



PMI RESEARCH & DEVELOPMENT

Safety Update Report

Tobacco Heating System 2.2 Regular

Appendix B - Description of Ongoing and Completed Studies

Report Number: PMI_SURV_2015_SUR01

Period Covered: 01 May 2014 to 30 April 2015

Product Name: Tobacco Heating System 2.2 Regular

Sponsor: Philip Morris Products S.A.
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Appendix A - Description of Ongoing and Completed Studies**Table 1 Description of Ongoing Studies**

Ongoing Studies								
Study ID	Country	Title	Design	Type	Study Population	Enrolled	First-Subject In	Exposed to THS 2.2
ZRHR-REXC-04-JP	Japan	Study to demonstrate reductions in exposure to selected smoke constituents in smoking, healthy subjects switching from conventional cigarettes to the Tobacco Heating System 2.2 (THS 2.2) or smoking abstinence, compared to smokers continuing to use conventional cigarettes for 5 days in confinement.	Randomized, controlled, open-label, 3-arm parallel group, single-center	Reduced exposure study	Male or female smoking, healthy adult Japanese subjects, aged from 23 to 65 years old.	166 subjects	23 July 2013	86 subjects

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Ongoing Studies								
Study ID	Country	Title	Design	Type	Study Population	Enrolled	First-Subject In	Exposed to THS 2.2
ZRHR-ERS-09-US	USA	A randomized, controlled, 2-arm parallel group, multi-center study, to evaluate biological and functional changes in healthy smokers switching to Tobacco Heating System 2.2 (THS 2.2) compared to continuing smoking conventional cigarettes for 26 weeks in an ambulatory setting	Randomized, controlled, open-label, 2-arm parallel group, multi-center	Exposure – response study	Male or female smoking, healthy adult subjects, aged at least 30 years old	Planned: 950 subjects	18 March2015	Planned: 475 subjects (exposed, as of 30-Apr-2015: N=40)

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Table 2 Description of Completed Studies

Completed Studies								
Study ID	Country	Title	Design	Type	Study Population	Enrolled	First-Subject In	Exposed To THS 2.2
ZRHR-PK-01-EU	UK	Study to investigate the nicotine pharmacokinetic profile and safety of Tobacco Heating System 2.2 (THS 2.2) following single use in smoking, healthy subjects compared to conventional cigarettes and nicotine nasal spray.	Single-center, open-label, randomized, controlled, crossover	PK/PD	Male or female smoking, healthy adult Caucasian subjects aged from 21 to 65 years old.	62 subjects	01 Nov 2013	62 Subjects
ZRHR-PK-02-JP	Japan	Study to investigate the nicotine pharmacokinetic profile and safety of Tobacco Heating System 2.2 (THS 2.2) following single use in smoking, healthy subjects compared to conventional cigarettes and nicotine gum.	Single-center, open-label, randomized, controlled, crossover	PK/PD	Male or female smoking, healthy adult Japanese subjects, aged from 23 to 65 years old.	62 subjects	31 Jul 2013	65 subjects

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Completed Studies								
Study ID	Country	Title	Design	Type	Study Population	Enrolled	First-Subject In	Exposed To THS 2.2
ZRHR-REXC-03-EU	Poland	Study to demonstrate reductions in exposure to selected smoke constituents in smoking, healthy subjects switching to the Tobacco Heating System 2.2 (THS 2.2) or smoking abstinence, compared to continuing to use conventional cigarettes, for 5 days in confinement.	Randomized, controlled, open-label, 3-arm parallel group, single-center	Reduced exposure study	Male or female smoking, healthy adult Caucasian subjects, aged from 23 to 65 years old.	169 subjects	29 June 2013	89 subjects

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Table 3 Estimated Cumulative Subject Exposure

Estimated cumulative subject exposure, based upon actual exposure data from completed assessment studies in humans and the enrolment/randomization schemes for ongoing studies.

Study ID	Study Arm	Number of Subjects
ZRHR-PK-01-EU	Conventional cigarettes	22
	THS 2.2	62
	Nicotine nasal spray	9
ZRHR-PK-02-JP	Conventional cigarettes	22
	THS 2.2	65
	Nicotine replacement therapy 2 mg gum	9
ZRHR-REXC-03-EU	Conventional cigarettes	41
	THS 2.2	89
	Smoking abstinence	39
ZRHR-REXC-04-JP	Conventional cigarettes	40
	THS 2.2	86
	Smoking abstinence	40
ZRHR-ERS-09-US	Conventional cigarettes	475 (planned)
	THS 2.2	475 (planned)
		40 (as of 30-Apr-2015)

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