APPENDIX A3.2.2-14

AEROSOL CHEMISTRY SELECTION JUSTIFICATION

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1. NEW BATCH RELEASE PROCESS AND CQAS FOR PLATFORM 1.

1.1. Introduction:

(b) (4)

, a revised list of parameters for platform 1 is then proposed and rational are described in this document.

A new batch release method (b) (4) was developed and validated. The method was already applied for the batch release of (b) (4) study.

In this document we describe the rational to apply the new analytical method and a revised list of critical to quality attributes (CQAs) to Platform 1. (b) (4)

1.2. Selection of CQA

CQAs should be judiciously selected to allow release of batches with evidence that the desired product quality is reached. CQAs should therefore cover different aspects of the quality of the product in order to allow detection of any possible deviation in product quality. CQAs are used to set product specifications. According to ICH guideline Q6, a specification is defined as a list of tests, references to analytical procedures, and appropriate acceptance criteria, which are numerical limits, ranges, or other criteria for the tests described. It establishes the set of criteria to which a product should conform to be considered acceptable for its intended use. "Conformance to specifications" means that the product, when tested according to the listed analytical procedures, will meet the listed acceptance criteria. Specifications are critical quality

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standards that are proposed and justified by the manufacturer and approved by regulatory authorities as conditions of approval.

In the framework of (b) (4) development, two categories of product specifications are defined:

1) (b) (4) *specifications*
These specifications are used as the basis for (b) (4)
(b) (4)
.

1) (b) (4) *specifications*
These specifications are used as basis for (b) (4)

Specifications parameters, through CQAs, are chosen to *confirm the quality* of the product
(b) (4)

(b) (4)

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1.3. Current chemical CQA for batch release of Platform I :

(b) (4)

[redacted]

1.4. New proposed CQA list and rationales

(b) (4)

[redacted] list for the reasons described below:

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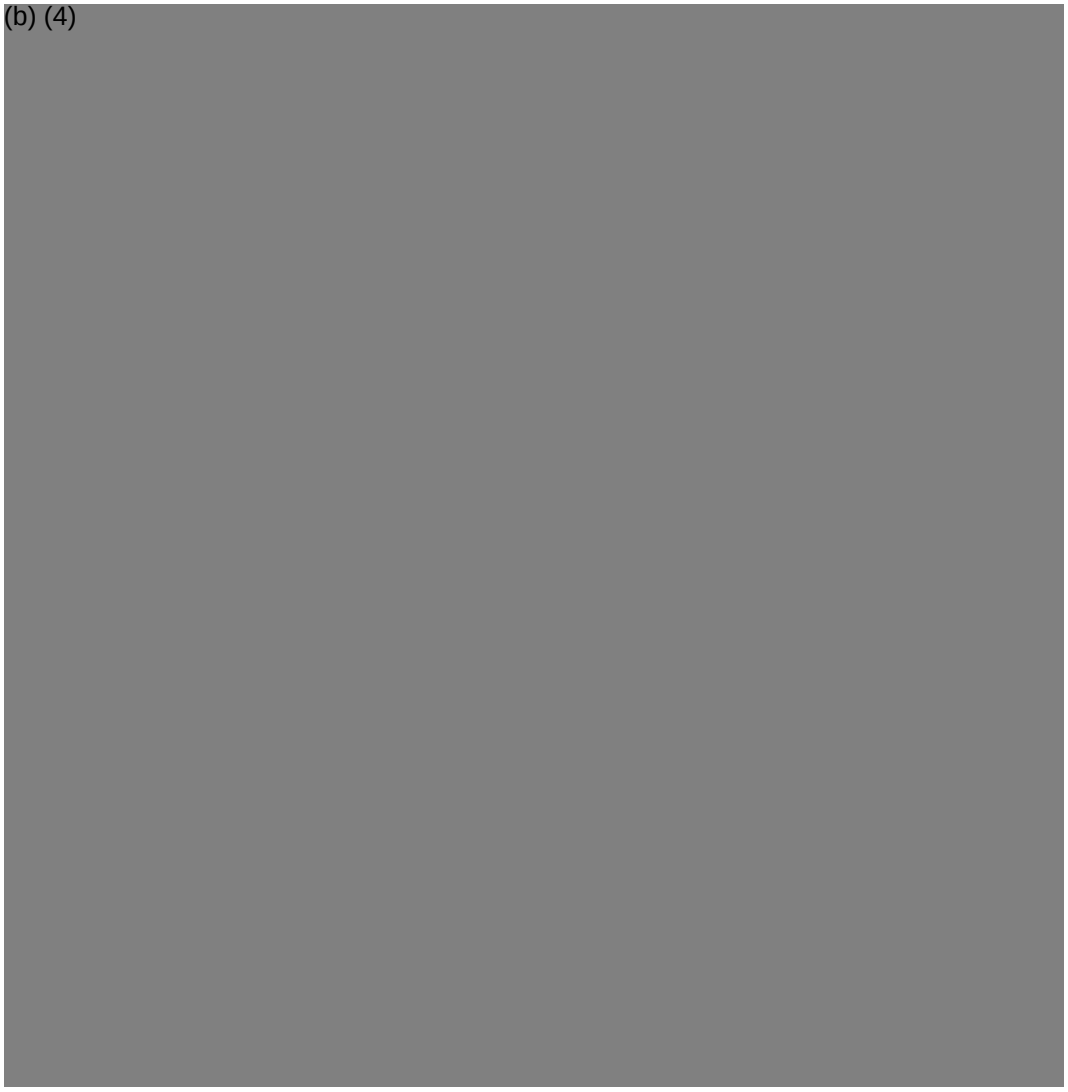
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- (b) (4)
- (b) (4)
- (b) (4)
- (b) (4)

We therefore propose the following (b) (4) as sufficient CQAs for batch release of platform I.

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1.5. **Critical to Quality Attributes selection for physical parameters**

To ensure a complete check of the quality of the product, in addition to the chemical parameters, the CQAs list should also cover the relevant physical parameters: deviations measured in the selected physical parameters should be indicative of deviations in product quality. Physical parameters should therefore cover product quality from sensory perception to product performance and product design, and should be complementary to the chemical parameters.

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The list of (b) (4) CQA remains the same as the currently used for batch release. We however propose to review the (b) (4) . This means that (b) (4)
(b) (4)

1.6. Batch release process

The new batch release process includes a new approach (b) (4) process is based on a (b) (4)
(b) (4) . The quality level is defined by (b) (4)).
The process also allows to (b) (4) based on historical results (see figure 1). (b) (4)
. Table 1 below shows an example of
(b) (4)

Table 1: (b) (4)

(b) (4)

(table continues)

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(b) (4)



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(b) (4)



Figure 1: scheme (b) (4)

1.7. Recommendation

We therefore recommend (b) (4) . This (b) (4)

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1.8. Review and approval

Name	Function	Justification	Signature	Date
Jeannet, Cyril	Manager Product Characterization	Author		28-Jun-2016
Maeder, Serge	Director PMI Testing Laboratories Governance	Approver		28.Jun.2016
Moores, Shelley	Manager QA Assessment & Quality Systems	QA Review		28-June-2016

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SCIENTIFIC REPORT

RATIONALE FOR THE SELECTION OF REDUCED RISK LIST OF CQA FOR P1 PRODUCT

Strategy	Develop RRPs
Program Name	Product Development
Project Name	P1 Product development WBS:J-1002RDA0016/0001/0001
Type of document	Scientific and technical report
Written by	Cyril Jeannet
Approved by*	Serge Maeder

*For proof of review and approval (Dates and electronic sign-off), refer to the EDMS history tab in the document properties.

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1 Introduction

Modified Risk Tobacco Products (MRTP) are intended to reduce harm or the risk of tobacco-related disease associated with commercially marketed tobacco products. The underlying Product Development (PD) assumption governing the development of next generation products (NGPs) is that "heating is better than burning" which should lead to produce a significantly different Modified Mainstream Aerosol (MMA) in terms of quality and quantity than Conventional Cigarette (CC) mainstream smoke. Therefore, it has been hypothesized that formation of some potentially harmful smoke constituents would not occur, or formation of some potentially harmful smoke constituents would occur in much smaller amounts, i.e., MMA is a subset of CC Mainstream Smoke (MS). In order to demonstrate the reduction of smoke constituents produced by MRTP, PMI R&D has established a list of 58 smoke constituents to be determined in RRP aerosol. The list is mainly based on the Health Canada list with additional compounds that have been selected using various criteria (e.g. combustion marker, biomarker of exposure, toxicological concerns etc.).

(b) (4) . The rational for the selection of the CQA was based on (b) (4) factors which were the (b) (4) (b) (4) .

2 Objective

The purpose of this document is to describe how a (b) (4) . The rationale described in this document is based on previous knowledge and statistical analyses of historical data.

3 Previous Knowledge

(b) (4)

(b) (4) results of these studies were then used to establish criteria for the selection of CQA by (b) (4)

(b) (4)
.

(b) (4) (b) (4) .

(b) (4)
:

(b) (4) :

(b) (4)

Where:

(b) (4)
(b) (4)

(b) (4)

(b) (4)

(b) (4) .

(b) (4) .

(b) (4)
highlighted as shown in the figure 1 below:

(b) (4)
.

(b) (4)

Figure 1: (b) (4)

(b) (4)

(b) (4)

n were used and shown in table 1 below. (b) (4)

(b) (4)

Table 1: (b) (4)

(b) (4)

(b) (4) .

(b) (4)

Table 2: (b) (4)

(b) (4)

A (b) (4) .

4 Conclusions

(b) (4) .

The proposed list of CQA was (b) (4) was approved as to be the list of CQA to be analyzed in (b) (4)) product in order assess (b) (4)) and then to (b) (4) The CQA will also be further used as (b) (4) (b) (4) .

(b) (4)

(b) (4)

5 Revision history

Version N°	Author	Description of change (including reason for change)	Type of change
1.0	Jeannet, Cyril	Original issue in a form of a Memo	
2.0	Jeannet, Cyril	Memo version introduced in a standard report format. Content of the document is not modified	2
3.0	Jeannet, Cyril	Approval Workflow	3
3.0SV	Jeannet Cyril	Submission version, with updated references	2

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

6 Approvals

	Name	Role	Signature	Date
Author	Cyril Jeannet	Manager Product Characterization		28-Jun-2016
Owner	Serge Maeder	Director PMI Testing Laboratories Governance		28. Jun. 2016
QA Review	Shelley Moores	Manager QA Assessment & Quality Systems		28 June 2016