TABLE OF CONTENTS

6.3.1 Summary of Intent to Use THS Assessment among Tobacco Non-Users 4
6.3.1.1 Background and Overview 4
6.3.1.2 Overall Approach.....6
6.3.1.2.1 Types of Studies.....6
6.3.1.2.2 Study Population 8
6.3.1.3 Development Phase 9
6.3.1.3.1 THS-PBA-02-US Study.....9
6.3.1.3.2 THS-PBA-03-US Study.....14
6.3.1.3.3 THS-PBA-04-US Study.....18
6.3.1.3.4 Conclusions across Developmental Studies.....20
6.3.1.4 Assessment Phase 20
6.3.1.4.1 THS-PBA-05-RRC-US Study.....23
6.3.1.4.2 THS-PBA-05-RRC2-US Study.....28
6.3.1.4.3 THS-PBA-05-REC-US Study.....32
6.3.1.4.4 Conclusions across Assessment Studies 35
6.3.1.5 References.....45

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

TABLE OF TABLES

Table 1 Overview of the Studies 5
Table 2 Measurement of Intent to Use THS in Quantitative PBA Studies 8
Table 3 Methodology of THS-PBA-02-US 10
Table 4 THS Messages tested in THS-PBA-02-US Study 13
Table 5 Methodology of THS-PBA-03-US 14
Table 6 Different Combinations of Evidence Statements and Warnings Tested in THS-PBA-03-US 15
Table 7 Proportion of Subjects with Positive Intention to Try and Intention to Use THS 2.2 in THS-PBA-03-US 17
Table 8 Methodology of THS-PBA-04-US 18
Table 9 Modified Risk Claims assessed in THS-PBA-04-US 19
Table 10 THS Communication Materials, Warning Type and Study Arms 22
Table 11 Measures of Intent to Use in the Assessment Phase 23
Table 12 Methodology of THS-PBA-05-RRC-US 24
Table 13 Proportion of Subjects with Positive Intention to Try THS and Comparators in THS-PBA-05-RRC-US 26
Table 14 Proportion of Subjects with Positive Intention to Use THS and Comparators in THS-PBA-05-RRC-US 27
Table 15 Methodology of THS-PBA-05-RRC2-US 28
Table 16 Proportion of Subjects with Positive Intention to Try THS and Comparators in THS-PBA-05-RRC2-US 30
Table 17 Proportion of Subjects with Positive Intention to Use THS and Comparators in THS-PBA-05-RRC2-US 31
Table 18 Methodology of THS-PBA-05-REC-US 32
Table 19 Proportion of Subjects with Positive Intention to Try THS and Comparators in THS-PBA-05-REC-US 34
Table 20 Proportion of Subjects with Positive Intention to Use THS and Comparators in THS-PBA-05-REC-US 35
Table 21 Positive Intention to Try among Adult Former Smokers and Adult Never Smokers following Exposure to THS Brochure by Study, Assessment Phase 39
Table 22 Positive Intention to Use among Adult Former Smokers and Adult Never Smokers following exposure to THS Brochure by Study, Assessment Phase 40

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 23 Positive Intention to Try among Adult Former Smokers and Adult Never Smokers exposed to Tobacco Sticks Pack by Study, Assessment Phase ... 41
Table 24 Positive Intention to Use among Adult Former Smokers and Adult Never Smokers exposed to Tobacco Sticks Pack by Study, Assessment Phase ... 42
Table 25 Positive Intention to Try among Adult Former Smokers and Adult Never Smokers exposed to THS Direct Mail by Study, Assessment Phase 43
Table 26 Positive Intention to Use among Adult Former Smokers and Adult Never Smokers exposed to THS Direct Mail by Study, Assessment Phase 44

TABLE OF FIGURES

Figure 1 Visual Aid for Intent to Use 6
Figure 2 Example of a THS Potential Product Message 11
Figure 3 Reduced Risk Claim (RRC) and associated Warning 21
Figure 4 Reduced Risk Claim 2 (RRC2) and associated Warning 21
Figure 5 Reduced Exposure Claim (REC) and associated Warning 21

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

6.3.1 Intent to Use among Tobacco Non-Users

6.3.1.1 Background and Overview

As stated in the MRTP Draft Guidance: "*A critical population health consideration under section 911(g)(1)(B) and 911(g)(2)(B)(iv) of the FD&C Act is the effect that an MRTP and its marketing will have on tobacco use initiation among non-users (both never users and former users). An MRTPA must contain scientific evidence regarding the effect the product and its marketing will have on increasing the likelihood that persons who do not use tobacco products will start using the tobacco product that is the subject of the application*" (lines 762-767) (FDA (Food and Drug Administration) 2012). In a pre-market setting, the effect of THS on initiation among non-users cannot be assessed. For that reason, behavioral intention, a person's perceived likelihood or "subjective probability that he or she will engage in a given behavior", is an appropriate proxy to best predict the behavior of using an MRTP (Fishbein 1975, Harakeh 2004, Pierce 1998). Furthermore, as per FDA recommendations, evaluation of how an MRTP labeling and advertising relate to likelihood to use the product ("Intent to Use") is an important consideration, particularly with regards to youth and young adults (lines 773-780) (FDA (Food and Drug Administration) 2012).

This section of the application summarizes the scientific evidence collected on the effect of *THS labeling and advertising* ("THS communication") on *Intent to Use* THS among adult non-users of CC, including both adult never smokers and adult former smokers.

PMI has designed a research program to study consumer perception and behavior, the Perception and Behavior Assessment (PBA) program (Section 2.7), that responds to FDA's recommendations as outlined in the MRTP Draft Guidance (FDA (Food and Drug Administration) 2012). One of the objectives of this program was to develop communications for THS that generate substantial interest in the intended consumer group, i.e. adult smokers with no intention to quit smoking, while generating low *Intent to Use* among those for whom THS is not intended, such as adult never smokers and adult former smokers. Results summarized in Section 6.2.2 demonstrate that THS communication generates high intention to use THS among current adult smokers.

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 1 Overview of the Studies

Study Name	Study Type	Cities	Study Period	Study Population	Age of Participants	THS Communications
THS-PBA-02-US	Qualitative	Boston, MA Chicago, IL Charlotte, NC Phoenix, AZ	Oct-Dec 2013	S-NITQ, S-ITQ, FS, NS[a]	21+	9 potential 'plain text' [b] messages
THS-PBA-03-US	Quantitative	Chicago, IL Marlton, NJ Phoenix, AZ Atlanta, GA	Oct-Dec 2014	S-NITQ, S-ITQ, FS, NS	LA+	3 potential 'plain text'[b] messages selected from THS-PBA-02-US
THS-PBA-04-US	Qualitative	Chicago, IL Phoenix, AZ	Dec 2014	AS, FS, NS	18+	5 potential branded[c] communication materials with claims selected from THS-PBA-02-US
THS-PBA-05-RRC-US	Quantitative	Paramus, NJ Dallas, TX St Louis, MO Los Angeles, CA	Jul 2015	S-NITQ, S-ITQ, FS, NS	LA+	3 branded[c] communication materials with claim #1 "Reduced risks of tobacco-related disease"
THS-PBA-05-RRC2-US	Quantitative	Marlton, NJ Chicago, IL Tampa, FL Denver, CO	Sep 2015	S-NITQ, S-ITQ, FS, NS	LA+	3 branded[c] communication materials with the claim #2 – "Reduced risk of harm"
THS-PBA-05-REC-US	Quantitative	Framingham, MA San Diego, CA St Louis, MO Baltimore, MD	Dec 2015	S-NITQ, S-ITQ, FS, NS	LA+	3 branded[c] communication materials with the claim #3 "Reduced body's exposure to harmful and potentially harmful chemicals"

Abbreviations.: AS = Adult Smokers; CC = Conventional Cigarettes; FS = Adult Former Smokers; HPHC = Harmful and Potentially Harmful Constituent; IDI = Individual Interviews; LA = Legal Smoking Age; NS = Adult Never Smokers; S-ITQ = Adult Smokers with the Intention to Quit; S-NITQ = Adult Smokers with No Intention to Quit;
[a] Adult Never Smokers participated only in Phase 2 of THS-PBA-02-US
[b] 'plain text' message describes the information communicated on the product
[c] The branded communication materials are THS label, labeling and marketing material. THS device was presented with *iQOS* commercial name and the Tobacco Sticks as *HeatSticks* with the *Marlboro* Brand.

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

6.3.1.2 Overall Approach

As summarized in Table 1, a total of 6 PBA studies were completed to develop and assess THS communication. These studies included qualitative and quantitative studies of either of 2 phases:

1. **Development phase**: 2 qualitative studies ([THS-PBA-02-US] and [THS-PBA-04-US]) and 1 quantitative study [THS-PBA-03-US]) to inform the development of the most appropriate *product communication*, as per the recommendations of the MRTP Draft Guidance (FDA (Food and Drug Administration) 2012) and IOM report (IOM (Institute of Medicine) 2012).
2. **Assessment phase**: 3 quantitative studies ([THS-PBA-05-RRC-US], [THS-PBA-05-RRC2-US] and [THS-PBA-05-REC-US]) to assess the appropriateness of proposed THS labels, labeling and advertising submitted in this application.

In these 6 studies, in addition to *Intent to Use* assessment, *Comprehension and Risk Perception* (discussed in detail in Section 6.4.1), as well as *Change in Intention to Quit Smoking* among adult smokers (discussed in detail in Section 6.2.2) were systematically assessed. Within each of the phases, the studies were conducted in a sequential manner (starting from [THS-PBA-02-US], followed by [THS-PBA-03-US] and [THS-PBA-04-US] for the development phase and starting from [THS-PBA-05-RRC-US] followed by [THS-PBA-05-RRC2-US] and finally [THS-PBA-05-REC-US] for the assessment phase) in order to leverage from the overall findings of one study to design the next one.

6.3.1.2.1 Types of Studies

6.3.1.2.1.1 Qualitative Studies

As recommended by the IOM in its report (IOM (Institute of Medicine) 2012), qualitative studies are particularly useful to perform formative and exploratory work in a developmental phase. Those studies were helpful to generate a broad understanding of various subpopulation reactions to different types of communication or variations of similar concepts.

Focus group discussions (FGDs) and individual interviews (IDIs) were used in [THS-PBA-02-US], while only IDIs were used in [THS-PBA-04-US]. In these qualitative studies, visual aids (in the form of lines anchored with 6 levels of intention to use) were used as the basis for discussion to allow participants to visually "rank" the potential messages or communication materials they were exposed to in terms of *Intent to Use* (Figure 1).

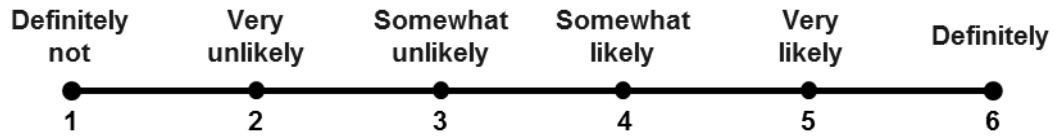


Figure 1 Visual Aid for Intent to Use

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

6.3.1.2.1.2 Quantitative Studies

The quantitative studies, [THS-PBA-03-US] in the development phase and [THS-PBA-05-RRC-US], [THS-PBA-05-RRC2-US], [THS-PBA-05-REC-US] in the assessment phase, were conducted in large samples of subjects using a 5-arm parallel-group research design to quantify *Intent to Use* THS. The 5 arms corresponded to 5 different *THS "plain text" Messages* (i.e., information communicated on the product) for [THS-PBA-03-US], and to 5 instances of *THS branded communication materials* (i.e., THS Brochure, Tobacco Sticks Pack, THS Direct Mail) for [THS-PBA-05-RRC-US], [THS-PBA-05-RRC2-US], [THS-PBA-05-REC-US]. In these studies, subjects were first exposed to an instance of *THS communication* and then presented with a battery of assessments administered in a fixed order using computer-assisted self-interview (CASI) methodology, to ensure consistency in the presentations of questions across interviews.

Intent to Use Assessment

Measure of *Intent to Use* following exposure to product information is a well-accepted proxy to assess the extent to which consumers may adopt a tobacco product (Shiffman 2004), (Parascandola 2008), no questionnaire has been identified as a standard and validated measure of *Intent to Use* in both current tobacco users and non-users. Acknowledging the lack of robust and validated measurement instruments, PMI has undertaken, as part of the PBA program, the development of new self-reported instruments based on best practices guidelines, including the current FDA guidance for patient-reported outcomes (PROs) in clinical trials (FDA (Food and Drug Administration) 2009). This project led to the development of the *Intent to Use Questionnaire* (ITUQ), comprised of two sets of single items assessing: (i) the intention to try (at least once) and (ii) intention to use (on a regular basis). The generation of items for ITUQ was based on the interpretation of the FDA draft guidance on MRTPs (FDA (Food and Drug Administration) 2012) and the IOM report ((IOM 2012)) complemented with the input from consumer focus groups and expert opinions. A *Research Summary Document* describing key methodologies and outcomes underlying the development of the Intent to Use Questionnaire (ITUQ) is presented in Appendix [A732 PBA01Sum]. Two sets of items from the ITUQ were used in quantitative PBA studies (i.e., [THS-PBA-03-US], [THS-PBA-05-RRC-US], [THS-PBA-05-RRC2-US] and THS-PBA-5-REC-US), yielding descriptive measures of: (i) Intention to Try (i.e., at least once) and (ii) Intention to Use (i.e., on a regular basis) (Table 2).

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 2 Measurement of Intent to Use THS in Quantitative PBA Studies

Items	Response Scale
Intention to Try items: How likely or unlikely are you… 1. to try THS 2. to try THS if one of your best friends were to offer THS to you **Intention to Use items**: 3. If you try THS and like it, how likely or unlikely are you to use THS regularly 4. If you try THS and like it, how soon would you being to use THS regularly	**For Items 1, 2 and 3:** 6-point Likert-like scale (1=definitely not, 2=very unlikely, 3= somewhat unlikely, 4=somewhat likely, 5=very likely, 6=definitely) **For item 4:** 6 ordinal timeframe response categories (1=within a week, 2=within a month, 3=within 3 months, 4=within 6 months, 5=more than 6 months, 6=never).

6.3.1.2.2 Study Population

The target population for the PBA studies was adults living in the United States. The sampling frame consisted of adults living in strategically selected areas forming a geographically diverse sample, such that the cities selected for sampling were within the 4 regions defined by the United States Census Bureau (Table 1). Subjects participating in PBA studies were recruited via telephone by independent vendors using a proprietary database.

Main Sample

In addition to adult smokers (see Section 6.2.2), the main study samples included adult never CC smokers and adult former CC smokers, defined in accordance with guidelines established by the World Health Organization (WHO (World Health Organization) 1998) based on subject's self-report of tobacco use:

- **Adult Never Smokers:** Adults having either never smoked at all, or never having been daily smokers and having smoked less than 100 CC.
- **Adult Former Smokers**: Adults having formerly been daily smokers (i.e., having smoked at least 100 CC) and, at the time of study, having quit smoking CC more than 30 days ago. In addition, in all quantitative studies, to ensure a sufficient number of long-term quitters , a minimum quota of subjects who have quit smoking over at least a total of twelve months ("long-term quitters") was used (approximately 30%).

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Oversample of Young Adults Never Smokers

In all quantitative studies (i.e., [THS-PBA-03-US], [THS-PBA-05-RRC-US], [THS-PBA-05-RRC2-US] and [THS-PBA-05-REC-US]), an oversampling of young Adult Never Smokers was recruited to approximate the same number of participants from each smoking group in the Main Sample. This intentional oversampling of young adults allows PMI to adequately describe responses within this younger group and infer the understanding and perception of the product messages and marketing materials in non-adults (PMI internal policy prohibits the conducting of studies relating to tobacco products involving minors). This is in line with the recommendations from the FDA, as stated in its preliminary responses to PMI meeting request STN: TC0000737 sent on September 3, 2013: "*FDA does not believe that it is necessary for applicants to conduct research with non-adult populations. However, FDA recommends that applicants provide information about the likely impact that marketing a product as modified risk may have on non-adults and their tobacco use behavior. This information may be inferred from studies with other similar populations, such as young adults.*" (P.004).

- **Legal Smoking Age to 25 years of age (LA-25) Never Smokers:** Young adults between legal smoking age and 25 years of age, who, having either never smoked at all, or never having been daily smokers and having smoked less than 100 CC.

6.3.1.3 Development Phase

This section reports only the main results on *Intent to Use* assessment among *adult non-users of tobacco* (i.e., former CC smokers and never CC smokers). More detail on the individual study results, including *Intent to Use* among adult current CC smokers (Section 6.2.2), *Comprehension, Risk Perception* (Section 6.4.1), as well as *Change in Intention to Quit Smoking* within adult smokers (Section 6.2.2) can be found in Section 7.3.2.

6.3.1.3.1 THS-PBA-02-US Study

The purpose of this study was to contribute to the development of *THS potential product Messages* by exploring how each element of different messages contributes to the *Comprehension* of the modified risk information, *Intent to Use* THS, and *Risk Perception* of THS compared to other tobacco and nicotine-containing products, and to the intention to quit tobacco use.

Methodology

A brief description of the study methods is provided in Table 3.

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 3 Methodology of THS-PBA-02-US

Study Title: Qualitative Study to Develop THS 2.2 Hypothetical Product Messages
Study Design: 4-cities, 2-phase, sequential, qualitative study. Phase 1 'Product Message Development' consisted of 1 pilot focus group discussion (FGD) and 20 FGDs, where participants shared their opinions and reactions to a variety of discussion topics in an interactive group setting to contribute to the development and refinement of the THS product messages. Phase 2 'Product Message Understanding' consisted of 1 pilot individual interview (IDI) and 37 IDIs conducted to collect detailed perceptions, opinions, beliefs, and attitudes of participants as well as of evaluating the clarity of the revised product messages resulting from Phase 1.
Subjects: Enrolled: 123 in FGDs and 38 in IDIs; Full analysis population (FAP): 117 in FDGs and 37 in IDIs; Number of adult smokers in the FAP: 93 in FGDs and 25 in IDIs; Number of adult former smokers in the FAP: 24 in FDGs and 6 IDIs; Number of adult never smokers in the FAP: 6 (IDIs).
Main Criteria for Inclusion: • Aged 21 or older • Adult Smokers with no Intention to Quit CC: currently smoking at least 1 CC/day, started more than 30 days ago with no intention to quit within 6 months; Adult Smokers with Intention to Quit CC: currently smoking at least 1 CC/day, started more than 30 days ago with the intention to quit within 6 months ; Adult Former Smokers: quit smoking CC more than 30 days ago; Adult Never Smokers (Phase 2 only): never smoked or never smoked daily and less than 100 CC
Methods: Moderators (5+ years of experience) conducted the FGDs and IDIs. A discussion guide was employed in each FGD and IDI in order to elicit participant feedback in a consistent manner across the various FGDs and IDIs.
Criteria of Evaluation: Verbal data, transcribed from the FGDs and IDIs, were examined for each potential product message in general, and by smoking status in particular, to identify the extent of endorsement.

The structure of the messages was identical across all messages and composed of information concerning THS features, risks, claims and intended users. The elements in the left panel included the "**Information section**" and the "**Intended Users Statement"**, which were constant across all the potential product messages tested. The elements in the right panel included the "**Evidence Statement"** and "**Important Warning"** and varied depending on the type of modified risk claim. An example is given in Figure 2.

Different formulations of messages were tested, varying the level of specificity of the claim (general *vs.* specific), type of claim (reduced exposure *vs.* reduced risk), and format (with or without a graph; important warning as a separate box or as part of the message). A summary of the modified risk claims assessed in [THS-PBA-02-US] are shown in Table 4 for Phase 1 and Phase 2.

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

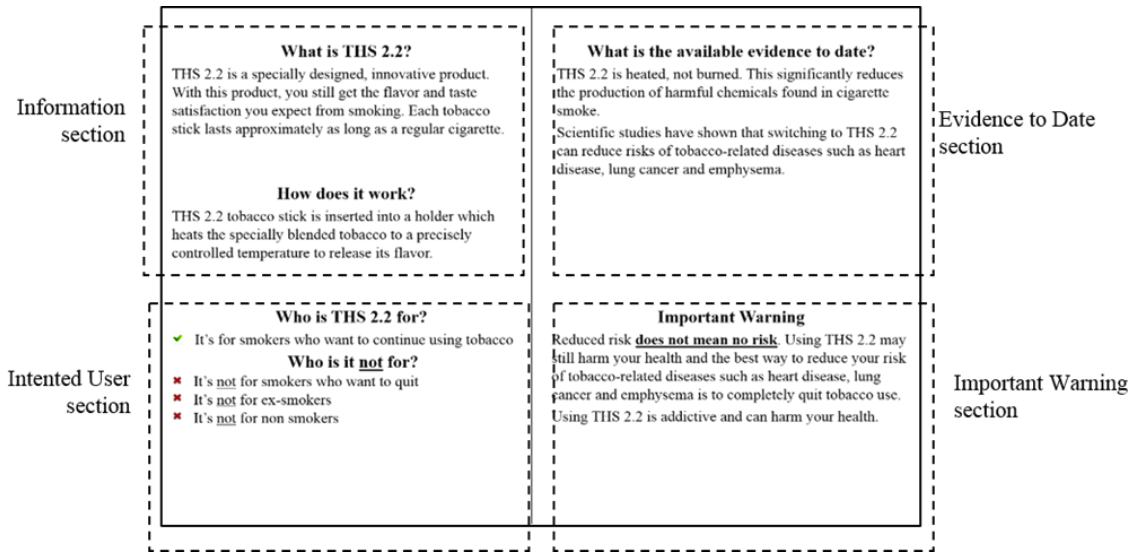


Figure 2 Example of a THS Potential Product Message

Results[1]

Based on the THS product description, and regardless of the type of claim presented in the product message, adult former smokers and adult never smokers clearly stated that they were definitely not interested in trying the product. Three key elements of the product message seemed particularly efficient to deter adult non-smokers from using THS:

(i) **Information section:** clear statement that THS contains tobacco.

> *"I am not saying that cigarettes are the cause of all bad health, a lot of things cause that problem. I just thought that it (quitting) works for me and I wouldn't do anything else to put in my mouth, to bring vapor or smoke in it after all I have gone through. This is tobacco and I don't want to have nothing to do with tobacco again."* (Former adult smoker, male, 51+, Phoenix)

(ii) **Important Warning Section:** clear statement on the risk of addiction and harm for the health.

> *"This one states that THS 2.2 does not produce smoke, or second hand smoke. But they have not demonstrated that it reduces the risk of tobacco related diseases. The fact that it can have risk of diseases is not something that I would be interested in."* (Adult never smoker female 36-50, Phoenix P2)

(iii) **Intended Users Section:** clear statement that non-smokers should not use THS, as it is only intended for smokers who want to continue using tobacco.

[1] Verbatims are shown for illustrative purposes.

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Overall, these qualitative findings indicate that adult former smokers and adult never smokers were not interested in the product proposition because THS contained tobacco, THS contains nicotine which is addictive and THS was not intended for them. These findings were used to craft the potential messages tested in the next study, [THS-PBA-03-US].

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 4 THS Messages tested in THS-PBA-02-US Study

	Specific Potential Claims	General Potential Claims
Phase 1		
Reduced Exposure	**A**. With THS 2.2, the production of carbon monoxide is reduced by more than 95%	**C**. Switching to THS 2.2 significantly reduces your body's exposure to many harmful chemicals found in cigarette smoke which are identified as likely causes of smoking-related diseases
	B. THS 2.2 produces at least 90% less second-hand smoke than CCs	**D**. THS 2.2 significantly reduces the production of harmful chemicals found in cigarette smoke
Reduced Risk	**E**. Switching to THS 2.2 can lower your cardiovascular disease risks	**H**. Switching to THS 2.2 can lower several risk factors that could lead to smoking-related diseases
	F. Switching to THS 2.2 improves several biomarkers, which are seen as early indicators of emphysema	**J**. Switching to THS 2.2 can reduce risks of smoking-related diseases
	G. Switching to THS 2.2 can improve the level of good cholesterol and can reduce the risk of clogging of arteries due to smoking	
Phase 2		
Reduced Exposure	**B**. THS 2.2 produces an aerosol. Unlike conventional cigarettes, THS 2.2 does not produce smoke or second-and smoke.	**C**. Switching to THS 2.2 significantly reduces your body's exposure to many harmful chemicals found in cigarette smoke which are identified as likely causes of tobacco-related diseases
	L. THS 2.2 significantly reduces the production of harmful chemicals, such as carbon monoxide which is reduced by 95%, found in cigarette smoke	
Reduced Risk	**E**. Switching to THS 2.2 can lower your cardiovascular disease risks	**H**. Switching to THS 2.2 can lower several risk factors that could lead to tobacco-related diseases
	K. Switching to THS 2.2 can improve lung function	**J**. Switching to THS 2.2 can reduce risks of tobacco-related diseases

Data Source: [THS-PBA-02-US Study Report Appendix c]

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

6.3.1.3.2 THS-PBA-03-US Study

The overall aim of this study was to further inform the selection of appropriate Product Messages using quantitative assessment of 5 potential "plain text" THS messages in terms of *Intent to Use* THS, *Comprehension* of different communication objectives, *Risk Perception* of THS and the comparators CC, NRTs, E-cigarettes, and Cessation, as well as Change in Intention to Quit Smoking within Adult Smokers with no Intention to Quit CC.

Methodology

A brief description of the study methods is provided in Table 5.

Table 5 Methodology of THS-PBA-03-US

Study Title: Study to Quantitatively Assess THS 2.2 Potential Messages
Study design: 4-cities, 5-arm parallel-group experiment. The 5 arms corresponded to the 5 different THS messages, each of them being tested by approximately equal numbers of subjects from different smoking status groups.
Subjects: *Full Sample* for analysis: 1713; Number of Adult Smokers with no Intention to Quit CC included in the *Main Sample*: 359; Number of Adult Smokers with Intention to Quit CC included in the *Main Sample*: 355; Number of Adult Former Smokers included in the *Main Sample*: 358; Number of Adult Never Smokers included in the *Main Sample*: 362; Number of Adult Never Smokers from the legal age of smoking to 25 years of age (*LA-25 Adult Never Smokers*) included in the *Full Sample*: 358 (including 79 from the main sample).
Main criteria for inclusion: • Aged 18 and above, or above state legal smoking age if above 18 years • Adult Smokers with no Intention to Quit CC: currently smoking at least 1 CC/day, started more than 30 days ago with no intention to quit within 6 months; Adult Smokers with Intention to Quit CC: currently smoking at least 1 CC/day, started more than 30 days ago with the intention to quit within 6 months; Adult Former Smokers: quit smoking CC more than 30 days ago; Adult Never Smokers: never smoked or never smoked daily and less than 100 CC
Methods: <u>Intent to Use</u> 2 sets of items from the Intent to Use Questionnaire (ITUQ) yielded descriptive measures of: • Intention to Try (i.e., to sample at least once; 2 items) • Intention to Use (i.e., for continued usage; 2 items)
Criteria for Evaluation: Positive *Intention to Try* THS (operationalized as the sum of % "*Very Likely"* and % "*Definitely"* responses for each item of Intention to Try) and Positive *Intention to Use* THS (operationalized as the sum of % "*Very Likely"* and % "*Definitely"* responses for the first item of *Intention to Use*), by study arm and smoking status group.

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Five messages were tested through combinations of 3 claims (selected based on [THS-PBA-02-US] findings) and different warnings. A summary of the different combinations of modified risk claims and warnings assessed in [THS-PBA-03-US] are shown in Table 6.

Table 6 Different Combinations of Evidence Statements and Warnings Tested in THS-PBA-03-US

	Claim	Warning
Message 1 **Reduced Exposure**	With the exception of nicotine, with THS 2.2 there is a significant reduction in the production of harmful or potentially harmful chemicals	• **It <u>has not been demonstrated</u>** that switching to THS 2.2 reduces the risk of developing tobacco-related diseases compared to smoking cigarettes. • THS 2.2 tobacco sticks contain nicotine which is addictive. • Using THS 2.2 can harm your health.
Message 2 **Reduced Exposure**	With the exception of nicotine, with THS 2.2 there is a significant reduction in the production of harmful or potentially harmful chemicals	• A significant reduction in the production of harmful chemicals, compared to cigarettes, **<u>does not mean a reduction in the risk of developing tobacco-related diseases</u>.** • THS 2.2 tobacco sticks contain nicotine which is addictive. • Using THS 2.2 can harm your health.
Message 3 **Reduced Exposure**	Scientific studies have shown that switching completely from cigarettes to THS 2.2 significantly reduces your body's exposure to harmful or potentially harmful chemicals.	• **It <u>has not been demonstrated</u>** that switching to THS 2.2 reduces the risk of developing tobacco-related diseases compared to smoking cigarettes. • THS 2.2 tobacco sticks contain nicotine which is addictive. • Using THS 2.2 can harm your health.
Message 4 **Reduced Exposure**	Scientific studies have shown that switching completely from cigarettes to THS 2.2 significantly reduces your body's exposure to harmful or potentially harmful chemicals.	• A significant reduction in your body's exposure to harmful chemicals, compared to cigarettes, **<u>does not mean a reduction in the risk of developing tobacco-related diseases</u>.** • THS 2.2 tobacco sticks contain nicotine which is addictive. • Using THS 2.2 can harm your health.
Message 5 **Reduced Risk**	Scientific studies have shown that switching completely from cigarettes to THS 2.2 can reduce the risks of tobacco-related diseases.	• Reduced risk **<u>does not mean no risk</u>.** The best way to reduce your risk of tobacco-related diseases is to completely quit tobacco use. • THS 2.2 tobacco sticks contain nicotine which is addictive. • Using THS 2.2 can harm your health.

Data Source: [THS-PBA-03-US Study Report Appendix 16.1.1]

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

The general structure of THS Message was similar across the five messages, with the exception that Message 1 and 2 contained a graphical display of HPHCs reduction (see THS-PBA-03-US Study Report Appendix 16.1.1).

Results

Results of [THS-PBA-03-US] in terms of *Intent to Use* THS (Intention to try and Intention to Use) are summarized in Table 7. Among Adult Former Smokers, across all *THS Messages*, positive Intention to Try *THS* ranged from 0% to 4.2% and positive Intention to Use THS regularly from 4.1% to 15.7%. Very few Adult Never Smokers in the Main Sample expressed a *positive Intent to Use* THS (≤3% for each of the 5 THS Messages for both positive Intention to Try and positive Intention to Use). Similarly, level of *Intent to Use* THS was low among LA-25 Adult Never Smokers (≤6% for each of the 5 THS Messages for both positive Intention to Try and positive Intention to Use). Similar to the findings of the first qualitative study [THS-PBA-02-US], this quantitative study provides evidence that *Intent to Use* THS was overall minimal among both adult former and adult never smokers, regardless of the type of messages. Furthermore, the study results showed no evidence that LA-25 never smokers have different patterns of *Intent to Use* THS compared to adult never smokers in general.

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 7 Proportion of Subjects with Positive Intention to Try and Intention to Use THS 2.2 in THS-PBA-03-US

		Message				
	Statistics	**1**	**2**	**3**	**4**	**5**
Try THS 2.2						
FS	N	72	72	73	71	71
	n (%)	3 (4.2)	3 (4.2)	0	2 (2.8)	2 (2.9)
	95% CI	(0.9, 11.7)	(0.9, 11.7)	(0.0, 4.9)	(0.3, 9.8)	(0.3, 9.9)
NS	N	74	71	72	72	71
	n (%)	0	1 (1.4)	0	0	0
	95% CI	(0.0, 4.9)	(0.0, 7.6)	(0.0, 5.0)	(0.0, 5.0)	(0.0, 5.1)
LA-25 NS	N	75	75	72	67	69
	n (%)	0	1 (1.3)	0	0	2 (2.9)
	95% CI	(0.0, 4.8)	(0.0, 7.2)	(0.0, 5.0)	(0.0, 5.4)	(0.4, 10.1)
Use THS regularly 2.2						
FS	N	72	72	73	71	71
	n (%)	3 (4.2)	4 (5.6)	3 (4.1)	3 (4.2)	11 (15.7)
	95% CI	(0.9, 11.7)	(1.5, 13.6)	(0.9, 11.5)	(0.9, 11.9)	(8.1, 26.4)
NS	N	74	71	72	72	71
	n (%)	0	1 (1.4)	1 (1.4)	2 (2.8)	1 (1.4)
	95% CI	(0.0, 4.9)	(0.0, 7.6)	(0.0, 7.5)	(0.3, 9.7)	(0.0, 7.6)
LA-25 NS	N	75	75	72	67	69
	n (%)	1 (1.3)	1 (1.3)	1 (1.4)	0	4 (5.8)
	95% CI	(0.0, 7.2)	(0.0, 7.2)	(0.0, 7.5)	(0.0, 5.4)	(1.6, 14.2)

Abbreviations: CC = conventional cigarettes; CI = confidence interval; FS = Adult Former Smokers; LA= legal smoking age; NS=Adult Never Smokers; THS = Tobacco Heating System.
Note: Positive intention was operationalized as the proportion of subjects whose response to the single item assessing intention to try/use THS was either "*Very Likely"* or "*Definitely"*.
Note: the 95% confidence intervals are calculated using the exact Clopper-Pearson method.
Data Source: [THS-PBA-03-US Study Report Table 15.2.2.1]

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

6.3.1.3.3 THS-PBA-04-US Study

Building upon the insights gained in [THS-PBA-02-US] and [THS-PBA-03-US], the purpose of this qualitative study was to contribute to the development of THS potential label, labeling and marketing material. To this end, the study examined how each element of the materials contributes to the *Comprehension* of the modified risk information, *Intent to Use* THS, and *Risk Perception* of THS, compared to other tobacco and nicotine-containing products as well as to quitting tobacco use.

Methodology

A brief description of the study methods is provided in Table 8.

Table 8 Methodology of THS-PBA-04-US

Study Title: Qualitative Study to Develop THS 2.2 Potential Label, Labeling and Marketing Material
Study design: 2-cities qualitative study, which consisted of 30 IDIs (including 2 pilot IDIs), designed to capture participants' comments and responses when exposed to specific label, labeling and marketing material.
Subjects: Enrolled: 30; Full analysis population (FAP): 28; Number of adult smokers in the FAP: 20; Number of adult former smokers in the FAP: 4; Number of adult never smokers in the FAP: 4.
Main Criteria for Inclusion: • Aged 18 or older • Adult Smokers: currently smoking at least 1 CC/day, started more than 30 days ago; Adult Former Smokers: quit smoking CC more than 30 days ago; Adult Never Smokers Phase 2 only: never smoked or never smoked daily and less than 100 CC
Methods: Moderators (5+ years of experience) were utilized to conduct the IDIs. A discussion guide was employed in each IDI in order to elicit participant feedback in a consistent manner across the various IDIs.
Criteria for Evaluation: Verbal data, transcribed from the FGDs and IDIs, were examined for each potential product message in general, and by smoking status in particular, to identify the extent of endorsement.

Five potential communication materials were assessed: (i) brochure, (ii) direct mail, (iii) advertising concept, (iv) point of sales advertisement, and (v) (b) (4). In the brochure and direct mail, 3 potential claims, selected on the basis of [THS-PBA-02-US] and [THS-PBA-03-US] findings, were included (Table 9).

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 9 Modified Risk Claims assessed in THS-PBA-04-US

Reduced Exposure A	Reduced Exposure B	Reduced Risk
• With the exception of nicotine, with the *iQOS* system there is a significant reduction in the production of harmful or potentially harmful chemicals.	• Scientific studies have shown that switching completely from cigarettes to the *iQOS* system significantly reduces your body's exposure to harmful or potentially harmful chemicals.	• Scientific studies have shown that switching completely from cigarettes to the *iQOS* system can reduce the risks of tobacco-related diseases.
Important Warning A	**Important Warning B**	**Important Warning C**
• It **has not been demonstrated** that switching to the *iQOS* system reduces the risk of developing tobacco-related diseases compared to smoking cigarettes. • HeatSticks™ contain nicotine which is addictive. • Using the *iQOS* system can harm your health.	• A significant reduction in your body's exposure to harmful chemicals, compared to cigarettes, **does not mean a reduction in the risk of developing tobacco-related diseases**. • HeatSticks™ contain nicotine which is addictive. • Using the *iQOS* system can harm your health.	• Reduced risk **does not mean no risk**. The best way to reduce your risk of tobacco-related diseases is to completely quit tobacco-use. • HeatSticks™ contain nicotine which is addictive. • Using the *iQOS* system can harm your health.

Data Source: [THS-PBA-04-US Study Report Appendix b]
iQOS is the commercial name and registered trademark for THS. *HeatSticks* is the commercial name and registered trademark for THS Tobacco Sticks.

Results[2]

Overall, comments made by Adult Former Smokers and Adult Never Smokers indicated no interest in using THS based on the different communication materials they were presented with. These groups, besides being simply uninterested in tobacco products, also expressed concerns with regards to health and addiction risks. These results are overall consistent with the first qualitative study [THS-PBA-02-US]. In terms of perception of the look and feel of the different communication materials presented, Adult Former Smokers and Adult Never Smokers described the materials as interesting from a design point of view; however, this was not associated with any intention to use THS.

> *"It tells me right away that it's a cigarette related product, some kind of cigarette related tobacco smoking device and I'm not interested. I'm not interested in starting to smoke, so thank you for the reduction of nicotine, but I'm still not interested."* (Never smoker, female, 36-50, Phoenix)

[2] Verbatims are shown for illustrative purposes.

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

"I just don't plan on ever smoking cigarettes or using tobacco really of any kind on a regular basis, so that is what would make it definitely not." (Never smoker, male, 26-35, Chicago)

6.3.1.3.4 Conclusions across Developmental Studies

At the stage of THS communication development, our findings indicate that THS communication materials were effective at detering non users of tobacco, especially never smokers, of using THS. This was evidenced consistently throughout 2 qualitative and 1 quantitative assessment in groups of adult former smokers and adult never smokers. Overall, *Intent to Use* THS was higher among adult former smokers compared to never smokers, in particular for THS communication that included a reduced risk claim (i.e., Message 5 in [THS-PBA-03-US]). This may reflect a general interest in tobacco products among adult former smokers who has a history of smoking habits and would thus remain interested in using tobacco products that are less harmful than CC. In sum, findings from the developmental studies provide evidence that the type of information communicated on THS and how this information is presented, in conjunction with other elements (brand, look and feel) in communication materials, is unlikely to encourage adult non-smokers to initiate tobacco use with THS. This evidence is particulary strong for adult never smokers. In addition, the findings from the development phase do not provide evidence suggesting that young adult never smokers would perceive THS differently from older adult never smokers.

6.3.1.4 Assessment Phase

Based on the insights generated during the development phase (Section 6.4.1.3.4), 3 types of communications were crafted for the assessment phase:

(1) A communication including Claim #1 "Reduced risks of tobacco-related diseases" based on Message 5 from study [THS-PBA-03-US] (Figure 3)

(2) A communication including Claim #2 – "Reduced risk of harm" (Figure 4).

(3) A communication including Claim #3 – "Reduced body's exposure to harmful and potentially harmful chemicals" based on Message 3 from study [THS-PBA-3-US] (Figure 5).

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

AVAILABLE EVIDENCE TO DATE:

- The *iQOS* system heats tobacco but does not burn it.
- This significantly reduces the production of harmful and potentially harmful chemicals.
- Scientific studies have shown that switching completely from conventional cigarettes to the *iQOS* system can reduce the risks of tobacco-related diseases.

IMPORTANT WARNING:

- Reduced risk does not mean no risk**.** The best way to reduce your risk of tobacco-related diseases is to completely quit tobacco use.
- HeatSticks™ contain nicotine, which is addictive.
- Using the *iQOS* system can harm your health.

Figure 3 Reduced Risk Claim (RRC) and associated Warning

AVAILABLE EVIDENCE TO DATE:

- Switching completely to *iQOS* presents less risk of harm than continuing to smoke cigarettes.

IMPORTANT WARNING:

- Less risk of harm does not mean no risk of harm. The best way to reduce your risk of tobacco-related diseases is to completely quit tobacco use.
- HeatSticks™ contain nicotine, which is addictive.

Figure 4 Reduced Risk Claim 2 (RRC2) and associated Warning

AVAILABLE EVIDENCE TO DATE:

- The *iQOS* system heats tobacco but does not burn it.
- This significantly reduces the production of harmful and potentially harmful chemicals.
- Scientific studies have shown that switching completely from conventional cigarettes to the *iQOS* system significantly reduces your body's exposure to harmful or potentially harmful chemicals.

IMPORTANT WARNING:

- It has not been demonstrated that switching to the *iQOS* system reduces the risk of developing tobacco-related diseases compared to smoking conventional cigarettes.
- HeatSticks™ contain nicotine, which is addictive.
- Using the *iQOS* system can harm your health.

Figure 5 Reduced Exposure Claim (REC) and associated Warning

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

The objective of the assessment phase was to describe responses to different instances of label, labeling and marketing material in the following populations: 1) Adult Smokers with no Intention to Quit CC, Adult Smokers with the Intention to Quit CC, Adult Former Smokers, and Adult Never Smokers (including LA-25 Never Smokers). The assessment phase included 3 studies, [THS-PBA-05-RRC-US] (Claim #1 RRC), [THS-PBA-05-RRC2-US] (Claim #2 RRC2), [THS-PBA-05-REC-US] (Claim #3 REC), all using a similar methodology and a randomized parallel 5-arm design, with subjects in each arm being presented with a single instance of THS communication material (Table 10).

Table 10 THS Communication Materials, Warning Type and Study Arms

		Type of Communication Material		
		THS 2.2 Brochure	**Tobacco Sticks Pack**	**THS 2.2 Direct Mail**
Warning Type	**Surgeon General[a]**	Arm 1	Arm 3	NA
	PMI[b]	Arm 2	Arm 4	Arm 5

Abbreviations: NA = not assessed.

[a] The Surgeon General (SG) warnings currently mandated for CC include: 1) "Smoking causes lung cancer, heart disease, emphysema, and may complicate pregnancy."; 2) "Quitting smoking now greatly reduces serious risks to your health."; 3) "Smoking by pregnant women may result in fetal injury, premature birth, and low birth weight."; 4) "Cigarette smoke contains carbon monoxide." Note: Subjects randomized to the Surgeon General warning were assigned 1 of the 4 warnings.

[b] The PMI Important Warning statements were adapted for each study to present a coherent set of information between the claim and the warning concerning the modified risk (see Figure 3, Figure 4, and Figure 5, for RRC, RRC2 and REC respectively).

Two warning types were used in the study to assess how *Comprehension, Risk Perception,* and *Intent to Use* were related to both the currently mandated Surgeon General warnings for CC and the Important Warning developed by PMI which was crafted in coherence with the rest of the message.

The section below reports only the main results on *Intent to Use* Assessment of [THS-PBA-05-RRC-US], [THS-PBA-05-RRC2-US] and [THS-PBA-05-REC-US] studies. More details can be found in the summary or full report of the individual studies presented in Section 7.3.2.

In all 3 PBA-05 studies, the ITUQ was used to assess *Intent to Use* (overarching concept including both Intention to Try and Intention to Use) THS and comparators (i.e., CC, E-cigarettes, and any nicotine-containing products). In order to limit the number of comparisons involved, assessments were selected on the basis of appropriateness as reported by participants in Cognitive Debriefing Interviews (CDIs) during the development of the ITUQ (details on the ITUQ development can be found in [A732 PBA01Sum]). Table 11 presents the product by smoking group combinations that were presented in PBA-05 studies. For example, in some cases, assessments for certain

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

groups were not done as this would have been inapplicable, e.g. assessing Intention to Try CC for current Adult Smokers.

Table 11 Measures of Intent to Use in the Assessment Phase

Measure	THS	CC	E-cigarettes	Any nicotine-containing products
Intention to Try (at least once)	All smoking status groups	Adult Never Smokers (including LA-25)	Adult Never Smokers (including LA-25)	Adult Never Smokers (including LA-25)
Intention to Try (if offered by a friend)	All smoking status groups	Adult Never Smokers (including LA-25)	Adult Never Smokers (including LA-25)	Adult Never Smokers (including LA-25)
Intention to Use (regularly)	All smoking status groups	Adult Former Smokers	Adult Former Smokers	Adult Former Smokers
Timing for Use (how soon will use)	All smoking status groups	–	–	–

6.3.1.4.1 THS-PBA-05-RRC-US Study

Methodology

A brief description of the study methods is provided in Table 12.

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 12 Methodology of THS-PBA-05-RRC-US

Study Title: Quantitative Assessment of THS 2.2 Label, Labeling, and Marketing Material with Reduced Risk Claims

Study Design: 4 cities, 5-arm parallel-group experiment. The 5 arms corresponded to 5 different combinations of communication materials and warning type, each of the materials being tested by approximately equal numbers of subjects from different smoking status groups.

Subjects: *Full Sample* (N=2255) stratified into Adult Smokers with no Intention to Quit CC (N=472), Adult Smokers with the Intention to Quit CC (N=472), Adult Former Smokers (N=471) and Adult Never Smokers (N=477). An additional oversampling of 478 Adult Never Smokers from the legal age of smoking to 25 years of age (*LA-25 Adult Never Smokers*) which includes 115 Adult Never Smokers from the *Main Sample*.

Main Criteria for Inclusion:

- Aged 18 and above, or above state legal smoking age if above 18 years
- Adult Smokers with no Intention to Quit CC[a]: currently smoking some days or every day, started more than 30 days ago with no intention to quit within 6 months; Adult Smokers with Intention to Quit CC[a]: currently smoking some days or every day, started more than 30 days ago with the intention to quit within 6 months; Adult Former Smokers: quit smoking CCs more than 30 days ago; Adult Never Smokers: never smoked or never smoked daily and less than 100 CC

Methods:

Intent to Use

2 sets of items from the Intent to Use Questionnaire (ITUQ) yielded descriptive measures of:

- Intention to Try (i.e., to sample at least once; 2 items)
- Intention to Use (i.e., for continued usage; 2 items)

Criteria for Evaluation:

Intent to Use:

Positive Intention to Try (operationalized as the sum of % "Very Likely" and % "Definitely" responses for each item of Intention to Try) and Positive Intention to Use (operationalized as the sum of % "Very Likely" and % "Definitely" responses for the first item of Intention to Use), by study arm and smoking status group.

[a] Include Regular Smokers (smoke at least 1 CC a day) and Intermittent Smokers (between 4 and 27 days per month, with no restrictions on total number of CC smoked over that period, between 10% and 40%).

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Mockup of THS Brochure, THS Tobacco Sticks Pack, and THS Direct Mail were presented branded (*iQOS* for THS and *Marlboro* for the Tobacco Sticks) to the subjects with a hypothetical price for the THS device (b) (4) and for a pack of 20 Tobacco Sticks (price of a *Marlboro* pack of CC in the specific city where the research took place). All materials included at least the following 2 elements:

1) Information on THS, including the modified risk claim that "Scientific studies have shown that switching completely from conventional cigarettes to the *iQOS* system can reduce the risks of tobacco-related diseases".
2) Warning Section (Surgeon General's warnings or PMI Important Warning)

The mockups are presented in THS-PBA-05-RRC-US study report Appendix 16.1.1.

Results

The overall pattern of results were consistent across the 2 domains of *Intent to Use* composed of Intention to Try (2 items) and Intention to Use (2 items). All results can be found in Study Report [THS-PBA-05-RRC-US] (Table 15.2.2.1.1 Table 15.2.2.1.3, and Table 15.2.2.1.4). For brevity in this section, we summarize only the results on the first item of each Intention to Try (Table 13) and Intention to Use (Table 14) domains, respectively.

Positive Intention to Try and positive Intention to Use THS were low among Adult Former Smokers for all materials tested, both with Surgeon General's warnings and PMI Important Warning: positive Intention to Try THS ranged from 3.2% to 9.6% (Table 13); positive Intention to Use THS ranged from 2.1% to 6.4% (Table 14). For Adult Never Smokers and LA-25 Adult Never Smokers groups, very few subjects expressed an *Intent to Use THS* (between 0.0% and 1.1% for each of the 5 study arms for both positive Intention to Try (Table 13) and positive Intention to Use (Table 14)).

Overall, these low levels of *Intent to Use THS* (Intention to Try for Adult Never Smokers and Intention to Use for Adult Former Smokers) were consistent with the low levels of *Intent to Use* CC and E-Cigarettes (Table 13 and Table 14).

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 13 Proportion of Subjects with Positive Intention to Try THS and Comparators in THS-PBA-05-RRC-US

		THS Brochure		Tobacco Sticks Pack		THS Direct Mail
	Statistics	**SG warnings**	**PMI Warning**	**SG warnings**	**PMI Warning**	**PMI Warning**
THS						
FS	N	94	94	93	94	96
	n (%)	9 (9.6)	4 (4.3)	7 (7.5)	3 (3.2)	5 (5.2)
	(95% CI)	(4.5, 17.4)	(1.2, 10.5)	(3.1, 14.9)	(0.7, 9.0)	(1.7, 11.7)
NS	N	95	95	96	94	96
	n (%)	1 (1.1)	1 (1.1)	0	0	1 (1.0)
	(95% CI)	(0.0, 5.7)	(0.0, 5.7)	(0.0, 3.8)	(0.0, 3.8)	(0.0, 5.7)
LA-25 NS	N	94	94	97	96	96
	n (%)	0	1 (1.1)	0	0	0
	(95% CI)	(0.0, 3.8)	(0.0, 5.8)	(0.0, 3.7)	(0.0, 3.8)	(0.0, 3.8)
CC						
NS	N	95	95	96	95	96
	n (%)	1 (1.1)	0	0	0	0
	(95% CI)	(0.0, 5.7)	(0.0, 3.8)	(0.0, 3.8)	(0.0, 3.8)	(0.0, 3.8)
LA-25 NS	N	95	94	97	96	96
	n (%)	0	1 (1.1)	0	1 (1.0)	0
	(95% CI)	(0.0, 3.8)	(0.0, 5.8)	(0.0, 3.7)	(0.0, 5.7)	(0.0, 3.8)
E-cigarettes						
NS	N	95	95	96	95	96
	n (%)	2 (2.1)	1 (1.1)	1 (1.0)	0	1 (1.0)
	(95% CI)	(0.3, 7.4)	(0.0, 5.7)	(0.0, 5.7)	(0.0, 3.8)	(0.0, 5.7)
LA-25 NS	N	95	94	97	96	96
	n (%)	4 (4.2)	3 (3.2)	1 (1.0)	1 (1.0)	2 (2.1)
	(95% CI)	(1.2, 10.4)	(0.7, 9.0)	(0.0, 5.6)	(0.0, 5.7)	(0.3, 7.3)

Abbreviations: CC = conventional cigarettes; CI = confidence interval; FS = Adult Former Smokers; LA = legal smoking age; NS = Adult Never Smokers; SG = Surgeon General; THS = Tobacco Heating System.
Note: positive intention was operationalized as the proportion of subjects whose response to the single item assessing intention to try THS was either "*Very Likely"* or "*Definitely"*.
Note: the 95% confidence intervals are calculated using the exact Clopper-Pearson method. Only relevant combinations of *smoking status group* and *comparator* were assessed, namely, those deemed most directly relevant to study objectives (as shown in the table).
Data Source: Study Report THS-PBA-05-RRC-US, Table 15.2.2.1.1, Table 15.2.2.1.3, and Table 15.2.2.1.4.

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 14 Proportion of Subjects with Positive Intention to Use THS and Comparators in THS-PBA-05-RRC-US

		THS Brochure		Tobacco Sticks Pack		THS Direct Mail
	Statistics	**SG warnings**	**PMI Warning**	**SG warnings**	**PMI Warning**	**PMI Warning**
THS						
FS	N	94	94	93	94	96
	n (%)	6 (6.4)	4 (4.3)	3 (3.2)	2 (2.1)	3 (3.1)
	(95% CI)	(2.4, 13.4)	(1.2, 10.5)	(0.7, 9.1)	(0.3, 7.5)	(0.6, 8.9)
NS	N	95	95	96	94	96
	n (%)	0	1 (1.1)	0	0	1 (1.0)
	(95% CI)	(0.0, 3.8)	(0.0, 5.7)	(0.0, 3.8)	(0.0, 3.8)	(0.0, 5.7)
LA-25 NS	N	94	94	97	96	96
	n (%)	0	0	0	0	0
	(95% CI)	(0.0, 3.8)	(0.0, 3.8)	(0.0, 3.7)	(0.0, 3.8)	(0.0, 3.8)
CC						
FS (use again)	N	94	94	93	94	96
	n (%)	3 (3.2)	0	0	1 (1.1)	0
	(95% CI)	(0.7, 9.0)	(0.0, 3.8)	(0.0, 3.9)	(0.0, 5.8)	(0.0, 3.8)
E-cigarettes						
FS	N	94	94	93	94	96
	n (%)	12 (12.8)	8 (8.5)	4 (4.3)	7 (7.4)	4 (4.2)
	(95% CI)	(6.8, 21.2)	(3.7, 16.1)	(1.2, 10.6)	(3.0, 14.7)	(1.1, 10.3)

Abbreviations: CC = conventional cigarettes; CI = confidence interval; FS = Adult Former Smokers; LA = legal smoking age; NS = Adult Never Smokers; SG = Surgeon General; THS = Tobacco Heating System.
Note: positive intention was operationalized as the proportion of subjects whose response to the single item assessing intention to use THS was either "*Very Likely"* or "*Definitely"*.
Note: the 95% confidence intervals are calculated using the exact Clopper-Pearson method. Only relevant combinations of *smoking status group* and *comparator* were assessed, namely, those deemed most directly relevant to study objectives (as shown in the table).
Data Source: Study Report THS-PBA-05-RRC-US, Table 15.2.2.1.1, Table 15.2.2.1.3, and Table 15.2.2.1.4.

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

6.3.1.4.2 THS-PBA-05-RRC2-US Study

Methodology

A brief description of study methods is provided in Table 15.

Table 15 Methodology of THS-PBA-05-RRC2-US

Study Title: Second Quantitative Assessment of THS 2.2 Label, Labeling and Marketing Material with Reduced Risk Claims
Study Design: 4 cities, 5-arm parallel-group experiment. The 5 arms corresponded to 5 different combinations of communication materials and warning type, each of the materials being tested by approximately equal numbers of subjects from different smoking status groups.
Subjects: *Full Sample* (N=2247) stratified into Adult Smokers with no Intention to Quit CC (N=475), Adult Smokers with the Intention to Quit CC (N=471), Adult Former Smokers (N=469) and Adult Never Smokers (N=468). An additional oversampling of 471 Adult Never Smokers from the legal age of smoking to 25 years of age (*LA-25 Adult Never Smokers*) which includes 107 Adult Never Smokers from the *Main Sample*.
Main Criteria for Inclusion: • Male and female aged 18 and above, or above state legal smoking age • Aged 18 and above, or above state legal smoking age if above 18 years • Adult Smokers with no Intention to Quit CC[a]: currently smoking some days or every day, started more than 30 days ago with no intention to quit within 6 months; Adult Smokers with Intention to Quit CC[a]: currently smoking some days or every day, started more than 30 days ago with the intention to quit within 6 months; Adult Former Smokers: quit smoking CCs more than 30 days ago; Adult Never Smokers: never smoked or never smoked daily and less than 100 CC
Methods: Intent to Use 2 sets of items from the Intent to Use Questionnaire (ITUQ) yielded descriptive measures of: • Intention to Try (i.e., to sample at least once; 2 items) • Intention to Use (i.e., for continued usage; 2 items)
Criteria of Evaluation: Intent to Use: Positive Intention to Try (operationalized as the sum of % "Very Likely" and % "Definitely" responses to the item Intention to Try) and Positive Intention to Use (operationalized as the sum of % "Very Likely" and % "Definitely" responses to the item Intention to Use Regularly), by study arm and smoking status group.

[a] Include Regular Smokers (smoke at least 1 CC a day) and Intermittent Smokers (between 4 and 27 days per month, with no restrictions on total number of CC smoked over that period, between 10% and 40%).

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Mockup of THS Brochure, Tobacco Sticks Pack and THS Direct Mail were presented branded (*iQOS* for THS and *Marlboro* for the Tobacco Sticks) to the subjects with a hypothetical price for the THS device ((b) (4) and for a pack of 20 Tobacco Sticks (price of a *Marlboro* pack of CC in the specific city where the research took place). All materials included at least the following 2 elements:

1) Information on THS, including the modified risk claim that "Switching completely to *iQOS* presents less risk of harm than continuing to smoke cigarettes"
2) Warning Section (Surgeon General's warnings or PMI Important Warning)

The mockups are presented in THS-PBA-05-RRC2-US study report Appendix 16.1.1.

Results

The overall pattern of results were consistent across the 2 domains of *Intent to Use* composed of Intention to Try (2 items) and Intention to Use (2 items). All results can be found in Study Report [THS-PBA-05-RRC2-US] (Table 15.2.2.1.1 Table 15.2.2.1.3, and Table 15.2.2.1.4). For brevity in this section, we summarize only the results on the first item of each Intention to Try and Intention to Use domains, respectively (Table 2).

Positive Intention to Try and positive Intention to Use THS were low among Adult Former Smokers for all materials tested, both with Surgeon General's warnings and PMI Important Warning: positive Intention to Try ranged from 2.1% to 7.6%, (Table 16); positive Intention to Use ranged from 1.1% to 5.3%, (Table 17). For Adult Never Smokers and LA-25 Adult Never Smokers groups, very few subjects expressed an *Intent to Use* (between 0% and 3% for positive Intention to Try for each of the 5 study arms (Table 16) and between 0% and 1.1% for positive Intention to Use (Table 17)). Overall, these low levels of *Intent to Use* THS were consistent with the low levels of *Intent to Use* CC and E-Cigarettes (Table 16 and Table 17).

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 16 Proportion of Subjects with Positive Intention to Try THS and Comparators in THS-PBA-05-RRC2-US

		THS Brochure		Tobacco Sticks Pack		THS Direct Mail
	Statistics	**SG warnings**	**PMI Warning**	**SG warnings**	**PMI Warning**	**PMI Warning**
THS						
FS	N	94	92	92	96	93
	n (%)	5 (5.3)	7 (7.6)	7 (7.6)	2 (2.1)	2 (2.2)
	(95% CI)	(1.7, 12.0)	(3.1, 15.1)	(3.1, 15.1)	(0.3, 7.3)	(0.3, 7.6)
NS	N	96	93	93	94	92
	n (%)	0	1 (1.1)	0	0	0
	(95% CI)	(0.0, 3.8)	(0.0, 5.8)	(0.0, 3.9)	(0.0, 3.8)	(0.0, 3.9)
LA-25 NS	N	89	92	101	95	94
	n (%)	1 (1.1)	0	3 (3.0)	1 (1.1)	1 (1.1)
	(95% CI)	(0.0, 6.1)	(0.0, 3.9)	(0.6, 8.4)	(0.0, 5.7)	(0.0, 5.8)
CC						
NS	N	96	93	93	94	92
	n (%)	0	0	0	0	0
	(95% CI)	(0.0, 3.8)	(0.0, 3.9)	(0.0, 3.9)	(0.0, 3.8)	(0.0, 3.9)
LA-25 NS	N	89	92	101	95	94
	n (%)	0	0	0	0	0
	(95% CI)	(0.0, 4.1)	(0.0, 3.9)	(0.0, 3.6)	(0.0, 3.8)	(0.0, 3.8)
E-cigarettes						
NS	N	96	93	93	94	92
	n (%)	1 (1.0)	0	0	1 (1.1)	1 (1.1)
	(95% CI)	(0.0, 5.7)	(0.0, 3.9)	(0.0, 3.9)	(0.0, 5.8)	(0.0, 5.9)
LA-25 NS	N	89	92	101	95	94
	n (%)	1 (1.1)	1 (1.1)	0	2 (2.1)	2 (2.1)
	(95% CI)	(0.0, 6.1)	(0.0, 5.9)	(0.0, 3.6)	(0.3, 7.4)	(0.3, 7.5)

Abbreviations: CC = conventional cigarettes; CI = confidence interval; FS = Adult Former Smokers; LA = legal smoking age; NS = Adult Never Smokers; SG = Surgeon General; THS = Tobacco Heating System.
Note: positive intention was operationalized as the proportion of subjects whose response to the single item assessing intention to tryTHS was either "*Very Likely* "or "*Definitely"*.
Note: the 95% confidence intervals are calculated using the exact Clopper-Pearson method. Only relevant combinations of *smoking status group* and *comparator* were assessed, namely, those deemed most directly relevant to study objectives (as shown in the table).
Data Source: Study Report THS-PBA-05-RRC2-US, Table 15.2.2.1.1, Table 15.2.2.1.3, and Table 15.2.2.1.4.

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 17 Proportion of Subjects with Positive Intention to Use THS and Comparators in THS-PBA-05-RRC2-US

		THS Brochure		Tobacco Sticks Pack		THS Direct Mail
	Statistics	**SG warnings**	**PMI Warning**	**SG warnings**	**PMI Warning**	**PMI Warning**
THS						
FS	N	94	92	92	96	93
	n (%)	5 (5.3)	1 (1.1)	3 (3.3)	2 (2.1)	1 (1.1)
	(95% CI)	(1.7, 12.0)	(0.0, 5.9)	(0.7, 9.2)	(0.3, 7.3)	(0.0, 5.8)
NS	N	96	93	93	94	92
	n (%)	0	1 (1.1)	0	0	1 (1.1)
	(95% CI)	(0.0, 3.8)	(0.0, 5.8)	(0.0, 3.9)	(0.0, 3.8)	(0.0, 5.9)
LA-25 NS	N	89	92	101	95	94
	n (%)	0	1 (1.1)	0	0	1 (1.1)
	(95% CI)	(0.0, 4.1)	(0.0, 5.9)	(0.0, 3.6)	(0.0, 3.8)	(0.0, 5.8)
CC						
FS (use again)	N	94	93	93	96	93
	n (%)	0	2 (2.2)	1 (1.1)	0	2 (2.2)
	(95% CI)	(0.0, 3.8)	(0.3, 7.6)	(0.0, 5.8)	(0.0, 3.8)	(0.3, 7.6)
E-cigarettes						
FS	N	94	93	93	96	93
	n (%)	8 (8.5)	6 (6.5)	4 (4.3)	6 (6.3)	7 (7.5)
	(95% CI)	(3.7, 16.1)	(2.4, 13.5)	(1.2, 10.6)	(2.3, 13.1)	(3.1, 14.9)

Abbreviations: CC = conventional cigarettes; CI = confidence interval; FS = Adult Former Smokers; LA = legal smoking age; NS = Adult Never Smokers; SG = Surgeon General; THS = Tobacco Heating System.
Note: positive intention was operationalized as the proportion of subjects whose response to the single item assessing intention to use THS was either "*Very Likely"* or "*Definitely"*.
Note: the 95% confidence intervals are calculated using the exact Clopper-Pearson method. Only relevant combinations of *smoking status group* and *comparator* were assessed, namely, those deemed most directly relevant to study objectives (as shown in the table).
Data Source: Study Report THS-PBA-05-RRC2-US, Table 15.2.2.1.1, Table 15.2.2.1.3, and Table 15.2.2.1.4.

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

6.3.1.4.3 THS-PBA-05-REC-US Study

Methodology

A brief description of the study methods is provided in Table 18.

Table 18 Methodology of THS-PBA-05-REC-US

Study Title: Quantitative Assessment of THS 2.2 Label, Labeling and Marketing Material with Reduced Exposure Claims
Study design: 4 cities, 5-arm parallel-group experiment. The 5 arms corresponded to 5 different combinations of communication materials and warning type, each of the materials being tested by approximately equal numbers of subjects from different smoking status groups.
Subjects: *Full Sample* (N=2272) stratified into Adult Smokers with no Intention to Quit CC (N=479), Adult Smokers with the Intention to Quit CC (N=479), Adult Former Smokers (N=480) and Adult Never Smokers (N=480). An additional oversampling of 480 Adult Never Smokers from the legal age of smoking to 25 years of age (*LA-25 Adult Never Smokers*) which includes 126 Adult Never Smokers from the *Main Sample*.
Main criteria for inclusion: • Aged 18 and above, or above state legal smoking age if above 18 years • Adult Smokers with no Intention to Quit CC[a]: currently smoking some days or every day, started more than 30 days ago with no intention to quit within 6 months; Adult Smokers with Intention to Quit CC[a]: currently smoking some days or every day, started more than 30 days ago with the intention to quit within 6 months; Adult Former Smokers: quit smoking CCs more than 30 days ago; Adult Never Smokers: never smoked or never smoked daily and less than 100 CC
Methods: <u>Intent to Use</u> 2 sets of items from the Intent to Use Questionnaire (ITUQ) yielded descriptive measures of: • Intention to Try (i.e., to sample at least once; 2 items) • Intention to Use (i.e., for continued usage; 2 items)
Criteria for Evaluation: <u>Intent to Use</u>: Positive Intention to Try (operationalized as the sum of % "Very Likely" and % "Definitely" responses to the item on Intention to Try) and positive Intention to Use (operationalized as the sum of % "Very Likely" and % "Definitely" responses to the item on Intention to Use Regularly), by study arm and smoking status group.

[a] Include Regular Smokers (smoke at least 1 CC a day) and Intermittent Smokers (between 4 and 27 days per month, with no restrictions on total number of CC smoked over that period, between 10% and 40%).

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Mockup of THS Brochure, Tobacco Sticks Pack and THS Direct Mail were presented branded (*iQOS* for THS and *Marlboro* for the Tobacco Sticks) to the subjects with a hypothetical price for the THS device ((b) (4) and for a pack of 20 Tobacco Sticks (price of a *Marlboro* pack of CC in the specific city where the research took place). All materials included at least the following 2 elements:

1) Information on THS, including the modified risk claim that "Scientific studies have shown that switching completely from cigarettes to the *iQOS* system significantly reduces your body's exposure to harmful or potentially harmful chemicals."
2) Warning Section (Surgeon General's warnings or PMI Important Warning)

The mockups are presented in THS-PBA-05-REC-US study report Appendix 16.1.1.

Results

The overall pattern of results were consistent across the 2 domains of *Intent to Use* composed of Intention to Try (2 items) and Intention to Use (2 items). All results can be found in Study Report [THS-PBA-05-REC-US] (Table 15.2.2.1.1 Table 15.2.2.1.3, and Table 15.2.2.1.4). For brevity in this section, we summarize only the results on the first item of each Intention to Try and Intention to Use domain, respectively (Table 2).

Positive Intention to Try and positive Intention to Use THS were low among Adult Former Smokers for all materials tested, both with Surgeon General's warnings and PMI Important Warning: positive Intention to Try ranged from 3.1% to 6.3% (Table 19); positive Intention to Use ranged from 1.0% to 5.2% (Table 20). For Adult Never Smokers and LA-25 Adult Never Smokers groups, very few subjects expressed an *Intent to Use* (between 0% and 2.1% for positive Intention to Try for each of the 5 study arms (Table 19) and between 0% and 1.1% for positive Intention to Use (Table 20)). Overall, these low levels of *Intent to Use* THS were consistent with the low levels of *Intent to Use* CC and E-Cigarettes (Table 19 and Table 20).

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 19 Proportion of Subjects with Positive Intention to Try THS and Comparators in THS-PBA-05-REC-US

		THS Brochure		Tobacco Sticks Pack		THS Direct Mail
	Statistics	**SG warnings**	**PMI Warning**	**SG warnings**	**PMI Warning**	**PMI Warning**
THS						
FS	N	96	96	96	96	96
	n (%)	4 (4.2)	3 (3.1)	6 (6.3)	3 (3.1)	4 (4.2)
	(95% CI)	(1.1, 10.3)	(0.6, 8.9)	(2.3, 13.1)	(0.6, 8.9)	(1.1, 10.3)
NS	N	96	96	95	96	95
	n (%)	2 (2.1)	0	0	1 (1.0)	0
	(95% CI)	(0.3, 7.3)	(0.0, 3.8)	(0.0, 3.8)	(0.0, 5.7)	(0.0, 3.8)
LA-25 NS	N	97	97	97	96	93
	n (%)	1 (1.0)	2 (2.1)	0	1 (1.0)	1 (1.1)
	(95% CI)	(0.0, 5.6)	(0.3, 7.3)	(0.0, 3.7)	(0.0, 5.7)	(0.0, 5.8)
CC						
NS	N	96	96	96	96	96
	n (%)	0	0	1 (1.0)	0	2 (2.1)
	(95% CI)	(0.0, 3.8)	(0.0, 3.8)	(0.0, 5.7)	(0.0, 3.8)	(0.3, 7.3)
LA-25 NS	N	97	97	97	96	93
	n (%)	0	0	1 (1.0)	0	2 (2.2)
	(95% CI)	(0.0, 3.7)	(0.0, 3.7)	(0.0, 5.6)	(0.0, 3.8)	(0.3, 7.6)
E-cigarettes						
NS	N	96	96	96	96	96
	n (%)	0	1 (1.0)	1 (1.0)	1 (1.0)	2 (2.1)
	(95% CI)	(0.0, 3.8)	(0.0, 5.7)	(0.0, 5.7)	(0.0, 5.7)	(0.3, 7.3)
LA-25 NS	N	97	97	97	96	93
	n (%)	1 (1.0)	4 (4.1)	1 (1.0)	1 (1.0)	2 (2.2)
	(95% CI)	(0.0, 5.6)	(1.1, 10.2)	(0.0, 5.6)	(0.0, 5.7)	(0.3, 7.6)

Abbreviations: CC = conventional cigarettes; CI = confidence interval; FS = Adult Former Smokers; LA = legal smoking age; NS = Adult Never Smokers; SG = Surgeon General; THS = Tobacco Heating System.
Note: positive intention was operationalized as the proportion of subjects whose response to the single item assessing intention to try THS was either "*Very Likely"* or "*Definitely"*.
Note: the 95% confidence intervals are calculated using the exact Clopper-Pearson method. Only relevant combinations of *smoking status group* and *comparator* were assessed, namely, those deemed most directly relevant to study objectives (as shown in the table).
Data Source: Study Report THS-PBA-05-REC-US, Table 15.2.2.1.1, Table 15.2.2.1.3, and Table 15.2.2.1.4.

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 20 Proportion of Subjects with Positive Intention to Use THS and Comparators in THS-PBA-05-REC-US

		THS Brochure		Tobacco Sticks Pack		THS Direct Mail
	Statistics	**SG warnings**	**PMI Warning**	**SG warnings**	**PMI Warning**	**PMI Warning**
THS						
FS	N	96	96	96	96	96
	n (%)	3 (3.1)	1 (1.0)	5 (5.2)	3 (3.1)	1 (1.0)
	(95% CI)	(0.6, 8.9)	(0.0, 5.7)	(1.7, 11.7)	(0.6, 8.9)	(0.0, 5.7)
NS	N	96	96	95	96	95
	n (%)	0	1 (1.0)	0	1 (1.0)	1 (1.1)
	(95% CI)	(0.0, 3.8)	(0.0, 5.7)	(0.0, 3.8)	(0.0, 5.7)	(0.0, 5.7)
LA-25 NS	N	97	97	97	96	93
	n (%)	0	1 (1.0)	0	1 (1.0)	0
	(95% CI)	(0.0, 3.7)	(0.0, 5.6)	(0.0, 3.7)	(0.0, 5.7)	(0.0, 3.9)
CC						
FS (use again)	N	96	96	96	96	96
	n (%)	0	0	1 (1.0)	2 (2.1)	1 (1.0)
	(95% CI)	(0.0, 3.8)	(0.0, 3.8)	(0.0, 5.7)	(0.3, 7.3)	(0.0, 5.7)
E-cigarettes						
FS	N	96	96	96	96	96
	n (%)	5 (5.2)	7 (7.3)	3 (3.1)	4 (4.2)	4 (4.2)
	(95% CI)	(1.7, 11.7)	(3.0, 14.4)	(0.6, 8.9)	(1.1, 10.3)	(1.1, 10.3)

Abbreviations: CC = conventional cigarettes; CI = confidence interval; FS = Adult Former Smokers; LA = legal smoking age; NS = Adult Never Smokers; SG = Surgeon General; THS = Tobacco Heating System.
Note: positive intention was operationalized as the proportion of subjects whose response to the single item assessing intention to use THS was either "*Very Likely"* or "*Definitely"*.
Note: the 95% confidence intervals are calculated using the exact Clopper-Pearson method. Only relevant combinations of *smoking status group* and *comparator* were assessed, namely, those deemed most directly relevant to study objectives (as shown in the table).
Data Source: Study Report THS-PBA-05-REC-US, Table 15.2.2.1.1, Table 15.2.2.1.3, and Table 15.2.2.1.4.

6.3.1.4.4 Conclusions across Assessment Studies

In the absence of epidemiological evidence on initiation among non-users, behavioral intention has been recommended by the IOM as an appropriate proxy to measure the likelihood that non-users would initiate use of an MRTP (IOM (Institute of Medicine) 2012). In that context, a total of 6 studies were conducted to develop and assess THS labeling and advertising materials that generate low *Intent to Use* among those for whom THS is not intended, i.e., tobacco non-users. Across these studies, several combinations of claims and warnings were tested for Intention to Try (at least once) and Intention to Use (regularly) THS, forming the overarching concept of *Intent to Use*. Results provided consistent evidence that *Intent to Use* THS is low among Adult Former Smokers and very low among Adult Never Smokers, with similar results for LA-25 Adult Never Smokers and older Adult Never Smokers.

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

To maximize the ecological validity and generalizability of the assessment, in [THS-PBA-05-RRC-US], [THS-PBA-05-RRC2-US], and [THS-PBA-05-REC-US] studies, subjects were exposed to hypothetical THS price information and branded labels, labeling and advertising in the form intended to be used for commercialization (i.e., physical mockups of the material rather than only information presented on a screen or on paper). This allowed for a more realistic evaluation of the interest that THS may generate in consumers. In addition, in the 3 PBA-05 studies, stratified randomization was used within a large sample to deliver a sample which was well powered and balanced in terms of age, sex and smoking status. Furthermore, quotas were used to ensure that the study sample provided a sufficient proportion of "recent quitters" (i.e., more than 30 days but less than 12 months) vs "long-term quitters" (i.e., more than 12 months) to best capture intentions of subgroups of adult former smokers who may have different likelihood to relapse. Additionally, the sample was geographically diverse, being drawn from the 4 main geographical regions of the US. Taking into consideration the robustness of the sampling design and the consistency across 3 independent studies testing different modified risk claims, overall results of the [THS-PBA-05-RRC-US], [THS-PBA-05-RRC2-US], and [THS-PBA-05-REC-US] studies provided data that the proposed labeling and advertising for THS are unlikely to produce initiation in adult never smokers, including young adults, or relapse in former smokers. Moreover, the 3 assessment studies tested communication materials using 3 main communication channels and, as results seem highly stable, they may be generalizable to other derivative materials which use similar communication channels.

THS Brochure

Intention to Try and Intention to Use for the subjects exposed to the THS Brochure are summarized in Table 21 and Table 22, respectively. The overall pattern of results for *Intent to Use* THS was broadly consistent across the 3 studies testing different variations of modified risk information:

- Consistently low levels of *Intent to Use* among Adult Former Smokers regardless of the type of claim and type of warning (positive Intention to Try ranged from 3.1% to 9.6%; positive Intention to Use ranged from 1.0% to 6.4%)
- Consistently very low levels of *Intent to Use* among Adult Never Smokers and LA-25 Adult Never Smokers (≤2.1% for each of the 2 subject groups across studies).
- Similar levels of Intent to Use THS and Intent to Use CC and E-cigarettes, within all 3 non-smoker groups.

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Tobacco Sticks Pack

Intention to Try and Intention to Use for the subjects exposed to the Tobacco Sticks Pack are summarized in Table 23 and Table 24 respectively. Similar to the results for THS Brochure, the overall pattern of results for *Intent to Use* THS based on the exposure to the Tobacco Sticks Pack was broadly consistent across the 3 studies:

- Consistently low levels of *Intent to Use* among Adult Former Smokers, regardless of the type of claim and type of warning (positive Intention to Try ranged from 2.1% to 7.6%; positive Intention to Use ranged from 2.1% to 5.2%).
- Consistently very low levels of *Intent to Use* among Adult Never Smokers and LA-25 Adult Never Smokers (≤3% for each of the 2 subject groups across studies).
- Similar levels of *Intent to Use* THS and *Intent to Use* CC and E-cigarettes, within all 3 non-smoker groups.

THS Direct Mail

The overall pattern of results of *Intent to Use* THS for subjects exposed to the THS Direct Mail was broadly consistent with results for the THS Brochure and the Tobacco Sticks Pack (Table 25 and Table 26):

- Consistently low levels of *Intent to Use* among Adult Former Smokers across the 3 studies (positive Intention to Try ranged from 2.2% to 5.2%; positive Intention to Use ranged from 1.0% to 3.1%).
- Consistently very low levels of *Intent to Use* among Adult Never Smokers and LA-25 Adult Never Smokers (≤1.1% for each of the 2 subject groups).
- Similar levels of *Intent to Use* THS and *Intent to Use* CC and E-cigarettes, within all 3 non-smoker groups.

Overall, [THS-PBA-05-RRC-US], [THS-PBA-05-RRC2-US], [THS-PBA-05-REC-US] studies showed consistent results on *Intent to Use* among non-users of CC across the 3 claims proposed, the different materials tested, and between the PMI and Surgeon General's warnings. There was very small Intention to Try/Use THS among adult never smokers (no more than 2.1 % of positive Intention to Try/Use in any of the study arms for the 3 studies). Similarly, positive responses throughout all tested materials were particularly low for LA-25 Adult Never Smokers (no more than 3.0% of positive Intention to Try/Use). *Intent to Use* THS was slightly higher for Adult Former Smokers (between 2.1% and 9.6% and between 1.0% and 6.4% of positive Intention to Try and Intention to Use, respectively, in any of the study arms for the 3 studies).

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Importantly from a public health perspective, the results provide evidence that the low levels of Intention to Try or Use THS in adult non-smokers were similar and not higher than what was observed for CC and E-cigarettes. We conclude that the remaining low to very low levels of *Intent to Use* THS among non-smokers exposed to THS communication materials were not specific to THS, but rather represent either a general interest in tobacco or nicotine-containing products and/or unsystematic variance within the data. In particular, it was expected that adult former smokers were likely to be more interested in trying/using THS than adult never smokers, considering their smoking history.

The results for young never smokers (LA-25 Adult Never Smokers) are consistent with those observed in Adult Never Smokers within the Main Sample. Thus our results provide evidence that exposure to the THS communications we tested was associated with low levels of intention within young never smokers, and a level which was comparable to never smokers of a wide age range. Our results suggest that THS is neither targeted towards, nor attractive to young non-smokers and is likely to have a non-differentiated effect compared to other commercial tobacco products already on the market when it comes to initiation of tobacco use among young adults.

Overall, results obtained from 3 distinct studies suggest that the THS Brochure, the Tobacco Sticks Pack, and the THS Direct Mail are all suitable not to generate *Intent to Use* among US non-smokers: they all provide consistent results in line with PMI's aims not to recruit new smokers or new tobacco users from the non-smoking section of the population and to dissuade adult former smokers from returning to tobacco. In addition, the type of warning (Important Warning or Surgeon General's warnings) does not seem to influence the potential effect of THS communication on *Intent to Use* among adult non-smokers. Finally, our results provide no evidence that exposure to THS communications would be more likely to encourage Adult Former Smokers and Adult Never Smokers to initiate tobacco use if THS would be marketed with a reduced risk claim compared to a reduced exposure claim.

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 21 Positive Intention to Try among Adult Former Smokers and Adult Never Smokers following Exposure to THS Brochure by Study, Assessment Phase

	THS-PBA-05-RRC-US		THS-PBA-05-RRC2-US		THS-PBA-05-REC-US	
	SG Warning n (%) 95% CI	PMI Warning n (%) 95% CI	SG Warning n (%) 95% CI	PMI Warning n (%) 95% CI	SG Warning n (%) 95% CI	PMI Warning n (%) 95% CI
THS						
FS	9 (9.6) (4.5, 17.4)	4 (4.3) (1.2, 10.5)	5 (5.3) (1.7, 12.0)	7 (7.6) (3.1, 15.1)	4 (4.2) (1.1, 10.3)	3 (3.1) (0.6, 8.9)
NS	1 (1.1) (0.0, 5.7)	1 (1.1) (0.0, 5.7)	0 (0) (0.0, 3.8)	1 (1.1) (0.0, 5.8)	2 (2.1) (0.3, 7.3)	0 (0) (0.0, 3.8)
LA-25 NS	0 (0) (0.0, 3.8)	1 (1.1) (0.0, 5.8)	1 (1.1)	0 (0) (0.0, 3.9)	1 (1.0) (0.0, 5.6)	2 (2.1) (0.3, 7.3)
CC						
NS	1 (1.1) (0.0, 5.7)	0 (0) (0.0, 3.8)	0 (0) (0.0, 3.8)	0 (0) (0.0, 3.9)	0 (0) (0.0, 3.8)	0 (0) (0.0, 3.8)
LA-25 NS	0 (0) (0.0, 3.8)	1 (1.1) (0.0, 5.8)	0 (0) (0.0, 4.1)	0 (0) (0.0, 3.9)	0 (0) (0.0, 3.7)	0 (0) (0.0, 3.7)
E-cigarettes						
NS	2 (2.1) (0.3, 7.4)	1 (1.1) (0.0, 5.7)	1 (1.0) (0.0, 5.7)	0 (0) (0.0, 3.9)	0 (0) (0.0, 3.8)	1 (1.0) (0.0, 5.7)
LA-25 NS	4 (4.2) (1.2, 10.4)	3 (3.2) (0.7, 9.0)	1 (1.1) (0.0, 6.1)	1 (1.1) (0.0, 5.9)	1 (1.0) (0.0, 5.6)	4 (4.1) (1.1, 10.2)

Abbreviations: CC = conventional cigarettes; CI = confidence interval; FS = Adult Former Smokers; LA = legal smoking age; NS = Adult Never Smokers; SG = Surgeon General; THS = Tobacco Heating System; RRC: reduced risk claim; RRC2: reduced risk claim 2; REC: reduced exposure claim.

Note: positive intention was operationalized as the proportion of subjects whose response to the single item assessing intention to try THS was either "Very Likely" or "Definitely".

Data Source: THS-PBA-05-RRC-US Study Report, Table 15.2.2.1.1, Table 15.2.2.1.3, and Table 15.2.2.1.4; THS-PBA-05-RRC2-US Study Report , Table 15.2.2.1.1, Table 15.2.2.1.3, and Table 15.2.2.1.4; THS-PBA-05-REC-US Study Report, Table 15.2.2.1.1, Table 15.2.2.1.3, and Table 15.2.2.1.4.

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 22 Positive Intention to Use among Adult Former Smokers and Adult Never Smokers following exposure to THS Brochure by Study, Assessment Phase

	THS-PBA-05-RRC-US		THS-PBA-05-RRC2-US		THS-PBA-05-REC-US	
	SG Warning n (%) 95% CI	PMI Warning n (%) 95% CI	SG Warning n (%) 95% CI	PMI Warning n (%) 95% CI	SG Warning n (%) 95% CI	PMI Warning n (%) 95% CI
THS						
FS	6 (6.4) (2.4, 13.4)	4 (4.3) (1.2, 10.5)	5 (5.3) (1.7, 12.0)	1 (1.1) (0.0, 5.9)	3 (3.1) (0.6, 8.9)	1 (1.0) (0.0, 5.7)
NS	0 (0) (0.0, 3.8)	1 (1.1) (0.0, 5.7)	0 (0) (0.0, 3.8)	1 (1.1) (0.0, 5.8)	0 (0) (0.0, 3.8)	1 (1.0) (0.0, 5.7)
LA-25 NS	0 (0) (0.0, 3.8)	0 (0) (0.0, 3.8)	0 (0) (0.0, 4.1)	1 (1.1) (0.0., 5.9)	0 (0) (0.0, 3.7)	1 (1.0) (0.0, 5.6)
CC						
FS	3 (3.2) (0.7, 9.0)	0 (0) (0.0, 3.8)	0 (0) (0.0, 3.8)	2 (2.2) (0.3, 7.6)	0 (0) (0.0, 3.8)	0 (0) (0.0, 3.8)
E-cigarettes						
FS	12 (12.8) (6.8, 21.2)	8 (8.5) (3.7, 16.1)	8 (8.5) (3.7, 16.1)	6 (6.5) (2.4, 13.5)	5 (5.2) (1.7, 11.7)	7 (7.3) (3.0, 14.4)

Abbreviations: CC = conventional cigarettes; CI = confidence interval; FS = Adult Former Smokers; LA = legal smoking age; NS = Adult Never Smokers; SG = Surgeon General; THS = Tobacco Heating System; RRC: reduced risk claim; RRC2: reduced risk claim; REC: reduced exposure claim.
Note: positive intention was operationalized as the proportion of subjects whose response to the single item assessing intention to use THS was either "Very Likely" or "Definitely".
Data Source: THS-PBA-05-RRC-US Study Report, Table 15.2.2.1.1, Table 15.2.2.1.3, and Table 15.2.2.1.4; THS-PBA-05-RRC2-US Study Report , Table 15.2.2.1.1, Table 15.2.2.1.3, and Table 15.2.2.1.4; THS-PBA-05-REC-US Study Report, Table 15.2.2.1.1, Table 15.2.2.1.3, and Table 15.2.2.1.4.

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 23 Positive Intention to Try among Adult Former Smokers and Adult Never Smokers exposed to Tobacco Sticks Pack by Study, Assessment Phase

	THS-PBA-05-RRC-US		THS-PBA-05-RRC2-US		THS-PBA-05-REC-US	
	SG Warning n (%) 95% CI	PMI Warning n (%) 95% CI	SG Warning n (%) 95% CI	PMI Warning n (%) 95% CI	SG Warning n (%) 95% CI	PMI Warning n (%) 95% CI
THS						
FS	7 (7.5) (3.1, 14.9)	3 (3.2) (0.7, 9.0)	7 (7.6) (3.1, 15.1)	2 (2.1) (0.3, 7.3)	6 (6.3) (2.3, 13.1)	3 (3.1) (0.6, 8.9)
NS	0 (0) (0.0, 3.8)	0 (0) (0.0, 3.8)	0 (0) (0.0, 3.9)	0 (0) (0.0, 3.8)	0 (0) (0.0, 3.8)	1 (1.0) (0.0, 5.7)
LA-25 NS	0 (0) (0.0, 3.7)	0 (0) (0.0, 3.8)	3 (3.0) (0.6, 8.4)	1 (1.1) (0.0, 5.7)	0 (0) (0.0, 3.7)	1 (1.0) (0.0, 5.7)
CC						
NS	0 (0) (0.0, 3.8)	0 (0) (0.0, 3.8)	0 (0) (0.0, 3.9)	0 (0) (0.0, 3.8)	1 (1.0) (0.0, 5.7)	0 (0) (0.0, 3.8)
LA-25 NS	0 (0) (0.0, 3.7)	1 (1.0) (0.0, 5.7)	0 (0) (0.0, 3.6)	0 (0) (0.0, 3.8)	1 (1.0) (0.0, 5.6)	0 (0) (0.0, 3.8)
E-cigarettes						
NS	1 (1.0) (0.0, 5.7)	0 (0) (0.0, 3.8)	0 (0) (0.0, 3.9)	1 (1.1) (0.0, 5.8)	1 (1.0) (0.0, 5.7)	1 (1.0) (0.0, 5.7)
LA-25 NS	1 (1.0) (0.0, 5.6)	1 (1.0) (0.0, 5.7)	0 (0) (0.0, 3.6)	2 (2.1) (0.3, 7.4)	1 (1.0) (0.0, 5.6)	1 (1.0) (0.0, 5.7)

Abbreviations: CC = conventional cigarettes; CI = confidence interval; FS = Adult Former Smokers; LA = legal smoking age; NS = Adult Never Smokers; SG = Surgeon General; THS = Tobacco Heating System; RRC: reduced risk claim; RRC2: reduced risk claim 2; REC: reduced exposure claim.
Note: positive intention was operationalized as the proportion of subjects whose response to the single item assessing intention to try THS was either "Very Likely" or "Definitely".
Data Source: THS-PBA-05-RRC-US Study Report, Table 15.2.2.1.1, Table 15.2.2.1.3, and Table 15.2.2.1.4; THS-PBA-05-RRC2-US Study Report, Table 15.2.2.1.1, Table 15.2.2.1.3, and Table 15.2.2.1.4; THS-PBA-05-REC-US Study Report, Table 15.2.2.1.1, Table 15.2.2.1.3, and Table 15.2.2.1.4.

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 24 Positive Intention to Use among Adult Former Smokers and Adult Never Smokers exposed to Tobacco Sticks Pack by Study, Assessment Phase

	THS-PBA-05-RRC-US		THS-PBA-05-RRC2-US		THS-PBA-05-REC-US	
	SG Warning	PMI Warning	SG Warning	PMI Warning	SG Warning	PMI Warning
	n (%) 95% CI	n (%) 95% CI	n (%) 95% CI	n (%) 95% CI	n (%) 95% CI	n (%) 95% CI
THS						
FS	3 (3.2) (0.7, 9.1)	2 (2.1) (0.3, 7.5)	3 (3.3) (0.7, 9.2)	2 (2.1) (0.3, 7.3)	5 (5.2) (1.7, 11.7)	3 (3.1) (0.6, 8.9)
NS	0 (0) (0.0, 3.8)	0 (0) (0.0, 3.8)	0 (0) (0.0, 3.9)	0 (0) (0.0, 3.8)	0 (0) (0.0, 3.8)	1 (1.0) (0.0, 5.7)
LA-25 NS	0 (0) (0.0, 3.7)	0 (0) (0.0, 3.8)	0 (0) (0.0, 3.6)	0 (0) (0.0, 3.8)	0 (0) (0.0, 3.7)	1 (1.0) (0.0, 5.7)
CC						
FS	0 (0) (0.0, 3.9)	1 (1.1) (0.0, 5.8)	1 (1.1) (0.0, 5.8)	0 (0) (0.0, 3.8)	1 (1.0) (0.0, 5.7)	2 (2.1) (0.3, 7.3)
E-cigarettes						
FS	4 (4.3) (1.2, 10.6)	7 (7.4) (3.0, 14.7)	4 (4.3) (1.2, 10.6)	6 (6.3) (2.3, 13.1)	3 (3.1) (0.6, 8.9)	4 (4.2) (1.1, 10.3)

Abbreviations: CC = conventional cigarettes; CI = confidence interval; FS = Adult Former Smokers; LA = legal smoking age; NS = Adult Never Smokers; SG = Surgeon General; THS = Tobacco Heating System; RRC: reduced risk claim; RRC2: reduced risk claim 2; REC: reduced exposure claim.
Note: positive intention was operationalized as the proportion of subjects whose response to the single item assessing intention to use THS was either "Very Likely" or "Definitely".
Source: THS-PBA-05-RRC-US Study Report, Table 15.2.2.1.1, Table 15.2.2.1.3, and Table 15.2.2.1.4; THS-PBA-05-RRC2-US Study Report , Table 15.2.2.1.1, Table 15.2.2.1.3, and Table 15.2.2.1.4; THS-PBA-05-REC-US Study Report, Table 15.2.2.1.1, Table 15.2.2.1.3, and Table 15.2.2.1.4.

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 25 Positive Intention to Try among Adult Former Smokers and Adult Never Smokers exposed to THS Direct Mail by Study, Assessment Phase

	THS-PBA-05-RRC-US	THS-PBA-05-RRC2-US	THS-PBA-05-REC-US
	PMI Warning n (%) 95% CI	PMI Warning n (%) 95% CI	PMI Warning n (%) 95% CI
THS			
FS	5 (5.2) (1.7, 11.7)	2 (2.2) (0.3, 7.6)	4 (4.2) (1.1, 10.3)
NS	1 (1.0) (0.0, 5.7)	0 (0) (0.0, 3.9)	0 v (0.0, 3.8)
LA-25 NS	0 (0) (0.0, 3.8)	1 (1.1) (0.0, 5.8)	1 (1.1) (0.0, 5.8)
CC			
NS	0 (0) (0.0, 3.8)	0 (0) (0.0, 3.9)	2 (2.1) (0.3, 7.3)
LA-25 NS	0 (0) (0.0, 3.8)	0 (0) (0.0, 3.8)	2 (2.2) (0.3, 7.6)
E-cigarettes			
NS	1 (1.0) (0.0, 5.7)	1 (1.1) (0.0, 5.9)	2 (2.1) (0.3, 7.3)
LA-25 NS	2 (2.1) (0.3, 7.3)	2 (2.1) (0.3, 7.5)	2 (2.2) (0.3, 7.6)

Abbreviations: CC = conventional cigarettes; CI = confidence interval; FS = Adult Former Smokers; LA = legal smoking age; NS = Adult Never Smokers; SG = Surgeon General; THS = Tobacco Heating System; RRC: reduced risk claim; RRC2: reduced risk claim 2; REC: reduced exposure claim.
Note: positive intention was operationalized as the proportion of subjects whose response to the single item assessing intention to try THS was either "Very Likely" or "Definitely".
Data Source: Study Reports THS-PBA-05-RRC-US, Table 15.2.2.1.1, Table 15.2.2.1.3, and Table 15.2.2.1.4; THS-PBA-05-RRC2-US, Table 15.2.2.1.1, Table 15.2.2.1.3, and Table 15.2.2.1.4; THS-PBA-05-REC-US, Table 15.2.2.1.1, Table 15.2.2.1.3, and Table 15.2.2.1.4.

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

Table 26 Positive Intention to Use among Adult Former Smokers and Adult Never Smokers exposed to THS Direct Mail by Study, Assessment Phase

	THS-PBA-05-RRC-US	THS-PBA-05-RRC2-US	THS-PBA-05-REC-US
	PMI Warning n (%) 95% CI	PMI Warning n (%) 95% CI	PMI Warning n (%) 95% CI
THS			
FS	3 (3.1) (0.6, 8.9)	1 (1.1) (0.0, 5.8)	1 (1.0) (0.0, 5.7)
NS	1 (1.0) (0.0, 5.7)	1 (1.1) (0.0, 5.9)	1 (1.1) (0.0, 5.7)
LA-25 NS	0 (0) (0.0, 3.8)	1 (1.1) (0.0, 5.8)	0 (0.0, 3.9)
CC			
FS	0 (0) (0.0, 3.8)	2 (2.2) (0.3, 7.6)	1 (1.0) (0.0, 5.7)
E-cigarettes			
FS	4 (4.2) (1.1, 10.3)	7 (7.5) (3.1, 14.9)	4 (4.2) (1.1, 10.3)

Abbreviations: CC = conventional cigarettes; CI = confidence interval; FS = Adult Former Smokers; LA = legal smoking age; NS = Adult Never Smokers; SG = Surgeon General; THS = Tobacco Heating System; RRC: reduced risk claim; RRC2: reduced risk claim 2; REC: reduced exposure claim.
Note: positive intention was operationalized as the proportion of subjects whose response to the single item assessing intention to use THS was either "Very Likely" or "Definitely".
Data Source: Study Reports THS-PBA-05-RRC-US, Table 15.2.2.1.1, Table 15.2.2.1.3, and Table 15.2.2.1.4; THS-PBA-05-RRC2-US, Table 15.2.2.1.1, Table 15.2.2.1.3, and Table 15.2.2.1.4; THS-PBA-05-REC-US, Table 15.2.2.1.1, Table 15.2.2.1.3, and Table 15.2.2.1.4.

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.

6.3.1.5 References

FDA (Food and Drug Administration). Guidance for industry - Modified risk tobacco product applications - Draft Guidance. 2012.

FDA (Food and Drug Administration). Guidance for industry - Patient-reported outcome measures: use in medical product development to support labeling claims. 2009.

Fishbein M, Ajzen I. Belief, attitude, intention and behavior: an Introduction to theory and research. ed.: Addison-Wesley Pub (Sd); 1975. Chapter 7 - Formation of intention. p.

Harakeh Z, Scholte RH, Vermulst AA, de Vries H, Engels RC. Parental factors and adolescents' smoking behavior: an extension of The theory of planned behavior. Prev Med. 2004; 39(5):951-61.

IOM. Scientific standards for studies on modified risk tobacco products Washington DC: The National Academies Press; 2012.

IOM (Institute of Medicine). Scientific standards for studies on modified risk tobacco products. Washington, DC: The National Academies Press. 2012.

Parascandola M, Hurd AL, Augustson E. Consumer awareness and attitudes related to new potential reduced-exposure tobacco products. Am J Health Behav. 2008; 32(4):431-7.

Pierce JP, Choi WS, Gilpin EA, Farkas AJ, Berry CC. Tobacco industry promotion of cigarettes and adolescent smoking. JAMA. 1998; 279(7):511-5.

Shiffman S, Pillitteri JL, Burton SL, Di Marino ME. Smoker and ex-smoker reactions to cigarettes claiming reduced risk. Tob Control. 2004; 13(1):78-84.

WHO (World Health Organization). Guidelines for Controlling and Monitoring the Tobacco Epidemic. ed.: World Health Organization; 1998. Monitoring tobacco use. p. 76-101.

Confidentiality Statement

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 applicable provisions of United States law. No part of this document may be publicly disclosed without the written consent of Philip Morris Products S.A.