

PMPSA’s supplemental modified risk tobacco product application for IQOS 3 does not adequately consider or address new published research on IQOS’s appeal to adolescents or young adults, consumer perceptions, or the likelihood that the proposed labeling and marketing will be misunderstood by consumers, particularly youth; FDA should not issue a reduced exposure MRTP order for IQOS 3

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Docket No. FDA-2021-N-0408

Modified Risk Tobacco Product Application: Application for the IQOS 3 System Holder
and Charger Submitted by Philip Morris Products S.A.

December 7, 2021

The supplemental modified risk tobacco product application for IQOS 3 (sMRTPA) does not adequately address new published research and information on the appeal of IQOS 3 to youth, consumer perceptions of IQOS 3, or the likelihood that the proposed labeling and marketing will mislead consumers, especially youth. The sMRTPA also does not demonstrate benefits to individual or population health. Therefore, FDA should not issue an MRTP order for IQOS 3.

1. Background

Philip Morris Products S.A. (PMPSA) submitted to FDA a supplemental modified risk tobacco product application (sMRTPA) for its IQOS 3 system holder and charger on March 18, 2021. In its sMRTPA, PMPSA stated that it was “not submitting new data for review in this sMRTPA for the IQOS 3 System” because “[s]tudies that supported the original MRGO [Modified Risk Granted Order for the IQOS 2.4 System] are the same and do not require reanalysis.”¹ Instead, PMPSA cross-referenced its previous MRTP and Premarket Tobacco Product Applications (PMTA) and stated that the IQOS 3 system generates an aerosol that is comparable to that generated by the IQOS 2.4 system, exposes users to similar levels of toxicants included in the FDA’s list of harmful and potentially harmful compounds (HPHCs) it analyzed in its IQOS 2.4 applications, and claimed that therefore there is sufficient evidence to support the modified risk claim that this product “significantly reduces the production of harmful and

¹ Philip Morris Products S.A. Modified Risk Tobacco Product (MRTP) Applications, IQOS 3 System Holder and Charger Supplemental MRTP, m1-1-Cover Letter. Available at <https://www.fda.gov/media/148606/download>.

potentially harmful chemicals.”² Among the cross-referenced application materials used to support the current sMRTPA for IQOS 3 is a list of references dated August 31, 2018, that PMPSA submitted as Amendment 2 to its MRTP for IQOS 2.4. (See PMPSA’s spreadsheet which included 7,733 references, attached to this comment). It appears, therefore, that ***the most recent scientific literature used to support PMPSA’s sMRTPA for IQOS 3 is at least three years old.***

Since PMPSA submitted its MRTPA for the IQOS 2.4, more than 100 papers have been published on IQOS (see attached spreadsheet with references to new literature published since September 2018). PMPSA’s Supplemental Premarket Tobacco Product Application (sPMTA)³ for IQOS 3, which is cross-referenced in and used to support the IQOS 3 sMRTPA, includes references for only 14 additional papers, only six of which were published since August 2018 (one of which is written in French). However, ***at least 57 papers published since 2018 that address the subject of this comment – prevalence and actual use patterns, appeal to adolescents and young adults, consumer perceptions, and the impacts of IQOS’s labeling and marketing on consumer understanding of the potential harms of IQOS – were not discussed in PMPSA’s sMRTPA for IQOS 3. To properly consider whether PMPSA’s proposed reduced exposure claims for IQOS 3 would benefit the public health, FDA’s review of these papers is essential.***

Although PMPSA failed to report this recent literature in its MRTP applications, ***FDA must base its decisions on the best available science.*** Therefore, we summarize below the new published research and have attached the list of articles to this comment. The new literature reinforces our conclusion that ***PMPSA failed to prove that IQOS would benefit the health of the population as a whole as required by section 911(g) of the Family Smoking Prevention and Tobacco Control Act (FSPTCA). Importantly, section 911(g)(4) unambiguously states that this demonstration of population and individual health benefits is required for reduced exposure as well as reduced risk MRTPAs.***

To obtain a “reduced exposure” marketing order, applicants are required (FSPTCA section 911(g)(2)) to demonstrate, among other things, that:

1. such order would be “appropriate to promote the public health”;
2. the labeling and advertising are limited to an explicit or implicit representation that the product contains a reduced level of a substance or presents a reduced exposure to a substance in tobacco smoke;
3. the product “*as actually used by consumers* will not expose them to higher levels of other harmful substances compared to the similar types of tobacco products then on the market” unless such increases are minimal; and

² Philip Morris Products S.A. Modified Risk Tobacco Product (MRTP) Applications, IQOS 3 System Holder and Charger Supplemental MRTP Application Executive Summary, Module 2.4 and Summary of Health Risk Investigations, Module 6.1. Available at: <https://www.fda.gov/tobacco-products/advertising-and-promotion/philip-morris-products-sa-modified-risk-tobacco-product-mrtp-applications>

³ Philip Morris Products S.A. IQOS 3 System Holder and Charger Supplemental Premarket Tobacco Product Application (PMTA), Module 9 (m9): References, posted July 1, 2021. Available at: <https://digitalmedia.hhs.gov/tobacco/hosted/mrtpa/pmi/Cross-referenced%20PMTA%20Submission%20%28PM0000364%29.zip>

4. testing of actual consumer perception shows that the labeling and marketing will not mislead consumers into believing that the product has been demonstrated to be less harmful or presents less risk of disease.

Because PMPSA's sMRTP application for IQOS 3 failed to meet these statutory requirements for its reduced exposure claims, FDA must reject the application and not issue a reduced exposure MRTP marketing order for IQOS 3.

Specifically:

- PMPSA's sMRTPA did not consider IQOS's appeal to youth, or the likelihood that adolescents or young adults will initiate tobacco use with IQOS or use IQOS with other tobacco products.
- Independent research not reported by PMPSA provides significant scientific evidence relevant to its sMRTPA for IQOS 3. In particular:
- Epidemiological studies indicate growing awareness, ever-use, and current use of IQOS among adolescents and young adults;
- Recent studies highlight the potential for growing susceptibility, use, and appeal of IQOS among youth;
- Studies analyzing consumers' perceptions show that IQOS packaging, labeling, and marketing mislead consumers into believing that IQOS has been demonstrated to be less harmful or presents less risk of disease;
- As actually used by consumers, IQOS is not associated with quitting smoking;
- Consumers do not understand what it means to "switch completely" and that they need to exclusively use IQOS to get the claimed benefits. Instead, dual- or poly-use of IQOS along with cigarettes, e-cigarettes, and/or other tobacco products is the predominant use pattern; and
- IQOS marketing increases youth appeal.
- Recent papers document aggressive marketing tactics used to promote IQOS in the US and globally that may encourage initiation and/or increase IQOS use among youth and other non-users.
- Recent literature emphasizes how FDA's actions have affected consumer behavior and supported industry marketing of IQOS.

Therefore, PMPSA failed to provide adequate scientific evidence demonstrating that IQOS would benefit the health of individuals and the "population as a whole," in particular non-users (including adolescents and young adults) as well as current users of other tobacco products.

- 2. PMPSA's sMRTPA did not consider IQOS's appeal to youth, or the likelihood that adolescents or young adults will initiate tobacco use with IQOS or use IQOS with other tobacco products; therefore, PMPSA 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**

In December 2017, we submitted three public comments^{4, 5, 6} regarding the IQOS 2.4 MRTPA (Docket Number: FDA-2017-D-3001) relevant to the impact of IQOS marketing on youth. Because PMPSA's sMRTPA for IQOS 3 is based entirely on its earlier PMTA and MRTPA for IQOS 2.4 and provides no additional scientific evidence or literature considering IQOS's potential appeal to youth or the likelihood of dual and poly-use (of IQOS plus one or more other tobacco products), the evidence and conclusions we presented in our earlier public comments are relevant to the current sMRTPA for IQOS 3. In those comments and a fourth comment we submitted in February 2020,⁷ attached and incorporated by reference, [lkl – attach earlier comments] we demonstrated with scientific evidence that PMPSA failed to consider IQOS's appeal to or impact on adolescents and young adults, failed to conduct or properly analyze actual consumer perception studies, failed to consider the impact on poly-use of novel tobacco products among adolescents, failed to appropriately consider the impact of IQOS's packaging and marketing, failed to consider the likelihood that IQOS's two menthol flavors would appeal to adolescents and young adults and encourage initiation among non-users, and failed to consider the likelihood that consumers, including adolescents and young adults, will misinterpret MRTP claims. Thus, we demonstrated that *Philip Morris had failed to prove that IQOS would benefit the health of the population as a whole as required by section 911(g)(4). Importantly, section 911(g) unambiguously states that this evidence is required for reduced exposure as well as reduced risk MRTPAs.*

3. Independent research shows growing awareness and use of IQOS among youth as well as adults, that IQOS packaging and marketing may mislead consumers into believing that IQOS is safe or less harmful, that consumers do not understand that they must switch completely from cigarettes to IQOS and use IQOS exclusively to get claimed benefits, and that aggressive marketing tactics may make IQOS more appealing to youth

In November 2018, we and our colleagues published seven relevant peer-reviewed papers including papers concerning IQOS's appeal to adolescents and young adults,⁸ how IQOS labeling will mislead consumers,⁹ the impact of IQOS's MRTP claims on adult and adolescent

⁴ 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, December 7, 2017, Docket Number: FDA-2017-D-3001.

⁵ Halpern-Felsher B, McKelvey K, Popova L, et al. The evidence cited in PMI's MRTP Application indicates that the proposed labeling and warnings for IQOS will mislead consumers, particularly youth, about the product, December 8, 2017, Docket Number: FDA-2017-D-3001.

⁶ Lempert LK, Popova L, Halpern-Felsher B, et al. Because PMI has not demonstrated that IQOS is associated with lower risks, FDA should not permit modified exposure claims, because such claims are likely to be misunderstood as modified risk claims, December 11, 2017, Docket Number: FDA-2017-D-3001.

⁷ Lempert LK, Kim M, Chaffee B, et al. FDA should not authorize Philip Morris International to market IQOS with claims of reduced risk or reduced exposure, February 23, 2020, Docket Number: FDA-2017-D-3001.

⁸ 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. *Tob Control*. 2018 Nov;27(Suppl 1):s41-s47. doi: 10.1136/tobaccocontrol-2018-054596. PMID: 30352843; PMCID: PMC6252490.

⁹ McKelvey K, Popova L, Kim M, Lempert LK, Chaffee BW, Vijayaraghavan M, Ling P, Halpern-Felsher B. IQOS labelling will mislead consumers. *Tob Control*. 2018 Nov;27(Suppl 1):s48-s54. doi: 10.1136/tobaccocontrol-2018-054333. Epub 2018 Aug 29. PMID: 30158208; PMCID: PMC6252493.

perceptions,¹⁰ consumer perceptions about IQOS in Japan and Switzerland,¹¹ the likelihood that IQOS's reduced exposure claims will be misunderstood as reduced risk claims,¹² the experience of IQOS among Korean young adults,¹³ and IQOS's marketing campaign in Israel.¹⁴

FDA is required (FSPTCA section 910(c)(2)(A)) to deny marketing authorization if a PMTA applicant fails to demonstrate that its product is "appropriate for the protection of the public health." However, in a June 2020 peer-reviewed paper¹⁵ that analyzed FDA's April 2019 order permitting IQOS 2.4 to be marketed in the US, we found that PMPSA failed to meet this statutory requirement. PMPSA failed to demonstrate reduction in long-term disease risks and failed to appropriately consider: IQOS emits some toxins at higher levels than conventional cigarettes; the health impacts of dual use; the product's attractiveness to youth; and that consumers do not accurately perceive the addictive risks of IQOS. Despite PMPSA failing to demonstrate that IQOS is "appropriate for the protection of the public health" and FDA's own scientists' recommendations and independent research (which is inherently more reliable than industry-conducted and/or funded research) showing that IQOS presents serious health risks to users, FDA disregarded valid scientific evidence and issued a marketing order for IQOS 2.4. ***That erroneous marketing order and FDA's Technical Project Lead Review explaining how it arrived at its decision were used to provide support for the IQOS 2.4 MRTPA order and the IQOS 3 PMTA marketing order, calling into question the validity of those orders which, in turn, are being used to support the current sMRTPA for IQOS 3.***

In addition to these papers that were available to FDA before it issued its reduced exposure MRTP order for IQOS 2.4, we summarize below ***57 peer-reviewed research papers published since August 2018 that address the awareness, use, and appeal of IQOS among youth; IQOS packaging, labeling, and marketing; actual consumer use and perceptions; and aggressive marketing tactics.*** These papers present clear evidence that permitting IQOS 3 to be marketed with reduced exposure MRTP claims is not appropriate for the public health because:

- a. there is growing awareness, ever-use, and current use of IQOS among adolescents and young adults;

¹⁰ El-Toukhy S, Baig SA, Jeong M, Byron MJ, Ribisl KM, Brewer NT. Impact of modified risk tobacco product claims on beliefs of US adults and adolescents. *Tob Control*. 2018 Nov;27(Suppl 1):s62-s69. doi: 10.1136/tobaccocontrol-2018-054315. Epub 2018 Aug 29. PMID: 30158212; PMCID: PMC6202195.

¹¹ Hair EC, Bennett M, Sheen E, Cantrell J, Briggs J, Fenn Z, Willett JG, Vallone D. Examining perceptions about IQOS heated tobacco product: consumer studies in Japan and Switzerland. *Tob Control*. 2018 Nov;27(Suppl 1):s70-s73. doi: 10.1136/tobaccocontrol-2018-054322. Epub 2018 May 15. PMID: 29764957; PMCID: PMC6252486.

¹² Popova L, Lempert LK, Glantz SA. Light and mild redux: heated tobacco products' reduced exposure claims are likely to be misunderstood as reduced risk claims. *Tob Control*. 2018 Nov;27(Suppl 1):s87-s95. doi: 10.1136/tobaccocontrol-2018-054324. Epub 2018 Sep 12. PMID: 30209208; PMCID: PMC6202239.

¹³ Kim J, Yu H, Lee S, Paek YJ. Awareness, experience and prevalence of heated tobacco product, IQOS, among young Korean adults. *Tob Control*. 2018 Nov;27(Suppl 1):s74-s77. doi: 10.1136/tobaccocontrol-2018-054390. Epub 2018 Aug 29. PMID: 30158210; PMCID: PMC6252497.

¹⁴ Rosen LJ, Kislev S. IQOS campaign in Israel. *Tob Control*. 2018 Nov;27(Suppl 1):s78-s81. doi: 10.1136/tobaccocontrol-2018-054619. Epub 2018 Oct 19. PMID: 30341089; PMCID: PMC6252485.

¹⁵ Lempert LK, Glantz S. Analysis of FDA's IQOS marketing authorisation and its policy impacts [published online ahead of print, 2020 Jun 29]. *Tob Control*. 2020;tobaccocontrol-2019-055585. doi:10.1136/tobaccocontrol-2019-055585.

- b. the labeling and advertising of IQOS represents, implicitly if not explicitly, that IQOS is safer than other tobacco products;
- c. consumer perception studies show that the labeling and marketing of IQOS mislead consumers into believing that IQOS has been demonstrated to be less harmful or presents less risk of disease than other tobacco products;
- d. actual use patterns demonstrate that consumers do not switch completely to IQOS but rather use IQOS concurrently with one or more other tobacco products which may expose them to higher levels of harmful substances; and
- e. PMI engages in aggressive marketing tactics that may encourage initiation and/or increase IQOS use among youth and other non-users; and
- f. consumers misinterpret FDA's marketing authorization of IQOS with reduced risk claims to mean that FDA endorses or approves IQOS, and the industry uses FDA's actions when marketing IQOS to further these misperceptions.

Therefore, pursuant to the statutory requirements (FSPTCA section 911(g)(2)) described above for issuing an MRTP reduced exposure order, ***FDA should not authorize the marketing of IQOS 3 with reduced exposure claims.***

a. Epidemiological studies indicate growing awareness, ever-use, and current use of IQOS among adolescents and young adults

Epidemiological studies on heated tobacco product (HTP) use conducted by independent, non-industry researchers in the US and abroad indicate growing awareness, ever-use, and current use of IQOS among adolescents and young adults. A 2021 analysis¹⁶ of data from the 2019 US National Youth Tobacco Survey (NYTS), a nationally representative survey of middle and high school students (n=19,018) showed that in weighted results, 12.8% of the overall sample was aware of heated tobacco products, 2.3% had ever tried them, and 1.6% were current (past 30-day) users. Awareness, ever-use, and current-use of HTP were higher among current tobacco users and dual/poly users and users of flavored tobacco. Youth use was particularly elevated if they reported a family member used HTP, suggesting children of adult HTP users may be at risk of HTP uptake. Another 2021 publication¹⁷ analyzing 2019 NYTS data reported similar findings and reported 12.8% of the overall sample was aware of heated tobacco products, 2.4% had ever tried them, and 1.6% were current (past 30-day) users. Among users, HTP use was greater with exposure to tobacco/cigarette marketing and with exposure to e-cigarette marketing. In a 2021 study¹⁸ analyzing data from the 2019 Tobacco Use Supplement to the Current Population Survey (n=42,477 US residents ages ≥18), awareness of HTP was higher among younger (18-24 years) males, current smokers, and e-cigarette users, and use was higher among younger tobacco users (cigarette, e-cigarette, and other tobacco products) living in metropolitan areas. Overall awareness of heated tobacco products was 8.6% and was highest among young adults ages 18-20 (13.3%). Ever use of HTP was also highest among those ages 18-20 (1.2% vs. 0.5% in the

¹⁶ Lee J, Thompson LA, Salloum RG. Heated tobacco product use among US adolescents in 2019: The new tobacco risk. *Tob Prev Cessat*. 2021 Jan 8;7:01. doi: 10.18332/tpc/130502. PMID: 33437895; PMCID: PMC7796675.

¹⁷ Dai H. Heated tobacco product use and associated factors among U.S. youth, 2019. *Drug Alcohol Depend*. 2020 Sep 1;214:108150. doi: 10.1016/j.drugalcdep.2020.108150. Epub 2020 Jul 2. PMID: 32645682.

¹⁸ Azagba S, Shan L. Heated Tobacco Products: Awareness and Ever Use Among U.S. Adults. *Am J Prev Med*. 2021 May;60(5):684-691. doi: 10.1016/j.amepre.2020.11.011. Epub 2021 Jan 29. PMID: 33518430.

sample overall). Use of cigarettes and use of e-cigarettes were associated with HTP awareness and use.

A 2021 study¹⁹ featuring a national panel survey conducted primarily in January 2020 of 20,449 US adults (age ≥ 18) found overall awareness (8.1%), ever use (0.55%), and current use (0.10%) of heated tobacco products were uncommon. However, the ratios of ever use to awareness and current use to ever use were similar to those reported for e-cigarettes in 2012, using similar methods. The authors conclude that these similarities suggest that ***HTP use could follow a similar trajectory as e-cigarette use if marketed aggressively, and that a predictable percentage of those who had experimented with HTPs would become continual users.*** The majority of respondents (54%) perceived HTPs to be equally harmful or less harmful than e-cigarettes; only 9% perceived HTP to be more harmful than e-cigarettes.

The findings in these papers reinforce the urgent need for FDA to monitor and restrict HTP marketing that targets or is appealing to youth.

East et al.²⁰ examined repeated cross-sectional data from national surveys of youth (ages 16-19) in the United States, Canada, and the United Kingdom. In the US and Canada, use of any tobacco or nicotine product increased in prevalence over the period from 2017-2019. Use of combustible tobacco did not decline, but use of e-cigarettes and smokeless tobacco increased. Past 30-day use of IQOS use was not assessed in 2017, but increased from 0.6% to 0.8% from 2018 to 2019 in the US.

Several other recent papers analyzed IQOS awareness and use in countries outside the US where IQOS has been available for a longer period of time. A 2020 study²¹ examined data from the 2018 Taiwan Global Youth Tobacco Survey, featuring a sample of nearly 50,000 junior and senior high school students. Past 30-day use of IQOS devices (2.3%) was near the prevalence of past 30-day e-cigarette use (2.7%) and about half the prevalence of cigarette smoking (5.7%). Another analysis²² of the 2018 Taiwan data found similar results. The authors noted that the prevalence of ever (4.2%) and past 30-day (2.3%) use of IQOS was achieved despite IQOS not being legally authorized in Taiwan (but accessible via sales in Japan and South Korea, among other countries), and that legal access could lead to greater levels of adolescent IQOS use. A study²³ using an online panel survey of Korean young adults (n=228, ages 18-24) conducted

¹⁹ Zhu SH, Ong J, Wong S, Cole A, Zhuang YL, Shi Y. Early adoption of heated tobacco products resembles that of e-cigarettes. Tob Control. 2021 Feb 4:tobaccocontrol-2020-056089. doi: 10.1136/tobaccocontrol-2020-056089. Epub ahead of print. PMID: 33542070.

²⁰ East KA, Reid JL, Rynard VL, Hammond D. Trends and Patterns of Tobacco and Nicotine Product Use Among Youth in Canada, England, and the United States From 2017 to 2019. J Adolesc Health. 2021 Apr 7:S1054-139X(21)00096-3. doi: 10.1016/j.jadohealth.2021.02.011. Epub ahead of print. PMID: 33839006.

²¹ Lee YC, Chang LC, Hsu C, Chen PC. Comparing the Characteristics of Cigarette Smoking and e-Cigarette and IQOS Use among Adolescents in Taiwan. J Environ Public Health. 2020 Jun 20;2020:7391587. doi: 10.1155/2020/7391587. PMID: 32655649; PMCID: PMC7322614.

²² Chang LC, Lee YC, Hsu C, Chen PC. Prevalence of heated tobacco product use among adolescents in Taiwan. PLoS One. 2020 Dec 21;15(12):e0244218. doi: 10.1371/journal.pone.0244218. PMID: 33347476; PMCID: PMC7751857.

²³ Kim J, Yu H, Lee S, Paek YJ. Awareness, experience and prevalence of heated tobacco product, IQOS, among young Korean adults. Tob Control. 2018 Nov;27(Suppl 1):s74-s77. doi: 10.1136/tobaccocontrol-2018-054390. Epub 2018 Aug 29. PMID: 30158210; PMCID: PMC6252497.

three months after introduction of IQOS to the Korean market in 2017 found awareness (38%), ever-use (5.7%), and current use (3.5%) of IQOS. ***All IQOS users also concurrently used conventional cigarettes and e-cigarettes.*** The authors note that the presence of cigarette smoking universally within the sample suggests that ***few smokers switched completely to the IQOS product.***

b. Recent studies highlight the potential for growing susceptibility, use, and appeal of IQOS among youth

Several recent studies analyzing the perceived relative harm of HTPs (including IQOS), e-cigarettes, and cigarettes indicate an overall lack of understanding of the addictiveness and relative harm of IQOS, especially among adolescents and young adults. In a large 2021 study²⁴ of 10th and 12th graders (n=150,516) in California high schools from September 2019 to March 2020, Li et al. found that 0.67% of youth ever used HTPs and 0.20% were past 30-day users. In addition, continuation and susceptibility rates were cause for concern. Nearly one-third (30.2%) of adolescents who had ever tried HTPs continued to use them and roughly one in five (18.3%) never users of HTPs indicated susceptibility to future use. Continuation and susceptibility rates varied by tobacco use status. Rates of both continuation and susceptibility were higher among students who had tried e-cigarettes, and higher still among students who had tried combustible cigarettes. Czoli et al.²⁵ examined the awareness and interest in IQOS among youth in Canada, England and the US in a large online survey conducted in the summer 2017. The study found that although IQOS was not yet available in the US (it was available in the UK and Canada at that time), youth in the US reported the highest awareness of IQOS. Interest and susceptibility to trying IQOS was higher among participants with experience smoking or using e-cigarettes than among never-smokers or never-ecigarette users; however, ***among never-smokers in the US, 21% reported interest and 26% reported susceptibility to try IQOS.***

A qualitative study by Kim et al.²⁶ investigated how US young adult poly-tobacco users reacted to, perceived, and developed interest in IQOS. ***Multiple product characteristics influenced the appeal of IQOS, including its sleek electronic design, novel technology, and the “no smoke” claim that led to the perception that smoking IQOS was safer than smoking conventional cigarettes.***

Another 2021²⁷ paper analyzed Fall 2019 data from US young adults (n=2375, ages 18-34) participating in a 2-year, 5-wave longitudinal study that examined the impact of vape retailing across 6 metropolitan statistical areas (MSAs), including Atlanta where IQOS was first introduced in the US in October 2019. 9.7% of all respondents had heard of heated tobacco products (HTPs), 3.5% had ever used them, and 2.4% had purchased HTPs at some point in the

²⁴ Li et al. (2021). Adolescent Use of and Susceptibility to Heated Tobacco Products. *Pediatrics* 148(2):e2020049597. DOI: <https://doi.org/10.1542/peds.2020-049597>.

²⁵ Czoli, C. D., et al. (2020). Awareness and interest in IQOS heated tobacco products among youth in Canada, England and the USA. *Tobacco Control* 29(1): 89-95, DOI: 10.1136/tobaccocontrol-2018-054654.

²⁶ Kim M, Watkins SL, Koester KA, Mock J, Kim HC, Olson S, Harvanko AM, Ling PM. Unboxed: US Young Adult Tobacco Users' Responses to a New Heated Tobacco Product. *Int J Environ Res Public Health*. 2020 Nov 3;17(21):8108. doi: 10.3390/ijerph17218108. PMID: 33153143; PMCID: PMC7662359.

²⁷ Berg, Carla J., et al. (2021). Heated Tobacco Product Awareness, Use, and Perceptions in a Sample of Young Adults in the United States. *Nicotine & Tobacco Research* 2021:1967–1971, DOI: 10.1093/ntr/ntab058.

past year. *HTPs were perceived as less addictive than cigarettes, smokeless tobacco, and e-cigarettes, and less harmful* and more socially acceptable than other tobacco products except for e-cigarettes. Because of the newness and limited availability of HTPs in the US at the time of data collection, the authors concluded that these perceptions, coupled with the many ways that young adults can access HTPs (vape shops, convenience stores, online, etc.), mean that *HTPs could have substantial penetration into the US young adult market* despite the self-reported low likelihood of future use.

In a 2018 publication,²⁸ McKelvey et al. systematically evaluated publicly available data from PMPSA's MRTP application for IQOS 2.4. The authors found that PMPSA submitted its own flawed research, which failed to prove that IQOS would not appeal to or prompt initiation among adolescents and young adults. The industry research did not demonstrate that IQOS would benefit the public health because *as actually used by consumers* (the statutorily required standard), consumers rarely "switch completely" to IQOS. PMPSA did not, but should have, included relevant, independent research conducted with adolescents, which suggests that IQOS's trendy packaging, marketing, and safety claims are likely to appeal to adolescents and young adults. Indeed, youth-focused empirical evidence related to the impact of tobacco products on youth should be included in all MRTPAs.²⁹

A 2021 study³⁰ assessing adult (age ≥18) e-cigarette users' preferences among cigarettes, e-cigarettes, and HTPs of various flavors and nicotine levels found that HTPs, as relatively new products, were in general less preferred than both cigarettes and e-cigarettes. However, *participants living in states where IQOS was being sold had similar preferences for cigarettes and HTPs*. The authors concluded that this finding indicates that although HTPs are still new to the US market, they are likely to be accepted in places near IQOS test markets.

c. Many recent peer-reviewed studies analyzing consumers' perceptions show that IQOS packaging, labeling, and marketing mislead consumers into believing that IQOS has been demonstrated to be less harmful or presents less risk of disease.

Understanding the health harm perceptions of IQOS is important because consumers' perceptions of the harmfulness of IQOS can influence their use. Perceptions of the reduced harm of IQOS relative to smoking is a commonly reported reason for using IQOS.^{31,32} Harm

²⁸ McKelvey, Karma, et al. (2018). Heated tobacco products likely appeal to adolescents and young adults. *Tobacco Control* 27:s41–s47. DOI: 10.1136/tobaccocontrol-2018-054596.

²⁹ Halpern-Felsher B, Henigan D, Riordan M, Boonn A, Perks SN, Krishnan-Sarin S, Vallone D. The Importance of Including Youth Research in Premarket Tobacco Product and Modified Risk Tobacco Product Applications to the Food and Drug Administration. *J Adolesc Health*. 2020 Sep;67(3):331-333. doi: 10.1016/j.jadohealth.2020.06.020. Epub 2020 Jul 14. PMID: 32674965.

³⁰ Yang, Yong, et al. (2021). Impact of flavours, device, nicotine levels and price on adult e-cigarette users' tobacco and nicotine product choices. *Tobacco Control* 0:1-8. DOI: 10.1136/tobaccocontrol-2021-056599.

³¹ Gravely S, Fong GT, Sutanto E, Loewen R, Ouimet J, Xu SS, Quah ACK, Thompson ME, Boudreau C, Li G, et al. Perceptions of harmfulness of heated tobacco products compared to combustible cigarettes among adult smokers in Japan: findings from the 2018 ITC Japan Survey. *Int J Environ Res Public Health*. 2020. <https://doi.org/10.3390/ijerph17072394>.

³² Sutanto E, Miller C, Smith DM, O'Connor RJ, Quah ACK, Cummings KM, Xu S, Fong GT, Hyland A, Ouimet J, Yoshimi I, Mochizuki Y, Tabuchi T, Goniewicz ML. Prevalence, Use Behaviors, and Preferences among Users of

perceptions of tobacco products can be influenced by several factors, including reduced-risk claims, manufacturer advertisements, and the appearance of packaging and labeling, including health warnings, and can drive decisions to use emerging products. While PMPSA claims that their target customers are conventional cigarette smokers, non-smokers may also start using IQOS if they believe this product is less harmful than other nicotine products. Therefore, it is important to examine relative harm perceptions of IQOS and how IQOS packaging, labeling, and marketing can influence those perceptions and possibly mislead consumers.

To obtain a “reduced exposure” marketing order, applicants are required (FSPTCA section 911(g)(2)) to demonstrate that the labeling and marketing will not mislead consumers into believing that the product has been demonstrated to be less harmful or presents less risk of disease. As we summarize below, independent research demonstrates, however, that consumers are, in fact, misled by the labeling and marketing of IQOS, and that they believe or perceive IQOS to be less harmful than cigarettes or e-cigarettes.

Independent research by El-Toukhy et al.³³ on what influences harm perceptions of heated tobacco products found that ***reduced exposure claims misled the public to perceive lower perceived risk, even though no lower risk claim was explicitly made***. Similarly, a qualitative study by East et al.³⁴ in the United Kingdom found that a key marketing feature of IQOS is the reduction in harmful chemicals produced compared to cigarette smoking (i.e., reduced exposure claims) and that ***consumers are highly receptive to this and interpreted IQOS as less harmful, healthier, or safer***.

In a 2018 examination of materials PMPSA submitted as part of their MRTP applications for IQOS 2.4, Popova et al.³⁵ found that ***Philip Morris’s own qualitative and quantitative studies consistently showed that reduced exposure claims are likely to be perceived as reduced risk claims***, a clear violation of the statutory burden placed on companies seeking reduced risk MRTP orders to demonstrate that consumers are not misled in this way.

A separate 2018 study³⁶ that also reviewed the data submitted by PMPSA in its 2016 MRTP applications found deficiencies in the evidence submitted regarding consumer understanding of MRTP claims and that PMPSA misrepresented their data on the impact of messaging on intentions to quit smoking. This suggests that ***consumers will not understand the condition of the claims—that they must quit using cigarettes completely to achieve the inferred***

Heated Tobacco Products: Findings from the 2018 ITC Japan Survey. Int J Environ Res Public Health. 2019 Nov 21;16(23):4630. doi: 10.3390/ijerph16234630. PMID: 31766410; PMCID: PMC6926809.

³³ El-Toukhy S, Baig SA, Jeong M, Byron MJ, Ribisl KM, Brewer NT. Impact of modified risk tobacco product claims on beliefs of US adults and adolescents. Tob Control. 2018 Nov;27(Suppl 1):s62-s69. doi: 10.1136/tobaccocontrol-2018-054315. Epub 2018 Aug 29. PMID: 30158212; PMCID: PMC6202195.

³⁴ East, K. A., et al. (2021). "I perceive it to be less harmful, I have no idea if it is or not:" a qualitative exploration of the harm perceptions of IQOS among adult users. Harm Reduct J 18(1): 42, DOI: 10.1186/s12954-021-00490-8.

³⁵ Popova, Lucy, et al. (2018). “Light and mild redux: heated tobacco products’ reduced exposure claims are likely to be misunderstood as reduced risk claims.” *Tobacco Control* 27:s87–s95. DOI: 10.1136/tobaccocontrol-2018-054324

³⁶ McKelvey, K., et al. (2018). "IQOS labelling will mislead consumers." *Tobacco Control* 27(Suppl1): s48-s54, DOI: 10.1136/tobaccocontrol-2018-054333

health benefits of IQOS. Rather, consumers are likely to misunderstand the unsupported claims of reduced risks to mean IQOS reduces harms from smoking.

A 2021 study³⁷ assessed the effects of IQOS's modified risk claims on consumer comprehension and risk perceptions of IQOS. This study was conducted by independent researchers, not by a tobacco company with a financial interest in the study outcomes, and it improved on the methodology of the data submitted by PMPSA, which did not include a control condition. The study tested three language features of IQOS modified risk claims: explanation of the term "switching completely" (absent vs present); language certainty (hypothetical, "may reduce" vs certain, "reduces"); and number of diseases (single, "lung cancer" vs multiple, "lung cancer, emphysema, heart disease, stroke) among two populations of interest, adult smokers (n=1523) and young adult nonsmokers (n=1391). The study found that modified risk claims that lack an explanation of what "switching completely" means are likely to be misinterpreted by consumers (especially smokers) to mean that one may continue to smoke cigarettes, and that more than brief corrective statements are required to correct this misperception. In addition, the study found that ***modified risk claims listing multiple diseases might mislead people, particularly non-smokers, to believe that MRTPs reduce the risks of other diseases not mentioned specifically in the claims.***

Sutanto et al.³⁸ studied the perceived relative harm of IQOS, e-cigarettes, and cigarettes among adults in Canada in Fall 2018, 1.5 years after IQOS was introduced in Canada. About half (48%) believed IQOS is less harmful than cigarettes. Both exclusive and dual e-cigarette users, but not exclusive smokers, believed IQOS is more harmful than e-cigarettes and less harmful than cigarettes compared to non-users. While PMPSA claims that their target customers are exclusive conventional cigarette smokers, the study found that exclusive smokers did not have higher odds of perceiving IQOS as less harmful than cigarettes compared to non-users.

A qualitative interview study³⁹ of 30 adults in London with experience using IQOS examined the factors that influence use. Because this study was also conducted independently of tobacco companies, it improves on the data submitted from the tobacco industry. The study found that perceptions of harm and motivations to reduce harm from smoking were very salient to users, and that ***IQOS packaging and warning labels (or lack thereof) impact harm perceptions. FDA regulation can impact these factors.*** In addition, participants were affected by other factors less directly related to FDA regulation, but about which FDA may need to provide more public education, including perceptions of their own physical experience using the devices, pricing, ability to use in smoke-free environments, and social factors. Only 9 of the 30 participants overall and 7 of 22 current IQOS users reported not smoking cigarettes at all (complete switching), providing further ***evidence that few consumers are "switching completely."*** In addition, some participants noted increased levels of consumption of HEETS compared to cigarettes, either because they used in more places or because they felt the HEETS

³⁷ Yang, Bo, et al. (2021). Effects of modified risk tobacco product claims on consumer comprehension and risk perceptions of IQOS. *Tobacco Control* 0:1-9, DOI: 10.1136/tobaccocontrol-2020-056191.

³⁸ Sutanto, E., et al. (2020). Perceived relative harm of heated tobacco products (IQOS), e-cigarettes, and cigarettes among adults in Canada: Findings from the ITC Project. *Tobacco Induced Diseases* 18: 81-81, DOI: 10.18332/tid/127233.

³⁹ Tompkins, C. N. E., et al. (2020). Factors that influence smokers' and ex-smokers' use of IQOS: a qualitative study of IQOS users and ex-users in the UK. *Tobacco Control*, DOI: 10.1136/tobaccocontrol-2019-055306.

were safer than cigarettes, highlighting the need to link IQOS to structured programs or smoking cessation programs to encourage complete switching, smoking cessation, and to avoid practices that may increase harm among users. ***In the absence of data on the long-term health impacts of using IQOS, consumers are using the device hoping it will improve health.***

In an experimental study of US adult current smokers conducted in October 2018, Lee et al.⁴⁰ described how evolving IQOS packaging designs change perceptions of the product's uniqueness, quality, and safety. In particular, the study found that linking IQOS products (Marlboro HEETS were used in this study, as Marlboro HeatSticks were not yet available in the US) with established cigarette brands (Marlboro cigarettes) changes how adult smokers respond to the product, and the design of IQOS packaging can imply modified risks to consumers.

In another study of IQOS packaging, Liu et al.⁴¹ conducted an eye-tracking study of US college students in October 2019 (after the launch of IQOS in Atlanta). They found that the promotional content attracted significantly more attention than the health warnings, and that attention to promotional content was associated with more favorable attitudes and intention to use IQOS among ever-vapers.

A 2021 analysis⁴² of IQOS Twitter discussions found that 32.3% were online marketing for IQOS (many describing HeatStick flavors and other product features) and 34.2% were personal testimonials related to IQOS use. ***Many of the personal testimonial tweets made harm reduction claims about IQOS which could be misleading, including saying that IQOS could help current smokers quit smoking combustible cigarettes, that IQOS is less harmful in comparison to combustible cigarettes,*** and that IQOS was either “95%” or “95 times less health adverse” for users than combustible tobacco or vaping. Additionally, many tweets referred to tobacco policy, including describing how IQOS may benefit from flavored tobacco product bans. ***Nearly 14% of the policy tweets described how IQOS could be used to circumvent clean air policies or how they could be used in areas that do not allow smoking or vaping.***

Whether heated tobacco products could be used for smoking cessation was examined in a 2021 study⁴³ of Japanese tobacco users. In this study, the authors offered smoking cessation programs (pharmacological support, counseling only, or information about cessation) to 158 healthy male adult Japanese tobacco users and then surveyed the quitting rate among them four months out. (“Quitting” was defined as no use of any nicotine containing tobacco products). The authors observed that ***participants who used heated tobacco products either exclusively or in conjunction with combustible cigarettes were less likely than exclusive cigarette users to quit tobacco.*** Based on these findings, the authors assert that HTPs should not be recommended as a cessation aid. Notably, ***the authors suggest that tobacco industry marketing may have created a***

⁴⁰ Lee, J. G. L., et al. (2019). Evolving IQOS packaging designs change perceptions of product appeal, uniqueness, quality and safety: a randomised experiment, 2018, USA. Tobacco Control 28(e1): e52-e55, DOI: 10.1136/tobaccocontrol-2018-054910.

⁴¹ Liu, J., et al. (2021). Do Young Adults Attend to Health Warnings in the First IQOS Advertisement in the U.S.? An Eye-Tracking Approach. Nicotine & Tobacco Research 23(5): 815-822, DOI: 10.1093/ntn/ntaa243.

⁴² Barker, J. O., et al. (2021). Categorizing IQOS-Related Twitter Discussions. International Journal of Environmental Research and Public Health 18(9), DOI: 10.3390/ijerph18094836.

⁴³ Kanai, Makkiko, et al. 2021. Association of heated tobacco product use with tobacco use cessation in a Japanese workplace: a prospective study. Thorax 76:615–617. DOI: 10.1136/thoraxjnl-2020-216253.

sense of reduced risk among tobacco users who could interpret industry messaging to mean “that switching from cigarettes to HTPs eliminates the need to quit tobacco,” which would help explain the “negative impact of HTP use on successful quitting.”

A 2020 article by Leas et al.⁴⁴ documented how as early as August 2019, just four months after FDA’s April 2019 order authorizing the marketing of IQOS in the US, Philip Morris already used covert marketing strategies implying that FDA endorsed its product, violated FDA tobacco product regulations, and circumvented the terms of the media channel it advertised on. PMI paid advertising that appeared on Google searches for IQOS featured the term “FDA Process” and links to the PMI Science website where the company claimed to be developing reduced harm tobacco products. The website implied that IQOS is a reduced harm product, but FDA had not authorized PMI to make such a MRTP claim in August 2019, or ever. (In July 2020, FDA authorized the marketing of IQOS 2.4 with reduced exposure MRTP claims, but explicitly prohibited Philip Morris to make reduced harm claims.) PMI’s disclaimers stating, “this is not for advertising purposes” did not cure the violation since the clickthrough to PMI’s reduced harm product website was linked directly to Google’s sponsored ads. The advertising also appeared to circumvent Google’s terms prohibiting tobacco advertising. ***This content was likely to mislead consumers to believe that the FDA had approved or endorsed IQOS and/or found IQOS to be less harmful than other tobacco products.***

- d. **Recent peer-reviewed studies show that *as actually used by consumers*, IQOS is *not* associated with quitting smoking, consumers do *not* understand what it means to “switch completely” and that they need to exclusively use IQOS to get the claimed benefits, and that dual- or poly-use of IQOS along with cigarettes, e-cigarettes, and/or other tobacco products is the predominant use pattern.**

To obtain a reduced exposure MRTP marketing order, PMPSA is required to demonstrate (FSPTCA section 911(g)(2)) that IQOS, *as actually used by consumers*, will not expose them to higher levels of other harmful substances compared to similar types of tobacco products currently on the market. However, several recent peer-reviewed studies of *actual use* patterns demonstrate that consumers do *not* switch completely to IQOS (or even understand what it means to “switch completely”). Rather, ***consumers typically use IQOS concurrently with one or more other tobacco products, and this dual- or poly-use may expose them to higher levels of other harmful substances.***

The assumption that smokers will switch completely to IQOS is not supported by the findings from several studies. A 2018 online survey⁴⁵ of California youth assessed their perceptions of IQOS and their comprehension of “switching completely” after viewing PMPSA’s MRTP marketing claims. The study found that **youth exposed to the reduced exposure claims as well as to the reduced risk claims believed that IQOS is a less harmful product in general, and that using IQOS will result in less risk of some health conditions.**

⁴⁴ Leas, E. C., et al. (2020). A Philip Morris advertisement for its heated tobacco product IQOS sets a troubling precedent. Tobacco Control: tobaccocontrol-2019-055363, DOI: 10.1136/tobaccocontrol-2019-055363.

⁴⁵ McKelvey K, Baiocchi M, Halpern-Felsher B. PMI’s heated tobacco products marketing claims of reduced risk and reduced exposure may entice youth to try and continue using these products. *Tobacco Control* 2020;**29**:e18-e24.

Additionally, more than 25% did not correctly understand that the meaning of “switching completely” meant not using *any* tobacco products besides IQOS. Yang et al.⁴⁶ found even lower comprehension of this key term among older adults.

A study⁴⁷ that used the 2018 International Tobacco Control Japan Survey queried regular HTP users as to why they used the product. Just over half used them to help in smoking cessation, but almost the same number used the product to partially replace cigarette use *so they would not have to completely quit smoking*. The authors concluded that in the latter case, “the harm reduction potential of HTPs suggested by the toxicity studies will be diminished.” Another study⁴⁸ using the same 2018 ITC Japan survey found that 68% of HTP users also currently used cigarettes.

Kim and colleagues conducted an online survey⁴⁹ of young Korean adults. They found that *“Current IQOS users were more likely to smoke conventional cigarettes and/or e-cigarettes, which contradicts the tobacco industry’s claims that conventional cigarette smokers will switch to heated tobacco products.”* Another study of Korean adults⁵⁰ used data from a large (n=21,100) health survey and found that *96% of current HTP users were dual users (IQOS and cigarettes)*. HTP use was *not* associated with an intention to quit smoking, and HTP use was added on top of smoking, rather than used as a substitute. HTPs did not help people reduce smoking cigarettes. Also contradicting the idea that HTPs help people quit smoking combustible cigarettes, Park et al.⁵¹ analyzed a November 2018 survey of Korean adult tobacco users and found that HTP users did not differ from conventional cigarette users regarding their intention to quit within one month, dual users (including those who used HTP with either combustible or electronic cigarettes) had a lower rate of intention to quit, and intention to quit within one month was lower among exclusive HTP users compared to exclusive e-cigarette users or smokers. Moreover, Park et al. found that more than half of HTP users were dual- or poly-users of HTP with combustible or electronic cigarettes, and ¾ of the dual/poly-users used HTPs as part of their product mix.

⁴⁶ Yang, Bo, et al. (2021). Effects of modified risk tobacco product claims on consumer comprehension and risk perceptions of IQOS. *Tobacco Control* 0:1-9, DOI: 10.1136/tobaccocontrol-2020-056191.

⁴⁷ Xu SS, Meng G, Yan M, Gravely S, Quah ACK, Ouimet J, O'Connor RJ, Sutanto E, Yoshimi I, Mochizuki Y, Tabuchi T, Fong GT. Reasons for Regularly Using Heated Tobacco Products among Adult Current and Former Smokers in Japan: Finding from 2018 ITC Japan Survey. *Int J Environ Res Public Health*. 2020 Oct 31;17(21):8030.

⁴⁸ Sutanto E, Miller C, Smith DM, O'Connor RJ, Quah ACK, Cummings KM, Xu S, Fong GT, Hyland A, Ouimet J, Yoshimi I, Mochizuki Y, Tabuchi T, Goniewicz ML. Prevalence, Use Behaviors, and Preferences among Users of Heated Tobacco Products: Findings from the 2018 ITC Japan Survey. *Int J Environ Res Public Health*. 2019 Nov 21;16(23):4630. doi: 10.3390/ijerph16234630. PMID: 31766410; PMCID: PMC6926809.

⁴⁹ Kim J, Yu H, Lee S, Paek YJ. Awareness, experience and prevalence of heated tobacco product, IQOS, among young Korean adults. *Tob Control*. 2018 Nov;27(Suppl 1):s74-s77.

⁵⁰ Hwang JH, Ryu DH, Park SW. Heated tobacco products: Cigarette complements, not substitutes. *Drug Alcohol Depend*. 2019 Nov 1;204:107576. doi: 10.1016/j.drugalcdep.2019.107576. Erratum in: *Drug Alcohol Depend*. 2020 Mar 1;208:107872.

⁵¹ Park, Jinju, et al. (2021). Perceptions of Heated Tobacco Products (HTPs) and Intention to Quit Among Adult Tobacco Users in Korea. *Journal of Epidemiology* 2022:1-6. DOI: 10.2188/jea.JE20200213.

A study⁵² conducted among Korean adults found that while dual use of heated tobacco products (including IQOS) and electronic cigarettes was associated with increased attempts to quit cigarette smoking, ***the use of HTPs alone or with e-cigarettes was associated with lower odds of successful cessation.*** Similarly, a qualitative study of Korean adults by Kim et al.⁵³ found that many used heated tobacco products along with cigarettes, and the typical trajectory was dual use, followed by a gradual return to exclusive smoking.

e. Recent peer-reviewed literature finds that IQOS marketing increases youth appeal

Recent studies address the impact of IQOS marketing on youth and address how IQOS marketing can lead to youth appeal because it creates misperceptions among adolescents and young adults about the relative harm of IQOS.

A 2021 paper⁵⁴ analyzed the effects of visual exposure to IQOS on young adults. In the Brett et al. study, young adult smokers viewed videos depicting IQOS or bottled water use, then measured (1) changes in participants' cigarette and e-cigarette desires and (2) latency to smoke cigarettes provided. Although most participants had not yet been using IQOS themselves, the study found ***visual exposure to IQOS use produced smoking urges and behaviors in young adult smokers.***

A systematic literature review by Ratajczak et al.⁵⁵ reported that there is substantial interest in heated tobacco products, including among nonsmokers and youth, suggesting that these products may ***“create new nicotine addicted populations.”*** A survey⁵⁶ of Italians aged 15+ queried participants about their awareness and use of IQOS. They found that more never smokers than smokers had already tried IQOS and, using language almost identical to Ratajczak et al.'s, said the findings suggested that “IQOS may create new nicotine addicted generations.” Another study⁵⁷ examining consumer perceptions and attitudes about IQOS in Japan and Switzerland found that the product was marketed and packaged as a sophisticated, high-tech, and aspirational product. This approach is likely particularly appealing to youth and young adults, raising concerns about youth appeal. A study⁵⁸ using data on US adolescents from the 2019 National Youth Tobacco Survey reported that youth who use tobacco products, particularly dual

⁵² Kim, J., Lee, S., Kimm, H., Lee, J. A., Lee, C. M., & Cho, H. J. (2021). Heated tobacco product use and its relationship to quitting combustible cigarettes in Korean adults. *Plos one*, 16(5), e0251243.

⁵³ Kim, K., et al. (2020). Gendered factors for heated tobacco product use: Focus group interviews with Korean adults. *Tobacco Induced Diseases* 18(May), DOI: 10.18332/tid/120103.

⁵⁴ Brett et al. (2021). Effects of Visual Exposure to IQOS Use on Smoking Urge and Behavior. *Tobacco Regulatory Science* 7(1):31-45. DOI: 10.18001/trs.7.1.3.

⁵⁵ Ratajczak A, Jankowski P, Strus P, Feleszko W. Heat Not Burn Tobacco Product-A New Global Trend: Impact of Heat-Not-Burn Tobacco Products on Public Health, a Systematic Review. *Int J Environ Res Public Health*. 2020 Jan 8;17(2):409.

⁵⁶ Liu X, Lugo A, Spizzichino L, Tabuchi T, Pacifici R, Gallus S. Heat-not-burn tobacco products: concerns from the Italian experience. *Tob Control*. 2019 Jan;28(1):113-114.

⁵⁷ Hair EC, Bennett M, Sheen E, Cantrell J, Briggs J, Fenn Z, Willett JG, Vallone D. Examining perceptions about IQOS heated tobacco product: consumer studies in Japan and Switzerland. *Tob Control*. 2018 Nov;27(Suppl 1):s70-s73.

⁵⁸ Lee J, Thompson LA, Salloum RG. Heated tobacco product use among US adolescents in 2019: The new tobacco risk. *Tob Prev Cessat*. 2021 Jan 8;7:01.

and poly tobacco users and those who use flavored products, are at increased risk of using heated tobacco products. Many other studies have documented the appeal of IQOS to youth (e.g., McKelvey et al.⁵⁹ described above) concluding that heated tobacco products likely appeal to adolescents and young adults and were discussed in an earlier public comment submitted by UCSF TCORS,⁶⁰ incorporated by reference and attached.

Several recent studies were conducted in Israel, where HTP use as well as e-cigarette use is expanding rapidly. Elbaz et al.⁶¹ looked at the proximity of IQOS and JUUL points of sale relative to every elementary, middle, and high school in Israel. They found that youth are greatly exposed to IQOS points of sale very close to their schools, and that points of sale were more densely located near schools in middle-SES neighborhoods. Bar-Zeev et al.⁶² described IQOS marketing at the point of sale in Israel and found that IQOS products were frequently placed in prominent locations in retail stores that were near youth-oriented merchandise and were easily viewed by youth. Although a small pilot study, it underscores the need for data on the impact of exposure to IQOS advertising on youth (including at the point of sale), which PMPSA failed to submit with its application materials. A commentary about the Bar-Zeev study by Halpern-Felsher⁶³ warns that this kind of misleading marketing of IQOS is especially disconcerting considering the numerous studies that link marketing of novelty tobacco products, product misperceptions, and subsequent tobacco use among youth.

f. Other recent papers document aggressive marketing tactics used to promote IQOS in the US and globally

Two recent studies by Berg et al. analyze IQOS marketing strategies in the US. In a mixed-methods study⁶⁴ of all IQOS ads run in the US from August 2019 to April 2021, Berg et al. compared and contrasted the periods before and after FDA's July 7, 2020 reduced exposure MRTP authorization for IQOS 2.4. Unsurprisingly, they found that most of the money spent on advertising across the study timeframe was spent after the authorization and included messages regarding reduced exposure, promoting switching from traditional cigarettes, and alluding to research to support claims of reduced exposure. IQOS ads featured women significantly more than men, and were frequently distributed via women's fashion and entertainment, pop culture, and gaming media channels with young audiences. Of particular concern, however, is that the ad content, occurrences, and amount of money spent on ads indicated that *the marketing was targeting women and young people under age 24*.

⁵⁹ 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. *Tob Control*. 2018 Nov;27(Suppl 1):s41-s47.

⁶⁰ 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>.

⁶¹ Elbaz, D. et al. (2021). Proximity of IQOS and JUUL points of sale to schools in Israel: a geospatial analysis. *Tobacco Control* 0:1-6, DOI: 10.1136/tobaccocontrol-2021-056718.

⁶² Bar-Zeev Y, Levine H, Rubinstein G, Khateb I, Berg CJ. IQOS point-of-sale marketing strategies in Israel: a pilot study. *Isr J Health Policy Res*. 2019;8(1):11. Published 2019 Jan 14. doi:10.1186/s13584-018-0277-1.

⁶³ Halpern-Felsher, B. (2019). Point-of-sale marketing of heated tobacco products in Israel: cause for concern. *Israel Journal of Health Policy Research* 8:47. DOI: 10.1186/s13584-019-0316-6.

⁶⁴ Berg, Carla J., et al. (2021.) IQOS marketing strategies in the USA before and after US FDA modified risk tobacco product authorization. *Tobacco Control* 0:1-10, DOI: 10.1136/tobaccocontrol-2021-056819.

Another 2021 study by Berg et al.⁶⁵ analyzing IQOS marketing found that Philip Morris employs innovative methods and non-traditional marketing distribution channels to promote and distribute IQOS. They assert that IQOS has the potential for rapid uptake and identify several key areas of concern warranting more research. They found a dearth of information about consumers' interpretations of and behavioral responses to health-related marketing content, such as modified exposure messages. ***The authors note that although the company claims to target only current combustible tobacco users, the literature shows that in some populations, IQOS use is equally prominent among smokers and nonsmokers, and that specific subgroups (e.g., young adults, women) are targeted.***

Churchill et al.⁶⁶ looked at the initial October 2019 launch of IQOS in the US in Atlanta, Georgia following FDA's April 2019 PMTA marketing authorization. The paper described the high-tech design of the flagship stores in shopping malls that emphasize the clean and high-tech aspects of IQOS compared with cigarettes. IQOS marketing includes promotional price bundles and the opportunity to participate in a "personal IQOS trial" for \$1.00. Employees use high-touch marketing techniques and smoke IQOS alongside the customer, engaging in conversation and discussing the taste and feel of the product. Further, Philip Morris took advantage of the EVALI outbreak occurring contemporaneously with the Atlanta launch and FDA's recommendations against using e-cigarettes and promoted IQOS as a potential (and implicitly safer) alternative not only to conventional cigarettes, but also to e-cigarettes.

In a 2021 paper by Leas et al.,⁶⁷ the authors analyzed Google shopping queries for vaping products, JUUL, and IQOS to determine shopping trends before and during the EVALI outbreak. The study found a decrease in queries for vapes and a decrease in queries specifically for JUUL, along with an increase in queries for IQOS at that time. In absolute terms, these rates translate into about 7.3 million fewer vape shopping searches, 1.1 million fewer JUUL shopping searches and 35,000 more IQOS shopping searches than expected for the time period. Several factors may have contributed to these observed changes in shopping queries, including concerns about the safety of vaping due to the EVALI crisis, decreases in the availability of some e-cigarettes including the withdrawal of flavored JUUL products, and PMI's press releases and launch of new IQOS stores during this time. The authors conclude that ***tobacco companies should be prohibited from using events such as disease outbreaks to position their products as less harmful*** unless they have obtained specific authorization to make such claims.

⁶⁵ Berg, Carla J. et al. (2021). IQOS Marketing in the US: The Need to Study the Impact of FDA Modified Exposure Authorization, Marketing Distribution Channels, and Potential Targeting of Consumers. *International Journal of Environmental Research and Public Health*, 18(19):10551. DOI: 10.3390/ijerph181910551.

⁶⁶ Churchill, V., et al. (2020). IQOS debut in the USA: Philip Morris International's heated tobacco device introduced in Atlanta, Georgia. *Tobacco Control*: tobaccocontrol-2019-055488, DOI: 10.1136/tobaccocontrol-2019-055488.

⁶⁷ Leas, E. C., et al. (2021). Google shopping queries for vaping products, JUUL and IQOS during the E-cigarette, or Vaping, product use Associated Lung Injury (EVALI) outbreak. *Tobacco Control*, DOI: 10.1136/tobaccocontrol-2021-056481.

Several studies document aggressive marketing of IQOS outside the US where IQOS has been available for a longer period. A November 2021⁶⁸ paper describes PMI's promotion of IQOS in New Zealand. Relying on an article that was funded by Philip Morris, PMI presents unsupported information suggesting that IQOS could help smokers quit using conventional cigarettes and conflates heated tobacco products with electronic cigarettes. Recent promotions on the IQOS New Zealand online store bundle PMI's e-cigarette brand VEEV with IQOS 3 and urge smokers to use VEEV "when you're on the go" and IQOS "when you have a moment to relax," thus *encouraging dual use of IQOS with e-cigarettes*.

Watts et al.⁶⁹ analyzed Philip Morris's lobbying activities and corporate strategies aimed at introducing IQOS in Australia where heated tobacco products were prohibited by bans on nicotine-containing products. The company actively lobbied Australian policymakers to overturn those bans and create a new product category that would exempt IQOS from these laws. Philip Morris simultaneously worked to establish high-end pubs, clubs and bars where they could sell IQOS once the desired legalization was achieved.

Another article⁷⁰ documented that Reviti, a wholly owned subsidiary of PMI, sold life insurance in the UK that offered substantial discounts on premiums to IQOS users, claiming that IQOS was the only available science-backed smokefree alternative. The discount to IQOS users in the short term was greater than the discount for quitting smoking, and the premium discounts also implied that using IQOS was 10 times healthier than using e-cigarettes. *This life insurance offer appears to be a novel marketing tool to promote health claims about IQOS.*

Misinformation was also used to promote IQOS in Turkey. A descriptive study⁷¹ of websites selling IQOS in Turkey documented the online promotion of IQOS in Turkey where tobacco marketing is prohibited. Despite advertising prohibitions, the online promotions include reduced risk claims and links to social media which are popular among youth. The study found that of 119 websites selling tobacco products, 41.2% sold e-cigarettes and 39.5% sold IQOS, the second most common product. *The websites selling e-cigarettes or IQOS were more likely to contain misinformation about the harmlessness of the product, and the websites had routing tabs to social media; approximately half were being directed to Facebook, WhatsApp, and Twitter (53.8%, 51.3%, and 49.6%, respectively).*

Mathers et al.⁷² documented PMI's activities selling IQOS in Ontario, Canada, where there are strict limitations on tobacco marketing. IQOS was promoted at tobacco retailers and using boutique stores featuring promotions including exchanging a pack of cigarettes or lighter

⁶⁸ Robertson L, Hoek J, Silver K. PMI New Zealand conflates IQOS heated tobacco products with electronic nicotine delivery systems. *Tobacco Control* Published Online First: 19 November 2021. doi: 10.1136/tobaccocontrol-2021-056964.

⁶⁹ Watts, C., et al. (2020). Creating a market for IQOS: analysis of Philip Morris' strategy to introduce heated tobacco products to the Australian consumer market. *Tobacco Control*, DOI: 10.1136/tobaccocontrol-2020-056057.

⁷⁰ Prochaska, J. J. and L. Henriksen (2020). PMI reduced-risk claims and upselling of IQOS via Reviti life insurance. *Tobacco Control* 29(e1): e136-e137, DOI: 10.1136/tobaccocontrol-2019-055145.

⁷¹ Çoban T, İncesoy AC, Demir B, et al. Evaluation of tobacco product-selling websites accessed using search engines. *Turk Thorac J* 2020; 21(6): 377-82.

⁷² Mathers A, Schwartz R, O'Connor S, Fung M, Diemert L. Marketing IQOS in a dark market. *Tob Control*. 2019;28(2):237-238. doi:10.1136/tobaccocontrol-2017-054216.

for an IQOS device, launch parties, “meet and greet” lunches, and after-hour events. IQOS boutique retail stores feature prominent “IQOS” and “Building a smoke-free future” signs, and sales representatives promote the product by smoking IQOS outside the stores. IQOS was also promoted online, and consumers were encouraged to register on the website. The article notes that without premarket approval, the Canadian government was not able to educate the public about the risks of IQOS. These kinds of marketing tactics that promote IQOS as sophisticated, high-tech products were also described in Hair et al.’s analysis⁷³ of IQOS marketing in Japan and Switzerland. ***These studies suggest that FDA needs to impose additional disclosure requirements about the risks of IQOS prior to granting (further) sales authorizations to IQOS.***

g. Recent literature emphasizes that FDA’s actions have misled consumers and supported industry marketing of IQOS

Many consumers misinterpret FDA’s marketing authorization of IQOS with reduced risk claims to mean that FDA endorses or approves IQOS, and the industry uses FDA’s actions when marketing IQOS to further these misperceptions both in the US and in other countries.

Ayers et al.⁷⁴ documented how PMI used the EVALI crisis to promote IQOS in a 2019 PMI press release about EVALI, which was published on the same day as the largest number of news stories on IQOS. The press release also announced FDA’s order authorizing the sale of IQOS in the US and said that FDA found that marketing IQOS would be “appropriate for the protection of public health” (quotes used in the original release). This statement in the press release could mislead the public to perceive FDA endorsement of the product or that the product reduces health risk.

As discussed in more detail above, Leas et al.⁷⁵ described how ***PMI used covert strategies to market IQOS implying that FDA endorsed its product*** and linking IQOS to reduced harm products. These promotions were likely to mislead consumers.

Independent studies of consumer perceptions substantiate that FDA’s authorization of products and industry claims affect perceptions of the product’s harmfulness. Mays et al.⁷⁶ surveyed US young adult smokers and non-smokers to assess the independent and interactive effects of including different health warnings and risk claims in IQOS ads. They found that among young adult smokers, some health warnings increased the advertisements’ perceived credibility and effectiveness at discouraging IQOS use, but ***among non-smokers, the FDA-authorized reduced exposure claim increased intentions to use IQOS.*** These results suggest that ***FDA’s authorization of reduced exposure claims may make it more likely that non-users will initiate tobacco use with IQOS.***

⁷³ Hair, Elizabeth C., et al. (2018). Examining perceptions about IQOS heated tobacco product: consumer studies in Japan and Switzerland. *Tobacco Control* 27:s70-s73, DOI: 10.1136/tobaccocontrol-2018-054322.

⁷⁴ Ayers, J. W., et al. (2021). Philip Morris International used the e-cigarette, or vaping, product use associated lung injury (EVALI) outbreak to market IQOS heated tobacco. *Tobacco Control*: tobaccocontrol-2021-056661, DOI: 10.1136/tobaccocontrol-2021-056661.

⁷⁵ Leas, E. C., et al. (2020). A Philip Morris advertisement for its heated tobacco product IQOS sets a troubling precedent. *Tobacco Control*: tobaccocontrol-2019-055363, DOI: 10.1136/tobaccocontrol-2019-055363.

⁷⁶ Mays, Darren, et al. 2021. Effects of IQOS health warnings and modified risk claims among young adult cigarette smokers and non-smokers. *Tobacco Control* 0:1–5. DOI: 10.1136/tobaccocontrol-2021-056810.

FDA's orders also have impact outside the US. FDA acknowledges on its own web page that many other countries rely on FDA for guidance on how to regulate recently developed products.⁷⁷ The 2021 paper by Lempert et al.⁷⁸ discussed why FDA's reduced exposure MRTP order for IQOS 2.4 is not a reliable global model. Although the order explicitly prohibits the marketing of IQOS with claims that IQOS reduces harm or the risk of tobacco-related diseases, the legal language is inherently confusing, and PMI is exploiting this confusion and using FDA's decision as the basis for marketing and public relations campaigns outside the US. A review by Kim⁷⁹ highlighted how events and policy decisions in the US affect consumer behavior in Korea. Kim describes how FDA's July 2020 reduced exposure authorization MRTP order for IQOS 2.4 complicated smoking-cessation efforts in Korea. The authors correctly warned that although FDA announced that IQOS produces fewer or lower levels of some toxins than combustible cigarettes, FDA's authorization does *not* mean that these products are safe, and there is no evidence that reducing the harmful chemical components leads to health benefits. FDA's exposure modification authorization for IQOS 2.4 was used to promote IQOS sales as a safer tobacco product in other countries.⁸⁰ In Thailand, ENDS advocates advertised that the FDA had found IQOS "appropriate for the protection of the public health".⁸¹

FDA must consider the scientific evidence presented in this large body of peer-reviewed studies that were not included in PMPSA's sMRTPA for IQOS 3. This new evidence reinforces our earlier papers and comments concluding that PMPSA failed to prove that IQOS would benefit the health of the population as a whole, including youth and other non-users and former users, as required by section 911(g).

4. Conclusion

As detailed above, published scientific *evidence that has not been reported by PMPSA* demonstrates that IQOS may appeal to adolescents and young adults, as well as other non-users and former users, and that the proposed reduced exposure claims, labeling and marketing of IQOS will likely be misunderstood by consumers, particularly youth.

Specifically:

⁷⁷ Office of the Commissioner. FDA Goes Global. FDA. Published April 24, 2019. Accessed November 16, 2021. <https://www.fda.gov/about-fda/changes-science-law-and-regulatory-authorities/fda-goes-global>

⁷⁸ Lempert LK, Bialous S, Glantz S. FDA's reduced exposure marketing order for IQOS: why it is not a reliable global model [published online ahead of print, 2021 Apr 2]. *Tob Control*. 2021;tobaccocontrol-2020-056316. doi:10.1136/tobaccocontrol-2020-056316.

⁷⁹ Kim JY. Directions and Challenges in Smoking Cessation Treatment. *Tuberc Respir Dis (Seoul)*. 2020;83(Supple 1):S1-S5. doi:10.4046/trd.2020.0150.

⁸⁰ University of Bath. PMI Promotion of IQOS Using FDA MRTP Order - TobaccoTactics. Published June 10, 2021. Accessed October 2, 2021. <https://tobaccotactics.org/wiki/pmi-iqos-fda-mrtp-order/>

⁸¹ Patanavanich R, Glantz S. Successful countering of tobacco industry efforts to overturn Thailand's ENDS ban. *Tob Control*. Published online November 23, 2020;tobaccocontrol-2020-056058. doi:10.1136/tobaccocontrol-2020-056058.

- PMPSA's sMRTPA did not consider IQOS's appeal to youth, or the likelihood that adolescents or young adults will initiate tobacco use with IQOS or use IQOS with other tobacco products.
- Independent research not reported by PMPSA provides significant scientific evidence relevant to its sMRTPA for IQOS 3. In particular:
- Epidemiological studies indicate growing awareness, ever-use, and current use of IQOS among adolescents and young adults;
- Recent studies highlight the potential for growing susceptibility, use, and appeal of IQOS among youth;
- Studies analyzing consumers' perceptions show that IQOS packaging, labeling, and marketing mislead consumers into believing that IQOS has been demonstrated to be less harmful or presents less risk of disease;
- As actually used by consumers, IQOS is not associated with quitting smoking;
- Consumers do not understand what it means to "switch completely" and that they need to exclusively use IQOS to get the claimed benefits. Instead, dual- or poly-use of IQOS along with cigarettes, e-cigarettes, and/or other tobacco products is the predominant use pattern; and
- IQOS marketing increases youth appeal.
- Recent papers document aggressive marketing tactics used to promote IQOS in the US and globally that may encourage initiation and/or increase IQOS use among youth and other non-users.
- Recent literature emphasizes how FDA's actions have affected consumer behavior and supported industry marketing of IQOS.

Because PMPSA and FDA have not presented or made publicly available evidence refuting these points, and have failed to otherwise demonstrate that IQOS 3 would benefit the health of individuals and of the population as a whole, we strongly recommend that FDA deny PMI's Supplemental MRTP application for IQOS 3.