

Appendix 22: THS-PBA-05-RRC-US Study Summary

Confidentiality Statement

Certain data and information contained in this document constitute trade secrets and confidential commercial information. The legal protections that apply to trade secrets and confidential information are hereby claimed under the applicable provisions of law. No part of this document may be publicly disclosed without the written consent of Philip Morris International Inc. of which Philip Morris Products SA is an affiliate.



PMI RESEARCH & DEVELOPMENT

Study Report

THS-PBA-05-RRC-US

Study Title	Quantitative Assessment of THS 2.2 Label, Labeling and Marketing Material with Reduced Risk Claims
Study Number:	THS-PBA-05-RRC-US
Product Name	THS 2.2 (Tobacco Heating System version 2.2)
Study Initiated (first subject enrolled):	01 July 2015
Study Completed (last subject completed):	21 July 2015
Principal Investigators:	Thomas Alfieri, PhD Director, Covance Market Access Services Inc. 10300 Campus Point Drive, Suite 225 San Diego, California, USA Sam Colman, MSc Director, Covance Market Access Services Inc. Level 3, 4 Research Park Drive North Ryde, NSW, Australia
Sponsor	Philip Morris International Management S.A. Avenue de Rhodanie, 50 1007 Lausanne Switzerland
Sponsor Signatories:	Felix Beacher PhD, Study Manager Pierpaolo Magnani, PBA Program Manager Gerd Kallischnigg MSc, Study Biostatistician
Version:	1.0
Report Date	24 May 2016

This study was conducted in accordance with Good Epidemiological Practice.

Confidentiality Statement

Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the provisions of applicable law. No part of this document may be publicly disclosed without the written consent of Philip Morris International Management S.A.

SYNOPSIS

Sponsor: Philip Morris International Management S.A	Individual Study Table Referring to Part of the Dossier	(For National Authority Use Only)
Name of Finished Product: THS 2.2 (Tobacco Heating System version 2.2)	Volume:	
Name of Active Ingredient: Not applicable	Page:	
Study Title: Quantitative Assessment of THS 2.2 Label, Labeling and Marketing Material with Reduced Risk Claims		
Principal Investigators: Thomas Alfieri, PhD Director, Covance Market Access Services Inc. 10300 Campus Point Drive, Suite 225 San Diego, California, USA Sam Colman, MSc Director, Covance Market Access Services Inc. Level 3, 4 Research Park Drive North Ryde, NSW, Australia		
Publication (reference): Not applicable		
Period of Study: First subject completed: July 1, 2015 Last subject last participation: July 21, 2015		
OVERALL AIM The overall aim of this study was to describe responses to different instances of THS 2.2 label, labeling and marketing material, within Adult Smokers with the Intention to Quit conventional cigarettes (CC), Adult Smokers with No Intention to Quit CC, Adult Former Smokers and Adult Never Smokers. OBJECTIVES Study objectives included the assessment of: <ul style="list-style-type: none"> • Intent to Use (THS 2.2, CC, E-cigarettes and any nicotine-containing products) • Change in Intention to Quit Smoking and All Tobacco, associated with exposure to the THS 2.2 material, within Adult Smokers with the Intention to Quit CC • Comprehension of the THS 2.2 material • Risk Perception for THS 2.2 and for the comparators CC, E-cigarettes, Nicotine Replacement Therapy products (NRTs) and Cessation. MEASURES Dimensions measured in this study were: <ul style="list-style-type: none"> • Intent to Use, • Change in Intention to Quit Smoking and All Tobacco (within Adult Smokers with the Intention to Quit CC) • Comprehension, • Risk Perception 		
METHODOLOGY Study design: This study had a randomized parallel five arm design, with subjects in each Arm being presented with a separate instance of THS 2.2 label, labeling and marketing material. Arm 1 corresponded to the THS 2.2 Brochure including the Surgeon General’s warnings. Arm 2 corresponded to the THS 2.2		

Confidentiality Statement

Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the provisions of applicable law. No part of this document may be publicly disclosed without the written consent of Philip Morris International Management S.A.

<p>Brochure including the “Important Warning” developed by PMI. Arm 3 corresponded to the HeatSticks™ Pack including the Surgeon General’s warnings. Arm 4 corresponded to the HeatSticks™ Pack including the PMI Important Warning. Arm 5 corresponded to the THS 2.2 Direct Mail including the PMI Important Warning. Assessments were conducted in a fixed order. The smoking status groups, which formed the Main Sample were: (1) Adult Smokers with No Intention to Quit CC, (2) Adult Smokers with the Intention to Quit CC, (3) Adult Former Smokers and (4) Adult Never Smokers. In addition, an “oversample” of young Adult Never Smokers from legal smoking age to 25 years (“LA-25 Adult Never Smokers”) was included. Within each Arm, each smoking status group was composed of an approximately equal number of subjects.</p>													
<p>Procedures: Study assessments were administered using a Computer-Assisted Self-Interview (CASI) methodology. Assessments involved exposure to randomized THS 2.2 label, labeling and marketing material and direct questioning. Intent to Use was assessed for THS 2.2, CC, E-cigarettes and “any nicotine-containing products” as appropriate. Change in Intention to Quit Smoking and All Tobacco were assessed within Adult Smokers with the Intention to Quit CC. Risk Perception was assessed for THS 2.2 and the comparators CC, E-cigarettes, NRTs and Cessation. The study was conducted solely in the United States.</p>													
<p>Number of Subjects (Planned and Analyzed):</p> <table><tr><td>Invited:</td><td>3,003 subjects</td></tr><tr><td>Screened:</td><td>2,655 subjects</td></tr><tr><td>Full Sample planned:</td><td>2,320 subjects</td></tr><tr><td>Full Sample actual:</td><td>2,255 subjects</td></tr><tr><td>Main Sample:</td><td>1,892 subjects</td></tr><tr><td>LA-25 Adult Never Smokers Sample:</td><td>478 subjects (including 115 Adult Never Smokers from the Main Sample)</td></tr></table>		Invited:	3,003 subjects	Screened:	2,655 subjects	Full Sample planned:	2,320 subjects	Full Sample actual:	2,255 subjects	Main Sample:	1,892 subjects	LA-25 Adult Never Smokers Sample:	478 subjects (including 115 Adult Never Smokers from the Main Sample)
Invited:	3,003 subjects												
Screened:	2,655 subjects												
Full Sample planned:	2,320 subjects												
Full Sample actual:	2,255 subjects												
Main Sample:	1,892 subjects												
LA-25 Adult Never Smokers Sample:	478 subjects (including 115 Adult Never Smokers from the Main Sample)												
<p>Inclusion Criteria:</p> <ul style="list-style-type: none">• Aged 18 years and above, or above state legal smoking age (age to be verified with photo ID)• Currently living in the United States• Signed Informed Consent Form (ICF)• Ability to understand written and spoken English• Ability to comply with study procedures in the judgment of the researcher <p>Exclusion Criteria:</p> <ul style="list-style-type: none">• Employed in the fields of market research, marketing, advertising, media or journalism, law, the tobacco industry, or the health sector• Participation in a consumer or clinical study in the past three months• Subject started smoking CC within the last 30 days• Subject quit CC less than 30 days ago• Subject did not fall into any of the smoking status groups (e.g. if a subject quit CC less than 30 days ago, or started smoking CC within the last 30 days)													
<p>Statistical Methods: Data analysis was descriptive in nature. Categorical outcome measures were described by presenting the number and proportion of subjects endorsing each questionnaire category. Continuous outcome measures were described by presenting the mean, standard deviation, median, minimum and maximum. In addition, unadjusted 95% confidence intervals were calculated as interval estimates for the outcome variables.</p>													
<p>Summary of the Results:</p> <p><i>Demographics and Subject Characteristics</i> Demographics and subject characteristics for the Main Sample were similar for the five study Arms. The mean age for the subjects allocated to the five study Arms ranged from 42.5 (SD: 14.52, 14.15) years of age for Arms 2 and 4, respectively, to 43.1 (SD: 14.33) years of age for Arm 5. For each of the five Arms most subjects categorized themselves as white (ranging from 70.2% for Arm 1 to 76.3% for Arms 2 and 3, respectively) and had at least a high school degree (ranging from 95.0% for Arm 4 to 97.1% for Arm 3). In the LA-25 Adult Never Smokers Sample, the mean age ranged from 21.2 (SD:</p>													

Confidentiality Statement

Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the provisions of applicable law. No part of this document may be publicly disclosed without the written consent of Philip Morris International Management S.A.

2.19) years of age in Arm 2 to 21.9 (SD: 2.20) years of age in Arm 1. Apart from age, the demographics and subject characteristics of the LA-25 Adult Never Smokers Sample were broadly consistent with the Main Sample.

THS 2.2 Brochure (Arms 1 and 2)

For the THS 2.2 Brochure (Arms 1 and 2) Intent to Use THS 2.2 was substantial within Adult Smokers with No Intention to Quit CC (positive Intention to Use THS 2.2 was 34.4% for Arm 1 and 38.9% for Arm 2^a) and was also substantial within Adult Smokers with the Intention to Quit CC (positive Intention to Use THS 2.2 was 34.0% for Arm 1 and 23.2% for Arm 2). Intent to Use THS 2.2 was low within Adult Former Smokers (positive Intention to Use THS 2.2 was 6.4% for Arm 1 and 4.3% for Arm 2), Adult Never Smokers (positive Intention to Use THS 2.2 was 0.0% for Arm 1 and 1.1% for Arm 2), and LA-25 Adult Never Smokers (positive Intention to Use THS 2.2 was 0.0% for Arm 1 and 0.0% for Arm 2). Within Adult Former Smokers, Adult Never Smokers and LA-25 Adult Never Smokers, Intent to Use THS 2.2 was of a similar level to Intent to Use any nicotine-containing products, CC and E-cigarettes. Intent to Use THS 2.2 was similar comparing the THS 2.2 Brochure with the Surgeon General's warnings (Arm 1) and the PMI Important Warning (Arm 2).

Within Adult Smokers with the Intention to Quit CC, there were low levels of Change in Intention to Quit (both Smoking and All Tobacco) following exposure to the THS 2.2 Brochure (Change in Intention to Quit Smoking and All Tobacco were respectively 5.3% and 7.4% for Arm 1, 11.6% and 11.6% for Arm 2^b). Levels of Change in Intention to Quit were similar comparing the THS 2.2 Brochure with the Surgeon General's warnings (Arm 1) and the PMI Important Warning (Arm 2).

For the THS 2.2 Brochure, comprehension (within the Main Sample) that the risk of tobacco-related diseases can be reduced by completely switching from CC to THS 2.2 was 62.5% for Arm 1 and 69.1% for Arm 2. Comprehension (within the Main Sample) that with THS 2.2 exposure to harmful and potentially harmful constituents (HPHCs) is significantly reduced was 61.7% for Arm 1 and 54.4% for Arm 2. Comprehension level for specific sections of the THS 2.2 Brochure was consistently high for both Arms 1 and 2 ($\geq 85\%$). Overall, the comprehension levels on risk of tobacco-related diseases within the LA-25 Adult Never Smokers were comparable with those observed in the Main Sample.

For both Arms 1 and 2, and within all smoking status groups, CC was consistently rated as having the highest mean Perceived Health Risk. For Adult Smokers with No Intention to Quit CC, Adult Smokers with the Intention to Quit CC and Adult Former Smokers, THS 2.2 was consistently rated as an "intermediate" mean Perceived Health Risk, in that it was associated with mean Perceived Health Risk ratings below those of the highest object (CC) and above the lowest object (consistently either NRTs or Cessation). Similarly, for Arms 1 and 2, within Adult Smokers with No Intention to Quit CC and Adult Smokers with the Intention to Quit CC, THS 2.2 was rated on Perceived Addiction Risk between the highest risk comparator (consistently CC) and the lowest comparator (NRTs or Cessation).

HeatSticks™ Pack (Arms 3 and 4)

For the HeatSticks™ Pack (both Arms 3 and 4) Intent to Use THS 2.2 was substantial within Adult Smokers with No Intention to Quit CC (positive Intention to Use THS 2.2 was 32.3% for Arm 3 and 28.4% for Arm 4) and was also substantial within Adult Smokers with the Intention to Quit CC (positive Intention to Use THS 2.2 was 24.7% for Arm 3 and 33.3% for Arm 4). Intent to Use THS 2.2 was low within Adult Former Smokers (positive Intention to Use THS 2.2 was 3.2% for Arm 3 and 2.1% for Arm 4), Adult Never Smokers (positive Intention to Use THS 2.2 was 0.0% for Arm 3 and 0.0% for Arm 4), and LA-25 Adult Never Smokers (positive Intention to Use THS 2.2 was 0.0% for

^a "Positive Intention to Use" was operationalized as the proportions of subjects indicating that they would either "Very likely" or "Definitely" use THS 2.2.

^b All Changes in Intention to Quit (for all Arms) were reductions from baseline.

Confidentiality Statement

Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the provisions of applicable law. No part of this document may be publicly disclosed without the written consent of Philip Morris International Management S.A.

Arm 3 and 0.0% for Arm 4). Within Adult Former Smokers, Adult Never Smokers and LA-25 Adult Never Smokers, Intent to Use THS 2.2 was of a similar level to Intent to Use any nicotine-containing products, CC and E-cigarettes. The overall pattern of Intent to Use THS 2.2 was similar comparing the HeatSticks™ Pack with the Surgeon General's warnings (Arm 3) and the PMI Important Warning (Arm 4).

Within Adult Smokers with the Intention to Quit CC, there were low levels of Change in Intention to Quit (both Smoking and All Tobacco) following exposure to the HeatSticks™ Pack (Change in Intention to Quit Smoking and All Tobacco were respectively 4.3% and 1.1% for Arm 3, and 8.3% and 2.1% for Arm 4). Levels of Change in Intention to Quit were similar comparing the HeatSticks™ Pack with the Surgeon General's warnings (Arm 3) and the PMI Important Warning (Arm 4).

For the HeatSticks™ Pack, comprehension (within the Main Sample) that the risk of tobacco-related diseases can be reduced by completely switching from CC to THS 2.2 was 74.4% for Arm 3 and 77.8% for Arm 4. Comprehension (within the Main Sample) that with THS 2.2 exposure to HPHCs is significantly reduced was 61.9% for Arm 3 and 63.3% for Arm 4. Comprehension level for specific sections was consistently high for both Arms 3 and 4 (>83%).

The overall pattern of Perceived Health Risk for Arms 3 and 4 was consistent with that for the THS 2.2 Brochure. Within all smoking status groups, CC was consistently rated as having the highest Health Risk. Also, for Adult Smokers with the Intention to Quit CC, Adult Smokers with No Intention to Quit CC and Adult Former Smokers THS 2.2 was consistently rated as an "intermediate" mean Perceived Health Risk, in that it was associated with mean Perceived Health Risk ratings between the highest object (CC) and the lowest object (consistently NRTs or Cessation). For both Arms 3 and 4, within all smoking status groups, mean Perceived Addiction Risk ratings for THS 2.2 were below those for CC.

THS 2.2 Direct Mail (Arm 5)

For the THS 2.2 Direct Mail Intent to Use THS 2.2 was substantial within Adult Smokers with No Intention to Quit CC (positive Intention to Use THS 2.2 was 29.5%) and was also substantial within Adult Smokers with the Intention to Quit CC (positive Intention to Use THS 2.2 was 25.5%). Intent to Use THS 2.2 was low within Adult Former Smokers (positive Intention to Use THS 2.2 was 3.1%), Adult Never Smokers (positive Intention to Use THS 2.2 was 1.0%), and LA-25 Adult Never Smokers (positive Intention to Use THS 2.2 was 0.0%). Within Adult Former Smokers, Adult Never Smokers and LA-25 Adult Never Smokers, Intent to Use THS 2.2 was of a similar level to Intent to Use any nicotine-containing products, CC and E-cigarettes.

Within Adult Smokers with the Intention to Quit CC, there were low levels of Change in Intention to Quit (both Smoking and All Tobacco) following exposure to the THS 2.2 Direct Mail (Change in Intention to Quit Smoking and All Tobacco were respectively 5.3% and 3.2%).

For the THS 2.2 Direct Mail, comprehension (within the Main Sample) that the risk of tobacco-related diseases can be reduced by completely switching from CC to THS 2.2 was 63.8%. Comprehension that with THS 2.2 exposure to HPHCs is significantly reduced was 49.1%. Comprehension level for specific sections was consistently high (≥86%).

The overall pattern of Perceived Health Risk for the THS 2.2 Direct Mail was broadly consistent with that for the THS 2.2 Brochure and HeatSticks™ Pack. Within all smoking status groups, CC was consistently rated as having the highest Health Risk. Also, for smokers (Adult Smokers with No Intention to Quit CC and Adult Smokers with the Intention to Quit CC) and Adult Former Smokers THS 2.2 was consistently rated as having mean Perceived Health Risk ratings below the highest object (CC) and above the lowest object (consistently NRTs). Similarly, within Adult Smokers with No Intention to Quit CC and Adult Smokers with the Intention to Quit CC, THS 2.2 was rated on Perceived Addiction Risk between the highest risk comparator (consistently CC) and the lowest comparator (NRTs or Cessation).

Confidentiality Statement

Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the provisions of applicable law. No part of this document may be publicly disclosed without the written consent of Philip Morris International Management S.A.

CONCLUSIONS AND RECOMMENDATIONS

The different instances of THS 2.2 label, labeling and marketing material tested in the current study (1. the THS 2.2 Brochure, 2. the HeatSticks™ Pack and 3. the THS 2.2 Direct Mail) were associated with the following:

1. Substantial levels of Intent to Use THS 2.2 within the intended section of the population, i.e. Adult Smokers with No Intention to Quit CC (positive Intention to Use THS 2.2 was between 28.4% and 38.9% across all Arms).
2. Low levels of Intent to Use THS 2.2 within Adult Former Smokers and Adult Never Smokers (across all Arms, positive Intention to Use THS 2.2 was $\leq 6\%$ for Adult Former Smokers, $\leq 2\%$ for Adult Never Smokers and $\leq 1\%$ for LA 25 Adult Never Smokers).
3. Substantial levels of Intent to Use THS 2.2 within Adult Smokers with the Intention to Quit CC (positive Intention to Use THS 2.2 was between 23.2% and 34.0% across all Arms). To some degree, these levels of Intent to Use THS 2.2 may represent an interest in using THS 2.2 as a temporary measure to aid quitting all tobacco. This was indicated by low levels of Change in Intention to Quit (both Smoking and All Tobacco) (Change in Intention to Quit was between 4.3% and 11.6%, across all Arms).
4. Intermediate levels of comprehension ($\geq 63\%$) that completely switching from CC to THS 2.2 can involve a reduction in risk of tobacco-related diseases, and a only small proportion of subjects ($< 6\%$ across all Arms) indicating that THS 2.2 is risk free.
5. Within Adult Smokers with No Intention to Quit CC, Adult Smokers with the Intention to Quit CC, and Adult Former Smokers, Perceived Health Risk for THS 2.2 was consistently below CC and higher than NRTs and Cessation.
6. Within Adult Smokers with No Intention to Quit CC and Adult Smokers with the Intention to Quit CC level of Perceived Addiction Risk for the THS 2.2 was below that of CC and higher than that of NRTs and/or Cessation.
7. No substantial differences between LA-25 Adult Never Smokers and Adult Never Smokers in general for Intent to Use and Perceived Health Risk for any study Arm.

Overall, the results of this study suggest that the THS 2.2 Brochure, the HeatSticks™ Pack and the THS 2.2 Direct Mail are all suitable to be used in marketing the THS 2.2 in the US.

Final Report Date: 24 May 2016

Prepared in: Microsoft Word 2013

Confidentiality Statement

Data and information contained in this document are considered to constitute trade secrets and confidential commercial information, and the legal protections provided to such trade secrets and confidential information are hereby claimed under the provisions of applicable law. No part of this document may be publicly disclosed without the written consent of Philip Morris International Management S.A.