December 5, 2025

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

Submitted electronically

RE: (1) Docket No. FDA-2021-N-0408, Modified Risk Tobacco Product Application: Renewal Application for IQOS 3.0 System Holder and Charger, Heated Tobacco Product, Submitted by Philip Morris Products S.A.; and

(2) Docket No. FDA-2017-D-3001, Modified Risk Tobacco Product Application: Renewal Applications for IQOS 2.4 System Holder and Charger, Marlboro Amber HeatSticks, Marlboro Green Menthol HeatSticks, and Marlboro Blue Menthol HeatSticks, Heated Tobacco Products and Heated Tobacco Product Consumables, Submitted by Philip Morris Products S.A.

The American Academy of Pediatrics, American Cancer Society Cancer Action Network, American Heart Association, American Lung Association, and Campaign for Tobacco-Free Kids submit these comments on the above-referenced modified risk tobacco product ("MRTP") renewal applications submitted by Philip Morris Products S.A., an affiliate of Philip Morris International (PMI and its affiliates hereinafter referred to as "PMI"), for the following products: IQOS 3.0 System Holder and Charger, IQOS 2.4 System Holder and Charger, Marlboro Amber HeatSticks, Marlboro Green Menthol HeatSticks, and Marlboro Blue Menthol HeatSticks. FDA previously authorized PMI to market these products with the following reduced exposure claims:

"AVAILABLE EVIDENCE TO DATE:

- The IQOS system heats tobacco but does not burn it.
- This significantly reduces the production of harmful and potentially harmful chemicals.

- Scientific studies have shown that switching completely from conventional cigarettes to the IQOS system significantly reduces your body's exposure to harmful or potentially harmful chemicals."[1]

INTRODUCTION

As detailed below, PMI has failed to meet the statutory standard for renewal of its modified risk granted orders ("MRGOs") for the following reasons:

1. Independent research since issuance of the original MRGO shows that the reduced exposure message is misinterpreted by consumers.

2. PMI's repeated misleading and deceptive statements regarding the orders fuel public misunderstanding about IQOS.

3. Independent studies published since the MRGOs contradict PMI's claims about IQOS use patterns, do not show that heated tobacco products ("HTPs") like IQOS provide a population-wide public health benefit, and raise doubts about potential individual benefits.

4. PMI's marketing and promotion of IQOS appeals to young people rather than its purported target population, existing adult smokers.

5. FDA's conclusions supporting a prohibition on menthol cigarettes contradict any justification for renewal of the MRGOs for the menthol-flavored IQOS products.

6. As discussed by members of the Tobacco Products Scientific Advisory Committee ("TPSAC") at the October 7, 2025 TPSAC Meeting discussing these renewal applications, actual patterns of use show that most IQOS users will not receive the benefits asserted in the claim (reduced exposure to harmful or potentially harmful chemicals), FDA's reference list of harmful and potentially harmful constituents ("HPHC") is outdated and likely underestimates IQOS users' exposure to HPHCs, and a lack of recent consumer perception research does not allow for an adequate evaluation of current consumer understanding of the claim.

Finally, FDA should reject the arguments PMI makes in its August 4, 2025 application amendment that IQOS does not meet the Food, Drug, and Cosmetic Act's ("FDCA") "cigarette" definition and thus should not required to display the statutory warnings applicable to cigarettes.

[1] Under the Family Smoking Prevention and Tobacco Control Act ("Tobacco Control Act"), such "reduced exposure" claims are a type of "modified risk" order. *See* 21 U.S.C. §§ 387k(b)(1) and (2)(A)(i).

PMI's interpretation of the statutory cigarette definition is overly narrow and the company's argument relies on a misreading of the PMTA Final Rule.[2]

These comments expand upon a letter that the undersigned sent to FDA in June 2024 outlining key developments related to IQOS. That letter ("June 2024 Letter") is attached and incorporated by reference.[3]

I. PMI's Authorized Reduced Exposure Message Is Being Misinterpreted.

Independent research released since the initial MRGO indicates that consumers continue to misinterpret the "reduced exposure" claims as meaning "reduced risk" and that the authorized claims have failed to educate consumers that complete switching from cigarettes to IQOS is necessary to achieve the claimed reduced exposures.

A. Consumers continue to misinterpret "reduced exposure" to mean "reduced risk."

One of the statutory *requirements* for authorization to make reduced exposure claims under 21 U.S.C. §§ 387g(2), the type of claims PMI seeks to renew here, is that applicants demonstrate – through "testing of actual consumer perception" – that "consumers will not be misled into believing that the product – (I) is or has been demonstrated to be less harmful; or (II) presents or has been demonstrated to present less of a risk of disease than 1 or more other commercially marketed tobacco products." 21 U.S.C. 387k(g)(2)(B)(iii). As detailed below, independent research consistently shows that consumers misinterpret claims of reduced exposure to mean reduced risk, including for IQOS products, strongly suggesting that PMI has failed to meet its statutory burden under 21 U.S.C. 387k(g)(2)(B)(iii).

In comments submitted to FDA on PMI's original modified risk tobacco product applications for IQOS 2.4 and IQOS 3, public health groups repeatedly highlighted research showing that consumers make the leap between claims of "reduced exposure" to mean claims of lowering risk.[4] Studies published since then have only reiterated these findings.

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[2] Premarket Tobacco Product Applications and Recordkeeping Requirements, 86 Fed. Reg. 55,300 (Oct. 5, 2021).

[3] The letter is also available here: https://assets.tobaccofreekids.org/content/what_we_do/federal_issues/fda/2024_06_27_Letter-to-FDA-re-IQOS-w-exhibits.pdf.

[4] Comments at 31-32 (Feb. 11, 2019), https://assets.tobaccofreekids.org/content/what_we_do/federal_issues/fda/regulatory/2019_02_11_Public_Health_Groups_Comments_IQOS_MRPTAs.pdf.

One study found that "reduced exposure messaging resulted in lower perceived relative harm, exposure and disease risk" compared to a control message among adult participants, and that "participants do not adequately distinguish between reduced exposure and reduced risk language—therefore not meeting the criteria for using this language in IQOS marketing."[5] These findings are reinforced by other recent studies showing that consumers, including youth,[6] do not distinguish between reduced exposure and reduced risk messages; instead, they interpret and respond to both types of statements similarly.[7]

Results from qualitative studies echo those from quantitative studies. One study found that most participants did not distinguish between reduced exposure and reduced risk messaging related to IQOS.[8] Another focus group study showed participants the modified exposure claims authorized by FDA for IQOS and found that participants were confused about the meaning of the reduced exposure statement, including some misinterpretation that, compared to cigarettes, IQOS "was less addictive and less dangerous, which was appealing."[9] Consistent with other research, this finding indicates that consumers continue to misinterpret the authorized claims to mean that IQOS use reduces consumers' disease risk.

TPSAC members expressed this same concern – that smokers still do not distinguish between reduced risk and reduced exposure – during their recent meeting:

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[5] Carla J. Berg et al., *Impact of FDA endorsement and modified risk versus exposure messaging in IQOS ads: a randomized factorial experiment among US and Israeli adults*, 33 TOBACCO CONTROL e69-e77 (2024), https://pubmed.ncbi.nlm.nih.gov/36428095/.

[6] Karma McKelvey et al., *PMI's heated tobacco products marketing claims of reduced risk and reduced exposure may entice youth to try and continue using these products*, 29 TOBACCO CONTROL e18-e24 (2020), https://doi.org/10.1136/tobaccocontrol-2019-055318.

[7] Andrew B. Seidenberg et al., *Effects of Modified Risk Tobacco Product Claims on Consumer Responses*, 26 NICOTINE & TOBACCO RESEARCH 435-443 (2024), https://doi.org/10.1093/ntr/ntad187.

[8] Carla J. Berg et al., *Qualitative Examination of US and Israeli Adults' Perceptions of IQOS Advertising Messages: Modified Exposure and Risk Statements, US FDA Endorsement, and Health Warnings*, 27 NICOTINE & TOBACCO RESEARCH 1083-1091 (2025), https://doi.org/10.1093/ntr/ntae266.

[9] Scott R. Weaver et al., *Perceptions and intentions regarding IQOS among current US adults who use cigarettes and/or electronic nicotine delivery systems*, TOBACCO CONTROL (Dec. 31, 2024), online ahead of print, https://doi.org/10.1136/tc-2024-058854.

TPSAC member Dr. Scout: "I'm also concerned about the idea that from the independent studies, the public is not understanding what reduced exposure is versus reduced risk."[10]

TPSAC member Dr. Lucy Popova: The "industry's presentation . . . [stated] that consumers continue to understand the reduced exposure claim. But what does it actually mean to correctly understand the claim? The way their studies measure it, they have a very specific answer in saying . . . [does] using IQOS less…expose people to less harmful chemicals? And it's very hard to answer this question incorrectly. Although even then, some people do. What we are seeing in our studies and studies done by other people in the U.S. and in other countries . . . is that the answers often depend on how you ask the question. … [A]nd this is a statutory question. Because the law itself says reduced exposure claim cannot be confused with reduced risk claim. And all the data show that people are very good at confusing them. When you ask people, does having less exposure to harmful chemicals mean you have less risk of disease? They say overwhelmingly, yes."[11]

In enacting the Tobacco Control Act, Congress was well-aware of the danger that consumers would misinterpret reduced exposure claims to mean reduced risk, and accordingly set a high statutory bar for authorization of modified exposure claims. The research discussed above, as well as PMI's misleading statements discussed in Part II, support the conclusion that IQOS has failed to meet its statutory burden under 387k(g)(2)(B)(iii) of showing that consumers do not misinterpret the reduced exposure claims to mean reduced risk.

B. Consumers continue to misunderstand the concept of complete switching in the reduced exposure message.

In the initial MRGO, FDA expressed concern that PMI failed to "assess how consumers perceive the health risks associated with *partially* switching from combusted cigarettes to IQOS."[12] The agency found it "likely" that "smokers would [mistakenly] expect at least some health benefit" from partial substitution, when in fact complete substitution is necessary "to achieve the benefits of the reduced exposure described in the modified risk claim."[13] FDA thus required postmarket

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[10] Tobacco Products Scientific Advisory Committee Meeting, Oct. 7, 2025, at 83, https://www.fda.gov/media/189658/download?attachment (hereinafter referred to as "TPSAC Meeting").

[11] *Id.* at 86.

[12] FDA, Scientific Review of Modified Risk Tobacco Product Application (MRTPA) Under Section 911(d) of the FD&C Act – Technical Project Lead (TPL) at 51-52 (July 7, 2020), https://www.fda.gov/media/139796/download?attachment (emphasis added) (hereinafter referred to as "IQOS TPL").

[13] *Id.* at 52.

surveillance "to ensure consumers understand that the benefits of reduced exposure cannot be achieved by continuing to smoke combusted cigarettes in addition to using IQOS."[14]

Recently published studies further confirm the concern expressed by FDA that the authorized claims do not adequately educate consumers that complete switching is needed to experience reduced exposure to harmful or potentially harmful chemicals. Consumers still believe that using IQOS and reducing the number of cigarettes smoked without fully quitting will reduce one's risk or exposure.[15] Some consumers, including youth,[16] do not fully understand what is meant by "switching completely."[17] Researchers have suggested including explicit language in modified risk messages to convey that partial switching does not reduce risk or exposure[18] or adding an explanation of "switching completely."[19]

At the recent TPSAC meeting, members also pointed out that smokers still do not understand that complete switching (i.e., no cigarettes) is necessary to achieve the benefits mentioned in the reduced exposure claims:

> Dr. Popova: "[E]ven though the claim says, switching completely, people do not understand what that means. We've done a study where we ask this question, …if you switch completely, how many cigarettes per day can you smoke? Zero? One to two? Three to four? Five to six? I don't know. As many as you want. And when we ask this question to people who don't smoke . . . like upper 60, 70 percent, they correctly say zero. When we ask this question to people who smoke, only about 10 percent say zero. Everybody else says—like a very large number says, 'I don't know.' But a lot of them say, like, 'A few

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[14] *Id.* at 52, 76.

[15] Carla J. Berg et al., *Qualitative Examination of US and Israeli Adults' Perceptions of IQOS Advertising Messages: Modified Exposure and Risk Statements, US FDA Endorsement, and Health Warnings*, 27 NICOTINE & TOBACCO RESEARCH 1083-1091 (2025), https://doi.org/10.1093/ntr/ntae266.

[16] Karma McKelvey et al., *PMI's heated tobacco products marketing claims of reduced risk and reduced exposure may entice youth to try and continue using these products*, 29 TOBACCO CONTROL e18-e24 (2020), https://doi.org/10.1136/tobaccocontrol-2019-055318.

[17] Bo Yang et al., *Effects of modified risk tobacco product claims on consumer comprehension and risk perceptions of IQOS*, 31 TOBACCO CONTROL e41-e49 (2022), https://doi.org/10.1136/tobaccocontrol-2020-056191.

[18] Andrew B. Seidenberg et al., *Effects of Modified Risk Tobacco Product Claims on Consumer Responses*, 26 NICOTINE & TOBACCO RESEARCH 435-443 (2024), https://doi.org/10.1093/ntr/ntad187.

[19] Bo Yang et al., *Effects of modified risk tobacco product claims on consumer comprehension and risk perceptions of IQOS*, 31 TOBACCO CONTROL e41-e49 (2022), https://doi.org/10.1136/tobaccocontrol-2020-056191.

cigarettes per day is okay.' It is complete switching. And even when we added a very clear statement that . . . 'Complete switching means smoking no cigarettes and only using IQOS product,' only 20 percent of people [responded] correctly . . . And this was a randomized experimental study that we published. So, that switching completely in the current language, how it is shown there, is not going to give people [the] full understanding that they do need to switch completely.…[P]eople have to really understand what it [complete switching] is. And only then can we realize any potential benefits from less exposure to harmful chemicals."[20]

TPSAC Chair Dr. Cristine Delnevo: "[Y]ou [Dr. Popova] kind of took the words out of my mouth when you tied the pattern of use to understanding the behavior. Understanding the risk, because if you don't understand…how complete switching is understood, then dual use…could very well be an inevitable behavior, depending on how people understand that."[21]

II. PMI's Misleading and Deceptive Statements Since Issuance of the Original MRGO Exacerbates Consumers' Misunderstanding.

The June 2024 Letter (at 6-8) documents how PMI has repeatedly made misleading and deceptive statements wrongly suggesting that FDA found that IQOS reduces the risk of disease. These statements exploit, and exacerbate, the tendency of consumers to interpret reduced exposure claims as indicating reduced risk.

It is important to note that at the time FDA authorized the reduced exposure claims under 21 U.S.C. § 387k(g)(2) for IQOS, the agency denied PMI's request to make a "reduced risk" claim under 21 U.S.C. § 387k(g)(1) that switching completely from conventional cigarettes to IQOS "can reduce the risks of tobacco-related diseases." FDA denied the reduced risk claim because the company failed to demonstrate that "as actually used by consumers, the products sold or distributed with the proposed modified risk information will significantly reduce harm and the risk of tobacco-related disease to individual tobacco users and benefit the population as a whole, taking into account both users of tobacco products and persons who do not currently use tobacco products."[22] The MRGO specifically instructed PMI that it "may not market these products with reduced risk claims."[23] Notably, PMI has since abandoned its efforts to secure authorization to make modified

[20] TPSAC Meeting at 86-87.

[21] *Id*. at 87.

[22] IQOS TPL at 8 (July 7, 2020), https://www.fda.gov/media/139796/download?attachment.

[23] Modified Risk Granted Orders – Exposure Modification at 2, https://www.fda.gov/media/139797/download?attachment.

risk claims, which at the least appears to be a recognition that it cannot meet the statutory standard for such claims.

Nonetheless, since FDA authorized the "reduced exposure" claims, PMI has made statements calculated to associate IQOS with a reduction in disease risk, in violation of the statute and FDA's instruction to the company to avoid reduced risk claims. For example:

- During a September 2020 webinar in the Philippines, a PMI official stated that "IQOS, our leading flagship brand in the reduced risk portfolio, was granted the modified risk tobacco claim in the United States."[24]

- An advertisement in Mexico published in June 2021 mentions that IQOS has "been authorized by the U.S. Food and Drug Administration as a product of 'modified risk'" and includes a quote from a PMI official about wanting to inform smokers about the "lower risk alternatives" that exist in Mexico.[25]

- Most recently, during an August 2025 hearing before the South African Parliament's Portfolio Committee on Health, a PMI official discussed FDA's authorization of its smoke-free products, including IQOS, and stated that "smoke-free products," contain "less than 90% of the 6,000 [chemicals] in cigarettes . . . in this case, the 90% I'm referring to is heated tobacco. So this to me as a scientist strongly suggests harm reduction. And it is on this basis . . . that FDA has authorized these products stating that they are appropriate for the protection of the public health."[26]

Additional misrepresentations of the modified exposure orders by PMI in the global context are discussed in the June 2024 Letter (at 7-8, and accompanying exhibits). PMI's repeated misuse of the FDA exposure modification orders is particularly troubling given consumers' well-documented tendency to interpret reduced exposure claims to mean reduced risk, as discussed earlier in these comments. PMI should not be rewarded for these misrepresentations by renewal of its MRGOs for IQOS.

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[24] June 2024 Letter at 8 (citing https://mb.com.ph/2020/09/07/philip-morris-urges-ph-to-adopt-us-fda-finding/) (emphasis added).

[25] June 2024 Letter at 8 (citing https://lifeandstyle.expansion.mx/bespoke-ad/2021/08/19/iqos-y-el-proceso-de-cambio-para-evolucionar and Exhibit 7).

[26] Parliament of the Republic of South Africa, *Portfolio Committee on Health, 26 August 2025*, at 3:59:00-4:00:10, YOUTUBE https://www.youtube.com/live/DOY6M0Tx0-s?t=14369s (last visited Sept. 23, 2025).

III. IQOS Does Not Provide a Population-Wide Public Health Benefit.

New information released since FDA granted the reduced exposure authorizations for IQOS 2.4 and IQOS 3 raises doubts about the products' benefit to public health. Independent studies of IQOS in other countries contradict PMI's claims of complete switching. Additionally, research on the health impacts of HTPs, including IQOS, which is the dominant brand on the market,[27] fail to show a population-wide public health benefit and raise concerns about individual risk as well.

Data on IQOS use in the United States is limited because, until March 2025, the products were available only in select U.S. cities and states between 2019-2021, before being pulled due to a patent infringement dispute.[28] PMI resumed IQOS sales in this country in March 2025, beginning with Austin, Texas, following a relaunch of its marketing campaign that began in October 2024,[29] and then in Fort Lauderdale, Florida in mid-2025.[30] However, IQOS has been available in other countries for much longer, such as Japan (where it has been available since 2014) and South Korea (available since 2017).[31]

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[27] PMI's press release for its 2025 2nd quarter earnings stated that its brands hold 76% of the global volume share in the heated tobacco products category. PMI Press Release, *Philip Morris International Reports 2025 Second Quarter & First Six-Months Results and Raises Full-Year Guidance; Second Quarter Reported Diluted EPS Grew 26.6% to $1.95, Adjusted Diluted EPS Grew 20.1% to $1.91, and by 18.9% excluding currency* at 1 (July 22, 2025), https://philipmorrisinternational.gcs-web.com/static-files/b5677465-b1cb-4835-88ba-7556cb767b38.

[28] *See* June 2024 Letter at 1-2.

[29] *Philip Morris' Heated tobacco device IQOS goes on sale in Texas*, REUTERS (March 31, 2025), https://www.reuters.com/business/healthcare-pharmaceuticals/philip-morris-heated-tobacco-device-iqos-goes-sale-texas-2025-03-27/; PMI, *Philip Morris International's 2023 Investor Day Transcript* (Sept. 28, 2023), https://philipmorrisinternational.gcs-web.com/static-files/539f900e-e06e-469d-8851-934a5c0bf334.

[30] PMI Press Release, *PMI U.S. Reveals Ft. Lauderdale as Next IQOS Launch City to Provide Residents 21+ Who Smoke a Better Alternative to Leave Cigarettes Behind*, BUSINESSWIRE (May 2, 2025), https://www.businesswire.com/news/home/20250502143425/en/PMI-U.S.-Reveals-Ft.-Lauderdale-as-Next-IQOS-Launch-City-to-Provide-Residents-21-Who-Smoke-a-Better-Alternative-to-Leave-Cigarettes-Behind.

[31] *See* Minji Kim, *Philip Morris International Introduces New Heat-not-burn Product,* IQOS, *in South Korea*, 27 TOBACCO CONTROL e76-e78 (2018), https://pmc.ncbi.nlm.nih.gov/articles/PMC5966325/pdf/nihms923244.pdf.

A. Independent data from other countries contradict PMI's claims about IQOS use and switching.

In its MRTP renewal applications, PMI submitted data from Germany, Japan, South Korea, and Italy to "supplement" U.S. data to support the company's assertion that "IQOS products have continued to prove successful in converting millions of adult smokers to this modified-risk tobacco product."[32] As mentioned in a previous letter from public health groups to FDA about PMI's global IQOS marketing targeted to youth, PMI did not adequately explain how the experience in these two countries would apply to the U.S. setting.[33] The sweeping redactions in the renewal applications make it impossible for the public and independent scientists to evaluate if that is still the case with the new data PMI submitted. Even so, independent, global data released since the original modified risk authorization show that IQOS usage patterns differ from what PMI claims.

A recent systematic review and meta-analysis of studies across several countries found that at least two-thirds of HTP users dual used with cigarettes, HTP use among adolescents was "not negligible," and that evidence did "not support these products as effective smoking cessation tools. In contrast, HTP users are more likely to start conventional cigarette smoking and less likely to quit conventional cigarettes."[34] Independent research from some of the countries that PMI references in its applications, including Japan and South Korea, also contradict PMI's claims about high rates of complete switching from cigarette smoking to IQOS.

As detailed more fully in the June 2024 Letter (at 4-5), data from the International Tobacco Control Policy Evaluation Project ("ITC") from Japan show much lower rates of IQOS users who had "completely transitioned" to IQOS in 2020 – just 17%, as compared with the 73% that PMI claimed in its Shareholder Report. In addition, these data show that dual use of cigarettes and HTPs is the dominant use pattern among those using HTPs rather than complete switching and that HTP uptake exceeds the reduction in cigarettes smoked so that users' overall tobacco consumption increased.[35] These findings are consistent with a pilot study in the U.S. that showed that most participants became dual users and the few smokers who switched to IQOS used more HeatSticks per day than they had smoked cigarettes before switching.[36] Other studies from Japan showed that

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[32] *See* Module 1.2 General Information, p. 8.

[33] Letter at 3 (May 14, 2019), https://assets.tobaccofreekids.org/content/what_we_do/federal_issues/fda/2019_05_14_youth_marketing_iqos.pdf

[34] Marco Scala et al., *Patterns of Use of Heated Tobacco Products: A Comprehensive Systematic Review*, 35 JOURNAL OF EPIDEMIOLOGY 213-221 (2025), https://doi.org/10.2188/jea.JE20240189.

[35] See June 2024 Letter at 4-5 (and sources cited therein).

[36] Matthew D. Stone et al., *Switching from cigarettes to IQOS: A pilot examination of IQOS-associated reward, reinforcement, and abstinence relief,* 238 DRUG AND ALCOHOL DEPENDENCE 109569 (2022), https://doi.org/10.1016/j.drugalcdep.2022.109569.

the majority of HTP users also smoked cigarettes concurrently and that HTP use was associated with decreased likelihood of smoking cessation and increased likelihood of smoking relapse.[37] The researchers in one study stated that "none of the assessed subgroups of established smokers showed positive associations between HTP use and smoking cessation, indicating that HTPs could serve as a disincentive to successful quitting and not as a cessation aid."[38]

Data from South Korea showed similar results to those for Japan. Notably, since South Korea allows the sale of e-cigarettes, like the U.S. but unlike Japan,[39] findings from South Korea may be more applicable to the U.S. experience. Analysis of ITC data from South Korea shows lower rates of complete switching compared to PMI's survey data, high rates of dual use (cigarettes and HTPs) and an increase in HTP use that outpaced the slight reduction in cigarettes smoked.[40] ITC data also showed that most HTP users in South Korea were using HTPs for reasons other than to quit or reduce cigarette smoking, indicating that they were intentionally supplementing their cigarette smoking with HTPs.[41] Similarly, several studies of dual users of cigarettes and HTPs in other data sources have found declines in visits to smoking cessation clinics,[42] lower likelihood of

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[37] Satomi Odani et al., *Heated tobacco products do not help smokers quit or prevent relapse: a longitudinal study in Japan*, 33 TOBACCO CONTROL 472-480 (2024), https://doi.org/10.1136/tc-2022-057613; Yusuke Matsuyama et al., *Heated tobacco product use and combustible cigarette smoking relapse/initiation among former/never smokers in Japan: the JASTIS 2019 study with 1-year follow-up*, 31 TOBACCO CONTROL 520-526 (2022), http://dx.doi.org/10.1136/bmjpo-2020-000755.

[38] Satomi Odani et al., *Heated tobacco products do not help smokers quit or prevent relapse: a longitudinal study in Japan*, 33 TOBACCO CONTROL 472-480 (2024), https://doi.org/10.1136/tc-2022-057613.

[39] Shihoko Koyama et al., *E-Cigarettes Use Behaviors in Japan: An Online Survey*, 19 INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH 892 (2022), https://doi.org/10.3390/ijerph19020892.

[40] See June 2024 Letter at 5 (and sources cited therein); Sungkyu Lee et al., *Patterns of cigarette, heated tobacco product, and nicotine vaping product use among Korean adults: Findings from the 2020 ITC Korea Survey*, 22 TOBACCO INDUCED DISEASES 63 (2024), https://doi.org/10.18332/tid/186273.

[41] Hong Gwan Seo et al., *Reasons for Initiation and Regular Use of Heated Tobacco Products among Current and Former Smokers in South Korea: Findings from the 2020 ITC Korea Survey*, 20 INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH 4963 (2023), https://doi.org/10.3390/ijerph20064963.

[42] Cheol Min Lee, *The Impact of Heated Tobacco Products on Smoking Cessation, Tobacco Use, and Tobacco Sales in South Korea*, 41 KOREAN JOURNAL OF FAMILY MEDICINE 273-281 (2020), https://doi.org/10.4082/kjfm.20.0140.

making quit attempts,[43] and no significant difference in intention to quit smoking compared to exclusive cigarette smokers.[44] Further, three studies of South Korean youth showed high rates of dual use of HTPs and cigarettes and negative or no association between HTP uptake and smoking cessation or quit attempts.[45]

Similarly, youth data from Hong Kong showed not only increases in HTP use within three years of IQOS introduction, but also high rates of dual use (HTPs and cigarettes) and lower likelihood of cigarette abstinence.[46] The studies from Hong Kong also found that the primary reason youth started using HTPs was out of curiosity or because of peer pressure, not to quit smoking,[47] reinforcing the concern that the novelty of these products attracts youth and can lead to addiction and dual use.

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[43] Cheol Min Lee et al., *Are Heated Tobacco Product Users Less Likely to Quit than Cigarette Smokers? Findings from THINK (Tobacco and Health IN Korea) Study*, 17 INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH 8622 (2020), http://dx.doi.org/10.3390/ijerph17228622.

[44] Doyeon Won et al., *Comparison of the Smoking Cessation of Heated Tobacco Product Users and Conventional Cigarette Smokers in Korea*, 44 KOREAN JOURNAL OF FAMILY MEDICINE 151-157 (2023), https://doi.org/10.4082/kjfm.22.0142; Dong-Hee Ryu et al., *Association between Intention to Quit Cigarette Smoking and Use of Heated Tobacco Products: Application of Smoking Intensity Perspective on Heated Tobacco Product Users*, 17 INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH 8471 (2020), http://dx.doi.org/10.3390/ijerph17228471.

[45] Seo Young Kang et al., *Prevalence and predictors of heated tobacco product use and its relationship with attempts to quit cigarette smoking among Korean adolescents*, 30 TOBACCO CONTROL 192-198 (2021), http://dx.doi.org/10.1136/; Heewong Kang et al., *Heated tobacco product use among Korean adolescents*, 29 TOBACCO CONTROL 466-468 (2020), http://dx.doi.org/10.1136tobaccocontrol-2019-054949; Haein Lee et al., *Associations between the Frequency and Quantity of Heated Tobacco Product Use and Smoking Characteristics among Korean Smoking Adolescents*, 53 JOURNAL OF KOREAN ACADEMY OF NURSING 155-166 (2023), https://doi.org/10.4040/jkan.22125.

[46] Wei Xia et al., *The association between heated tobacco product use and cigarette cessation outcomes among youth smokers: A prospective cohort study*, 132 JOURNAL OF SUBSTANCE ABUSE TREATMENT 108599 (2022), https://doi.org/10.1016/j.jsat.2021.108599; Laurie Long Kwan Ho et al., *Awareness and Use of Heated Tobacco Products among Youth Smokers in Hong Kong: A Cross-Sectional Study*, 17 INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH 8575 (2020), http://dx.doi.org/10.3390/ijerph17228575.

[47] Wei Xia et al., *The association between heated tobacco product use and cigarette cessation outcomes among youth smokers: A prospective cohort study*, 132 JOURNAL OF SUBSTANCE ABUSE TREATMENT 108599 (2022), https://doi.org/10.1016/j.jsat.2021.108599; Laurie Long Kwan Ho et al., *Awareness and Use of Heated Tobacco Products among Youth Smokers in Hong Kong: A*

Thus, the available independent research fails to substantiate PMI's claims that IQOS benefits individual or population health and, in fact, contradicts what PMI has submitted.

B. Newer studies raise doubts about individual- and population-level health benefits from IQOS.

Newer, independent data invalidate PMI's reduced exposure claim and justify denial of the renewal applications.

Increasing research documenting the harmful chemicals present in IQOS sticks and aerosol has found variations in levels of nicotine, tobacco-specific nitrosamines, and other toxicants in IQOS sticks and emissions depending on where and when products were purchased[48] and what flavors were tested,[49] indicating that potential health impacts may not be consistent across products within the same brand or from different countries, and further complicating assessments of health risks and transferability of findings. Studies – including analysis by FDA[50] – have also found that IQOS aerosol can contain higher levels of certain chemicals compared to cigarettes even beyond FDA's harmful or potentially harmful chemicals ("HPHCs") list, with one study identifying key features that argue for classifying IQOS aerosol as smoke.[51] In particular, real-life conditions, in which substances deposited in the device during use are reheated repeatedly, can generate more HPHCs and particles.[52] One study stated, "When compared with an array of cigarettes, IQOS did

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Cross-Sectional Study, 17 INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH 8575 (2020), http://dx.doi.org/10.3390/ijerph17228575.

[48] Noel J. Leigh et al., *Nicotine, Humectants, and Tobacco-Specific Nitrosamines (TSNAs) in IQOS Heated Tobacco Products (HTPs): A Cross-Country Study*, 12 TOXICS 180 (2024), https://doi.org/10.3390/toxics12030180.

[49] Michele Davigo et al., *Impact of More Intense Smoking Parameters and Flavor Variety on Toxicant Levels in Emissions of a Heated Tobacco Product*, 26 NICOTINE AND TOBACCO RESEARCH 571-579 (2024), https://doi.org/10.1093/ntr/ntad238.

[50] IQOS TPL at 12 (July 7, 2020), https://www.fda.gov/media/139796/download?attachment.

[51] Ola Ardati et al., *Impact of smoking intensity and device cleaning on IQOS emissions: comparison with an array of cigarettes*, 33 TOBACCO CONTROL 449-456 (2024), http://dx.doi.org/10.1136/tc-2022-057802; Clement N. Uguna et al., *Should IQOS Emissions Be Considered as Smoke and Harmful to Health? A Review of the Chemical Evidence*, 7 ACS OMEGA 22111−22124 (2022), https://doi.org/10.1021/acsomega.2c01527.

[52] *Id;* Malak El-Kaassamani et al., *Analysis of mainstream emissions, secondhand emissions and the environmental impact of IQOS waste: a systematic review on IQOS that accounts for data source*, 33 TOBACCO CONTROL 93-102 (2024), http://dx.doi.org/10.1136/tobaccocontrol-2021-056986.

not have consistently reduced emission of toxicants."[53] FDA should take these newer studies into consideration when deciding on whether or not to renew these orders. At the very least, FDA should require additional independent research to determine the potential for harm from these chemicals before re-authorizing the claims.

At the October meeting, TPSAC members expressed that the more recent toxicological research led them to doubt the validity of the reduced exposure claim.

> Temporary TPSAC member Dr. Irina Stepanov: "[A]s was reviewed through independent studies…[the] biomarkers of potential harm in long-term users of IQOS are not—even though they're slightly reduced compared to smokers, but not statistically or substantially different from smokers. So, that is a concern and indicator that the picture is not clear cut. You cannot just simply extrapolate reduced exposures to harmful and potentially harmful constituents and long-term biological effects. . . . So, I would humbly and respectfully disagree that there are no new toxicological concerns coming from these assessments of 80 compounds that close to half of them have some carcinogenic and mutagenic potential properties."[54]
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> TPSAC member Dr. Nancy Rigotti: "It looks like we're maybe finding out that maybe the aerosol in these products is not as harmless. We never thought it was harmless. . . . But it's a little more harmful than we thought it was maybe going to be. And if people are not really switching completely, then the amount of actual risk reduction that the human would have is going to be less."[55]
>
> Temporary TPSAC member Dr. Judith Zelikoff: "[A]t this point, we have no evidence that convinces me that there will be no chronic concerns. . . ."[56]
>
> Dr. Popova: "[W]hen the decision was made in 2022 [*sic*], there was [a] preponderance of evidence that the exposure to harmful chemicals is definitely lower than cigarettes—than in conventional cigarettes. Since then, as we've seen today, we've had some additional studies come up. And we also have comments say that the list of chemicals needs to be

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[53] Ola Ardati et al., *Impact of smoking intensity and device cleaning on IQOS emissions: comparison with an array of cigarettes*, 33 TOBACCO CONTROL 449-456 (2024), http://dx.doi.org/10.1136/tc-2022-057802.

[54] TPSAC Meeting at 77-78.

[55] *Id.* at 79.

[56] *Id.* at 76.

expanded. So, that raises new questions and brings up the issue of whether the previous conclusion that this is definitely less harmful…might not be as solidly yes as before."[57]

While not the subject of these applications, more recent data on potential risks from using IQOS is still relevant to consider. Conclusive information on the long-term health effects from IQOS and other HTPs are not yet available, but data on short-term impacts on health reaffirm that HTPs present significant health risks.

Reviews of available research have found "a considerable body of evidence indicating that HTP use has adverse cardiovascular and respiratory effects"[58] and limited findings that HTP use could reduce health risks compared to cigarette smoking. A systematic review of research related to biomarkers of potential harm and adverse effects from HTP use concluded that "the existing data indicate HTPs have the potential to be harmful to both smokers and non-smokers, and that potential benefits in smokers switching to HTPs may be restricted to a limited subset of biomarkers whose clinical relevance is unclear."[59] In an accompanying commentary, one of the authors of the study stated that "the evidence we reviewed was inconclusive. Though most studies suggested that heated tobacco products might reduce risks of disease compared with smoking, other studies found no difference, or even the potential of increased risk. Compared with quitting smoking completely, use of heated tobacco products had more consistently harmful effects."[60]

Additionally, as part of a January 2022 report, the Cochrane Library reviewed the available studies on heated tobacco products for smoking cessation and concluded that, "No studies reported on the use of heated tobacco for cigarette smoking cessation, so their effectiveness for this purpose remains uncertain."[61]

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[57] *Id.* at 93-94.

[58] Malgorzata Znyk et al., *The Health Effects of Heated Tobacco Product Use—A Narrative Review*, 13 HEALTHCARE 2042 (2025), https://doi.org/10.3390/healthcare13162042.

[59] Sophie Braznell et al., *Impact of heated tobacco products on biomarkers of potential harm and adverse events: a systematic review and meta-analysis*, TOBACCO CONTROL (April 25, 2024), online ahead of print, https://doi.org/10.1136/tc-2024-059000.

[60] Jamie Hartmann-Boyce, *As heated tobacco products reenter the US market, evidence on their safety remains sparse – new study*, THE CONVERSATION (May 1, 2025), https://theconversation.com/as-heated-tobacco-products-reenter-the-us-market-evidence-on-their-safety-remains-sparse-new-study-254278.

[61] Harry Tattan-Birch et al., *Heated tobacco products for smoking cessation and reducing smoking prevalence,* COCHRANE DATABASE OF SYSTEMATIC REVIEWS, Issue 1. Art. No.: CD013790, at 21 (2022), https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013790.pub2/epdf/full.

Finally, given the unreliability of research funded and produced by tobacco companies, including PMI, it is critical that FDA consult independent studies to decide these renewal applications, and not simply the company's data. For decades, the tobacco industry has manipulated science to sow doubt in true research and generate findings that fit their narrative and promote their products. Newer research shows PMI still engages in this strategy to support IQOS.[62] Systematic reviews have called attention to the large volume of industry-funded studies and high risk of bias in their findings compared to independent research, specifically that research funded by tobacco companies generally produce more favorable findings for HTPs.[63] By inundating the research space with their studies, tobacco companies also create the false perception that a large body of research supports HTP use. For instance, both the Braznell and Cochrane systematic reviews explicitly noted the dominance of available research attributable to tobacco companies and the unclear or high risk of bias in reviewed studies produced by tobacco companies.[64] The industry's approach to conducting research also factors into its biased findings. For instance, one review highlighted the industry's frequent use of "surrogate outcomes" which is the use of non-human or laboratory testing to draw conclusions on human effects but that may not actually represent true impacts on humans.[65]

IV. PMI's Current and Historical Marketing of IQOS Is Not Aimed at Today's Adult Smokers.

PMI's marketing activities for IQOS both in the U.S. and abroad demonstrate that the company does not intend to solely switch smokers to IQOS. The most recent data from the National Health Interview Survey, from 2024, show that most adults in the U.S. who smoke are male and

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[62] Sophie Braznell et al., *"Keep it a secret": Leaked Documents Suggest Philip Morris International, and Its Japanese Affiliate, Continue to Exploit Science for Profit*, 27 NICOTINE AND TOBACCO RESEARCH 794-804 (2025), https://doi.org/10.1093/ntr/ntae101.

[63] Harumitsu Suzuki et al., *Comparison of Publications on Heated Tobacco Products With Conventional Cigarettes and Implied Desirability of the Products According to Tobacco Industry Affiliation: A Systematic Review*, 26 NICOTINE AND TOBACCO RESEARCH 520-526 (2024), https://doi.org/10.1093/ntr/ntad205; Sarah Ghazi, *A scoping review of the toxicity and health impact of IQOS*, 22 TOBACCO INDUCED DISEASES 97 (2024), https://doi.org/10.18332/tid/188867.

[64] Sophie Braznell et al., *Impact of heated tobacco products on biomarkers of potential harm and adverse events: a systematic review and meta-analysis*, TOBACCO CONTROL (Apr. 25, 2024), online ahead of print, https://doi.org/10.1136/tc-2024-059000; Harry Tattan-Birch et al., *Heated tobacco products for smoking cessation and reducing smoking prevalence,* COCHRANE DATABASE OF SYSTEMATIC REVIEWS, Issue 1. Art. No.: CD013790, at 21 (2022), https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013790.pub2/epdf/full.

[65] Harumitsu Suzuki et al., *Comparison of Publications on Heated Tobacco Products With Conventional Cigarettes and Implied Desirability of the Products According to Tobacco Industry Affiliation: A Systematic Review*, 26 NICOTINE AND TOBACCO RESEARCH 520-526 (2024), https://doi.org/10.1093/ntr/ntad205.

between 35-64 years old.[66] PMI's marketing tactics for IQOS clearly show that the company is targeting a much broader audience than just adult smokers.

As we have highlighted for FDA in previous comments[67] and letters,[68] PMI's marketing has focused on treating IQOS as a lifestyle object rather than a tool to help smokers completely switch or quit. For example, one of the first print ads for IQOS in the U.S. appeared in Vogue magazine, and in many countries, PMI partnered with fashion magazines and fashion designers to promote IQOS. More recent studies consistently found that after the initial MRGO, IQOS ads targeted women by being placed in magazines most popular with women or used themes more commonly associated with women, such as fashion.[69]

Recent marketing for IQOS in other countries provide additional clues about PMI's plans for IQOS in the U.S. PMI recruited electronic dance music DJ Steve Aoki to perform in concerts in the Philippines and Japan and collaborated with Aoki to release limited-edition devices and clothing available worldwide.[70] PMI joined with Rolling Stone UK for a Future of Music concert,

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[66] National Center for Health Statistics, *Percentage of current cigarette smoking for adults aged 18 and over, United States, 2019—2024*, National Health Interview Survey. Generated interactively: Sept. 11 2025, https://wwwn.cdc.gov/NHISDataQueryTool/SHS_adult/index.html.

[67] Comments at 16-18 (Feb. 11, 2019), https://assets.tobaccofreekids.org/content/what_we_do/federal_issues/fda/regulatory/2019_02_11_Public_Health_Groups_Comments_IQOS_MRPTAs.pdf.

[68] Letter at 1-5 (Mar. 23, 2018), https://assets.tobaccofreekids.org/press_office/2018/2018_03_28_IQOS_global_marketing.pdf; Letter at 1-3 (and accompanying exhibits) (May 14, 2019), https://assets.tobaccofreekids.org/content/what_we_do/federal_issues/fda/2019_05_14_youth_marketing_iqos.pdf.

[69] Zongshuan Duan et al., *IQOS marketing strategies and expenditures in the United States from market entrance in 2019 to withdrawal in 2021*, 25 NICOTINE AND TOBACCO RESEARCH 1789-1803 (2023), https://doi.org/10.1093/ntr/ntad096; Carla J. Berg et al., *IQOS marketing strategies in the USA before and after US FDA modified risk tobacco product authorization*, 32 TOBACCO CONTROL 418-427 (2023), http://dx.doi.org/10.1136/tobaccocontrol-2021-056819; Ollie Ganz et al., *IQOS print magazine advertising characteristics and reach before and after FDA authorisation as a modified risk tobacco product*, 33 TOBACCO CONTROL 680-683 (2024), http://dx.doi.org/10.1136/tc-2022-057741.

[70] *Smoke-free alternative*, DAILY TRIBUNE (Philippines) (Mar. 21, 2025), https://tribune.net.ph/2025/03/21/smoke-free-alternative. On April 15, 2025, tobacco control and public health organizations filed a complaint with the Philippines' Department of Trade and Industry objecting to a PMI-sponsored Steve Aoki Live event occurring in the country because of the event's use of "promotional content appealing to minors." The event was announced on the IQOS Philippines' official Instagram page. Letter from Child Rights Network et al. to Atty. Marcus N. Valdez, Dep't of Trade and Industry (Apr. 15, 2025),

described as "a night filled with music from cutting-edge artists, showcasing the trends and sounds that are shaping the future."[71] PMI continues to tie IQOS to the fashion industry, such as a Kuwaiti artist recruited to design IQOS accessories described in a sponsored post in Vogue Arabia magazine[72] and artists in Egypt who designed IQOS-branded items like t-shirts, tote bags, and towels in what is described as a "lifestyle campaign."[73] These tactics are aimed at recruiting younger people with suggestions of new ways to have fun, not adults looking to quit smoking.

PMI's activities in its relaunch of IQOS in Austin, TX, and Fort Lauderdale, FL, also do not appear to be aimed at the current adult smoking population, but rather young adults. PMI has joined with *Rolling Stone* magazine to sponsor music concerts purportedly only open to people registered with IQOS Circle, but social media posts show that unregistered people have also been able to attend.[74] PMI launched a marketing campaign in Fort Lauderdale, FL, with an exclusive concert featuring Grammy-winning artists Lauryn Hill and Wyclef Jean.[75] Images at these events show many young people attending. Research has tied exposure to tobacco marketing at music events to more positive views of tobacco products and higher likelihood of trying tobacco products.[76]

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https://seatca.org/dmdocuments/DTI%20Complaint%20PMFTC-Aoki%20event%2015Apr2025.pdf.

[71] *Rolling Stone UK partners with IQOS and ZYN to elevate the Future of Music*, ROLLING STONE UK (February 10, 2025), https://www.rollingstone.co.uk/music/rolling-stone-uk-partners-with-iqos-and-zyn-to-launch-the-future-of-music-event-47244/.

[72] Sponsored Content By Philip Morris Kuwait W.L.L, *Inside Abrar Zenkawi's Collaboration for the IQOS ILUMA i Kuwait Launch*, VOGUE ARABIA (August 14, 2025), https://www.voguearabia.com/sponsored/article/inside-abrar-zenkawis-collaboration-for-the-iqos-iluma-i-kuwait-launch.

[73] SDWorks, *IQOS "Curious Minds" Campaign, 2025*, accessed September 22, 2025, https://sdw-eg.com/IQOS-Curious-Minds-Campaign.

[74] Noahisburningnow Instagram post, October 20, 2024, https://www.instagram.com/p/DBWlmSWJ6Mx/; "Austin show - 10/19/24," r/LCDSoundsystem, Reddit, https://www.reddit.com/r/LCDSoundsystem/comments/1g535tb/austin_show_101924/; "secret austin show 10.19," r/LCDSoundsystem, Reddit, https://www.reddit.com/r/LCDSoundsystem/comments/1g6s2wa/secret_austin_show_1019/.

[75] Sarah Todd, *With aura readings and a Lauryn Hill concert, Philip Morris rolls out a new tobacco product in the U.S.*, STAT (May 28, 2025), https://www.statnews.com/2025/05/28/iqos-philip-morris-heated-tobacco-product-american-rollout-viewed-skeptically-anti-smoking-groups/.

[76] National Cancer Institute, *The Role of the Media in Promoting and Reducing Tobacco Use*, Tobacco Control Monograph No. 19, Bethesda, MD: U.S. Department of Health and Human

Researchers recently described a pop-up store in Austin, TX: "Colorful IQOS devices and accessories decorated the shelves and video screens showed upbeat ads with young adults and slogans like 'less smell than cigarettes' and 'the HEET of the moment.'"[77] PMI's IQOS.US Instagram page contains posts about "pre-fest" and "post-fest" events in Austin around the South By Southwest (SXSW) music festival in early October 2025.[78]

At the October TPSAC meeting, several members expressed concern about PMI's marketing for IQOS, referring to IQOS-sponsored music concerts and music festivals, and how evidence has shown that their strategies do not attract the adults who smoke, as PMI claims.

> TPSAC member Dr. Sven Jordt: "I remain also concerned about the marketing tactics of PMI that supposedly emphasized the modified risk or reduced risk but always end up with large numbers of young users who usually have lower smoking rates than older users, especially male young users. . . . Having been to Europe this summer, I've seen IQOS advertising at Pride parades and other big, big festivals. …I assume the same will happen here in the United States and this [is] incompatible with the assumed targeting of older smokers."[79]
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> Dr. Scout: "I think the available evidence that you can see the marketing strategies by PMI that are occurring currently in other countries strongly shows that they are attempting to get into the youth-adjacent market. And that is a very visible play on their parts. …I think a lot is to be gleaned by the marketing tactics. So, the idea that…we're talking electronic dance music concerts and special drops of clothing and…DJ collaborations…tells us a lot about whether this is actually about being targeted at people who are existing smokers, who are looking to convert, and reduce that smoking risk. Because that's not a population with

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Services, National Institutes of Health, National Cancer Institute, NIH Pub. No. 07-6242, at 160 (June 2008), https://cancercontrol.cancer.gov/sites/default/files/2020-08/m19_complete.pdf; U.S. Department of Health and Human Services, *Eliminating Tobacco-Related Disease and Death: Addressing Disparities—A Report of the Surgeon General*, Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, at 421 (2024), https://www.hhs.gov/sites/default/files/2024-sgr-tobacco-related-health-disparities-full-report.pdf.

[77] Victoria Churchill, et al., "The Return of IQOS – A Visit to Austin, Texas," TOBACCO CONTROL BLOG (2025), https://blogs.bmj.com/tc/2025/10/13/the-return-of-iqos-a-visit-to-austin-texas/.

[78] Iqos.us Instagram post, October 3, 2025, https://www.instagram.com/p/DPWR5Z9E4fB/?img_index=4.

[79] TPSAC Meeting at 93.

the highest smoking rate, and that's not the population that's even looking to consider cessation seriously."[80]

Dr. Delnevo: "[W]hat we see from the international studies…about who the IQOS users are internationally. And just seeing some of the marketing rollout in Austin, Texas, it does seem like, at least initially, those consumers skew younger. And these are groups of individuals that right now have very low rates of combusted cigarette use."[81]

Dr. Popova: "What…PMI and the other companies should be doing is really telling those smokers, and they have the list of them, they know who they are. It's like, 'Cigarettes are really, really bad.…you should switch to this product.' And that's what the marketing . . . [should] be, instead of advertising at the electronic festivals or in Austin music stuff."[82]

PMI's activities seen thus far in the U.S. and documented from around the world plainly show that the company does not plan to limit its marketing exposure only to adults who smoke. There are clear methods to accomplish that, yet PMI continues to engage in strategies that ensure that the products appeal to a broad audience – including youth and young adults.

V. FDA's Conclusions Supporting a Rule Prohibiting Menthol Cigarettes Undercut Any Justification for Renewal of the MRGOs for Menthol-Flavored IQOS Products.

The MRGOs that PMI seeks to renew applies to two menthol-flavored HeatSticks (Marlboro Green Menthol and Marlboro Blue Menthol). Since those orders were issued, FDA proposed a Rule prohibiting menthol as a characterizing flavor in cigarettes, and asked for comment on possible exceptions to the Rule for certain products that meet the statutory definition of "cigarette," including "noncombusted" products, such as IQOS.[83] Over 100 public health, medical, education, civil rights, and community organizations submitted comments on the Proposed Rule, arguing that no such exception for IQOS or other heated products would be appropriate for the protection of the public health.[84]

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[80] *Id.* at 89.

[81] *Id.* at 92.

[82] *Id.* at 94.

[83] FDA, Proposed Rule, Tobacco Product Standard for Menthol in Cigarettes, 87 Fed. Reg. 26,454, 26,487 (May 4, 2022) ("Proposed Menthol Rule").

[84] Comments filed in Docket No. FDA-2021-N-1349 (Aug. 2, 2022), at 29-30, https://assets.tobaccofreekids.org/content/what_we_do/federal_issues/fda/Support_Prohibiting_Menthol_Cigarettes_8_2_2022.pdf.

As detailed in those comments (at 29-30) and discussed in the June 2024 Letter (at 10-12), key findings that FDA made in the Preamble to the Proposed Rule regarding the effects and negative impacts of menthol in traditional combusted cigarettes are relevant to IQOS and other heated tobacco products. For example, FDA concluded that "menthol in cigarettes increases smoking initiation" because it "produces a minty taste and cooling sensation when inhaled" thereby "masking the harshness and irritation of tobacco and reducing unpleasant smoking experiences that can deter new users from repeated experimentation."[85] These findings, premised on menthol's sensory effects, likely would also apply to heated cigarettes that contain menthol, like the Marlboro Green and Blue Menthol HeatSticks.

FDA also found that the interaction of menthol and nicotine in the brain enhances nicotine addition, particularly among young people: "The combined effects of nicotine and menthol in the developing brain make youth who smoke menthol cigarettes particularly vulnerable to the effects of menthol on nicotine dependence."[86] These findings rest on menthol's flavor and sensory effects and the interaction between menthol and nicotine in the brain – features that are present in the Menthol HeatSticks. Thus, all menthol-flavored IQOS products would be expected to have a similar impact.

Finally, FDA noted that due to the industry's decades-long targeting of Black communities and other underserved populations with marketing for menthol cigarettes, members of these groups "are more likely to report smoking menthol cigarettes than other population groups" and thus "bear a disproportionate burden of tobacco-related morbidity and mortality."[87] There is a significant risk that these same population groups will be disproportionately represented among users of IQOS menthol-flavored products with resulting increased addiction and dual use, without countervailing smoking cessation benefits. Thus, FDA's conclusions supporting a prohibition of menthol cigarettes contradict any justification for continued or future authorization of menthol-flavored IQOS.

VI. The TPSAC Meeting Revealed Additional Concerns About Renewing the MRGOs.

At their October 7, 2025 meeting, TPSAC members raised several additional concerns that warrant consideration by FDA. Many comments focused on data – both newer toxicological data and a lack of recent consumer perception data – that make it difficult to decide the renewal applications. For instance, despite not being explicitly asked to vote on renewing this order, Dr. Zelikoff stated, "[I]f you're considering the totality of evidence, I think it's very difficult, because I don't think there are sufficient studies that have been brought up to show that totally, it's [IQOS]

[85] Proposed Menthol Rule at 26,463-64.

[86] *Id.* at 26,465.

[87] *Id.* at 26,458.

safer. So, if I had to make a decision right now . . . I would say that without more evidence showing that it's a modified [risk] product, I would have to say no. I don't favor renewal."[88]

Similarly, TPSAC Chair Dr. Cristine Delnevo stated, "[W]hile the product may be a lower exposure product compared to combustible cigarettes, there's a lot of unanswered questions regarding the population itself."[89] This lack of data led Dr. Delnevo to express that it was difficult to lean either way on deciding on these applications. She stated, "And so, did I hear anything today that would have me lean towards rescinding the MRTP? No, I didn't. Did I hear any evidence that would make me want to renew the MRTP? No, I didn't."[90]

Given its tasked role to advise FDA on its decisions, TPSAC's inability to evaluate the applications based on the available data indicates that FDA should deny this renewal. PMI has the statutory burden of demonstrating that the claim remains true. Based on the information submitted to TPSAC and FDA, including newer research, there are significant doubts that, as actually used, IQOS 2.4 and IQOS 3 exposes users to fewer toxicants compared to combusted cigarettes. Thus, the renewal applications should be denied.

A. Actual patterns of use of IQOS demonstrate that most IQOS users will not receive the benefits stated in the authorized claim (reduced HPHC exposure).

Based on independent data provided to TPSAC and data from other countries provided by PMI, several members observed that the actual patterns of IQOS use likely will not lead to reduced HPHC exposure compared to combusted cigarettes. If few people completely switch from cigarettes to IQOS, making dual use the likely dominant use pattern in the U.S., as it is in other countries, then the reduced exposure claim is not accurate for the vast majority of IQOS users.

> Dr. Popova: "I think what we've seen when IQOS was first introduced here, there was very little uptake of it. So, in terms of what is the likely pattern of IQOS use behavior will be, based on what we've seen here…it will be very few people who actually [use]… it and among those who do… it's highly likely they will be mostly dual users. So, when we are discussing the toxicological evidence and trying to answer the question, how much of the risk reduction, how can we translate the reduction of exposure to risk reduction? I think we really need to consider how people will be using this in the real world. And from what we know now, it's really people will be dual using. . . . . [F]rom all the evidence from other products and what we know before, it's highly unlikely that dual use will provide reduction

[88] TPSAC Meeting at 101.

[89] *Id.*

[90] *Id.* at 102.

in exposure and reduction in harms. And it's much more likely that we'll actually increase the risk in both of those."[91]

Dr. Stepanov: "[S]tudies are limited. They were halted, unfortunately. But there is a trend. If you look at the data, there is a trend that over the 18-month period, I think, in both studies, the one in 2020 and 2021…the proportion of participants who use IQOS exclusively trends to go down. And the proportion of the study population that are dual users [that] report smoking is going up."[92]

Dr. Scout: "[T]he independent studies show that really, what we're dealing with is a lot of dual use. And so it strikes me that… we've got a fair amount of limitations if we're only looking at studies that look at single use, which only affect a small minority of the number of people using IQOS."[93]

Some TPSAC members expressed concern about the levels of dual use found in the studies and questioned if this might lead to higher exposure to HPHCs and potentially greater health risks.

Dr. Scout: "I'm particularly concerned about the static level of dual use in at least one of the studies, saying that it's going on for longer. And that dual use is going to affect, it looks like between two-thirds up to, like, 85 percent of the people who might be moving from combustible cigarettes over to IQOS. And that being the case, it makes me really wonder about the way this is set up right now, the claim is about complete elimination. But if most all the people go through the journey where they have at least a period, if not an indefinite period, of dual use, then it seems that there is at least a potential harm step in the middle that is not being considered in the larger calculus of the route, even if they are among the smaller group that end up solely using IQOS at the end."[94]

Dr. Zelikoff: "[A]ccording to the background document, they have found that dual users do have greater health effects than just independent users on their own. And I don't think that people will actually take into account exclusive use only."[95]

TPSAC members also identified the need for more data on those who used IQOS and cigarettes to better inform the question about whether reduced exposure occurs when most people dual use.

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[91] *Id.* at 84.

[92] *Id.* at 85.

[93] *Id.* at 72.

[94] *Id.* at 83.

[95] *Id.* at 74.

> TPSAC member Dr. Nancy Rigotti: "[I]t seems like because of the concern about how much dual use there's probably going to be when this product is in real-world use, I think it's going to be important that looking carefully at what that means and how much risk reduction actually occurs, compared to cigarettes but also compared to HPHCs [*sic*] [HTPs] only, would be very helpful going forward."[96]
>
> Dr. Stepanov: "[W]hat is the proportion of the overall population that are predominant IQOS users versus people who just reduce their cigarettes per day by one or two cigarettes and are likely to be exposed to a more complex and potentially higher levels of toxicants, including some unique chemicals that come from these products? So I just [want] to second the proposal that dual use needs to be taken into consideration in these models."[97]

With the recognition that dual use would be the most likely pattern of IQOS use in the U.S., the lack of data provided by PMI about potential exposure and harm to this population, and the continued finding that consumers misunderstand "reduced exposure" as "reduced risk" while also misunderstanding "complete switching," PMI has failed to meet its burden in demonstrating that the orders should be renewed at this time.

B. The reference HPHC list being used by the FDA is outdated.

Several members suggested that, considering new constituent data found in IQOS aerosol, the current list of harmful and potentially harmful constituents ("HPHC list") is outdated, making it difficult to truly evaluate the relative exposure and harm from IQOS use compared to combusted cigarettes. These newer chemicals found in IQOS have the potential to cause harm that isn't currently associated with chemicals in cigarette smoke. That would make the reduced exposure claim inaccurate, and warrant further study before FDA can effectively decide on renewing this order.

> Dr. Scout: "I also am concerned because if we think about it, so far, we're still using an HPHC [list] that was developed before this item even came to market. And in 2019, TPSAC did suggest adding a bunch of chemicals that were more relevant to this type of product to the HPHC [list] and updating it. And here we are in 2025, and those chemicals are still not actually on the HPHC [list] yet so I would strongly encourage TPSAC to use their own updated HPHC [list]."[98]
>
> Dr. Jordt: "I would like to reiterate Dr. Scout's concern…about the deficiency of the HPHC list the FDA is working with and making conclusions on. . . . The list is completely

[96] *Id.* at 74.

[97] *Id.* at 74-75.

[98] *Id.* at 72.

outdated, it's from 2012. It only basically lists compounds that are present in combusting cigarettes but not even in e-cigarettes or in these heated tobacco products. And we just learned that in addition to the standard HPHCs that, some of them were reduced, there was an increase in some other compounds that are not on the list, but that are carcinogens. We're talking about, like, glycidol. We['re] talk[ing] about 2-Furanmethanol. There are compounds that have cardiovascular effects, such as 2-chloro-1,2-propanediol that was also mentioned. I don't even know where this comes from. PMI has complete control over the constituents. Why is there a chlorinated compound being formed? Where is this from? Is it from a sweetener, like sucralose or other compounds? So, I'm concerned FDA has insufficient tools to make conclusions based on the deficient HPHC lists and neglects concerns related to these compounds that are not on the list but are known carcinogens or cardiovascular toxicants."[99]

C. The lack of recent consumer perception research makes it difficult to adequately evaluate current understanding of the claim.

Several TPSAC members expressed concern about the lack of data to inform the decision on these applications. This lack of recent data is even more problematic considering how different the current marketplace is compared to when IQOS was first introduced, with the variety of e-cigarettes and nicotine pouches now being sold.

Dr. Delnevo: "We heard from PMI earlier, the totality of the evidence. We heard that phrase a couple times. The vast majority of IQOS users. Those data are 4 years old. There's no new consumer testing about perception. The data from the PACS study was also collected a number of years ago. And the tobacco marketplace looks quite different from 5 years ago. And so, the population impacts and the patterns of use are not the same as they used to be. And so, I'm left with the question of, do today's consumers, those that smoke cigarettes, understand the reduced risk statement [*sic*]? And would they be receptive to using this product? And the simple answer is we don't know. And while the disruption in the sales of products in the U.S. is a valid reason for the gaps in those post-market surveillance studies, the absence of that data is data that TPSAC would normally expect and would want to rely on when renewing and reviewing an MRTP renewal. And so that's problematic."[100]

Dr. Zelikoff: "[T]his is a 1-year, one-and-a-half year data collection. And despite the fact that it was mentioned that these data will reflect future data, I humbly disagree with that. I think that it's certainly the more numbers you have, the more people, all surveys, for the

[99] *Id.* at 77.

[100] *Id.* at 101-102.

most part have some bias within it. They're self-reported. And so, I think that we have to consider that as well."[101]

Dr. Delnevo: "I understand that there was disruption in the marketplace with availability of the product[,] which did prevent some of the studies from going ahead. It was a little disappointing that supplementary studies on the perceived understanding of the reduced risk [*sic*] claim couldn't have been done, even if the product wasn't available. You're not testing necessarily the use or the uptake of the product. But still understanding that people who smoke cigarettes understand the modified risk claim seemed like that was something that could have been done, even in the absence of the product in the marketplace. And it's not like the product hasn't been available in the marketplace, and it would have been useful to at least hear a little bit about what has been happening in the Austin test market, which has been going on for several months, with regards to the types of consumers that are using that particular product. It seems like it would have been possible to at least share and present at least a little bit of data on that."[102]

The change in today's tobacco product landscape led some TPSAC members to question whether the reduced exposure message would encourage IQOS uptake among users of non-cigarette tobacco products, and the potential health impacts of such uptake. Dr. Popova posed, "[W]hat is the gateway effect . . . would people switch from e-cigarettes to IQOS? And would this be a higher or lower harm, based on just the fact that it's tobacco. And there is potentially some combustion that actually does occur with higher temperatures, or in all the chemicals we've seen. Would this be a risk reduction or not? And then with the proliferation of nicotine pouches . . . which is quite popular among the young male population, would this be the easy shifting side by side?"[103]

The scant consumer perception data that PMI provided in its applications is deficient, outdated, and irrelevant to today's marketplace. PMI could have – but chose not to – conduct more perception studies even while the products were not being sold in the U.S. There are too many unanswered questions about how today's consumers will react to the reduced exposure claim for FDA to renew the orders at this time.

VII. IQOS Is a Cigarette Under the FDCA.

PMI argues that to qualify as a cigarette under the FDCA, a tobacco product must be:

> both (1) 'a roll of tobacco wrapped in paper or in any substance not containing tobacco'; and (2) 'includes tobacco, in any form that is functional in the product,

[101] *Id.* at 74.

[102] *Id.* at 83-84.

[103] *Id.* at 89.

> which because of its appearance, the type of tobacco used in the filler, or its packaging and labeling, is likely to be offered to, or purchased by, consumers as a cigarette.' Thus, whether a product meets the definition of a cigarette hinges on whether the product, because of its appearance, filler, packaging, and labeling, is likely to be marketed to, and perceived by, consumers as a cigarette.[104]

And, according to PMI, because IQOS is not likely to be marketed or perceived as a cigarette, it does not meet this definition and should be exempt from the statutory warnings required for cigarettes.

Setting aside PMI's debatable contention that IQOS is not likely to be marketed or perceived as a cigarette, the company's reading of the FDCA definition of a cigarette is incorrect. The FDCA's cigarette definition has two subparts – (A) and (B) – and, as the statutory text makes clear, any product that meets *either* subpart is considered a cigarette. The full FDCA definition is below.

> The term "cigarette"—
>
> **(A)** means a product that—
>
> **(i)** is a tobacco product; and
>
> **(ii)** meets the definition of the term "cigarette" in section 1332(1) of title 15;[105] and
>
> **(B)** includes tobacco, in any form, that is functional in the product, which, because of its appearance, the type of tobacco used in the filler, or its packaging and labeling, is likely to be offered to, or purchased by, consumers as a cigarette or as roll-your-own tobacco.

PMI reads subpart (B), which uses the word "includes," as narrowing the definition in subpart A. That simply cannot be squared with the ordinary meaning of "include" nor with caselaw interpreting that term in various statutory contexts. For example, Merriam Webster defines "include" to mean to "comprise *as part* of a whole or group."[106] The Supreme Court has also noted that the "word 'includes' is usually a term of enlargement, and not of limitation." *Burgess v. U.S.*,

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[104] Amendment at 2 (citing 21 U.S.C. § 387(3) and 15 U.S.C. § 1332(1)).

[105] 15 U.S.C. § 1332(1), in turn, states: (1)The term "cigarette" means—

(A) any roll of tobacco wrapped in paper or in any substance not containing tobacco, and

(B) any roll of tobacco wrapped in any substance containing tobacco which, because of its appearance, the type of tobacco used in the filler, or its packaging and labeling, is likely to be offered to, or purchased by, consumers as a cigarette described in subparagraph (A).

[106] Merriam-Webster, *Include*, https://www.merriam-webster.com/dictionary/include (last visited Nov. 24, 2025) (emphasis added).

553 U.S. 124, 131 n.3 (2008) (quoting 2A N. Singer & J. Singer, Sutherland on Statutory Construction § 47:7, p.305 (7th ed. 2007)).

Thus, any product that is a tobacco product under the FDCA[107] and meets the cigarette definition in 15 U.S.C 1332(1) is a cigarette under the FDCA. Here, PMI does not contest that IQOS meets the FDCA definition of a tobacco product nor that IQOS is a "roll of tobacco wrapped in paper or in any substance not containing tobacco," thus meeting the cigarette definition in 15 U.S.C. § 1332(1). Therefore, FDA should reject PMI's argument that IQOS is not a cigarette under the FDCA and is accordingly exempt from displaying the mandatory cigarette warnings.

PMI also misleadingly asserts that the PMTA Final Rule "created a new product category for HTPs." While the PMTA Final Rule created a new HTP category for the purposes of facilitating an efficient PMTA submission and review process, it explicitly stated that this "categorization of HTPs in § 1114.7(c)(3)(iii) and (i)(2)(ii) does not extend to other legal requirements beyond those associated with unique identification and product characterization for premarket review."[108] The PMTA Final Rule also clearly contemplated that some products that are cigarettes under the statute would fall into the HTP category for PMTA review purposes.[109] In any event, FDA does not have the authority to amend the *statutory* cigarette definition or to determine that some products that meet the definition should not be treated as such. That authority rests with Congress. FDA should reject PMI's misguided arguments that IQOS products are not cigarettes under the FDCA, and thus exempt from displaying the required cigarette warning statements.

CONCLUSION

For these reasons, we urge FDA to deny the MRTP renewal applications and reject the argument that IQOS is not a cigarette under the FDCA.

Respectfully submitted,

American Academy of Pediatrics

American Cancer Society Cancer Action Network

American Heart Association

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[107] *See* 21 U.S.C. § 321(rr).

[108] 86 Fed. Reg. at 55,318 n.15.

[109] *Id.* (The Heated Tobacco Product (HTP) "PMTA review category should be used for (among others) tobacco products that meet the definition of a cigarette but are not combusted…").

American Lung Association

Campaign for Tobacco-Free Kids