December 10, 2021

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm 1061
Rockville, MD 20852

Re: Docket No. FDA–2021–N–0408, Modified Risk Tobacco Product Application for the IQOS 3 System Holder and Charger Submitted by Philip Morris Products S.A.

The undersigned public health organizations submit these comments on the above-referenced modified risk tobacco product (MRTP) application, which according to the applicant, Philip Morris Products S.A. (Philip Morris or PM), was submitted as a "supplemental" MRTP.[1] Philip Morris states it submitted no new data for its IQOS 3 supplemental MRTP application, relying only on the studies that supported the original MRTP order granted by FDA for the IQOS 2.4 System and Heatsticks, and where relevant, studies that supported the supplemental Premarket Tobacco Product Application (PMTA) for the IQOS 3 System.[2]

We oppose grant of this MRTP for the following reasons:

(1) The application itself, and the process used by FDA for review of the application, are inconsistent with the relevant statutory requirements.

(2) FDA must not grant the MRTP application without clarifying whether IQOS 3 includes Bluetooth technology that allows for interaction between the manufacturer and the user, to the detriment of public health.

(3) Granting of the MRTP will extend to a new product the deficiencies in FDA's grant of an MRTP for IQOS 2.4.

(4) New research and data since FDA's grant of an MRTP for IQOS 2.4 further support denial of MRTPs for both IQOS 2.4 and IQOS 3.

[1] Letter to Dir. Matthew R. Holman, FDA, Office of Science, from Philip Morris Products S.A., 1 (Mar. 18, 2021), https://www.fda.gov/media/148606/download.

[2] *Id.* at 2.

I. THE SUPPLEMENTAL MRTP FOR IQOS 3 AND THE PROCESS FOR REVIEW OF THE SUPPLEMENTAL MRTP, ARE INCONSISTENT WITH THE STATUTORY REQUIRMENTS FOR MRTP APPLICATIONS

A. The Use of a Supplemental MRTP is Not Authorized by the Statute and FDA's Authority to Permit Such an Application Has Not Been Established

The MRTP submitted by Philip Morris for IQOS 3 is designated by the company as a "supplemental" MRTP. The statutory authority for FDA to permit or grant such "supplemental" MRTP applications is unclear and the agency has never solicited public comment on its legal authority or its implementation of such a pathway for modified risk products.

There is no reference to "supplemental" applications in Section 911 of the Food, Drug and Cosmetic Act, as amended by the Family Smoking Prevention and Tobacco Control Act (Tobacco Control Act or TCA),[3] the only provision of the TCA authorizing modified risk products. Moreover, there is no reference to "supplemental" MRTP applications in the Draft Guidance on Modified Risk Tobacco Applications, issued March, 2012;[4] nor is there any rule providing for such applications and specifying the conditions that must be met in order to use such applications.[5] FDA has never asserted its legal authority to diverge from the requirements imposed by Section 910 by permitting "supplemental" applications nor explained the policy reasons for doing so. The public has never had the opportunity to comment on a proposal to require a form of application that may call for information to be supplied by the applicant that differs from that required by Section 910.

Instead, in this case, FDA made a determination, without reference to any general legal authority, to allow PM to submit a "supplemental" application, with less information about the product at issue than that required by the statute. It communicated that determination through a letter sent to PM and disclosed by FDA only pursuant to a Freedom of Information Act request by the Campaign for Tobacco-Free Kids. It is only in that letter that FDA set out the criteria that a company must meet to diverge from the requirements of Section 910. FDA has never published these criteria, nor requested public comment on them.

There is a substantial risk that the mechanism of "supplemental" applications will become a vehicle for evasion of the statutory requirements for modified risk applications, leading to an incomplete consideration by the FDA of the full range of scientific and policy questions that must be thoroughly vetted through the application process. In this case, as discussed below, the "supplemental" application pathway has evaded required referral of the application to the Tobacco Product Scientific Advisory Committee (TPSAC). Therefore, FDA should not grant this, or any other, "supplemental" MRTP application without publishing, and seeking public comment on, the concept of such an application, the proposed criteria for use of such an

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[3] 21 U.S.C. §387k.

[4] FDA Draft Guidance, *Modified Risk Tobacco Applications* (Mar. 2012), https://www.fda.gov/media/83300/download.

[5] This is in contrast to Supplemental Premarket Tobacco Product Applications, the criteria for which are set out in 21 C.F.R. §1114.15.

application, its policy justification and FDA's legal authority to grant an application that provides less information about the product and proposed claim than is required by Section 910.

B. The Failure of FDA to Refer the PM Application to TPSAC is Not in Compliance with the Statute

The Philip Morris "supplemental" application for IQOS 3 appears to be the first MRTP application considered by the FDA and not referred to TPSAC for any purpose. Instead of announcing the date of a TPSAC meeting to consider the application, FDA's website advises the public to "Refer to January 24-25, 2018 meeting materials." https://www.fda.gov/tobacco-products/advertising-and-promotion/modified-risk-tobacco-products#summary The referenced meeting considered the MRTP for IQOS 2.4, a product that is unquestionably different in its characteristics from IQOS 3.

The failure to refer this MRTP application to TPSAC is in clear violation of Section 911 (f)(1) of the TCA, which provides that "[t]he Secretary *shall* refer to the Tobacco Products Scientific Advisory Committee *any* application submitted under this section."[6] (emphasis added). Section 911 also provides that TPSAC "*shall* report its recommendations on the application to the Secretary" within 60 days of the referral. [7] As described in our October 19, 2020 letter to Director Zeller, the mandatory referral of MRTP applications to TPSAC is a key component of the statutory scheme for the scientific evaluation of such applications by the FDA, distinguishing the modified risk evaluation process from the premarket review of new tobacco products, where referral to TPSAC is discretionary, as well as the discretionary role of other scientific advisory committees respecting FDA review of new products under other sections of the Food, Drug and Cosmetic Act.[8] We are concerned that the agency's failure to follow the law in referring the PM application to TPSAC is yet another indication of its marginalization of TPSAC's role in modified risk proceedings, as discussed in detail in our October, 2020 letter. Indeed, as that letter also indicates, the absence of agency deference to TPSAC's findings concerning IQOS 2.4 further indicates the marginalization of TPSAC.

It may well be that there is no need for TPSAC to do an extensive review of the Philip Morris application. FDA can certainly recommend to TPSAC that its role be limited in light of the claimed similarities between IQOS 2.4 and IQOS 3. But the statute does not permit FDA to avoid referral to TPSAC altogether. If TPSAC is to have a limited role with respect to this application, that determination ultimately must be made by TPSAC.

[6] 21 U.S.C. §387k(f)(1).

[7] 21 U.S.C. §387k(f)(2).

[8] See letter from American Academy of Pediatrics et al. to Mr. Mitchell Zeller re Role of Tobacco Products Scientific Advisory Committee in Modified Risk Tobacco Product Proceedings (Oct.19, 2020), https://www.tobaccofreekids.org/assets/content/what_we_do/federal_issues/fda/2020_10_10_Letter-to-FDA-on-TPSAC-role-MRTP-proceedings.pdf.

II. FDA MUST MAKE CLEAR TO THE PUBLIC WHETHER THE IQOS 3 MODIFIED RISK PRODUCT WILL FEATURE BLUETOOTH CAPABILITY, WHICH RAISES SERIOUS PUBLIC HEALTH CONCERNS

The redactions in the posted modified risk application and the cross-referenced supplemental PMTA (sPMTA) for IQOS 3 make it impossible for the public to know whether or not the IQOS 3 device under consideration includes technology that facilitates data collection and communication between users and tobacco companies. This is a critical gap, given the public health implications of such technology on product use and consumer perceptions of the product, particularly in relation to modified risk marketing.

The concerns related to Bluetooth technology in IQOS devices were addressed in a letter that public health groups sent to FDA in July 2020.[9] Because the specifications of this version of the device are blocked from the public, it is unclear if it contains the same features as those in the IQOS 3 models available in other countries, though the MRTP Executive Summary alludes to such features: "Also described in the sPMTA, the IQOS 3 System includes modifications to incorporate the evolution of electronics technology and aligns the U.S. version of the device more closely with the IQOS version currently commercialized outside the U.S."[10] but all specifics in both this MRTP application and the cross-referenced sPMTA have been redacted. According to websites, this technology allows connection to an app that, among other capabilities, locates the device, shows nearby retailers selling IQOS and HeatSticks, allows HeatStick purchases directly through the app, and can connect users to IQOS customer support.[11] In addition to raising important privacy concerns, this technology in tobacco products is a threat to public health because it gives profit-maximizing manufacturers of highly addictive products access to user data that will be used to sustain addiction.

For instance, at the January 2018 TPSAC meeting for the IQOS 2.4 MRTP application, Moira Gilchrist, Vice President of Scientific & Public Communications for Philip Morris International (PMI), described this communication feature in IQOS devices sold in other countries that could prompt users if the device and app detected that they hadn't used their device recently: "You know, for example, a message may come up, hey, you haven't used your IQOS device today. Have you stopped smoking or is it because you've gone back to combustible cigarettes?"[12] For a user who stopped use of all tobacco products, including IQOS, this type of message could lead to relapse. There is nothing preventing tobacco companies from using collected data to maximize user addiction to increase profits. One published paper warned, "[T]he fact that IQOS measures a user's puff-by-puff heating profile, integrates IQOS's Bluetooth capability with mobile phones and computers, and automatically reminds consumers to continuously use the device and to reorder tobacco sticks suggests that it calibrates the

[9] See letter from American Academy of Pediatrics et al. to Mr. Mitchell Zeller re Bluetooth Technology in Tobacco Products (July 16, 2020), https://www.tobaccofreekids.org/assets/content/what_we_do/federal_issues/fda/regulatory/2020_07_16-Letter-to-FDA-re-Bluetooth-Technology-in-Tobacco-Products.pdf.

[10] Executive Summary, p. 9.

[11] *Understanding the IQOS Connect App*, Heat180 (Aug. 13, 2019), https://heat180.com/understanding-the-iqos-connect-app/.

[12] PMI Presentation to TPSAC, Transcript (Jan. 25, 2018), https://www.fda.gov/media/111450/download.

delivery of nicotine to ensure not only 'satisfaction', but also the potential for PMI to customise the dose, speed of delivery and continuous use of nicotine to maximise addictive potential for individual users."[13]

FDA must make it clear to the public whether IQOS 3, which has received a premarket order and is the subject of the pending MRTP application, features Bluetooth technology. If it does, the agency must carefully and thoroughly evaluate the information provided to determine how these added features will interact with the modified risk messaging to impact public health.

III. GRANTING THE MRTP APPLICATION FOR IQOS 3 WILL EXTEND TO THAT PRODUCT THE ERRORS MADE BY FDA IN GRANTING THE MODIFIED RISK APPLICATION FOR IQOS 2.4

Most of the undersigned organizations opposed the MRTP for IQOS 2.4 and incorporate those comments by reference here.[14] Granting the MRTP application for IQOS 3 would extend the flaws in FDA's analysis of IQOS 2.4 to another product. The pending application for IQOS 3 should be seen by the agency as an opportunity to correct its errors by revisiting the modified risk order as to IQOS 2.4 and denying the application as to IQOS 3.

A. Lack of data on youth use and youth perception of products and marketing should render any tobacco product application deficient.

As the groups on this comment have raised repeatedly in prior comments and letters submitted to FDA, the companies' failure to submit, and the agency's failure to require, data on youth perceptions of IQOS and other modified risk products prevents FDA from fully evaluating the public health impact of these products on the population.[15] As noted by Institute of Medicine:

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[13] Lauren Lempert & Stanton Glantz, *Heated tobacco product regulation under US law and the FCTC*, 27 Tobacco Control, s118-s125 (2018), https://pubmed.ncbi.nlm.nih.gov/30291201/.

[14] Campaign for Tobacco-Free Kids (CTFK) et al., *Comment Letter on Modified Risk Tobacco Product Applications for IQOS system with Marlboro HeatSticks, IQOS system with Marlboro Smooth Menthol HeatSticks, and IQOS system with Marlboro Fresh Menthol HeatSticks submitted by Philip Morris, S.A.*, 2, 8-14 (Feb. 11, 2019), https://www.tobaccofreekids.org/assets/content/what_we_do/federal_issues/fda/regulatory/2019_02_11_Public_Health_Groups_Comments_IQOS_MRPTAs.pdf.

[15] CTFK, *Comment Letter on Applications for iQOS system with Marlboro Heatsticks, iQOS system with Marlboro Smooth Menthol Heatsticks, and iQOS system with Marlboro Fresh Menthol Heatsticks Submitted by Philip Morris Products S.A.*, 13-16 (Jan. 3, 2018), https://www.tobaccofreekids.org/assets/images/content/2018_01_03_CTFK_IQOS_comments.pdf; CTFK, *Comment Letter on Notice of Meeting re Tobacco Product Application Review*, 4-6 (Dec. 7, 2018), https://www.tobaccofreekids.org/assets/content/what_we_do/federal_issues/fda/2018_12_07_CTFK_Comments_premarket_review_meeting.pdf; CTFK et al., *Comment Letter on Modified Risk Tobacco Product Applications for IQOS system with Marlboro HeatSticks, IQOS system with Marlboro Smooth Menthol HeatSticks, and IQOS system with Marlboro Fresh Menthol HeatSticks submitted by Philip Morris, S.A.*, 2, 8-14 (Feb. 11, 2019), https://www.tobaccofreekids.org/assets/content/what_we_do/federal_issues/fda/regulatory/2019_02_11_Public_Health_Groups_Comments_IQOS_MRPTAs.pdf; CTFK et al., *Comment Letter on Proposed Rule for Premarket Tobacco Product Applications and Recordkeeping Requirements*, 21-25 (Dec. 16, 2019), https://www.tobaccofreekids.org/assets/content/what_we_do/federal_issues/fda/PublicHealthGroupsCommentsonPMTAProposedRule.pdf; CTFK et al., *Principles to Guide FDA Premarket Review of E-Cigarettes and Other*

> …adolescents' perceptions of the risks and benefits of cigarette smoking play an important role in adolescents' decisions to smoke. … Given that adolescence is a period of heightened vulnerability for the initiation of tobacco use, it is important to evaluate whether adolescents accurately understand the purported benefits of an MRTP.[16]

And:

> Of particular importance are adolescents' perceptions of the risks and benefits of using the product, and whether they intend to initiate tobacco use with the MRTP rather than a traditional tobacco product because they believe the former is a 'safe' alternative.[17]

FDA's granting of a modified risk order for IQOS 2.4, despite the lack of that fundamental data, will be compounded if FDA also grants a modified risk order for this MRTP application.

PMI's statements about potential impact on youth use in this MRTP application are not based on any actual data of youth initiation because yet again, it did not submit any for FDA to evaluate. For instance, in the Executive Summary, PMI stated, "Such conclusion is based on the demonstrated comparability of the IQOS 3 System to the IQOS 2.4 System in performance, use patterns, product consumption, and user profiles, successful switching of adult smokers to this modified-risk tobacco product as well as minimal use among non-users of tobacco products (including youth)."[18] It further stated, "[g]iven the product similarities, there is no evidence of increased risk for youth initiation and use for the IQOS 3 system as compared to the IQOS 2.4 System."[19] However, because PMI did not provide sufficient data to support its prediction of "minimal use" of IQOS 2.4 among U.S. youth in its initial MRTP application, the company's comparison between IQOS 3 and IQOS 2.4 as to youth appeal is not meaningful.

FDA's own social scientists expressed concern about this lack of data in FDA's Decision Summary for the IQOS 2.4 MRTP application:

Deemed Products, 3-4 (Aug. 10, 2020), https://www.tobaccofreekids.org/assets/content/what_we_do/federal_issues/fda/regulatory/2020_08_10_Premarket-Principles.pdf; FDA, *February 6, 2019 TPSAC Meeting Transcript*, 69-71 (Feb. 6, 2019), https://www.fda.gov/media/122002/download; CTFK et al., *Comment Letter to FDA about the Youth-Oriented Marketing of the IQOS Heated Cigarette Product in Other Countries* (May 14, 2019), https://www.tobaccofreekids.org/assets/content/what_we_do/federal_issues/fda/2019_05_14_youth_marketing_iqos.pdf; CTFK et al., *Necessity of Adolescent Risk Perception Data in Modified Risk Tobacco Applications* (Feb. 15, 2019), https://www.tobaccofreekids.org/assets/content/what_we_do/federal_issues/fda/regulatory/2019_02_15_Public-Health-Groups-Adolescent-Risk-Perception.pdf; CTFK, *Comments on Public Scientific Workshop on Youth Tobacco Cessation: Science and Treatment Strategies*, 6-7 (May 31, 2019), https://www.tobaccofreekids.org/assets/content/what_we_do/federal_issues/fda/regulatory/2019-05-31_FDA-Youth-Cessation-Workshop-Comments.pdf.

[16] Institute of Medicine, *Scientific Standards for Studies on Modified Risk Tobacco Products,* at 194 (2012). ("IOM Report")

[17] IOM Report, p. 200.

[18] Executive Summary, p. 5.

[19] Executive Summary, p. 18.

> The social science review concludes that based on the information submitted by the applicant, we have concerns with respect to: the lack of information about youth under age 18, as well as the lack of a discussion of submitted data's applicability to youth and the lack of presentation of the data in stratified categories that would allow us to make inferences about youth, the potential for initiation among young adult never smokers, and the potential for dual use among current smokers with only a one cigarette per day decrease in use frequency. Philip Morris Products S.A.'s premarket tobacco product applications do not contain sufficient information to address these concerns from a Social Science perspective.[20]

Yet the technical project lead overruled these concerns and granted the order. FDA should not grant another modified risk order based on a previous order that was not supported by sufficient data.

B. FDA failed to consider research showing consumers misunderstand reduced exposure as meaning reduced risk.

It is irresponsible for FDA to grant a modified risk order for IQOS 3 when it has not evaluated the impact of the reduced exposure messaging on consumers' understanding and behavior. Public health groups had raised concerns about consumers' misperceptions of reduced exposure claims in our previous comments.[21] While IQOS may present users with lower exposure to chemical constituents, consumer misinterpretation of that claim as a reduced risk statement will have important implications for public health.

As discussed in those previous comments, in data submitted by PMI, FDA found a sizeable portion of consumers incorrectly responding that using IQOS reduces one's risk.[22] An independent study similarly found that consumers consistently believed quantity translated into level of risk (i.e., lower quantity equaled lower risk).[23] Further, comments submitted by researchers at the University of North Carolina referenced their study finding that "Claims of less exposure were associated with lower perceived risk" and that "Reduced exposure claims also led to higher susceptibility to use the MRTP because of lower perceived risk." They concluded, "These results suggest that the exposure modification order pathway is not likely viable because reduced exposure claims may lower perceived risk and increase susceptibility to use."[24]

Granting a modified risk order for IQOS 3 would compound the public health risk of marketing products with reduced exposure claims, where the evidence establishes the likelihood that those claims will be misinterpreted to suggest reduced risk of disease.

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[20] FDA, Technical Project Lead Review for PMI heated tobacco products, at 83 (Apr. 29, 2019).

[21] CTFK et al. *supra* note 14, at 31-32.

[22] FDA Briefing Document, at 54.

[23] Lucy Popova, Lauren K. Lempert & Stanton A. Glantz, *Light and mild redux: heated tobacco products' reduced exposure claims are likely to be misunderstood as reduced risk claims*, *Tobacco Control* 27:s87–s95 (2018).

[24] Comments by Byron, MJ., et al., Comment ID FDA-2017-D-3001-0239, Tracking number 1k3-9879-mi34, 2 (Jan. 25, 2019), https://www.regulations.gov/comment/FDA-2017-D-3001-0239.

IV. NEW INFORMATION SINCE FDA GRANTED THE MRTP APPLICATION FOR IQOS 2.4 RAISES NEW DOUBTS ABOUT THE PUBLIC HEALTH IMPACT OF MODIFIED RISK STATUS FOR BOTH IQOS 2.4 AND IQOS 3

Since FDA granted the modified risk order for PM's IQOS 2.4 product in July 2020, not enough time has passed for the postmarket surveillance studies required in the IQOS 2.4 modified risk order to reveal any noticeable trends. As a result, at this time FDA does not have a complete picture of the impact of the 2.4 order on public health. The early postmarket surveillance data submitted in the pending IQOS modified risk application that relate to the 2019 marketing order for IQOS 2.4 likely do not provide enough data specific to the modified risk marketing. A full analysis is vital for understanding if the reduced exposure message is actually converting adult smokers to IQOS – which PM listed as the first of its "Good Conversion Principles"[25] – or having no effect on that population, or, even worse, encouraging non-tobacco users to use IQOS. It would be premature to make any decision on this MRTP application until data show the previous modified risk order has had a positive impact on public health.

Instead, since the initial modified risk order was issued, new studies have been published and new information about the company's actions have come to light. FDA should consider this new information before proceeding with this application. It is notable that the company omitted the studies that had been published at the time this MRTP application was submitted.

A. Additional information about the health impact of using IQOS.

Because IQOS and other heated tobacco products are still relatively new to the market, their long-term health consequences are still unknown. Even if IQOS presents lower exposure of some toxins to users compared to cigarette smokers, recent studies suggest biological changes from using heated tobacco products that could impact health. A systematic review of literature, published by both tobacco companies and various independent sources, found evidence to "suggest that there may be a positive correlation between the use of HTP and the occurrence of respiratory diseases, particularly negative impacts on lung physiology, human bronchial epithelial cells, AEP, allergic rhinitis and asthma," in addition to observations of an "[i]ncrease of the level of oxidative stress, mitochondrial dysfunction and increase[d] infections in the respiratory track." The researchers also found possible reduced risk of cardiovascular disease and other related indicators.[26] A separate study, however, suggested heated tobacco products were "an emerging threat to cardiovascular health."[27] Before authorizing a reduced exposure claim for a new heated tobacco product, FDA must take account of the most recent studies addressing the health effects of these products.

B. IQOS marketing in the U.S. raises questions about PM's intent

[25] PMI, Cross-Referenced IQOS 3 System Holder and Charger Supplemental Premarket Tobacco Product Application (PMTA), Module 4: Labeling and Marketing, 4.2 Marketing Plans, Appendix 4, 30-Day Notification for PM0000424 - PM0000426 and PM0000479, 4 (Jun. 7, 2019).

[26] Malgorzata Zynk et al., *Exposure to Heated Tobacco Products and Adverse Health Effects, a Systematic Review*, International Journal of Environmental Research and Public Health, 18(12):6651 (2021).

[27] Nicholas D. Fried & Jason D. Gardner, *Heat-not-burn tobacco products: an emerging threat to cardiovascular health*, American Journal of Physiology, Heart and Circulatory Physiology, 319(6):H1234-H1239, (2020).

The MRTP application for IQOS 3 assures FDA that "[t]he marketing and advertising restrictions implemented for the IQOS 2.4 System will also apply to the IQOS 3 System and hence ensure that IQOS is only sold to current adult smokers who would otherwise continue smoking and are at least 21 years old." Recent studies, however, show that current IQOS marketing in the U.S. has not effectively reached adult smokers, but instead is reaching other audiences.

An analysis of IQOS ads before and after FDA's modified risk order showed "a surge in adspend after IQOS received FDA modified exposure authorisation." In addition, the study found that, despite PM's claims of targeting adult smokers, most of the ads placed were in channels that targeted young women, who typically have lower smoking rates.[28] This second finding is, unfortunately, not a surprise. Public health groups had raised concerns about PM's global marketing for IQOS that has been heavily focused on women's fashion and style in a previous letter to FDA[29] and in our comments to FDA on the MRTP application for IQOS 2.4.[30]

C. More recent studies continue to show confusion about the modified risk messaging proposed by PM in its IQOS 2.4 application.

i. Misunderstanding "switch completely."

In its Decision Summary for the IQOS 2.4 MRTPA, FDA found that PM failed to provide data assessing consumer understanding about what "switching completely" meant: "The applicant's proposed exposure reduction claim specifies that smokers can obtain the stated exposure benefits by switching completely to IQOS, but the applicant did not provide evidence related to consumer understanding of this component of the information and the need to use IQOS exclusively."[31] Some TPSAC members "also expressed concern about the lack of evidence that consumers understood that complete switching was necessary to achieve the purported benefits communicated in the modified risk claims."[32] FDA recommended that "Because consumers need to switch completely to achieve the benefits of reduced exposure described in the modified risk claim, **postmarket surveillance should be conducted to ensure consumers understand that the benefits of reduced exposure cannot be achieved by continuing to smoke combusted cigarettes in addition to using IQOS**."[33] Before deciding on the IQOS 3 MRTP application, FDA should evaluate whether or not consumer understanding of "switching completely" has improved, in part based on the postmarket surveillance studies Altria/PMI should be conducting, as well as other independent studies.

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[28] Carla J. Berg et al., *IQOS marketing strategies in the USA before and after US FDA modified risk tobacco product authorisation*, Tobacco Control, Online ahead of print, doi: 10.1136/tobaccocontrol-2021-056819 (October 19, 2021).

[29] CTFK et al., *Comment Letter to FDA about the Youth-Oriented Marketing of the IQOS Heated Cigarette Product in Other Countries* (May 14, 2019), https://www.tobaccofreekids.org/assets/content/what_we_do/federal_issues/fda/2019_05_14_youth_marketing_iqos.pdf.

[30] CTFK et al. *supra* note 14 at 31-32.

[31] FDA Decision Summary, pp. 13, 49, 51.

[32] FDA Decision Summary, p. 19.

[33] (emphasis in original) FDA Decision Summary, p. 52. See also, FDA Decision Summary, p. 13.

A study published this year further demonstrates the necessity for such information and consumer education about "completely switching." This study evaluating consumer understanding of PM's modified risk messaging proposed in its IQOS 2.4 MRTP application found the majority of smokers surveyed misunderstood the phrase "switching completely" to mean that they could still smoke some cigarettes per day. Providing additional explanation about what was meant by the phrase improved smokers' understanding that "switching completely" meant zero cigarettes, but the majority still did not know or answered incorrectly (some cigarettes per day allowed). The authors recommended, "FDA should require PMI to demonstrate efforts to bring smokers' understanding of 'switching completely' closer to non-smokers' and to develop communications (included in product promotions, website marketing and 'personal experience') that directly address that."[34] As far as we can tell from the available parts of the IQOS 3 MRTP application, PM did not provide any information showing that it has attempted to further educate consumers about "switching completely." Thus, there is every reason to assume that smokers will fail to accurately understand the message that they must switch completely from cigarettes to IQOS 3 to reduce exposure to harmful constituents.

ii. Misunderstanding reduced exposure as reduced risk.

Findings from a study published in February 2020 suggested that "youth interpreted PMI's reduced exposure claim similar to how they interpreted the reduced risk claim: that IQOS is less harmful or risky than other tobacco products."[35] While this study was limited in size, it provides at least preliminary data that FDA should consider in evaluating the IQOS 3 MRTP application. This finding also provides additional evidence of the importance of requiring data on youth perceptions in MRTP applications.

A study published in May 2021 found that young adults exposed to a message about "significantly reduced" levels of harmful chemicals from heated tobacco products (HTPs) compared to cigarettes were more likely to perceive HTPs as less harmful.[36]

iii. Impact of claims on non-smokers versus smokers

PM should be required to demonstrate not only that the reduced exposure claim does not have a negative impact on non-tobacco users, but also that the reduced exposure claim motivates adult smokers to completely switch to IQOS. Instead, some early evidence shows that a reduced exposure claim could have a negative impact on non-tobacco-users *and* no effect on adult smokers.

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[34] Bo Yang, Zachary B. Massey, & Lucy Popova, *Effects of modified risk tobacco product claims on consumer comprehension and risk perceptions of IQOS*, Tobacco Control, Online ahead of print, doi: 10.1136/tobaccocontrol-2020-056191 (Mar. 6, 2021).

[35] Karma McKelvey, Michael Baiocchi, & Bonnie Halpern-Felsher, *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 29(e1):e18-e24 (2020).

[36] Julia C. Chen-Sankey et al., *Effect of a hypothetical modified risk tobacco product claim on heated tobacco product use intention and perceptions in young adults*, Tobacco Control, Online ahead of print, doi: 10.1136/tobaccocontrol-2021-056479 (May 31, 2021).

The study from May 2021 also found that reported intention to use HTPs even after exposure to that message did not change among past-30 day cigarette smokers, indicating that the message was not effective at moving cigarette smokers to HTPs. The authors stated, "If future evidence shows that MRTP claims fail to increase HTP uptake among cigarette smokers and that relative lower harm perceptions of HTPs and higher intentions of using HTPs compared with cigarettes lead to HTP uptake among non-cigarette-smoking individuals, then the FDA should re-evaluate the authorisation of MRTP status for HTPs."[37]

A study published in October 2021 found that among young adult nonsmokers, "PMI's reduced exposure claim increased IQOS use intentions relative to ads with no claims."[38] This finding is particularly concerning given that Altria increased advertising spending in media channels with broad population exposure after the modified risk order for IQOS 2.4 was granted, as described previously.[39]

That same study from October 2021 found no effect of the reduced exposure claim on young adult smokers' intentions to use IQOS.[40] The study published in May 2021 showed participants a hypothetical MRTP claim that the researchers developed, not the claim used by PM, but also found that the claim did not change smokers' intentions to use HTPs. The authors stated, "This finding may not support the FDA's original intent of HTP MRTP authorisation to help adult cigarette smokers completely transition away from smoking conventional cigarettes through using HTPs. The FDA may need to further evaluate the appeal of HTP MRTP claims in adult cigarette smokers and determine whether such claims may increase smokers' complete switching to HTPs, a behavioural change that may benefit the overall population health."[41] The absence of an impact should be sufficient to disallow such a claim, particularly if research shows a negative effect on non-smokers.

D. PMI is acting in bad faith by misstating, or enabling misinterpretation, of FDA's MRTP order in other countries.

Although FDA's decisions about IQOS are only valid for its marketing in the U.S., the original IQOS marketing order has been used by PMI to mislead consumers and regulators across the globe to believe that FDA has strongly endorsed IQOS. One of the most egregious examples is a flyer about IQOS distributed outside the U.S. by PMI in June, 2019, referencing the marketing order for IQOS 2.4 and featuring CTP Director Mitch Zeller:[42]

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[37] *Id.*

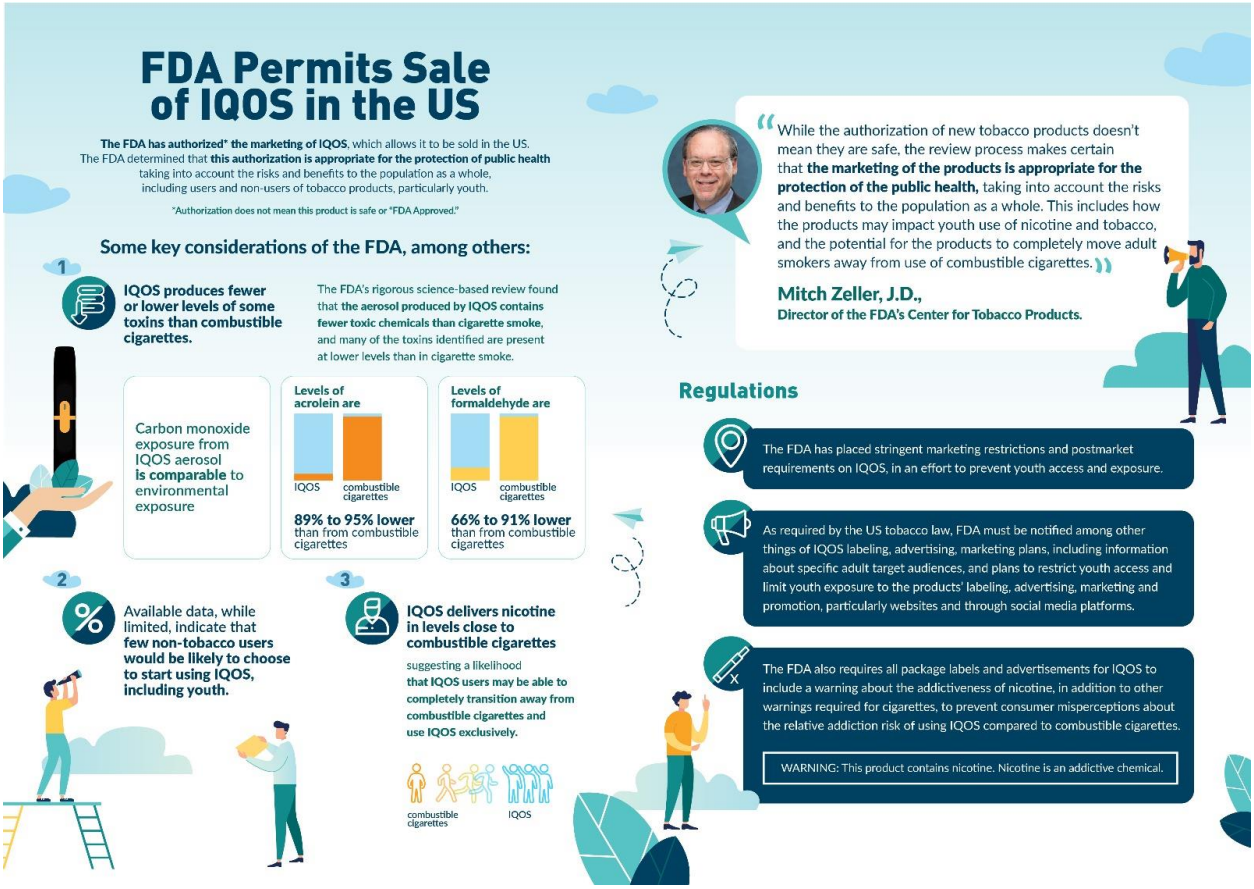
[38] Darren Mays et al., *Effects of IQOS health warnings and modified risk claims among young adult cigarette smokers and non-smokers*, Tobacco Control, Online ahead of print, doi: 10.1136/tobaccocontrol-2021-056810 (Oct. 29, 2021).

[39] Carla J. Berg, *supra* note 28.

[40] Darren Mays et al., *supra* note 38.

[41] Julia C. Chen-Sankey et al., *supra* note 36.

[42] Lauren K. Lempert & Stanton Glantz, *Analysis of FDA's IQOS marketing authorization and its policy impacts*, 30 Tobacco Control 413, Fig. 2 (2021), https://tobacco.ucsf.edu/sites/g/files/tkssra4661/f/wysiwyg/PMI-IQOS-FDA-PHOTO-2019-07-16-08-48-13.jpg.



In fact, the marketing granted order letter for IQOS 2.4 explicitly informed PM that "you may not make any express or implied statement or representation directed to consumers that conveys, or misleads or would mislead consumers into believing, among other things, that the new tobacco products specified in Appendix A are 'approved' by FDA." Certainly, a flyer promoting IQOS with an image of a smiling CTP Director conveys approval of the product.

A study published in October 2021 cited several additional examples of PMI using FDA's modified risk order "to promote IQOS globally…including efforts to minimize government regulation of IQOS."[43] The University of Bath has similarly documented instances where PMI representatives have used FDA's decision to influence regulations for heated tobacco products in various countries.[44]

Surely, FDA did not intend for its marketing order or modified risk order to mislead consumers or impact regulations in other countries. Thus, in evaluating the IQOS 3 application, it is entirely appropriate for FDA to consider the misuse of its modified exposure order for IQOS 2.4 in other countries.

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[43] Carla J. Berg et al., *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 18:10551 (2021).

[44] University of Bath, *PMI Promotion of IQOS Using FDA MRTP Order* (Jun. 10, 2021), https://tobaccotactics.org/wiki/pmi-iqos-fda-mrtp-order/.

For these reasons, we urge FDA to deny the MRTP application for IQOS 3 and to revisit the modified risk order for IQOS 2.4.

Respectfully submitted,

American Academy of Pediatrics

American Cancer Society Cancer Action Network

American Heart Association

American Lung Association

Campaign for Tobacco-Free Kids

Truth Initiative