

**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**

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***Philip Morris International's (PMI) Modified Risk Tobacco Product (MRTP) application for IQOS does not adequately consider IQOS's appeal to or impact on youth or adolescents, and does not provide the necessary scientific evidence to support its MRTP claims of reduced risk or reduced exposure, especially as these claims affect youth and adolescents. Therefore, FDA should deny PMI's MRTP application for IQOS.***

**1. Background**

PMI is seeking FDA authorization to market their IQOS heating system with three flavors of their "HeatSticks" as a MRTP with three claims:

- (1) Switching completely from cigarettes to the IQOS system can reduce the risks of tobacco-related diseases;
- (2) Switching completely to IQOS presents less risk of harm than continuing to smoke cigarettes; and
- (3) Switching completely from cigarettes to the IQOS system significantly reduces your body's exposure to harmful and potentially harmful chemicals.

Section 911 of the Family Smoking Prevention and Tobacco Control Act<sup>1</sup> and FDA's Guidance for Industry on Modified Risk Tobacco Product (MRTP) Applications<sup>2</sup> spell out the rigorous requirements that MRTP applicants must meet before a product can be deemed a "modified risk tobacco product" and can be marketed with MRTP claims. In particular, to market IQOS with the MRTP claims stated above, PMI must prove using substantial and objective scientific evidence that the new product, *as it is actually used by consumers*, will:

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<sup>1</sup> Family Smoking Prevention and Tobacco Control Act, 21 U.S.C. §387k, Pub. L. 111-31, 123 Stat. 1776 (2009).

<sup>2</sup> Food and Drug Administration, Modified Risk Tobacco Product Applications, Draft Guidance (March 2012). Available at <https://www.fda.gov/downloads/TobaccoProducts/GuidanceComplianceRegulatoryInformation/UCM297751.pdf>

- (1) Significantly reduce harm and the risk of tobacco-related disease to individual tobacco users; and
- (2) benefit the health of the population as a whole, taking into account both users of tobacco products and persons who do not currently use tobacco products.

In fulfilling the MRTP application requirements specified in section 911(g), FDA recommends in its MRTP Guidance that applicants submit, among other things, the following data and information:

- 1) Scientific evidence regarding the effect that IQOS and its marketing will have on increasing the likelihood that *non-users* (including never users and former users) will start using the product (Guidance, p. 20);
- 2) Data and information on how consumers *actually use* IQOS, including data and information addressing concurrent use of multiple products containing nicotine or tobacco (Guidance, p. 15), and scientific evidence demonstrating that consumers actually use the product in a way that exposes them to the claimed reduced level of substances or harm (Guidance, p. 17);
- 3) Human studies that evaluate consumer understanding and perceptions of the product, including its labeling, marketing, and advertising, including:
  - a. The ability of consumers to understand the modified risk claims and the significance of the information in the context of one's health;
  - b. Consumers' beliefs about the health risks of using the product relative to other tobacco products;
  - c. Consumer beliefs about the health risks of using the product relative to cessation aids; and
  - d. Consumer beliefs about the risks of using the product relative to quitting all tobacco use (Guidance, pp. 20-21)

*Despite the requirements of the law and these explicitly stated FDA guidelines, PMI has met none of them with respect to the use of IQOS among adolescents. In addition, the discussion of the effects of IQOS on young adults is cursory at best. For these reasons, explained more fully below, FDA should deny PMI's MRTP application for IQOS.*

- 2. Because PMI's MRTP application did not consider the impact of IQOS on adolescent use, it did not demonstrate that the product, as actually used by consumers, will benefit the health of the population as a whole, including current non-users; in particular, it did not provide any scientific evidence regarding the effect that IQOS and its marketing would have on increasing the likelihood that adolescents who are currently not tobacco users will start using IQOS.**

Despite section 911(g)'s requirement, PMI failed to provide adequate scientific evidence demonstrating that IQOS would "benefit the health of the population as a whole," in particular non-users (including adolescents and young adults) as well as current users of other tobacco products.

PMI merely claimed that in a pre-market setting, the effect of IQOS on initiation among non-users could not be assessed. For that reason, PMI used "behavioral intention," 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 MRTTP (Chapter 6.3.1). . ***Other factors that PMI did not consider, including willingness to use tobacco, perceived social norms, peer influences, and perceptions and attitudes towards the specific tobacco product is more predictive of use than intentions alone.***<sup>3</sup> As detailed below, ***it is incorrect to assume that intentions are the primary drivers of behavior, especially for adolescents***

**a. Intentions are not a proxy for actual behavior, especially for adolescents**

According to older decision-making theories such as the Social Cognitive Theory,<sup>4</sup> the Health Belief Model,<sup>5</sup> the Theory of Reasoned Action,<sup>6</sup> and the Theory of Planned Behavior,<sup>7</sup> people's behaviors are largely shaped by their intentions to engage in that behavior. These intentions are, in turn, shaped by their perceptions of behavior-related risks and benefits. While these theories have some merit, they are largely relying on cognitive processes, whereby one is expected to have a deliberate, planned decision to or not to engage in a behavior. In these cases, intentions are more likely to lead to behavior. However, as discussed in detail below, studies show that these cognitive models do not accurately or fully predict how adolescents decide whether or not to engage in a behavior, including tobacco use.

In contrast, current research demonstrates that decision-making does not only involve a deliberate, analytic process. Instead, many decisions, including adolescents' decisions to use tobacco, are based more on heuristic, reactive, and affective processes.<sup>8</sup> While adolescents may not have an active plan in mind to smoke, they often find themselves in situations in which they would consider smoking even though they were originally committed to avoiding it. Willingness to smoke is shaped by perceptions, including perceived peer norms and peer acceptance of smoking as well as images associated with smoking. For example, adolescents are less likely to smoke if they hold negative images that smokers are dirty, wrinkled, and have yellow teeth. In contrast, adolescents who are exposed to positive images of smokers are more likely to view smoking favorably and therefore try smoking.<sup>9</sup> Indeed, willingness is a better predictor of

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<sup>3</sup> Gerrard, M., Gibbons, F.X., Benthin, A.C., & Hessling, R.M. (1996). A longitudinal study of the reciprocal nature of risk behaviors and cognitions in adolescents: What you do shapes what you think and vice-versa. *Health Psychology, 15*, 344-354.

<sup>4</sup> Bandura, A. (1994). Social cognitive theory and exercise of control over HIV infection. In R.J. DiClemente & J.L. Peterson (Eds.), *Preventing AIDS: Theories and methods of behavioral interventions*. New York: Plenum Press

<sup>5</sup> Rosenstock, I.M. (1974). Historical origins of the health belief model. In M.H. Becker (Ed.), *The Health Belief Model and Personal Health Behavior* (pp. 1-8). Thorofare, NJ: Charles B. Slack.

<sup>6</sup> Fishbein M, Ajzen I. Belief, attitude and behavior. *Reading, MA: Addison-Welsey Publishing Co.* 1975.

<sup>7</sup> Ajzen I. From intentions to actions: A theory of planned behavior. In: *Action control*. Springer; 1985:11-39.

<sup>8</sup> Meg Gerrard et al., A Dual-Process Approach to Health Risk Decision Making: The Prototype Willingness Model, 28(1) *Developmental Review* 29 (2008).

<sup>9</sup> McKelvey, K., Popova, L., Pepper, J., Brewer, N., Halpern-Felsher, B. Adolescents Have Unfavorable Opinions of Adolescents Who Use E-cigarettes. In Review.

tobacco use than intentions and should be used in studies examining whether and why an adolescent would use any tobacco product.<sup>10,11</sup>

**b. PMI's application did not include information from studies with adolescents younger than 18**

*In addition to inappropriately relying on intentions as a proxy for actual behavior and behavior change, none of PMI's cited studies were conducted with adolescents younger than 18. PMI does not provide any reliable information in its application on whether adolescents would be interested in using IQOS, if adolescents would initiate nicotine use with IQOS, if adolescents would switch from another tobacco product to IQOS, or if adolescents would use IQOS along with other tobacco products.*

*One way to obtain information on adolescents' interests and behavior is to conduct studies with adolescents. However, neither PMI nor any other tobacco company should be permitted to conduct research on youth below the legal age for tobacco use (21, to be conservative) because they could use such information to design marketing campaigns to attract youth to their products. A different way to get at adolescents' interest and behavior is relying on research on other, similar products, such as electronic cigarettes, conducted with no direct or indirect involvement of tobacco companies or their agents.<sup>12</sup> There is a rich literature on adolescents conducted independent 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.*

In particular, it is important to consider IQOS and PMI's MRTP application in the context of recent experience with e-cigarettes and other novel tobacco products. Since e-cigarettes were first introduced in the U.S. less than a decade ago, there has been a rapid rise in the use of e-cigarettes,<sup>13</sup> a nicotine product that has been marketed with claims of reduced harm similar to PMI's claims about its IQOS product. E-cigarette use is especially common among adolescents and young adults. On the U.S. market since 2007, past 30-day use of e-cigarettes has

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<sup>10</sup> Gerrard, M., Gibbons, F.X., Benthin, A.C., & Hessling, R.M. (1996). A longitudinal study of the reciprocal nature of risk behaviors and cognitions in adolescents: What you do shapes what you think and vice-versa. *Health Psychology, 15*, 344-354; Meg Gerrard et al., A Dual-Process Approach to Health Risk Decision Making: The Prototype Willingness Model, 28(1) *Developmental Review 29* (2008).

<sup>11</sup> Gerrard M, Gibbons FX, Stock ML, Lune LS, Cleveland MJ. Images of smokers and willingness to smoke among African American pre-adolescents: An application of the prototype/willingness model of adolescent health risk behavior to smoking initiation. *Journal of Pediatric Psychology.* 2005 Feb 23;30(4):305-18.

<sup>12</sup> Institute of Medicine. 2012. *Scientific Standards for Studies on Modified Risk Tobacco Products*. Washington, DC: The National Academies Press. <https://doi.org/10.17226/13294>.

<sup>13</sup> McMillen RC, Gottlieb MA, Schaefer RM et al., Trends in Electronic Cigarette Use Among U.S. Adults: Use is increasing in both smokers and non-smokers. *Nicotine Tob Res.* 2015 Oct;17(10):1195-202

surpassed use of conventional cigarettes, with use prevalence of 11.3% among high school students (8.0% for cigarettes).<sup>14</sup> Among young adults 18-24 years old, 23.5% have ever used an e-cigarette.<sup>15</sup> Youth are also most likely to use flavored e-cigarette and other tobacco products.<sup>16</sup>

***The available evidence reported in scientific studies on currently marketed novel tobacco products (including e-cigarettes) conducted independent of the tobacco industry suggest that the introduction of novel IQOS products will attract adolescent non-users into initiating tobacco use with IQOS.*** Adolescents' decisions to adopt use of any tobacco product are based on several considerations, including whether the product appeals to them, the product's flavors, smell and taste, the product's perceived harm reduction, and the ease and location of use.<sup>17</sup> The marketing of IQOS with harm reduction claims and the claim that they are "smokeless" makes it likely that these products will appeal to youth.

The experience with e-cigarettes, which have also been promoted with harm reduction and "smokeless" messages, is directly relevant to adolescents' likely reaction to IQOS. In addition, both have a modern hi-tech image, another common characteristic that raises concerns that IQOS will attract youth. Many adolescents at low risk of initiating nicotine use with conventional

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<sup>14</sup> Jamal A, Gentzke A, Hu SS, et al. Tobacco Use Among Middle and High School Students — United States, 2011–2016. *MMWR Morb Mortal Weekly Rep* 2017; 66:597–603. DOI: <http://dx.doi.org/10.15585/mmwr.mm6623a1>; Syamlal G, King BA, Mazurek JM. Tobacco Use Among Working Adults — United States, 2014–2016. *MMWR Morb Mortal Weekly Rep* 2017;66:1130–1135. DOI: <http://dx.doi.org/10.15585/mmwr.mm6642a2>; see also Centers for Disease Control and Prevention. "National Youth Tobacco Survey (NYTS)." 2015. Web. 22 Aug. 2016; Centers for Disease Control and Prevention "Youth and Tobacco Use." 2016. Web. 22 Aug. 2016; Barrington-Trimis JL, Urman R, Leventhal AM, et al. E-cigarettes, cigarettes, and the prevalence of adolescent tobacco use. *Pediatrics*. 2016;138(2):10.1542/peds.2015-3983. Epub 2016 Jul 11; Gilreath TD, Leventhal A, Barrington-Trimis JL, et al. Patterns of alternative tobacco product use: Emergence of hookah and E-cigarettes as preferred products amongst youth. *Journal of Adolescent Health*. 2016;58(2):181-185; NIDA. Tobacco/nicotine and E-cigs. <https://www.drugabuse.gov/drugs-abuse/tobacconicotine-e-cigs>. Updated 2017. Accessed 09/12, 2017.

<sup>15</sup> QuickStats: Percentage of adults who ever used an e-cigarette and percentage who currently use e-cigarettes, by age group. National Health Interview Survey, United States, 2016. *MMWR Morb Mortal Weekly Report*, 2017;66:892. DOI: <http://dx.doi.org/10.15585/mmwr.mm6633a6>

<sup>16</sup> Ambrose BK, Day HR, Rostron B, et al. Flavored tobacco product use among us youth aged 12-17 years, 2013-2014. *JAMA*. 2015;314(17):1871-1873; Brown JE, Luo W, Isabelle LM, Pankow JF. Candy flavorings in tobacco. *N Engl J Med*. 2014;370(23):2250-2252; Feirman SP, Lock D, Cohen JE, Holtgrave DR, Li T. Flavored tobacco products in the united states: A systematic review assessing use and attitudes. *Nicotine Tob Res*. 2016;18(5):739-749; Wagoner KG, Cornacchione J, Wiseman KD, Teal R, Moracco KE, Sutfin EL. E-cigarettes, hookah pens and vapes: Adolescent and young adult perceptions of electronic nicotine delivery systems. *Nicotine Tob Res*. 2016.

<sup>17</sup> McKelvey, K., Ramos, M., Reditis, M., Ramamurthi, D., Halpern-Felsher, B. A Qualitative Analysis of Adolescents' Appeal of Various Tobacco Products. In preparation.

cigarettes initiate with e-cigarettes.<sup>18</sup> Adolescents who initiate nicotine use with e-cigarettes are more susceptible to smoking combustible cigarettes.<sup>19</sup> This experience with e-cigarettes raises the concern that adolescents will use both IQOS and other tobacco products concurrently, just as adolescents are dual and poly-users of e-cigarettes along with other tobacco products.<sup>20</sup>

### **3. PMI's application does not consider the impact of poly-use of novel tobacco products among adolescents**

***PMI ignores evidence that adolescent and young adult smokers who use novel tobacco products often use two or more kinds of tobacco products concurrently.***<sup>21</sup> Although PMI's own studies show that IQOS is often/sometimes actually used with conventional cigarettes, they fail to analyze the impact of this dual use. In particular, 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). According to

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<sup>18</sup> Dutra, LM, Glantz, SA. E-cigarettes and national adolescent cigarette use: 2004-2014. *Pediatrics*. 1239(2), 2017; Wills TA, Sargent JD, Knight R, Pagano I, Gibbons FX. E-cigarette use and willingness to smoke: a sample of adolescent non-smokers. *Tob Control*. 2016 Apr;25(e1):e52-9; Barrington-Trimis JL, Urman R, Leventhal AM, et al. E-cigarettes, cigarettes, and the prevalence of adolescent tobacco use. *Pediatrics*. 2016;138(2):10.1542/peds.2015-3983. Epub 2016 Jul 11

<sup>19</sup> Barrington-Trimis JL, Urman R, Leventhal AM, et al. E-cigarettes, cigarettes, and the prevalence of adolescent tobacco use. *Pediatrics*. 2016;138(2):10.1542/peds.2015-3983. Epub 2016 Jul 11; Association Between Initial Use of e-Cigarettes and Subsequent Cigarette Smoking Among Adolescents and Young Adults: A Systematic Review and Meta-analysis. Soneji S, Barrington-Trimis JL, Wills TA, Leventhal AM, Unger JB, Gibson LA, Yang J, Primack BA, Andrews JA, Miech RA, Spindle TR, Dick DM, Eissenberg T, Hornik RC, Dang R, Sargent JD. *JAMA Pediatr*. 2017 Aug 01;171(8):788-797; Barnett TE, Soule EK, Forrest JR, Porter L, Tomar SL. Adolescent electronic cigarette use: Associations with conventional cigarette and hookah smoking. *Am J Prev Med*. 2015;49(2):199-206; Miech RA, O'Malley PM, Johnston LD, Patrick ME. E-cigarettes and the drug use patterns of adolescents. *Nicotine Tob Res*. 2016;18(5):654-659; 16. Leventhal AM, Strong DR, Kirkpatrick MG, et al. Association of electronic cigarette use with initiation of combustible tobacco product smoking in early adolescence. *JAMA*. 2015;314(7):700-707; E-cigarette use and willingness to smoke: a sample of adolescent non-smokers. Wills TA, Sargent JD, Knight R, Pagano I, Gibbons FX. *Tob Control*. 2016 Apr;25(e1):e52-9.

<sup>20</sup> Barnett TE, Soule EK, Forrest JR, Porter L, Tomar SL. Adolescent electronic cigarette use. *Nicotine Tob Res*. 2016;18(5):654-659; Barrington-Trimis JL, Urman R, Leventhal AM, et al. E-cigarettes, cigarettes, and the prevalence of adolescent tobacco use. *Pediatrics*. 2016;138(2):10.1542/peds.2015-3983. Epub 2016 Jul 11

<sup>21</sup> Jamal A, Gentzke A, Hu SS, Cullen KA, Apelberg BJ, Homa DM, et al. Tobacco use among middle and high school students - United States, 2011-2016. *MMWR Morb Mortal Wkly Rep*. 2017;66(23):597-603.

PMI's 2016 full-year report,<sup>22</sup> 21-31% of users across multiple countries are dual-users with 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. While this information is based on adults there is no reason to expect that youth would not behave similarly. Indeed, dual and poly-use of tobacco products is more common among youth than adults.<sup>23</sup>

***PMI should have used the available experience with e-cigarettes collected independent of the tobacco industry to draw reasonable inferences about how IQOS would affect youth, but did not. The fact that PMI did not address these issues at all is a major shortcoming of the application that should lead FDA to deny the application.*** Indeed, section 911(d) of the Tobacco Control Act requires every MRTP application to include "(5) all documents (including underlying scientific information) relating to research findings conducted, supported, or possessed by the tobacco product manufacturer relating to the effect of the product on tobacco-related diseases and health-related conditions, *including information both favorable and unfavorable* to the ability of the product to reduce risk or exposure and relating to human health; (6) data and information on how consumers actually use the tobacco product... [emphasis added]." In its Guidance on MRTP applications, FDA explains that the term "possessed" includes research "findings from studies not conducted or supported by the manufacturer, but which it has received or has reviewed..." Further, FDA's Guidance states: "*FDA expects that the applicant will include*, among other things, as part of its submission of relevant documents, study reports, study protocols, and raw data... [emphasis added]." It is not credible for PMI to argue that it does not know about or has not reviewed the literature on the experience of e-cigarettes and adolescents, even if it did not conduct its own studies.

**4. 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.**

***The IQOS product, packaging, name, and store designs imitate Apple's iPhone and other i-products that are exceptionally popular with young people.***

Piper Jaffray's October 11, 2017 "Taking Stock with Teens" survey of 6,100 U.S. teens showed that Apple's iPhone continues to rise in popularity among teens, with 78% of U.S. teens saying they owned an iPhone, and 82% of teens saying their next smartphone will be an iPhone.<sup>24</sup> An April 2017 Fortune Magazine article led with the statement: "Teenagers are

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<sup>22</sup> <https://www.pmi.com/investor-relations/overview/event-details/?eventId=5246224>, Slide p. 19

<sup>23</sup> Kowitt, SD, Patel, T., Ranney, LM, Huang, LL, Sutfin, EL, Goldstein, AO. Poly-tobacco use among high school students. *Int J Environ Res Public Health*. 2015 Nov; 12(11): 14477–14489. Published online 2015 Nov 13. doi: 10.3390/ijerph121114477. PMID: PMC4661661; Soneji, S., Sargent, J, Tanski, S Multiple tobacco product use among US adolescents and young adults. *Tobacco control*, 25(2), 2016.

<sup>24</sup> [Piper Jaffray, Taking Stock with Teens – Fall 2017, October 11, 2017. Available at [www.piperjaffray.com/3col.aspx?id=4610](http://www.piperjaffray.com/3col.aspx?id=4610) ]

obsessed with Apple’s iPhone,” based on the Spring 2017 edition of Piper Jaffray’s teen survey in which 76% of U.S. teenagers said they had an iPhone, and 81% said their next smartphone will be an iPhone.<sup>25</sup> ***Considering IQOS’s similar design to iPhone (and the fact that PMI also calls it IQOS), it is reasonable to assume that adolescents will find IQOS’s design appealing, and will begin to use IQOS either alone or coupled with other tobacco products.***

Indeed, one of the common reasons young adults try e-cigarettes was novelty/technological appeal.<sup>26</sup> Therefore, it is especially concerning that the IQOS product design closely mimics Apple’s iPhone and other savvy, high-tech electronic products. The packaging resembles iPhones and other high-end smartphones, where the device and parts are neatly placed on molded plastic trays inside a glossy white box (Figure 1). Such marketing tactics are likely to appeal to adolescent and young adult never-smokers, making them more likely to try IQOS like many adolescents and young adults were attracted to try e-cigarettes.

***Adding to these concerns, the IQOS flagship stores in Seoul, Korea, visited in June 2017, look remarkably similar to high-end technology brand stores such as Apple or Microsoft stores in the U.S.***<sup>27</sup> (Figure 2). The design of the store and the way the products are displayed on the table in a spacious store contrasts sharply from a normal corner store where cigarette packs are tightly stacked, and gives a clean and refined look and feel to IQOS. Stores located in other countries have similar tech-savvy atmosphere, such as the IQOS store in Amsterdam, Netherlands (Figure 3).

##### **5. 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**

The IQOS heatsticks currently come in three flavors, Marlboro HeatSticks, Marlboro Smooth Menthol HeatSticks, and Marlboro Fresh Menthol HeatSticks. (PMI’s application is silent on whether or not there will be more flavors of IQOS in the future.) Flavor or “taste” is one of the most commonly used marketing techniques to entice young people to use a product; in particular, sweet and salty flavors are used to promote food (mostly candy and snacks<sup>28</sup>) to children.<sup>29</sup> ***PMI completely ignored all the evidence that menthol products would attract youth***

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<sup>25</sup> .[Reisinger, D., Fortune. Apple’s iPhone is the Dominant Smartphone Among Teenagers, April 11, 2017. Available at [fortune.com/2017/04/11/apple-iphone-teenagers/](http://fortune.com/2017/04/11/apple-iphone-teenagers/) ]

<sup>26</sup> Choi K., Fabian L., Mottey N., & Corbett A.(2012). Young adults’ favorable perceptions of snus, dissolvable tobacco products, and electronic cigarettes: Findings from a focus group study. *American Journal of Public Health, 102*, 2088–2093; Pokhrel P, Herzog TA, Muranaka N, Fagan P. Young Adult E-Cigarette Users’ Reasons for Liking and Not Liking E-Cigarettes: A Qualitative Study. *Psychol Health. 2015;30(12):1450-1469.*

<sup>27</sup> Kim M. Philip Morris International Introduces New Heat-Not-Burn Product, IQOS, in South Korea. *Tobacco Control. 2017.*

<sup>28</sup> Jenkin G, Madhvani N, Signal L, Bowers S. A systematic review of persuasive marketing techniques to promote food to children on television. *Obesity reviews. 2014;15(4):281-293.*

<sup>29</sup> Jenkin G, Madhvani N, Signal L, Bowers S. A systematic review of persuasive marketing techniques to promote food to children on television. *Obesity reviews. 2014;15(4):281-293.*

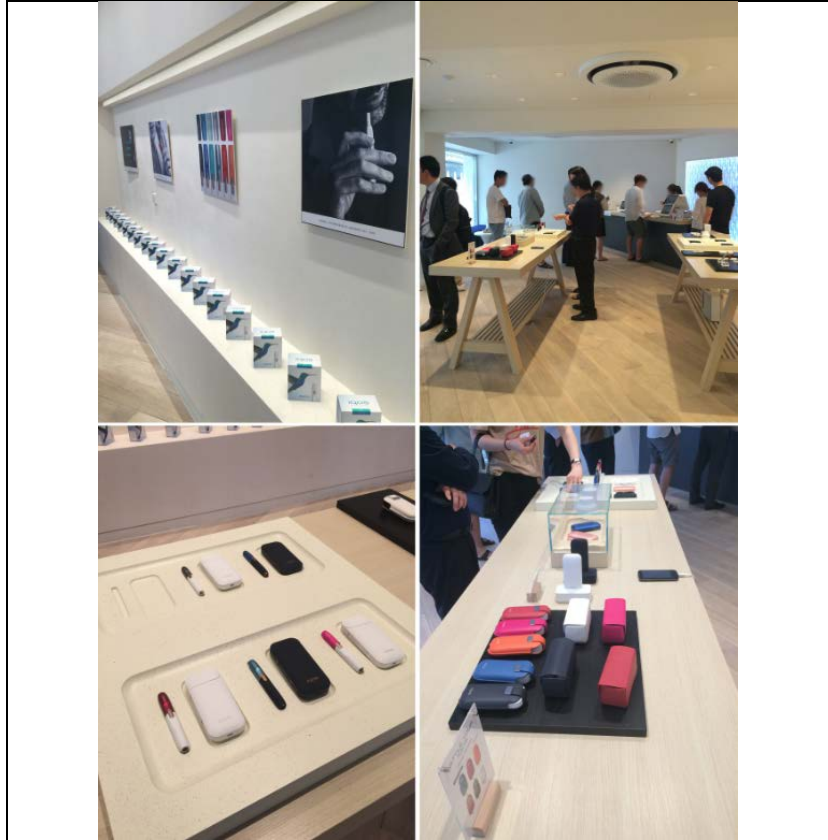


*and that adolescents will find these flavors appealing and therefore more likely to be used by them.*



*Figure 1. Packaging of IQOS (top: picture taken by Minji Kim) resembles that of high-end smartphone (bottom: Apple iPhone 7; source: phonearena.com<sup>30</sup>).*

<sup>30</sup> [https://www.phonearena.com/news/Apple-iPhone-7-unboxing-hands-on-with-the-speedy-new-water-resistant-iPhone\\_id85512](https://www.phonearena.com/news/Apple-iPhone-7-unboxing-hands-on-with-the-speedy-new-water-resistant-iPhone_id85512)



*Figure 2. IQOS Flagship store in Seoul, Korea, June 2017. Photos by Minji Kim, PhD.*



*Figure 3. IQOS Flagship store in Amsterdam, Netherlands, September 2017. Photo by Minji Kim, PhD.*

Exposure to flavored products and ads for such products is positively associated with youth consumption.<sup>31</sup> Research on newer tobacco products, including e-cigarettes, comports with these findings. Flavored tobacco products play an important role for online e-cigarette marketing and boosts user interaction and positive emotion.<sup>32</sup> Further, compared to ads for unflavored tobacco products, flavored e-cigarette advertisements elicit greater appeal and interest in buying and trying e-cigarettes.<sup>33</sup> The appeal of ads for flavors has been linked to rapid and persistent adoption of e-cigarettes among youth,<sup>34</sup> and 75% of US youth stated they would not use e-cigarettes without flavors.<sup>35</sup> Ads depicting flavors using colorful images make e-liquids attractive to youth,<sup>36</sup> and a 2014 content analysis of e-cigarette retail websites, which showed ads were appealing to youth.<sup>37</sup> Questions remain including whether the flavors will be attractive to adolescents who have never used a tobacco product or to adolescents who currently use at least one product. PMI did not present any information or studies on the IQOS advertisements for these flavored tobacco products that would permit an assessment of whether the ads will be appealing and misleading to youth, as we have seen in studies on e-cigarettes.<sup>38</sup>

## **6. PMI's arguments that modified risk claims will not attract never-smokers are illogical and inconsistent with the available evidence.**

PMI's application states that adult never-smokers in their study reported greater perceptions of risk for IQOS than current or former smokers (section 6.4.4.1-3), and 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). PMI's reasoning and interpretation of their results is not logical. Many studies have shown that non-tobacco users report greater perceptions

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<sup>31</sup> Cairns G, Angus K, Hastings G, Caraher M. Systematic reviews of the evidence on the nature, extent and effects of food marketing to children. A retrospective summary. *Appetite*. 2013;62:209-215

<sup>32</sup> Liang Y, Zheng X, Zeng DD, Zhou X. Impact of flavor on electronic cigarette marketing in social media. 2015:278-283

<sup>33</sup> Vasiljevic M, Petrescu DC, Marteau TM. Impact of advertisements promoting candy-like flavoured e-cigarettes on appeal of tobacco smoking among children: An experimental study. *Tob Control*. 2016;25(e2):e107-e112.

<sup>34</sup> Liang Y, Zheng X, Zeng DD, Zhou X. Impact of flavor on electronic cigarette marketing in social media. 2015:278-283 Vasiljevic M, Petrescu DC, Marteau TM. Impact of advertisements promoting candy-like flavoured e-cigarettes on appeal of tobacco smoking among children: An experimental study. *Tob Control*. 2016;25(e2):e107-e112.

<sup>35</sup> Zhu SH, Sun JY, Bonnevie E, et al. Four hundred and sixty brands of e-cigarettes and counting: Implications for product regulation. *Tob Control*. 2014;23 Suppl 3:iii3-9

<sup>36</sup> Sterling KL, Fryer CS, Nix M1, Fagan P. Appeal and Impact of Characterizing Flavors on Young Adult Small Cigar Use. *Tob Regul Sci*. 2015 Apr;1:42-53. Epub 2015 Mar 1.

<sup>37</sup> Grana RA, Ling PM. "Smoking revolution": A content analysis of electronic cigarette retail websites. *Am J Prev Med*. 2014;46(4):395-403

<sup>38</sup> (Choi, Fabian, Mottey, Corbett, & Forster, 2012; Feirman et al., 2016; Kong, Morean, Cavallo, Camenga, & Krishnan-Sarin, 2015; Wagoner et al., 2016).

of tobacco-related risk, compared to tobacco users.<sup>39</sup> However, you cannot then extend these findings to mean that non-users will never go on to use tobacco. Perceptions can change over time, and across products. ***Instead, the relevant question is how non-tobacco users perceive IQOS compared to other tobacco products, and whether the marketing and appeal of this new tobacco product will result in lower perceptions of risk of IQOS compared to other tobacco products, which then will result in use.***

In addition, PMI ignores the fact that most tobacco use begins before age 18. There is no reason to expect that IQOS would be any different, particularly in light of the fact that e-cigarettes, a similar product, have been more popular with youth than adults.

***The question PMI should have asked (and that the FDA should ask) is whether IQOS, with lower perceived risks, encourages never-smokers -- including adolescents and young adults -- who would otherwise not use any tobacco products to be more likely to try the IQOS product.*** Indeed, exposure to e-cigarette advertisements causes increases in smoking urge among adult former and current smokers<sup>40</sup> and reduces adolescent never-smokers' perceived risks of regular cigarettes.<sup>41</sup> Indeed, the fact that e-cigarettes are perceived as less harmful than regular cigarettes by adolescents and young adult never-smokers<sup>42</sup> is one reason that they are often the first tobacco product adolescents and young adults use, which also predicts future cigarette use.<sup>43</sup> According to PMI's application, while non-smokers' perceived risk score for IQOS are higher than current and former smokers in PMI's studies after seeing the modified risk claims (section 6.4.4.1-3), the scores are significantly lower than the non-smokers' perception of risks for

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<sup>39</sup> Roditis, M., Delucchi, K., Cash, D., & Halpern-Felsher, B. Adolescents' Perceptions of Health Risks, Social Risks, and Benefits Differ across Tobacco Products. *Journal of Adolescent Health*. 2016 May, 58(5):5558-66.

<sup>40</sup> Durkin SJ, Bayly M, Wakefield MA. Can E-Cigarette Ads Undermine Former Smokers? An Experimental Study. *Tob Regul Sci*. 2016;2(3):263-277; Maloney EK, Cappella JN. Does Vaping in E-Cigarette Advertisements Affect Tobacco Smoking Urge, Intentions, and Perceptions in Daily, Intermittent, and Former Smokers? *Health Communication*. 2016;31(1):129-138.

<sup>41</sup> Kim M, Popova L, Halpern-Felsher BL, Ling PM. Effects of E-Cigarette Advertisements on Adolescents' Perceptions of Cigarettes. *Health communication*. In Press; Petrescu DC, Vasiljevic M, Pepper JK, Ribisl KM, Marteau TM. What Is the Impact of E-Cigarette Adverts on Children's Perceptions of Tobacco Smoking? An Experimental Study. *Tob Control*. 2016.

<sup>42</sup> Roditis, M., Delucchi, K., Cash, D., & Halpern-Felsher, B. Adolescents' Perceptions of Health Risks, Social Risks, and Benefits Differ across Tobacco Products. *Journal of Adolescent Health*. 2016 May, 58(5):5558-66

<sup>43</sup> Kalkhoran S, Glantz SA. E-Cigarettes and Smoking Cessation in Real-World and Clinical Settings: A Systematic Review and Meta-Analysis. *The Lancet Respiratory Medicine*. 2016;4(2):116-128; Leventhal AM, Strong DR, Kirkpatrick MG, et al. Association of Electronic Cigarette Use with Initiation of Combustible Tobacco Product Smoking in Early Adolescence. *JAMA*. 2015;314(7):700-707; Miech R, Patrick ME, O'Malley PM, Johnston LD. E-Cigarette Use as a Predictor of Cigarette Smoking: Results from a 1-Year Follow-up of a National Sample of 12th Grade Students. *Tob Control*. 2017.

regular cigarettes. *Like e-cigarettes, PMI's results show that nonsmokers (which would include adolescents and young adults) are more likely to try IQOS than regular cigarettes.*

In considering PMI's claims about the impact of reduced risk perceptions on behavior of non-users, it is important to consider parallels with e-cigarettes when they first entered the market. Many e-cigarette users started using e-cigarettes because they perceive these e-cigarettes as less harmful (i.e., "reduced risk") than cigarettes and to be effective as smoking cessation aids.<sup>44</sup> An analysis of e-cigarettes retail websites showed that 95% of the 59 included websites made explicit claims that e-cigarettes can aid in smoking cessation or improve health.<sup>45</sup> Websites that compared cigarettes with e-cigarettes stated that e-cigarettes were cleaner (95% of the websites), cheaper (93% of the websites), could be used to circumvent indoor clear air policies (71% of the websites), and could aid in smoking cessation (64% of the websites). A study of the content of websites of e-cigarette manufacturers in China showed similar claims of health-related benefits, reduced secondhand smoke exposure, and utility for smoking cessation.<sup>46</sup> These explicit claims were made in the absence of consistent evidence pointing to benefits in health or smoking cessation.

Furthermore, these claims often led to a belief among both cigarette smokers and nonsmokers (including adolescents) that e-cigarettes are therefore a less harmful choice for any user (that is, not just in comparison to cigarettes), which in turn resulted in e-cigarette initiation among non-smokers.<sup>47</sup> In particular, adolescents believe that e-cigarettes are less harmful than cigarettes and all other tobacco products,<sup>48</sup> that e-cigarettes are acceptable and socially normative (with sizeable proportions (20-28%) agreeing that it is ok to use e-cigarettes indoors and

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<sup>44</sup> Roditis M, Delucchi K, Cash D, Halpern-Felsher B. Adolescents' perceptions of health risks, social risks, and benefits differ across tobacco products. *Journal of Adolescent Health*. 2016;58(5):558-566; Kong G, Morean ME, Cavallo DA, Camenga DR, Krishnan-Sarin S. Reasons for electronic cigarette experimentation and discontinuation among adolescents and young adults. *Nicotine Tob Res*. 2015;17(7):847-854; El-Toukhy S, Choi K. A risk-continuum categorization of product use among US youth tobacco users. *Nicotine Tob Res*. 2016.

<sup>45</sup> Grana, RA and Ling P. Smoking revolution: a content analysis of electronic cigarette retail websites. *Am J Prev Med*. 2014; 46(4): 395-403; Klein EG, Berman M, Hemmerich N, Carlson C, Htut S, Slater M. Online E-cigarette marketing claims: A systematic content and legal analysis. *Tobacco Regulatory Science*. 2016;2(3):252-262.

<sup>46</sup> Yao T, Jiang N, Grana R et al., A content analysis of electronic cigarette manufacturer websites in China. *Tob Control*. 2016; 25(2):188-94

<sup>47</sup> Gorukanti, A, Delucchi, K., Ling, P.P, Fisher-Travis, R, Halpern-Felsher, B. Adolescents' Attitudes towards E-cigarette Ingredients, Safety, Addictive Properties, Social Norms, and Regulation. *Preventive Medicine*. 2016 Oct 20; Roditis, M., Delucchi, K., Cash, D., & Halpern-Felsher, B. Adolescents' Perceptions of Health Risks, Social Risks, and Benefits Differ across Tobacco Products. *Journal of Adolescent Health*. 2016 May, 58(5):5558-66

<sup>48</sup> Roditis, M., Delucchi, K., Cash, D., & Halpern-Felsher, B. Adolescents' Perceptions of Health Risks, Social Risks, and Benefits Differ across Tobacco Products. *Journal of Adolescent Health*. 2016 May, 58(5):5558-66 ; Roditis, M.L., & Halpern-Felsher, B. Adolescents' perceptions of risks and benefits of conventional cigarettes, e-cigarettes and marijuana: A Qualitative Analysis. *Journal of Adolescent Health*. 2015 Aug; 57(2); 179-85.

outdoors),<sup>49</sup> and that such perceptions and attitudes are directly related to initiation and use of e-cigarettes.<sup>50</sup> Despite studies showing negative health effects of e-cigarettes, adolescents report believing that e-cigarettes are safer than cigarettes, can help people quit smoking conventional cigarettes, and contain none or just limited amounts of nicotine. Adolescents also consider e-cigarettes to be trendier, more prevalent, and more acceptable than conventional cigarettes.<sup>51</sup> The lowest perceptions of harm and the most positive attitudes regarding e-cigarettes have been reported among adolescents who have used e-cigarettes.<sup>52</sup> Given the similarities between IQOS and e-cigarettes (electronic, hi-tech, and claims of reduced harm, a better alternative to cigarettes, no “smoke”) it is reasonable to expect that IQOS will be popular with youth, because they will make similar assumptions about the risks associated with IQOS, and will be willing to initiate and use IQOS.

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<sup>49</sup> Gorukanti, A. Delucchi, K., Ling, P.P, Fisher-Travis, R. Halpern-Felsher, B. Adolescents' Attitudes towards E-cigarette Ingredients, Safety, Addictive Properties, Social Norms, and Regulation. *Preventive Medicine*. 2016 Oct 20.

<sup>50</sup> Gorukanti, A. Delucchi, K., Ling, P.P, Fisher-Travis, R. Halpern-Felsher, B. Adolescents' Attitudes towards E-cigarette Ingredients, Safety, Addictive Properties, Social Norms, and Regulation. *Preventive Medicine*. 2016 Oct 20; Roditis, M., Delucchi, K., Cash, D., & Halpern-Felsher, B. Adolescents' Perceptions of Health Risks, Social Risks, and Benefits Differ across Tobacco Products. *Journal of Adolescent Health*. 2016 May, 58(5):5558-66 ; Pepper, JK, Emery, SL, Ribisl, KM, Rini, CM, Brewer, NT. How risky is it to use e-cigarettes? Smokers' beliefs about their health risks from using novel and traditional tobacco products. *J Behav Med*. 2015 Apr;38(2):318-26.

<sup>51</sup> Anand V, McGinty KL, O'Brien K, Guenther G, Hahn E, Martin CA. 2015. E-cigarette Use and Beliefs Among Urban Public High School Students in North Carolina. *The Journal of adolescent health : official publication of the Society for Adolescent Medicine*. 57(1):46-51; Hammal F, Finegan BA. 2016. Exploring Attitudes of Children 12–17 Years of Age Toward Electronic Cigarettes. *Journal of Community Health*. 1-7; Trumbo CW, Harper R. Use and perception of electronic cigarettes among college students. 2013. *J Am Coll Health*. 61(3):149-155. Roditis, M.L., & Halpern-Felsher, B. Adolescents' perceptions of risks and benefits of conventional cigarettes, e-cigarettes and marijuana: A Qualitative Analysis. *Journal of Adolescent Health*. 2015 Aug; 57(2); 179-85.

<sup>52</sup> Ambrose BK, Rostron BL, Johnson SE, et al. 2014. Perceptions of the relative harm of cigarettes and e-cigarettes among U.S. youth. *Am J Prev Med*. 47(2 Suppl 1):S53-60; Anand V, McGinty KL, O'Brien K, Guenther G, Hahn E, Martin CA. 2015. E-cigarette Use and Beliefs Among Urban Public High School Students in North Carolina. *The Journal of adolescent health : official publication of the Society for Adolescent Medicine*. 57(1):46-51; Kong G, Morean ME, Cavallo DA, Camenga DR, Krishnan-Sarin S. Reasons for Electronic Cigarette Experimentation and Discontinuation Among Adolescents and Young Adults. *Nicotine Tob Res* 2015;17(7):847-54 (PMC PMC4674436) ; Chaffee BW, Gansky SA, Halpern-Felsher B, Couch ET, Essex G, Walsh MM. Conditional risk assessment of adolescents' electronic cigarette perceptions. *American Journal of Health Behaviors*; 2015 May; 39(3):421-432; Roditis, M.L., & Halpern-Felsher, B. Adolescents' perceptions of risks and benefits of conventional cigarettes, e-cigarettes and marijuana: A Qualitative Analysis. *Journal of Adolescent Health*. 2015 Aug; 57(2); 179-85. Trumbo & Harper, 2013)

*Thus, exposure to the marketing of IQOS focusing on claims of reduced risks is likely to cause similar harmful effects on never- and former-smokers, and could cause youth and adolescent never-smokers to initiate nicotine use with IQOS. PMI's application is silent on these important issues.*

## 7. Conclusion

*When evaluating whether PMI should be allowed to market IQOS as a MRTP, FDA must consider that adolescents who otherwise would not have used any tobacco product might find IQOS appealing and will initiate using IQOS as their first tobacco product. This is especially likely given adolescents' attraction to flavored tobacco products, the appeal of novel and technology-centric products among adolescents, and the tendency for the public at large, including adolescents, to misinterpret reduced harm claims.*

Further, FDA must consider whether the evidence submitted by PMI were *independent studies*, and not studies that were conducted by PMI or influenced or paid by PMI.<sup>53</sup> In particular, FDA must review independent studies of adolescents' perceptions of IQOS and the marketing claims made about IQOS, as well as independent studies that examine whether in the real world adolescents are more or less likely to initiate with IQOS compared to other tobacco products. FDA should review studies that examine adolescent consumers,' potential consumers,' and non-consumers' perceptions of IQOS products, and their use in the real world. FDA must evaluate whether and to what extent adolescents initiate with IQOS, whether they are likely to use both IQOS and other tobacco products, and whether adolescents initiating with IQOS will be more likely to subsequently initiate cigarette use. *Because PMI's did not submit with its MRTP application such rigorous, independent studies and because the application made no consideration of potential impact on adolescents, FDA does not have sufficient evidence on which to determine the public health impact of IQOS on the population as a whole as required by section 911(g), and should deny PMI's application.*

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<sup>53</sup> Institute of Medicine. 2012. *Scientific Standards for Studies on Modified Risk Tobacco Products*. Washington, DC: The National Academies Press. <https://doi.org/10.17226/13294>.