

Appendix. Expanded Systematic Evaluation of Evidence Required by the Tobacco Control Act and Evidence Provided by PMI vs Extant Evidence to Support or Refute MRTP Claims.

Evidence Required by Tobacco Control Act	PMI's Evidence	Extant Evidence as of 1 June 2018
<p>Will IQOS and its marketing increase the likelihood that AYA <i>non-users</i> (including never users and former tobacco products users) will start using the product?</p>	<p>PMI did not provide this evidence.</p> <p>PMI claimed that that in a pre-market setting, the effect of IQOS on initiation among non-users could not be assessed. Instead, PMI used “behavioral intentions” which it defined as a person's perceived likelihood or subjective probability that he or she will engage in a given behavior as a proxy to predict the behavior of using an MRTP (section 6.3.1).</p>	<p>Large proportions of non-users are using IQOS and other non-cigarette tobacco products. In Italy, 45% of IQOS ever-users were never-smokers.</p> <p>Studies have found evidence of gateway from e-cigarettes to combusted tobacco products.</p> <p>Intentions are not a suitable proxy for actual behavior, especially for adolescents.¹⁻¹⁰</p> <p>Awareness and use of HTP products in the US were higher among young adults compared to older adults.^{11, 12}</p>
<p>Does IQOS expose consumers to the claimed reduced level of harm considering how consumers <i>actually use</i> IQOS, including concurrent use of multiple nicotine or tobacco products?</p>	<p>Given that dual and poly use were the prevailing patterns in the PMI studies, PMI did not demonstrate that IQOS, as actually used by consumers, reduced levels of harm.</p> <p>PMI reports (section 3.5.3 and 6.2.2) that 22.4% of US study participants still were using both regular combustible cigarettes and IQOS after 6 weeks. In other countries, dual use of IQOS and combustible cigarettes ranged from 27% (Germany) to 39% (Switzerland) after 4 weeks (section 3.5.3, Table 5 of PMI application). According to PMI's 2016 full-year report, 21-31% of users across multiple countries are dual-users, with a substantial portion of their tobacco use (>30%) from products other than IQOS, including regular combustible cigarettes. Another 7-15% are “Predominant (70-95% IQOS)” users, meaning they still use regular cigarettes along with IQOS up to 30% of the time.</p> <p>Of those who used HeatSticks at least 100 times (37% of all participants who completed the 6-week study), only 16% used</p>	<p>Epidemiologic evidence suggests that for other non-cigarette tobacco products, switching completely has not been the most common outcome.</p> <p>For example, among US adults who use electronic cigarettes, 75% to 82% use e-cigarettes in combination with at least one other form of combustible tobacco, and only 20% of e-cigarette users are recent quitters of combustible cigarettes.^{5, 10} In Japan, 72% of those who use HTP or e-cigarettes also concurrently used combustible tobacco products.¹³ Adolescent and young adult smokers who use novel tobacco products often use two or more kinds of tobacco products concurrently.¹⁴⁻¹⁷</p> <p>Meta-analysis showed use of e-cigarettes as cessation aid reduced odds of quitting cigarettes by 28% compared to those who used any other means of quitting.¹⁸</p>

	<p>HeatSticks exclusively by the end of the study period, suggesting that while HeatSticks users have the "potential" to completely switch, of 968 daily cigarette smokers who were given HeatSticks and completed the 6-week FAS study, only 58 (6%) "completely switched" to the IQOS product. No long-term studies were conducted to assess whether participants would return to cigarette use beyond 6 weeks.</p>	
<p>Does IQOS advertising or labeling enable the public to:</p> <p>a. comprehend the modified risk claims and the significance of the information in the context of one's health</p> <p>b. understand the health risks of using the product relative to <u>other tobacco products</u></p> <p>c. understand the health risks of using the product relative to <u>cessation aids</u></p> <p>d. understand the health risks of using the product relative to <u>quitting all tobacco use</u></p>	<p>PMI's application did not include information from studies with adolescents younger than 18.</p> <p>Adult never-smokers in PMI study reported greater perceptions of risk for IQOS than current or former smokers (section 6.4.4.1-3). PMI argues that IQOS will not cause or motivate "non-users to be interested in the product because it is still considered a risky product" (section 6.4, p. 70).</p> <p>Non-smokers' perceived risk for IQOS was higher than current and former smokers in PMI's studies after seeing the modified risk claims (section 6.4.4.1-3), although perceived risk was significantly lower than the non-smokers' perception of risks for regular cigarettes.</p> <p>PMI reports that adult current and former smokers perceived health risks of IQOS greater than risks associated with NRT use (THS-PBA-03 and in THS-PBA-05-REC_US). Both smokers and non-smokers rated the risks of IQOS on the levels similar to the health risks of e-cigarettes.</p>	<p>There is an extensive literature on adolescents conducted independently of the industry that PMI could have, but did not, present on current, former and non-users of cigarettes to understand their intentions as well as their willingness to use IQOS. This research also provides insights on the extent to which warning messages and ads influence youth perceptions and willingness to use IQOS.^{1, 2, 7}</p> <p>The actual marketing of IQOS to date in other countries demonstrates that PMI has not adequately protected against use by nonsmokers and suggests that the product's name, physical appearance, and retail environment will appeal to young people.^{9, 13, 19}</p> <p>PMI's arguments that modified risk claims will not attract never-smokers are illogical and inconsistent with the available evidence. Although users of tobacco products typically have lower risk perceptions than non-users, it is not only perceptions of risk that make non-users try new products.^{9, 20-22} Perceptions of benefits play a significant role in predicting smoking initiation among youth.^{1, 2, 7, 8} However, PMI did not evaluate perceived benefits.</p> <p>PMI's MRTP application failed to consider the likelihood that IQOS's two menthol flavors would appeal to youth and adolescents and encourage initiation among non-users.²³⁻²⁸</p> <p>Given that the PMI studies found that users and non-users rated health</p>

		risks of IQOS and e-cigarettes at the similar level, the experience with e-cigarettes is directly applicable to IQOS and could have been relied upon by PMI in their MRTTP application.
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