

**PMI's December 22, 2017 amendment to its IQOS MRTP application  
failed to address concerns about dual use, flavors, risk perceptions, and its  
Population Health Impact Model**

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On October 1, 2018 FDA posted amendments to PMI's IQOS MRTP application, including PMI's December 22, 2017 response to FDA's November 22, 2017 information request. PMI's response did not adequately address discrepancies between data provided by PMI and FDA's own analysis regarding the extent to which smokers switch completely to IQOS vs using IQOS concurrently with cigarettes. Further, PMI's response did not adequately address FDA's questions regarding perceptions of IQOS or intention to try or use IQOS among current, former, or never smokers, including under age youth. Finally, PMI's response failed to address several concerns about its Population Health Impact Model.

**1. FDA Question 16, pp. 28-30**

FDA noted in Question 16 of its November 22, 2017 information request that in the IQOS MRTP application's Executive Summary, PMI provided data from a Japanese Market Research Panel of adult IQOS purchasers suggesting that 65% of smokers within this panel converted to exclusive IQOS use. However, FDA's own analysis of post-market cross-sectional study data showed that 85% of IQOS users continued to smoke cigarettes in addition to IQOS. FDA asked PMI to explain the discrepancy and provide additional information on the extent to which Japanese smokers switch completely to IQOS vs dual use with cigarettes.

PMI claims (page 28-30 of their response) that the two studies are too different to compare and the study FDA used for its estimates is not supposed to be used for the purpose of estimating the prevalence of complete switching to IQOS. However, the post-market cross-sectional study data do provide numbers on what proportion of IQOS users switch completely. Because the post-market cross-sectional study is representative of the overall adult population and captures behavior of adult smokers in the real world, this study is appropriate for estimating the prevalence of switching and dual use rates. The Market Research Panel is limited to people who purchased IQOS and registered it, which provides valid estimates of switching rates only for this limited population of users. Comparing the designs of two studies, the cross-sectional study is actually better suited to make population-level estimates of complete switching from smoking combusted cigarettes to IQOS that the FDA is looking for.

A recent peer reviewed study of young adults 19-24 of IQOS in Korea found that all the current IQOS users were triple users of conventional cigarettes and electronic cigarettes (e-cigarettes). There were no IQOS-only users and one IQOS ever user was a non-cigarette smoker.<sup>1</sup>

The main point PMI makes is that post-market research is needed. While this is true for all new tobacco products, such research should not be conducted by PMI because doing so could become cover for PMI to do market research on youth and young adults. The 2012 Surgeon General's Report on Preventing Tobacco Use Among Youth and Young Adults<sup>2</sup> recognizes that the tobacco industry receives benefits from this kind of market research:

Investment in these programs provides a venue for the industry to conduct research on determinants of smoking among youth for the stated purpose of developing its prevention programs. However, this information could inform the companies' tobacco marketing efforts to youth (Mandel et al. 2006). Tobacco industry research on youth has included Philip Morris' "Teenage Attitudes and Behaviors Study," which tracked the smoking behavior and motivations of approximately 20,000 11–17-year-olds annually, with a total of 180,000 teens being surveyed between 1999 and 2007 (Philip Morris USA 2008b). Although tobacco companies assert that there is a "firewall" between the research done for the department concerned with preventing smoking by youth and their cigarette marketing efforts, Philip Morris has acknowledged that it rotates employees through both departments (Tobacco on Trial 2005).<sup>2</sup>

Any future studies conducted by PMI should not be studies of select users who purchase and register with IQOS, but rather be studies of representative samples of the adult population in order to estimate real-world rates of switching and dual use.

## **2. FDA Question 17, pp. 31-34**

In Question 17 FDA asked PMI to confirm whether the IQOS products used by participants in Japanese post-market studies are the same as the products in the MRTPA.

PMI claimed in its response that while the products (and product codes) are not identical "due to continuous improvement of the product, and manufacturing site differences, they are comparable in their performance."

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<sup>1</sup> Kim J, Yu H, Lee S, Paek Y-J. Awareness, experience and prevalence of heated tobacco product, IQOS, among young Korean adults. 2018: tobaccocontrol-2018-054390.

<sup>2</sup> U.S. Department of Health and Human Services. Preventing Tobacco Use Among Youth and Young Adults: A Report of the Surgeon General, p. 563. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2012.

While PMI's argument (pages 31-34) is valid, it raises another question: If PMI moved on to "higher-quality" IQOS versions, which version(s) will be introduced in the US? Would the older or the newer versions be marketed? Would PMI be continuously making changes to the products after they are allowed in the US, similar to how they did in Japan? If so, then research must be conducted on both the new and the older versions to allow comparison and to determine effects with the newer product(s).

### 3. FDA Question 18, pp. 35-48

FDA requested that PMI submit information on perceptions of IQOS, intention to try or use IQOS, or intention to quit cigarette smoking or quit all tobacco use among current and former smokers by whether the participant was assigned to view a Regular, Smooth Menthol, or Fresh Menthol package. Additionally, FDA requested that PMI submit any information that describes perceptions of IQOS or intention to try or use IQOS among never smokers and legal age to 25 year old never smokers.

PMI had not done these analyses at the time of the application and did not have sufficient sample size to detect differences. They re-analyzed the data and in its December 2017 response reported the results for intent to try and use, risk perceptions, and change in intentions to quit smoking or tobacco (PMI Response pages 35-48, attached Appendix SRP1\_Q18-A1\_PMTA-05-NOC-US-Analysis Tables, and attached powerpoint discussing PMTA-05-NOC from PMI's January 2018 TPSAC presentation). The results were not statistically different due to very small sample sizes. However, the perceived risk scores for both health risks and addiction for "smooth menthol" were lower across current and former smokers, which might indicate that the word "smooth" is understood by smokers to communicate lower harm, similar to "light" and "mild" that are specifically prohibited by the Family Smoking Prevention and Tobacco Control Act.

PMI responded that non-smokers (including young adult non-smokers) were only shown "regular" products, justifying doing so by saying that "the Regular pack of HeatSticks would the type NS [non-smokers] would be most likely to see in a real world situation" because "regular (non-menthol)" cigarettes comprise approximately a third of the cigarette market in the United States (NSDUH Report, Recent Trends in Menthol Use, 2011." (p. 42, 02\_Response-to-FDA-InfoRequest)

There are four problems with PMI's response. First, PMI is misquoting the information from the NSDUH report. The report actually stated: "In 2010, an estimated 20.7 million Americans were current smokers of menthol cigarettes, accounting for more than one third of all smokers in the Nation."<sup>3</sup> Second, the rates of menthol use are much higher among youth and young adults as well as African Americans and the rates of use of menthol cigarettes are increasing.<sup>4</sup> Third, many non-smokers start their smoking with menthol cigarettes, a fact that the tobacco industry has long

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<sup>3</sup> Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. (November 18, 2011). *The NSDUH Report: Recent Trends in Menthol Cigarette Use*. Rockville, MD. Available at [https://www.samhsa.gov/data/sites/default/files/WEB\\_SR\\_088/WEB\\_SR\\_088/WEB\\_SR\\_088.htm](https://www.samhsa.gov/data/sites/default/files/WEB_SR_088/WEB_SR_088/WEB_SR_088.htm)

<sup>4</sup> <https://truthinitiative.org/news/menthol-facts-stats-and-regulations>

been exploiting.<sup>5</sup> Fourth, people are more likely to use menthol/mint and other flavored non-cigarette tobacco products, such as e-cigarettes, including Juuls.<sup>6</sup> Therefore, the data PMI submitted only shows non-smokers' responses to Regular products, so do not allow for the estimation of non-smokers' interest in the IQOS, which is likely to be greater than for non-mentholated product.

#### **4. FDA Question 19, pp. 48-50**

FDA noted in Question 19 that PMI did not provide any information about perceptions and intention to try or use IQOS among youth under age 18.

FDA has repeatedly asked and recommended PMI to “provide information about the likely impact that marketing a product as modified risk may have on non-adults and their tobacco use behavior.” PMI deflected this request by stating that they will not conduct studies on youth (Response pages 48-50). However, FDA is not asking for new studies. PMI could simply summarize the extensive existing literature on the likely impact that a modified risk tobacco product would have on non-users, using the example of electronic cigarettes. PMI chose not to do that, likely because the available evidence overwhelmingly indicates that a new modified risk product would appeal to adolescents and increase their rate of tobacco use as we are currently seeing with e-cigarettes and, for the first time in many years, with increasing cigarette use rates.<sup>7</sup> We addressed this issue in detail in our comment on PMI's IQOS MRTP application<sup>8</sup> and in a recently published peer reviewed paper.<sup>9</sup>

#### **5. FDA Questions 21, 22, and 23, pp. 52-61**

FDA solicits more information on PMI's Population Health Impact Model (PHIM), including notes on data files and information on the mathematical and computational structure of the P-Component of the PHIM to help FDA understand verification and validation including assumptions associated with the input parameters and validity of outputs.

Philip Morris provided more detail on the mechanics of running the PHIM, including SAS code, further information about input parameters for the simulation and sensitivity analyses, and a technical description of how they generated the tobacco use histories in

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<sup>5</sup> Klausner K. Menthol cigarettes and smoking initiation: a tobacco industry perspective. *Tobacco Control* 2011;20:ii12-ii19. =

<sup>6</sup> McKelvey, K., Baiocchi, M., Halpern-Felsher, B. Adolescents' and Young Adults' Use and Perceptions of Pod-based electronic cigarettes. *JAMA Network Open* 2018;1(6):1-13.

<sup>7</sup> CNBC. As vaping surges, teen cigarette smoking ticks up after decades of decline.

<https://www.cnbc.com/2018/10/22/teen-cigarette-smoking-ticks-up-as-vaping-surges.html> Published October 22, 2018.

<sup>8</sup> Halpern-Felsher B, McKelvey K, Kim M, et al. PMI's MRTP Application for IQOS Does Not Consider IQOS's Appeal to Youth or Adolescents, or the Likelihood that Youth and Adolescents will Initiate Tobacco Use with IQOS or Use IQOS with Other Tobacco Products, Docket Number: FDA-2017-D-3001, December 7, 2017. Available at: <https://www.regulations.gov/document?D=FDA-2017-D-3001-0148>.

<sup>9</sup> McKelvey K, Popova L, Kim M, Chaffee BW, Vijayaraghavan M, Ling P, Halpern-Felsher B. Heated tobacco products likely appeal to adolescents and young adults. *Tobacco Control*. 2018 Nov 1;27(Suppl 1):s41-7.

the model (Response pages 52-61 and attached Appendix SRP1\_Q22-A1\_Notes-PHIM-V4-project). These details, while helpful, do not address the concerns we raised about the model in our comment on PMI's IQOS MRTP application<sup>10</sup> <<cite the comment>> and in a recently published peer reviewed paper,<sup>11</sup> including mortality from only 4 diseases; ignoring morbidity; ignoring other tobacco products; optimistic assumptions about transition probabilities for initiation, cessation, and dual use; and not considering the impact of IQOS on non-users.

## Summary

The material PMI submitted in response to these questions fall short. The studies provided by PMI do not adequately determine if people will completely switch from cigarettes to IQOS or will become dual or poly users as found in other studies, do not provide enough information on which IQOS product(s) are being considered, and do not consider the role of flavors in the onset and continuation of IQOS usage.

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<sup>10</sup> Max W, Lempert L, Sung H-Y, et al. Philip Morris's Population Health Impact Model Based on Questionable Assumptions and Insufficient Health Impact Measures Does Not Adequately Support its MRTP Application, Docket Number: FDA-2017-D-3001, November 22, 2017. Available at: <https://www.regulations.gov/document?D=FDA-2017-D-3001-0121>.

<sup>11</sup> Max WB, Sung H, Lightwood J, et al. Modelling the impact of a new tobacco product: review of Philip Morris International's Population Health Impact Model as applied to the IQOS heated tobacco product Tobacco Control 2018;27:s82-s86.