading test. The PIXE cascade impactor is dismantled and the plates' weight recorded.

5.7 Data Processing

The calculation of the MMAD and GSD will be performed using SAS software version 9.2. For this a nonlinear regression analysis of the normalized mass fraction nMfi vs the respective Mid-Point Diameter Di using the model function (Hinds 1999, p. 92) will be used based on the minimum squared errors.

5.8 Respirability acceptance criteria based on aerosol measured MMAD and GSD

The key objective of performing these tests is to ensure that tested aerosols are respirable which means that more than 80% of the total inhaled aerosol is transferred in the human lung alveolar region. Table 2 summarizes the different (MMAD, GSD) couples for which the aerosol is respirable. Each member of each couple represents the maximum value for which the aerosol is respirable. For example, for a GSD of 1.6, the MMAD should not exceed 0.9 µm in order to classify the aerosol as respirable, considering the method variability (see Table 2, right column). For a perfectly mono-disperse aerosol (GSD = 1.0), the maximum possible MMAD characterizing it respirable is 2.5 µm.

Table 2: MMAD and GSD upper limit values for which the aerosol is respirable (assuming lognormal distribution)

Theoretical upper limit values		Upper limit values for MMAD taking into account method variability
MMAD [µm]	GSD [-]	MMAD [µm]
2.5	1.0	2.4
2.1	1.1	2.0
1.7	1.2	1.6
1.5	1.3	1.4
1.3	1.4	1.2
1.1	1.5	1.0
1.0	1.6	0.9
0.9	1.7	0.8
0.8	1.8	0.7
0.7	1.9	0.6
0.6	2.1	0.5
0.5	2.3	0.4
0.4	2.6	0.3
0.3	3.0	0.2

6 EXPERIMENTAL REPORT

All data, results, discussions, observations and possible deviations from experimental protocol will be fully described in the related experimental report.

7 CONCLUSIONS

Conclusions will be fully described in the related experimental report.

8 REFERENCES

- Health Canada, Official Method T-115, Determination of "Tar", Nicotine and Carbon Monoxide in Mainstream Tobacco Smoke, December 31, 1999
- Aerosol Technology,W.C. Hinds, second edition

9 REVISION HISTORY

Version N°	Description of change	Type of change
1.0	Original issue (signed on February 18th 2016)	1
2.0	Some links and references were removed from the text and addtional references were added (signed on may 27th 2016).	1
3.0	In Table 2 "units" were added in the column title as "[µm]" for MMAD and "[-]" for GSD, meaning an unitless value.	1

(1. Major change/new version; 2. Minor change; 3. Review without change)

10 ABBREVIATIONS

Abbreviations		
DSD	:	Droplet Size Distribution
GSD	:	Geometric Standard Deviation
MMAD	:	Mass Median Aerodynamic Diameter
MRTP	:	Modified Risk Tobacco Product
P1		Platform 1
PDSP	:	Programmable Dual Syringe Pump
PM2.5	:	Particulate Matter
THS	:	Tobacco Heated System