Module 6 : Research

6.4 Consumer Understanding and Perceptions

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1. CONSUMER UNDERSTANDING AND PERCEPTIONS

1.1. Introduction

To measure the potential benefit of marketing a MRTP to the public, the FDA Modified Risk Tobacco Product Applications Guidance recommended investigating several areas, including the effect of marketing on consumer understanding and perceptions[1]. In this section, we provide data from both pre-market studies included in the original MRTPA[2], and postmarket studies conducted both within the U.S. and internationally, on the effect of *IQOS* marketing on consumer understanding and perceptions. In addition, we cross-reference Module 7 of the original MRTPA for the Authorized *IQOS* products with related appendices and data, and with subsequent amendments, and Module 7 of the supplemental PMTA for the Authorized *IQOS* 3 System (PM0000634), as well as Module 7 of the supplemental MRPTA for *IQOS* 3 System (MR0000192).

1.2. U.S. Pre-market Studies

1.2.1. Background

To provide data on the effect of *IQOS* marketing on consumer understanding and perceptions, PMI conducted a U.S. premarket quantitative study (THS-PBA-05-REC-US)[3] to assess the effect of the authorized reduced exposure claim, included as part of the THS Label, Labeling and Marketing Materials (LLM), on consumer understanding and perception among adult users and non-users of tobacco products. A summary of the methodology of this study is presented in section 6.2 (Table 1).

Below, we provide a brief summary of previously submitted evidence from this U.S. pre-market quantitative study that aimed to assess, among others, the Comprehension of the modified risk claim and Risk Perception of the Authorized *IQOS* System (THS 2.2), among adult users and non-users of tobacco products, following exposure to THS LLM with the authorized reduced exposure claim.

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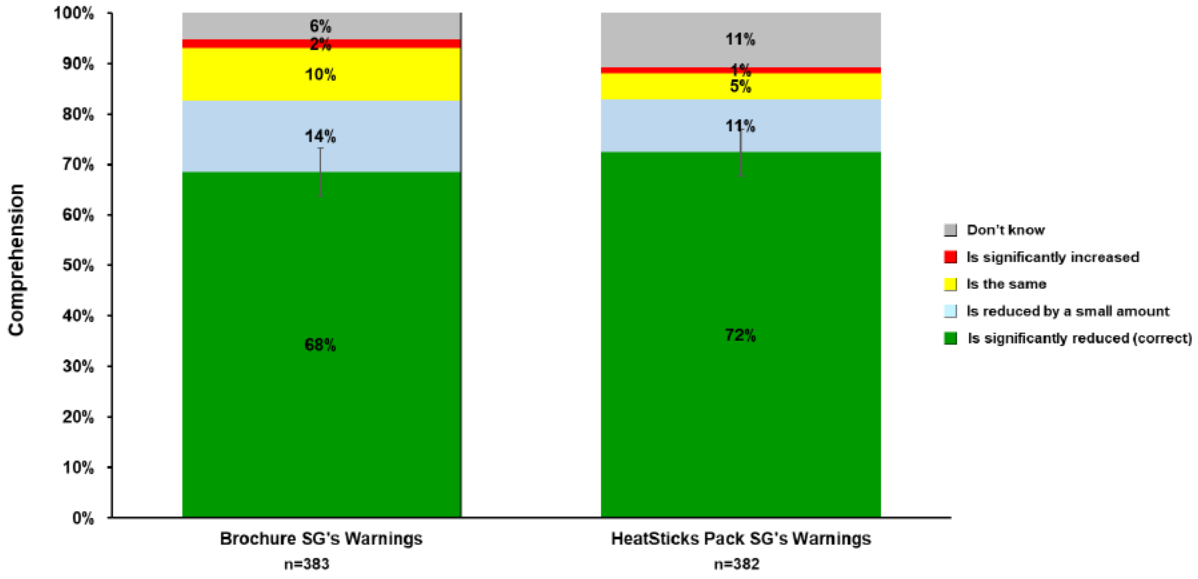
[1] FDA. Modified Risk Tobacco Product Applications. Guidance for Industry. Rockville, MD: U.S. Department of Health and Human Services. March 2012. https://www.fda.gov/downloads/TobaccoProducts/Labeling/RulesRegulationsGuidance/UCM297751.pdf.

[2] Modified Risk Granted Orders (MRGOs) – Exposure Modification issued on July 7, 2020 for the *IQOS* 2.4 System (MR0000133) with three (3) variants of *HeatStick* (MR0000059 - MR0000061)

[3] MO PM0000424-PM0000426, PM0000479 dated April 30, 2019 (section 6.2.2 Product Usage) and MGO MR0000059-MR000061 and MR0000133 dated July 7, 2020 (section 6.2.2 Product Usage)

1.2.1. Effect of THS Label, Labeling and Marketing Material on Comprehension

In the THS-PBA-05-REC-US study, the evaluation of the ability of adult users and non-users of tobacco products to understand information on the reduced exposure to HPHCs of THS 2.2 in comparison to conventional cigarettes was based on the level of correct comprehension of one communication objective: "exposure to harmful and potentially harmful chemicals is significantly reduced with THS 2.2 compared to conventional cigarettes". The levels of correct comprehension that Exposure to HPHCs is significantly reduced with THS 2.2 compared to conventional cigarettes ranged between 68% and 72% in the two study arms with the Surgeon General's Warnings (Figure 1).



Abbreviation: SG, Surgeon General.
Note: Error bars presented are 95% confidence intervals for the proportion correct
Data Source: THS-PBA-05-REC-US Study Report Figure 15.1.2.2.1 (Original IQOS 2.4 MRTPA submission dated Dec 5, 2016

Figure 1 Comprehension of Level of Exposure to Harmful and Potentially Harmful Chemicals Associated with the THS 2.2 Brochure and Associated with the HeatSticks Pack Within the Main Sample in THS-PBA-05-REC-US

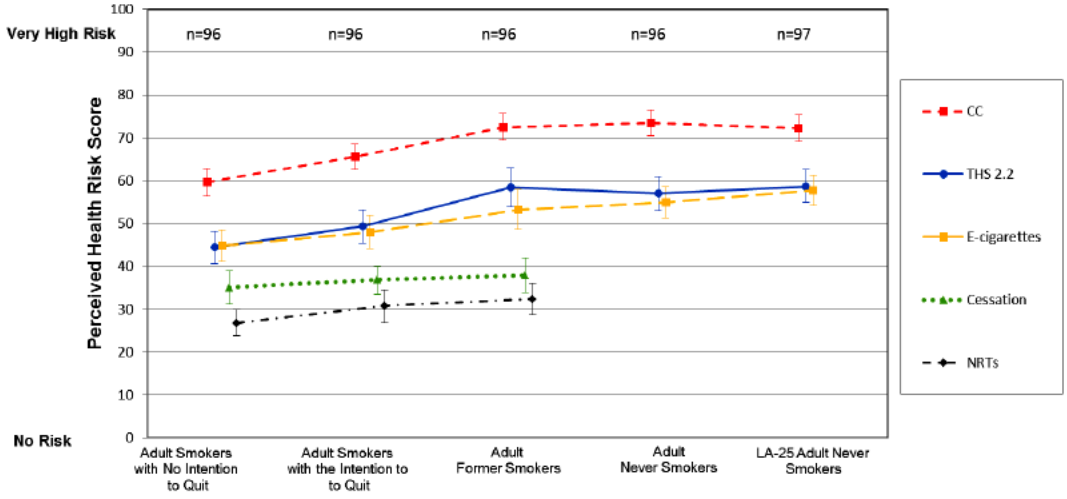
1.2.2. Effect of THS Label, Labeling and Marketing Material on Perceived Health Risk

The THS-PBA-05-REC-US study also found that among current smokers, the perceived health risk score[4] for THS 2.2 ranged between a lowest of 41.8 and a highest of 49.3 in the two study arms with the Surgeon General's Warnings, which corresponds to a moderate perceived risk. Moreover, among current smokers, THS 2.2 was consistently rated as having a lower perceived health risk than cigarettes (score range between a lowest of 59.6 to a highest of 65.7), which is in line with the relative health risks of the product that are reasonably likely (MRTP TPL).[5] Former smokers and never smokers rated the perceived health risk of THS 2.2 to be 49.3 and 58.5, respectively, which was higher than the lowest score rating observed among current smokers with intention to quit (41.8) and smokers with no intention to quit (42.1). Results also showed that, among either current smokers or former smokers, the perceived health risk related to THS 2.2 was higher than the perceived health risk for the lowest comparator, for instance, nicotine replacement therapy products which was rated to have a perceived health risk within a range of 26.9-32.5. The latter findings means that individuals perceived that there is risk associated with using THS 2.2 (i.e., using THS 2.2 is not risk free). These findings were observed for all tested LLM (i.e., THS 2.2 Brochure, *HeatSticks* Pack and THS 2.2 Direct Mail[6]) as well as across all subject groups (i.e., adult smokers, adult former smokers, and adult never smokers) (see Study Methodology section 6-2 Table 1). The Perceived Health Risk following the exposure of THS 2.2 Brochure with Surgeon General's Warnings (Arm 1) and the Perceived Health Risk following the exposure of *HeatSticks* Pack with Surgeon General's warnings (Arm 3) can be found in (Figure 2).

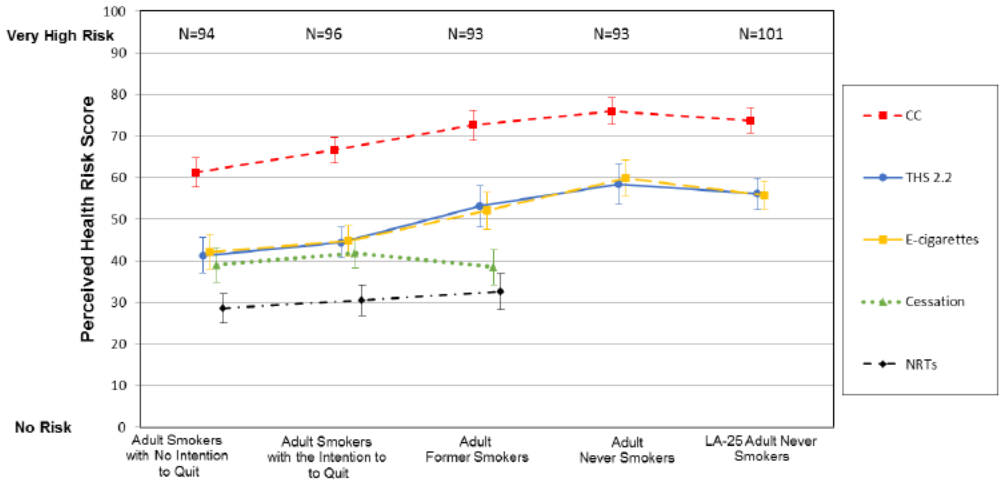
[4] Perceived health risk of *IQOS* was assessed using the validated ABOUT™ Perceived Risk Instrument, an 18-item, psychometrically valid measure of risk perceptions for various tobacco-types and levels of smoking status.

[5] Technical Project Lead (TPL) Review for the MRTP exposure modification orders granted on July 7, 2020.

[6] Results for PMI warnings are not presented herein and have been described in more details in sections 6.2.2, 6.3.1, 6.4 and 7.3.2 of the original MRTPA.



THS 2.2 Brochure, SG warnings (Arm 1)



HeatSticks™ Pack, SG warnings (Arm 3)

Abbreviations: CC = conventional cigarette; LA = legal age; NRT = nicotine replacement therapy. SG, Surgeon General.
Error bars are the 95% confidence intervals of the mean.
Note: connecting lines are only to highlight clustering of outcomes for each comparator along the x-axis.

Data Source: Study Report THS-PBA-05-REC-US, Figure 15.1.3.1.1 and Figure 15.1.3.1.3, described in sections 7.3.2, 6.2.2, 6.3.1, and 6.4 of the original MRTPA for IQOS 2.4.

Figure 2 Perceived Health Risk – THS 2.2 Brochure with Surgeon General's Warnings, Arm 1 and HeatSticks Pack with Surgeon General's warnings, Arm 3 in THS-PBA-05-REC-US

1.2.3. Conclusion of Pre-market U.S studies

Based on TPL review of the THS-PBA-05-REC-US consumer perception study, which was part of the original MRTPA, the FDA concluded that:

"*The results of applicant's consumer perception studies support that consumers generally comprehend the modified risk information in the context of total health. In particular, the results indicate that consumers understand that the product is not without risks and that it is more harmful than quitting smoking. Consumers also generally perceive the product as less harmful than combusted cigarettes, which is in line with the relative health risks of the product that are reasonably likely".*[7]

Although PMP S.A. has not conducted any new Tobacco Product Perception and Intention (TPPI) studies for the Authorized *IQOS* System in the United States, the results and conclusions from the U.S. premarket THS-PBA-05-REC-US study remain valid and relevant as confirmed by postmarket study data from U.S. and international markets, as outlined in section 1.3 and in section 1.4.

1.3. U.S. Postmarket Studies

1.3.1. Background

As part of the PMSS Plan for *IQOS* pursuant to the MRGOs issued by the FDA, PMP S.A. has implemented the *IQOS* cross-sectional Postmarket Adult Consumer Study (PACS) among qualified adult ever established *IQOS* users aged 21 years of age or older. The *IQOS* Cross-sectional PACS permits the evaluation of the impact of the marketing of the *IQOS* System with the authorized modified risk claim on consumer understanding and perception as highlighted by FDA TPL review[8] comment which stated that *'…postmarket surveillance should be conducted to ensure consumers understand that the benefits of reduced exposure cannot be achieved by continuing to smoke combusted cigarettes in addition to using IQOS'.*

A summary of the latest version of this study, which is part of our approved PMSS program, is provided in Section 8.1. The cessation of sales of *IQOS* due to the ITC order has limited our ability to study and surveil *IQOS* use (see section 8.1). As such, timing and plans for PMSS have been adjusted as documented in the letter sent to FDA on January 14, 2022[9]. Changes include pausing the *IQOS* Cross-sectional PACS. A summary of the *IQOS* Cross-sectional PACS methodology is presented in section 6-2 (Table 1).

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[7] Technical Project Lead (TPL) Review for the MRTP exposure modification orders granted on July 7, 2020.

[8] Scientific Review of Modified Risk Tobacco Product Application (MRTPA) Under Section 911(d) of the FD&C Act – Technical Project Lead, p. 53, July 6, 2020.

[9] Letter « Adjustment to the Postmarket Surveillance and Studies (PMSS) Plan forMR0000059 - MR000061 and MR0000133 » dated January14, 2022.

1.3.2. Consumer Understanding from IQOS Cross-sectional PACS

Before pausing the *IQOS* Cross-sectional PACS, the study did provide data to evaluate consumers' understanding of the influence that switching completely from cigarettes to *IQOS* has on exposure to HPHCs as well as their understanding as to what may reduce their exposure to HPHCs.

Among current established *IQOS* users (n=439), the majority of users (80.9%) understood that the exposure to HPHCs was lower when switching completely from cigarettes to *IQOS*. Moreover, only a smaller proportion of established *IQOS* users thought *IQOS* posed the same exposure (8.9%) or no exposure (4.8%) to HPHCs (Figure 3).

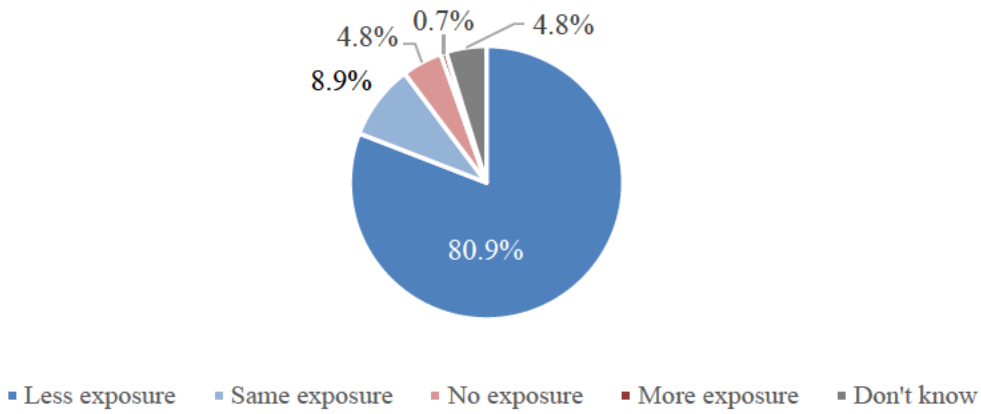

Figure 3 Perception about harmful or potentially harmful chemical exposure when switching completely from cigarettes to IQOS

Source: "IQOS Cross-sectional PACS" - Final Study Report - Wave 1[10]: Table 11

When asked what smokers must do to reduce their exposure (n=355), the majority (85.4%) thought they should stop smoking completely and only use *IQOS*. A smaller proportion (7.9%) thought they should smoke fewer cigarettes and also use *IQOS* (Figure 4).

[10] 2022 Annual report and PMSS plan submitted on April 29, 2022, P01-1_-_IQOS_Cross-Sectional_PACS_-_Wave_1_Final_Study_Report

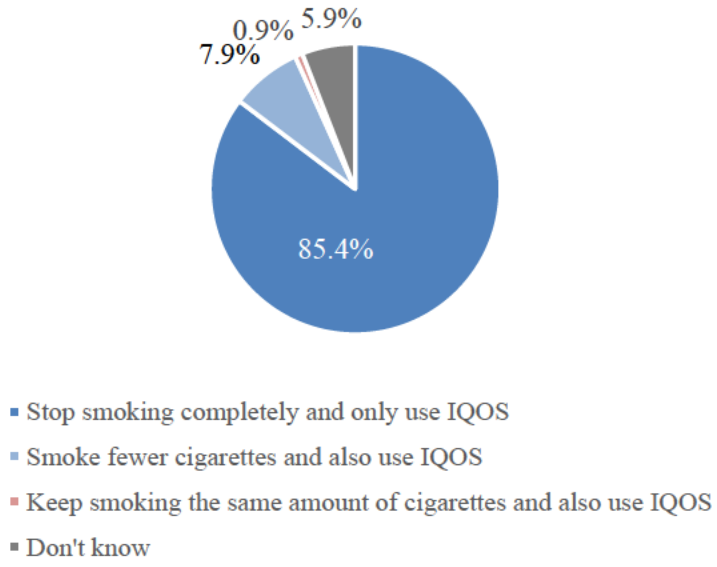

Figure 4 Understanding of what smokers must do to reduce their exposure to harmful or potentially harmful chemicals

Source: "IQOS Cross-sectional PACS" - Final Study Report - Wave 1[11]: Table 11

1.3.3. Perceived Health Risk from IQOS Cross-sectional PACS

Perceived health risks of *IQOS* and cigarettes were evaluated as part of the *IQOS* Cross-Sectional PACS, also using the ABOUT™ Perceived Risk Instrument for general risk assessment (PRI-G) (Cano et al., 2018). The resulting PRI-G Health Risk composite score was used to compare risk perceptions of one tobacco product to another at particular usage levels.

Overall, *IQOS* users perceived the risk of smoking cigarettes to be higher than the risk associated with using *IQOS*. This higher risk perception score for cigarettes was consistently observed among both current *IQOS* users who continued to smoke cigarette (64.1) and current *IQOS* users who quit smoking cigarettes (68.6) (Table 1). The mean composite score of the risk of using *IQOS* was lower among current *IQOS* users who quit smoking (i.e., used *IQOS* exclusively) (42.7) compared to current *IQOS* users who were also current cigarette smokers (45.8) or former *IQOS* users who had the highest risk perception of *IQOS* (47.1). Thus, it can be concluded that the results of the post-market study confirmed the findings of the perceived health risk of *IQOS* observed in the U.S. pre-market studies described in section 1.2.

[11] 2022 Annual report and PMSS plan submitted on April 29, 2022, P01-1_-_IQOS_Cross-Sectional_PACS_-_Wave_1_Final_Study_Report

Table 1 Risk Perceptions of *IQOS* and Cigarette

	Ever Established *IQOS* Users (n=463)		Current Established *IQOS* Users who smoke cigarettes (n=214)		Current Established *IQOS* Users who quit smoking cigarettes (n=99)		Former Established *IQOS* Users (n=24)	
	%	95% CI	%	95% CI	%	95% CI	%	95% CI
IQOS	44.41	(42.88; 45.94)	45.81	(43.41; 48.22)	42.72	(39.28; 46.15)	47.14	(40.77; 53.52)
Cigarettes	65.37	(63.77; 66.97)	64.10	(61.82; 66.39)	68.64	(64.90; 72.37)	64.48	(57.81; 71.14)

Source: "IQOS_Cross-sectional_PACS_TLF_Pre-Group'[12] : Table 8

1.3.4. Conclusion of U.S. Postmarket studies

In summary, U.S. postmarket results from the first wave of the *IQOS* Cross-sectional PACS demonstrated that adult current established *IQOS* users understood that *IQOS* was not risk free and that switching completely to *IQOS* would reduce exposure to HPHCs compared to smoking cigarettes.

1.4. PMP S.A. International Postmarket Data: Repeated Cross-sectional Post-Market Surveys (PMX studies)

1.4.1. Background

PMI has gathered data on the perceived health risk of using *IQOS* as part of PMI repeated cross-sectional post-market studies (PMX studies) in Italy and Japan. These cross-sectional surveys are conducted in nationally representative random samples of legal age adult participants from the general population (n > 5,000; 4-6 waves distributed over the year) coupled with surveys in large samples of *IQOS* users (n > 1,400; 4 waves distributed over the year) randomly selected from registered *IQOS* owners of PMI's country-associated *IQOS* Owner databases. Similarly to the methodology described for our pre-market TPPI study and post-market cross-sectional PACS study conducted in the U.S., perceived health risk was assessed using the validated ABOUT™ Perceived Risk Instrument (score from 0 [no-risk] to 100 [very-high risk]) (Cano, 2018).

[12] Annual Report 2022 PMSS report *IQOS*_Cross-sectional_PACS_TLF_Pre-Group_V1.0_20220110

In Italy, in study Year 2 (2019-2020), current *IQOS* users (N=1,401) perceived the health risk associated with smoking cigarettes (score: 64.3) to be higher compared to the health risk associated with using *IQOS* (score: 44.4) resulting in a health risk score difference of 19.6. The health risk associated with using *IQOS* (score: 44.4) also indicates that *IQOS* was not perceived as risk-free[13].

In Japan, five-year trend data have been collected. Across Year 1 (2016-2017) to Year 5 (2021-2022) (Figure 5), it can be observed that self-reported perceived health risk associated with smoking cigarettes remained stable with a score of 63.7 in Year 1, 62.1 in Year 2 (2017-2018), 63.3 in Year 3 (2018-2019), 62.2 in Year 4 (2020-2021), and 63.0 in Year 5, respectively. This score corresponds to high perceived risk. In contrast, the self-reported perceived health risk associated with using *IQOS* increased from 44.0 in Year 1, to 45.9 in Year 2, and to 48.6 in Year 3, respectively. The perceived health risk score for *IQOS* subsequently stabilized in Year 4 (49.4) and Year 5 (49.6) corresponding to a moderate perceived risk.

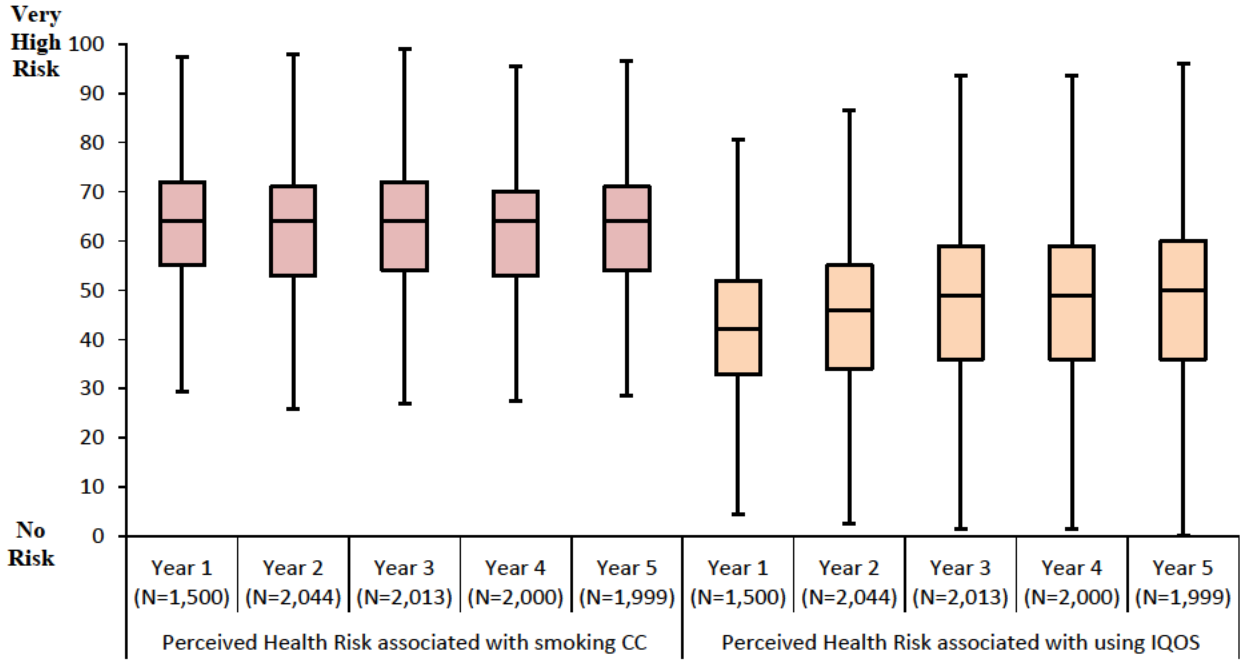

Figure 5 Perceived Health Risk Associated with Cigarettes /Using *IQOS* - Trend Data - *IQOS* Users in Japan.

Abbreviation: CC = conventional cigarette
Source: Appendix 7-a03-P1-PMX-01-JP-study-report-year-5

[13] Source: Appendix 7-a04-P1-PMX-02-IT-study-report-year-2

1.4.1. Conclusion of International Postmarket studies

Data from our international PMX studies shows that adult *IQOS* users perceived the health risks associated with using *IQOS* to be lower than the health risks associated with smoking cigarettes. At the same time, adult *IQOS* users perceived that there are health risks associated with using *IQOS* (i.e., using *IQOS* is not risk free). In addition, the same studies show that perceived health risk of cigarettes continues to be higher than perceived health risk of *IQOS* and that over time perceived health risk of *IQOS* has increased although it continues to be lower than perceived health risk of cigarettes (AlMoosawi, 2022).

1.5. Independent Studies

PMP S.A. analysis and PMP S.A. literature review of independent studies submitted to the FDA as part of PMP S.A.'s Annual Reporting[14] related to the Marketing Order for the Authorized *IQOS* Systems show that risk communication may influence use behavior of HTPs, including *IQOS*, as well as adoption and transitioning to exclusive use. Since PMP S.A.'s 2023 Annual Reporting[15], PMP S.A. has not identified any further independent studies in the context of risk communication.

2. CONCLUSION

The results of the U.S. pre-market study, submitted as part of the original MRTPA, showed that consumers were able to understand that, upon switching completely from CC to *IQOS*, they would benefit from a reduction of exposure to HPHCs. A high level of understanding that completely switching to *IQOS* would reduce exposure to HPHCs compared to smoking was also found in the U.S. postmarket study.

Findings from U.S. pre-market studies as well as U.S. and international post-market studies also consistently demonstrate that adult users and non-users of tobacco products perceive the health risks associated with using *IQOS* to be lower than the health risks associated with smoking cigarettes. Moreover, our study data show that they perceive that there is risk associated with using *IQOS* (i.e., using *IQOS* is not risk free). Importantly, both adult former smokers and adult never smokers also perceived that there are health risks associated with using *IQOS* and that this perceived risk was higher than the perceived health risks reported by adult current smokers.

Finally, our analysis and our literature review of independent studies show that risk communication influences use behavior. Findings point towards the importance of providing accurate and non-misleading information to smokers to ensure adult smokers are able to make

[14] For the list of Annual Reports see section 4.2 Marketing Plan

[15] 2023 Annual Report and PMSS report submitted on April 28, 2023

informed decisions about the risks and benefits of various tobacco products to help facilitate their transition from cigarettes to smoke-free products, such as *IQOS*, and prevent potential relapse into cigarettes.

Thus, the combined evidence from our pre-market and post-market studies conducted in the U.S. and internationally provides evidence that *IQOS* continues to satisfy MRTP requirements in accordance with section 911(g)(2)(B) of the FD&C Act as evidence continue to show that *consumers generally comprehend the modified risk information in the context of total health,* that *consumers understand that the product is not without risks and that it is more harmful than quitting smoking* and that *consumers also generally perceive the product as less harmful than combusted cigarettes, which is in line with the relative health risks of the product that are reasonably likely.*[16]

3. REFERENCES

AlMoosawi, S., Bajec, M., Mainy, N., Kallischnigg, G., Zwisele, B., Fischer, K., Magnani, P. and Roulet, S., 2022. Risk perception of IQOS™ and cigarettes: Temporal and cross-country comparisons. SSM-Population Health, 18, p.101123.

Cano, S., Chrea, C., Salzberger, T., Alfieri, T., Emilien, G., Mainy, N., ... & Weitkunat, R. (2018). Development and validation of a new instrument to measure perceived risks associated with the use of tobacco and nicotine-containing products. *Health and Quality of Life Outcomes*, *16*(1), 1-15.

[16] Technical Project Lead (TPL) Review for the MRTP exposure modification orders granted on July 7, 2020.