APPENDIX A3.2.1-2

TARGET PRODUCT PROFILE AND PRODUCT TEST SPECIFICATION

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Platform 1 Target Product Profile THS 2.2 (THD 2.4) – Product Test Specification

#	TPP Clause	Relevance	Product Test Specification	Measurement Method / Test protocol
1	**Product Promise / Unique Selling Proposition**			
1.1	Potential to reduce the health risk associated with conventional cigarette smoking as demonstrated under real-life conditions through substantiation of exposure reduction and favorable changes in clinical risk endpoints in the short-term approaching what is observed on smoking cessation.	• Unmet consumer need (reduced health risk) • Key part of RRP concept (heating versus burning reduces health risk	1.1.1 Product design and characterization are defined prior to the start of Human studies	Product & Performance Specifications FDS/FTS/FTR
			1.1.2 Safety and hazard assessment is completed and product is approved for use prior to clinical trial	Non-clinical assessment protocol
			1.1.3 Product meets criteria outlined in the Non-clinical Assessment Guidelines	Non-clinical assessment protocol
			1.1.4 Under exclusive switching from conventional cigarettes to RRP, the reductions (target is 50%) in the levels of biomarkers of exposure to selected HPHCs are statistically significant as compared to levels upon continuing smoking of conventional cigarettes	Clinical assessment protocol
			1.1.5 Under exclusive switching from conventional cigarettes to RRP, the reductions in the levels of biomarkers of exposure to selected HPHCs, corresponds to an at least 50% reduction as compared to CC and approaches levels observed upon smoking cessation.	Clinical assessment protocol
			1.1.6 Under ambulatory, ad-libitum use conditions levels of all biomarkers of exposure in non-exclusive RRP users are not higher than those observed in conventional cigarette smokers	Clinical assessment protocol
			1.1.7 Under ambulatory, ad-libitum use conditions selected clinical risk endpoints favorably change with a preserved effect of at least 50% observed after smoking cessation and demonstrate risk reduction on the individual level compared to continued use of CC	Clinical assessment protocol
			1.1.8 Based on the assessment of exposure-emergent adverse events, there is no signal for increased risks in RRP switchers (all adverse events, serious adverse events, severe adverse events) as compared to smoking conventional cigarettes	Clinical assessment protocol

Platform 1 Target Product Profile THS 2.2 (THD 2.4) – Product Test Specification

#	TPP Clause	Relevance	Product Test Specification	Measurement Method / Test protocol
1.2	Significant reduction in the visibility and smell intensity of the environmental aerosol when compared to environmental tobacco smoke produced by conventional cigarettes	• Unmet consumer need (personal and social) • Better in reduction compared to conventional cigarettes	1.2.1 At least 80% of panelists note a reduction in perception of environmental aerosol generated in sensory assessment of room	IAC protocol / *Consider ASTM E1958 - 12 'Standard Guide for Sensory Claim Substantiation'*
			1.2.2. Adult smoker acceptance of visibility and smell of environmental aerosol in Home Usage Test (more than 50% of panelists rate visibility and smell as acceptable or better than conventional cigarettes	Whole Offer Test (WOT) protocol
1.3	Significant reduction in the amount of harmful and potentially harmful constituents in the environmental aerosol when compared to environmental tobacco smoke produced by conventional cigarettes	• Key part of RRP concept (heating versus burning reduces generation of harmful smoke constituents) Defined by the Integrated Product Assessment Strategy (INAS 2010)	1.3.1 The Environment Aerosol does not negatively impact Indoor Air Quality as proven with our internal assessment	Assessment approach as proposed by Council of Fellows (CoF): Comparative assessment of environmental tobacco smoke from conventional cigarettes and aerosols produced by the use of modified tobacco products in indoor environment.
			1.3.2 In line with Japan & Italy regulations supported by market specific 3rd parties' validation.	3rd party documentation gathering Japan and Italy requirements for Indoor Air Quality
1.4	HeatStick can be safely disposed of in regular waste bins with no fire hazard		1.4.1 Product complies with adapted ignition propensity test	Non Applicable to current Platform design
2	**Consumer Acceptance and Understanding**			
	Consumer experience			
2.1	(b) (4)		2.1.1 (b) (4)	
2.2			2.2.1	
2.3			2.3.1	
2.4			2.4.1	

Platform 1 Target Product Profile THS 2.2 (THD 2.4) – Product Test Specification

#	TPP Clause	Relevance	Product Test Specification	Measurement Method / Test protocol
		(b) (4)	2.4.2 (b) (4)	
2.5	(b) (4)	• (b) (4)	2.5.1 2.5.2	
2.6	Effective substitute for conventional cigarettes	• Successful substitution of conventional cigarettes (Evaluation of subjective effects allow to predict successful suppression of withdrawal symptoms)	2.6.1 Domains Considered (i) withdrawal; (ii) positive and negative reinforcement effects (iii) craving; 2.6.2 Nicotine pharmacokinetics after single use of RRP is comparable to the nicotine pharmacokinetic profile observed after single use of Conventional Cigarette (CC) to support user acceptance. 2.6.4 Evaluation of subjective effects as a measure of potential product acceptance (e.g. relief of craving and withdrawal symptoms and positive/negative affect) – Single use of RRP relieves abstinence symptoms to ≥80% of the level achieved after single use of a conventional cigarettes 2.6.5 Under ad-libitum use, nicotine exposure measured through nicotine equivalents (NEq) is comparable in RRP users (including dual users) as compared to CC smokers	Product Assessment: Clinical Assessment Plan Subjective symptoms, examples • MCEQ (Modified Cigarette Evaluation Questionnaire). Total score and all subscales • QSU (Questionnaire of Smoking Urges)-Brief. Total score and 2 subscales • MNWS (Minnesota Nicotine Withdrawal Scale). Total score, all subscales, all individual symptoms • Evaluation of adverse events (mainly in the CNS (Central Nervous System) domain)
2.7	(b) (4)	• (b) (4)	Product Development: 2.7.1 (b) (4) Product Assessment: 2.7.3 (b) (4)	Commercialization: (b) (4) Product Assessment: (b) (4)

Platform 1 Target Product Profile THS 2.2 (THD 2.4) – Product Test Specification

#	TPP Clause	Relevance	Product Test Specification	Measurement Method / Test protocol
	Functionality			
2.8	(b) (4)	• (b) (4)	Product Development: 2.8.1 (b) (4) 2.8.2 (b) (4) 2.8.3 (b) (4) 2.8.4 (b) (4) 2.8.5 (b) (4) Commercialization: 2.8.6 (b) (4)	Product Development: - (b) (4) Market Research: (b) (4)
2.9	(b) (4)	• (b) (4)	Product Development: 2.9.1 (b) (4) Commercialization: 2.9.2 (b) (4)	Product Development: (b) (4) Commercialization: (b) (4)
2.10	(b) (4)	• (b) (4)	Product Development: 2.10.1 (b) (4) 2.10.2 (b) (4) Commercialization: 2.10.3 (b) (4)	Product Development: (b) (4) Commercialization: (b) (4)

Platform 1 Target Product Profile THS 2.2 (THD 2.4) – Product Test Specification

#	TPP Clause	Relevance	Product Test Specification	Measurement Method / Test protocol
2.11	(b) (4)	• (b) (4) • (b) (4)	Product Development: 2.11.1 (b) (4)	Product Development: Design Verification Report
	Understanding			
2.12	Consumers are provided with substantiated and meaningful information about the product risks (consistent with relevant law)	• Public Health concern	Product Assessment: 2.12.1 The perception of risk reduction consumer have of using the RRP is not below **or equal to** their risk perception related to smoking cessation	PBA (Perception and Behavior Assessment) /Market Research: PBA 05 study report
2.13	Consumer perceptions of product risk are demonstrated to be correct in at least 80% of respondents (and to the extent possible, this level of consumer understanding is accepted by public health agencies/regulators)	• Public Health concern	Product Assessment: 2.13.1 Consumer understanding and perceptions appropriately assessed and pass fail criteria justified and documented	Market Research: PBA05 study report
2.14	Consumer communications (to the extent they are permitted by relevant law) are substantially understood as intended by at least 80% of respondents in launch markets	• Public Health concern	Product Development 2.14.1 User manual describes appropriate use and foreseeable misuse	Product Development - User manual
			Market Research: 2.14.2 User manual rated as simple to understand in Home Usage Test (at least 80% of panelists rate user manual as simple to understand)	Market Research: - Qualitative, WOT, Home Usage Test studies reports
			2.14.3 Consumer comprehension of instructions for use appropriately assessed and pass fail criteria justified and documented	- PBA 06 study report
3	**Appearance & Features:**			
3.1	Format & size: (b) (4)	• (b) (4)	Product Development: 3.1.1 (b) (4) 3.1.2 (b) (4)	Product Development: Functional Test Report

Platform 1 Target Product Profile THS 2.2 (THD 2.4) – Product Test Specification

#	TPP Clause	Relevance	Product Test Specification	Measurement Method / Test protocol
	Packaging: HeatSticks; minimum 20 stick/pack; (b) (4) Device; Contains one main unit and 1 holder	• Minimize barriers to enter new category/ritual • Commercial viability	Commercialization: 3.2.1 HeatSticks packaging industrial design capable of containing at least 20 cigarettes 3.2.2 (b) (4) 3.2.3 Device packaging industrial design allows for the inclusion of one main unit and one holder	Product Design Innovation and User experiences • Market research studies
4	**Safety and Hazards**			
4.1	Levels of harmful and potentially harmful constituents in mainstream aerosol, and its biological activity, are below those found in conventional cigarette smoke	• Key part of RRP concept (heating versus burning reduces generation of harmful constituents) Equivalence between Product Assessment and Commercial versions	Product Development: 4.1.1 Compliance to Product Performance Specifications Product Assessment (as per CMC Assessment Plan): 4.1.2 (b) (4) 4.1.3 Deliveries of all 47 Health Canada List targeted smoke constituents in mainstream aerosol are below the relative 95th percentile of Conventional Cigarette market map median for each of the 47 constituent, calculated on per mg nicotine basis using the HC intense smoking regime 4.1.4 Based on the nicotine bridging method (b) (4) (b) (4) April 2006; Urban et al., 2012), medians of deliveries of all 58 targeted smoke constituents are below the median of the distribution of a representative sample of references from Conventional Cigarette market map, all smoked under Human Puffing Behavior conditions (smoking machine conditions that are derived from 95th percentile of the nicotine uptake distribution; Zenzen et al., 2012) 4.1.5 Under Human Puffing Behavior smoking regimen (Zenzen et al., 2012), levels of delivery of high temperature pyrolysis/combustion markers as contained in the PMI 58 MMA Constituent List is below set limits	Product Development Functional Test Report Product Assessment: Product Assessment & Toxicological Assessment to define Document links to: CMC Assessment Plan (CMCAP); Nonclinical Assessment Plan (NCAP) CoF Review: Chemical Assessment of Modified Tobacco Products Mainstream Aerosols (MMA) Conventional Cigarette Market Map

Platform 1 Target Product Profile THS 2.2 (THD 2.4) – Product Test Specification

#	TPP Clause	Relevance	Product Test Specification	Measurement Method / Test protocol
			Product Assessment THS2.2 as per Nonclinical Assessment Plan (NCAP): 4.1.6 *In vitro* assays listed by the Nonclinical Assessment Plan (NCAP) show reduction in hazard of THS2.2 vs. a sample of conventional cigarette types from the current market map (comparison methodology detailed in NCAP) 4.1.7 (b) (4) 4.1.8 (b) (4) 4.1.9 (b) (4) 4.1.10 (b) (4)	
4.2	Main stream aerosol contains no new harmful and potentially harmful constituents when compared to a representative sample of conventional cigarettes from the conventional cigarette market map	• Key part of RRP concept (heating versus burning does not generate new harmful smoke constituents)	Tox Assessment: 4.2.1 No constituents in mainstream aerosol detected in THS 2.2 with the potential to introduce novel hazard when compared to a representative sample of conventional cigarettes from the Conventional Cigarette Market Map 4.2.2 *In vitro/in vivo* assays listed by the Nonclinical Assessment Plan (NCAP) show no indication for novel hazard when compared to a representative sample of conventional cigarette types from the current market map and (b) (4) (b) (4)	Tox Assessment: Toxicological Assessment to define Document links to: CMC Assessment Plan (CMCAP); Nonclinical Assessment Plan (NCAP) Conventional Cigarette Market Map

Platform 1 Target Product Profile THS 2.2 (THD 2.4) – Product Test Specification

#	TPP Clause	Relevance	Product Test Specification	Measurement Method / Test protocol
4.3	Main stream aerosol harmful and potentially harmful constituents -to-nicotine ratios are below those for conventional cigarettes under extreme conditions	• Key part of RRP concept (product performance does not vary with smoking topography) Defined by the Integrated Product Assessment Strategy (INAS 2010)	Product Assessment: 4.3.1 (b) (4)	Product Testing: (b) (4)
4.4	Main stream aerosol is in the inhalable range, with poorly soluble particles at a level lower than found in the aerosol of conventional cigarette smoke	• Public health concern	Product Assessment: 4.4.1 The device shall produce a consistent aerosol droplet size distribution with MMAD <2.5µm and 1st and 3rd quartile no more than 25% below and above the MMAD respectively.	Product Testing: Due Diligence Assessment 1 Report
4.5	Bill of materials, product design, indirect materials, manufacturing process and equipment pass PMI toxicological assessment and are approved for use	• Due diligence assessment to ensure no new risks are introduced	Tox Assessment: 4.5.1 Toxicological assessment 4.5.2 Bill of materials, product design, indirect materials, manufacturing process and equipment are approved for use	Tox Assessment: SAR (Safety Assessment Requests) associated to respective studies or commercial launches.
4.6	Device self-cleaning emissions are not of toxicological concern	• Key part of RRP concept (heating versus burning reduces generation of harmful smoke constituents)	Tox Assessment: 4.6.1 Below Threshold of Toxicological Concern (TTC)	Tox Assessment: Functional Test Specifications
5	**Regulatory**			
5.1	(b) (4)	• Ensures product is (b) (4)	CA (Corporate Affairs)/Commercialization: 5.1.1 (b) (4)	CA/Commercialization: (b) (4)
5.2	Complies with market-specific ceilings on tar, nicotine and CO in priority launch markets	• Ensures compliance with market-specific tobacco regulations	CA/Commercialization: 5.2.1 Measured tar, nicotine and CO levels are below market-specific ceilings for priority launch markets	Product Testing: ISO smoking report
5.3	Complies with market-specific labeling requirements	• Ensures compliance with market-specific tobacco regulations	Commercialization: 5.3.1 Compliance	Commercialization: • Legal assessment

Platform 1 Target Product Profile THS 2.2 (THD 2.4) – Product Test Specification

#	TPP Clause	Relevance	Product Test Specification	Measurement Method / Test protocol
5.4	(b) (4)	• (b) (4)	CA/Commercialization: 5.4.1 (b) (4)	Tox Assessment: • (b) (4)
5.5	Complies with all requirements for CE marking (or equivalent) in priority launch markets	• Mandatory to demonstrate conformity with the essential requirements of the applicable EC directives (or equivalent) prior to placing on the market	Product Development: 5.5.1 Compliance with Low Voltage Directive 2006/95/EC 5.5.2 Compliance with Electromagnetic Compatibility Directive 2004/108/EC 5.5.3 Compliance with IEC 62133 5.5.4 Compliance with UN 38.3	Product Development: Functional Test Report (device) 3rd party device Certification
5.6	Complies with the General Product Safety Directive (2001/95/EEC) (or equivalent legislation) in priority launch markets	• Device put on the market should be safe i.e. pose no threat or only a reduced threat in accordance with the nature of its use	Product Development: 5.6.1 Compliance	Product Development: Functional Test Report 3rd party device Certification
5.7	Complies with the Waste Electrical and Electronic Equipment Directive (2002/96/EEC) (or equivalent legislation) in priority launch markets	• Environmental concern. Mandatory for electrical devices	Product Development: 5.7.1 Compliance	Supply Chain • Infrastructure for collecting waste devices in place
5.8	Complies with the Packaging/Packaging Waste Directive (94/62/EC) (or equivalent legislation) in priority launch markets	• Environmental concern. Mandatory for packaging of device and HeatSticks	Commercialization: 5.8.1 Compliance	PRC: • Material evaluation and approval
5.9	Complies with the Hazardous Materials Directive (2002/95/EC) (or equivalent legislation) in priority launch markets	• Electronic equipment put on the market should not contain hazardous materials	Product Development: 5.9.1 Compliance	Product Development: • Functional Test Report

Platform 1 Target Product Profile THS 2.2 (THD 2.4) – Product Test Specification

#	TPP Clause	Relevance	Product Test Specification	Measurement Method / Test protocol
5.10	Complies with the Batteries and Battery Waste Directive (2006/66/EC) (or equivalent legislation) in priority launch markets	• Environmental concern. Mandatory for devices containing batteries	Product Development: 5.10.1 Compliance	Supply Chain • Infrastructure for collecting waste devices in place
6	**Robustness**			
6.1	The system operation should be characterized under predefined set of temperatures and humidity conditions	• Predictable performance • Commercial viability	Product Development: 6.1.1 Performance is reported 6.1.2 Device meets functional specifications in the temperature/humidity range as required for testing and analysis in the respective ICH and WHO guidelines 6.1.3 HeatSticks meet specifications (chemical, and physical profiles as well as appearance) in the temperature/humidity range as required for testing and analysis in the respective ICH and WHO guidelines 6.1.4. Sensorial evaluations on both Regular & Menthol are acceptable by panelists	Product Development • Robustness Report (6.11 → 6.1.3) • 6.1.4 – Sensory Evaluation reports
7	**Commercial**			
7.1	(b) (4)	• (b) (4)	Operations: 7.1.1 (b) (4)	(b) (4) (b) (4)
7.2	(b) (4)	• (b) (4)	(b) (4) 7.2.1 (b) (4) 7.2.2 (b) (4) 7.2.3 (b) (4) 7.2.4 (b) (4)	(b) (b) (4) (b) (4) (b) (4)

Platform 1 Target Product Profile THS 2.2 (THD 2.4) – Product Test Specification

#	TPP Clause	Relevance	Product Test Specification	Measurement Method / Test protocol
7.3	(b) (4)	• (b) (4)	Product Development: 7.3.1 (b) (4)	Product Testing: (b) (4) (b) (4)
7.4	(b) (4)	• (b) (4)	Product Development: 7.4.1 (b) (4)	(b)

Notes:

All measurements except specifically mentioned are done under normal conditions (22 degres Celsius, 60% relative humidity)
THS: Tobacco Heating System
THD: Tobacco Heating Device
FDS: Functional Design Specifications
FTS: Functional Test Specifications
FTR: Functional Test report
AUC: Area Under the concentration Curve
LTN: Low Tar and Nicotine
MMA: Modified Tobacco Products Mainstream Aerosols
MMAD: Mass Median Aerodynamic Diameter
MTP: Modified Tobacco Product
HeatSticks = Tobacco Sticks

Platform 1 Target Product Profile THS 2.2 (THD 2.4) – Product Test Specification

Revision History:

Version	Author	Description	Type of change
0.11	Gilchrist, Moira	Original issue	1
2.0	Lycee, Stephane	Major Changes	1
3.0	Lycee, Stephane	Minor Changes prior to City Launches	2
4.0	Apetrei, Cristina	Major Changes	1
4.0 SV	Apetrei, Cristina	Submission Version	2

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

Review and Approval:

Name	Function	Justification	Date and Signature
Apetrei, Cristina	Project Manager Electronic Devices	Signed as Author	14.07.2016
Scharer, Michael	Director Electronic Devices	Signed as Owner	14/07/2016
Florence Kapp	QA Officer Audit	Signed as QA Reviewer	14/7/2016