From: Nandini Duraiswamy
To: TPSAC
Subject: Fwd: [EXTERNAL] CTP Scientific Advisory Committee Meeting - Oct 7th 2025
Date: Monday, August 18, 2025 9:12:04 AM

Feedback to the Advisory Committee at the end.
Thank you.

---------- Forwarded message ---------
From: **AskCTP** <AskCTP@fda.hhs.gov>
Date: Mon, Aug 18, 2025 at 8:54 AM
Subject: RE: [EXTERNAL] CTP Scientific Advisory Committee Meeting - Oct 7th 2025
To: Nandini Duraiswamy <(b) (6) >

Dear Nandini Duraiswamy:

Thank you for contacting the Center for Tobacco Products. Please submit all comments and suggestions regarding Tobacco Products Scientific Advisory Committee to TPSAC@fda.hhs.gov.

Sincerely,

Center for Tobacco Products

Food and Drug Administration

CTP Call Center: 1-877-CTP-1373

www.fda.gov/tobaccoproducts

From: Nandini Duraiswamy <(b) (6) >
Sent: Thursday, August 14, 2025 1:26 PM

To: AskCTP <AskCTP@fda.hhs.gov>
Subject: [EXTERNAL] CTP Scientific Advisory Committee Meeting - Oct 7th 2025

Hello CTP,

Congratulations on the FDA public meeting to be held on Oct 7th 2025 regarding tobacco products. Here are a couple of suggestions for the Advisory Committee to invite speakers who may be able to incorporate science and evidence at the public meeting.

(1) On the FDA website, I see that the discussion will involve IQOS products which seemed to be very popular in the UK (at least at Heathrow Airport). I have heard anecdotally that this product uses an actual cigarette and is different from other vaping devices that have been approved by the FDA. Dr. S Guha and Dr. A Dibaji from CDRH-OSEL have previously performed a scientific investigation related to vaping devices, and I suggest that their reviews and recommendations be considered for further research related to IQOS devices as well.

(2) UK is also coordinating the quit smoking program (www.nhs.uk/quit). As I was dropping Lyft customers in and around VA-DC-MD area, I noticed that the tobacco business is quite widely used here and is difficult to comprehend if the quit smoking programs implemented locally and widely across the country carry value. It would be great to see the efforts here being coordinated with those outside the country, particularly the process and efficiency. I hope your public meeting will involve relevant speakers in this area too.

Thank you for your attention,

Sincerely,

-Nandini Duraiswamy

From: Carlos F. Orta
To: TPSAC
Cc: Carlos F. Orta
Subject: [EXTERNAL] TLC Support Letter for Renewal of the MRTP
Date: Thursday, September 11, 2025 8:03:04 PM
Attachments: TLC - FDA-Harm-Reduction-Pending-Applications-Letter- 09 11 2025.pdf

September 11, 2025

Rachel Jang, PharmD, DFO
Center for Tobacco Products
U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Tobacco Products Scientific Advisory Committee (TPSAC) Members,

The Latino Coalition (TLC) is a 501(c)(4) nonprofit organization established to research and address issues that directly affect the well-being of Latinos in the USA.

We are writing in support of the modified risk tobacco product (MRTP) authorization renewal previously granted to Philip Morris Products S.A.'s IQOS 2.4 and IQOS 3.0 System Holder and Charger, along with Marlboro Amber, Green Menthol and Blue Menthol Heatsticks.

According to the CDC[1], Hispanic people in the U.S., on average, 8.0% of Hispanic adults in the U.S. smoke cigarettes. The Hispanic/Latino population comprise 19% of the U.S. population or an estimated 62 million people (including Puerto Rico).[2] We represent the nation's second largest racial/ethnic population segment (after non-Hispanic White people).[3] However, significant differences in disease prevalence, access to care, and health outcomes exist for Hispanic/Latino communities in the U.S.[4]

Advances in science and technology have enabled the society to reduce the adverse effects of continuing with harmful behavior such as smoking, known as harm reduction. Harm reduction strategies can limit the impact our choices have across a range of issues, including on ourselves, others, and the society at large. Innovation has led to the development of scientifically substantiated better alternatives to smoking that have the potential to present less risk of harm than cigarettes for adults who would otherwise continue to smoke.

The U.S. Food and Drug Administration (FDA) has recognized that tobacco products exist on a

spectrum with combustible cigarettes as the most harmful type of tobacco product. Cigarettes burn at high temperatures to produce tobacco smoke; this mix of chemicals —not nicotine— cause the serious health effects including fatal lung diseases, like chronic obstructive pulmonary disease (COPD) and cancer. Non-combusted products on the other hand—such as heat-not-burn products and other smokeless tobacco products—generally have lower health risks than cigarettes.
As acknowledged by the FDA, nicotine is not the primary cause of the harms associated with smoking combustible cigarettes, it is the toxicants in combustible cigarette smoke that are responsible for the vast majority of smoking-related death and disease.

The MRTP pathway, authorized by Congress and established by the U.S. Food and Drug Administration (FDA), plays a pivotal role in evaluating and regulating tobacco products that reduce health risks compared to conventional cigarettes. This pathway is crucial in promoting public health by providing consumers with less harmful alternatives to traditional tobacco products. This is also an opportunity to encourage development and innovation of products that can make a major difference in death and disease from smoking and/or tobacco use.

The science and data remain consistent, and these products contain significantly lower levels of harmful chemicals compared to cigarettes. Years of data also shows that switching to IQOS reduces the risk of smoking-related diseases.

TLC encourages you to recommend the renewal of the MRTP authorization for these products. We need to provide comprehensive support to move people away from smoking combustible cigarettes. For those who are not able yet to quit nicotine, moving away to safer alternative could be an option. Existing efforts to discourage people from smoking must continue, but supplementing these measures with a tobacco harm reduction approach can accelerate a decline in smoking.

Let's prioritize public health by ensuring access to safer alternatives while maintaining rigorous standards.

Attached please find the original, signed letter. Please confirm receipt of this email and attachment.

Regards,

(b) (6)

Carlos F. Orta

President & CEO
The Latino Coalition
E: (b) (6)

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[1] Hispanic and Latino People Experience a Health Burden From Commercial Tobacco | Tobacco - Health Equity | CDC

[2] *Id*.

[3] *Id*.

[4] *Id*.

THE LATINO COALITION

September 11, 2025

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Center for Tobacco Products
U.S. Food & Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

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[1] Hispanic and Latino People Experience a Health Burden From Commercial Tobacco | Tobacco - Health Equity | CDC
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Let's prioritize public health by ensuring access to safer alternatives while maintaining rigorous standards.o

Regards,

(b) (6)

Carlos F. Orta
President & CEO
The Latino Coalitiono
E: (b) (6)

September 23, 2025

Rachel Jang, PharmD, DFO
Center for Tobacco Products
Food and Drug Administration
Document Control Center
Building 71
10903 New Hampshire Ave.
Silver Spring, MD 20993-0002

Dear Dr. Jang:

The Hispanic Leadership Fund is a nonpartisan advocacy organization dedicated to promoting public policy that strengthens liberty, opportunity, and prosperity for all. On behalf of our members across the country I write to support the renewal of the modified risk granted orders previously issued to Philip Morris Products S.A.'s IQOS 2.4, IQOS 3.0 and the relevant HeatSticks products.

As the largest U.S. minority group, the Hispanic community accounts for 18.5% of the current U.S. population[1] and are projected to grow to approximately 27.5% by 2060.[2] Of the approximately 62 million Hispanics who reside in the U.S., 8.0% currently smoke cigarettes.[3] While this rate is lower than the general population (12.5%), tobacco use is the single most important preventable risk factor to premature death among Hispanics.[4]

The U.S. Food and Drug Administration (FDA) has a vital role to play to reduce the harm caused by combustible cigarettes. The FDA has recognized that the health risks for different tobacco products exist on a spectrum.[5] In fact, in July 2020, the FDA authorized the marketing of IQOS under its Modified Risk Tobacco Products (MRTP) process[6], citing

[1] U.S. Census Bureau, Population Division. Annual Estimates of the Resident Population by Sex, Race and Hispanic Origin for the United States: April 1, 2010 to July 1, 2019 (NC-EST2019-SR11H). 2020
[2] Vespa, Jonathan, Lauren Medina and David M. Armstrong, "Demographic Turning Points for the United States: Population Projections for 2020 to 2060," Current Population Reports, P25-1144, U.S. Census Bureau, Washington, DC, 2020
[3] Cornelius ME, Loretan CG, Wang TW, Jamal A, Homa DM. Tobacco Product Use Among Adults — United States, 2020. MMWR Morb Mortal Wkly Rep 2022;71:397–405. DOI: https://www.cdc.gov/mmwr/ volumes/71/wr/mm7111a1.htm
[4] *Id*.
[5] The Relative Risks of Tobacco Products | FDA
[6] "FDA Authorizes Marketing of IQOS Tobacco Heating System with 'Reduced Exposure' Information," FDA, 07/07/2020, https://www.fda.gov/news-events/press-announcements/fda-authorizes-marketing-iqos-tobacco-heating-system-reduced-exposure-information.

its ability to promote public health. At the time, the agency concluded that IQOS could reduce the risk of morbidity and mortality among individual tobacco users and thus be a benefit to public health. This decision followed years of rigorous scientific evaluation, demonstrating that IQOS aligns with the FDA's public health goals under the Family Smoking Prevention and Tobacco Control Act.

IQOS is a scientifically backed, innovative tobacco heating system that offers adult smokers a less harmful alternative to conventional cigarettes. The "heat-not-burn" mechanism significantly reduces the production of harmful and potentially harmful chemicals (HPHCs). The FDA's own analysis supports this claim, confirming that completely switching from combustible cigarettes to IQOS reduces a user's exposure to these harmful chemicals.[7]

Combustible cigarettes remain the leading cause of preventable deaths in the U.S., responsible for over 480,000 fatalities annually and costing the economy hundreds of billions of dollars.[8] The fact is that millions of Americans continue to smoke. Providing adult smokers with access to reduced-risk alternatives like IQOS is essential to achieving meaningful reductions in smoking-related harm.

Adult smokers deserve access to truthful, science-based information about the risks and benefits of tobacco products. However, misinformation about the relative risks of non-combustible alternatives remains widespread. Many smokers are unaware that products like IQOS can reduce their exposure to harmful chemicals compared to combustible cigarettes.

The MRTP process was specifically designed to address this issue, allowing manufacturers to provide accurate information about reduced-risk products.[9] Denying the renewal of IQOS's MRTP designation would not only undermine this process but also deprive consumers of a critical tool to make better choices. It would signal that the regulatory system fails to prioritize innovation and the public's right to know scientifically accurate information.

(b) (6)

Mario H. Lopez
President

[7] Rahman Basaran, et al., "An Overview of iQOS® as a New Heat-Not-Burn Tobacco Product and Its Potential Effects on Human Health and the Environment," NIH, 07/10/2019, https://pmc.ncbi.nlm.nih.gov/articles/PMC7227951/.
[8] "Burden of Cigarette Use in the U.S," CDC, https://www.cdc.gov/tobacco/campaign/tips/resources/data/cigarette-smoking-in-united-states.html.
[9] "Modified Risk Tobacco Products," FDA, https://www.fda.gov/tobacco-products/advertising-and-promotion/modified-risk-tobacco-products.

GOLDWATER
INSTITUTE

September 25, 2025
Goldwater Institute Comments in Support of Modified Risk Tobacco Product Renewal Applications for IQOS and HeatSticks
RE: Docket No. FDA-2021-N-0408

The Goldwater Institute, a public policy research and advocacy organization based in Phoenix, Arizona, is pleased to submit these comments in support of the renewal of the modified risk granted orders issued for IQOS and HeatStick heated tobacco products.

The core of our mission is to defend and strengthen the freedom guaranteed to all Americans, and a crucial component of that mission is ensuring individuals have the freedom to make informed choices that are consistent with their own health and well-being. This includes access to accurate, truthful, and scientifically supported information about consumer products. The FDA's initial authorization of IQOS as a modified risk product was a landmark decision that recognized the importance of providing adult smokers with a potentially less harmful alternative to combustible cigarettes. We urge the FDA and the Tobacco Products Scientific Advisory Committee to renew this authorization, as it remains a decision consistent with individual liberty, public health, and sound economic policy.

The public health toll of combustible cigarettes is a significant and ongoing crisis. Recent data from public health organizations continues to reinforce this reality. The U.S. Centers for Disease Control and Prevention estimates that smoking-related healthcare expenditures and productivity losses still amount to hundreds of billions of dollars annually. Recent figures indicate that the total annual cost of smoking in the U.S. is over $600 billion, with more than $240 billion in healthcare spending and nearly $372 billion in lost productivity.[1] This burden is disproportionately carried by taxpayer-funded programs, with Medicaid alone accounting for tens of billions of dollars in smoking-related costs each year.[2]

The FDA's own proposed regulations to cap nicotine levels in cigarettes underscore the agency's understanding of the profound public health challenge posed by nicotine addiction and combustible cigarettes. While we support market-based solutions and individual choice, we recognize that the FDA has a mandate to protect public health.

Allowing the continued, truthful communication of reduced-exposure claims for IQOS products is a vital and effective component of that mandate.

The scientific community has had several more years to study heated tobacco products since the initial authorization of IQOS. The evidence submitted by PMI and reviewed by the FDA's

GOLDWATER
INSTITUTE

TPSAC in 2017 showed a significant reduction in harmful and potentially harmful constituents in the IQOS aerosol compared to cigarette smoke. Subsequent studies have continued to support this finding.

A key study published in a peer-reviewed journal found that adult smokers who switched completely to the IQOS system for six months showed statistically significant improvements in five of eight key biomarkers of effect associated with smoking-related diseases. This research, conducted on a large cohort of U.S. smokers, found that the improvements were in the same direction as those seen in individuals who quit smoking altogether.[3.] These findings directly support the FDA's initial determination that "switching completely from conventional cigarettes to the IQOS system significantly reduces your body's exposure to harmful or potentially harmful chemicals."

Furthermore, the fact that IQOS heats tobacco rather than burns it remains a scientifically sound basis for the reduced-exposure claim. The temperature difference—up to 350°C for IQOS versus over 600°C for cigarettes—fundamentally changes the chemical profile of the aerosol, reducing the production of thousands of combustion-related toxins.[4.]

The renewal of the modified risk granted orders for IQOS products would uphold the principle of providing truthful information to consumers, while also acknowledging that a free-market approach to harm reduction—where less harmful alternatives can compete on a level playing field—is a powerful driver of public health improvements and taxpayer savings.

Sincerely,

Jen Springman
Coalitions Manager
Goldwater Institute

on the continuum of risk, where combusted tobacco products like cigarettes occupy the highest risk position, and non-combusted alternatives, including heated tobacco products (HTPs) like IQOS, offer substantially reduced harm.[1]

The continuum of risk is a well-established framework in tobacco control, endorsed by scientific consensus and regulatory bodies. It posits that tobacco and nicotine products exist on a spectrum of harm, with the level of risk determined primarily by the delivery method and the presence of combustion. Combusted products, such as cigarettes, are at the most harmful end because burning tobacco at high temperatures (over 600°C) generates thousands of toxic chemicals, including over 70 known carcinogens. In contrast, non-combusted products, like smokeless tobacco or medicinal nicotine, are at the lower end. Heated tobacco products, which heat tobacco to around 350°C without burning it, fall in between, producing an aerosol with significantly fewer and lower levels of harmful constituents.[2] This framework is not merely theoretical; it is grounded in extensive research demonstrating that switching to lower-risk products can reduce individual and population-level health risks. For instance, the National Academies of Sciences, Engineering, and Medicine have acknowledged that e-cigarettes, another non-combusted product, likely expose users to fewer toxicants than combustible cigarettes, supporting the harm reduction potential of such alternatives.[3] Extending this logic to HTPs like IQOS is consistent with promoting public health by encouraging smokers to migrate down the risk continuum.

Scientific evidence specifically on IQOS underscores its position on the lower end of the risk continuum compared to cigarettes. Studies have shown that IQOS produces vapor containing nearly 90% fewer toxic substances than cigarette smoke, including reduced levels of volatile organic compounds, polycyclic aromatic hydrocarbons, and other harmful chemicals.[4] For example, nicotine levels in IQOS aerosol are comparable to those in cigarettes, ensuring satisfaction for smokers, but concentrations of nitrosamines and carbon monoxide are dramatically lower—approximately one-fifth and 1% of cigarette levels, respectively. This reduction in toxicants translates to lower environmental and second-hand exposure risks, as IQOS emissions contain fewer submicron particles that linger in the air compared to cigarette smoke. Such findings align with the harm reduction paradigm, where the goal is to minimize exposure to combustion byproducts without necessarily eliminating nicotine use.

Further supporting this, a scoping review of IQOS toxicity and health impacts compiled data from various studies, revealing that while results vary by funding source, manufacturer-conducted research consistently demonstrates reduced toxicity and carcinogenicity in animal models exposed to IQOS aerosol versus cigarette smoke.[5] In chronic exposure experiments using mice, IQOS showed lower impacts on lung inflammation, emphysematous changes, and cardiovascular systems after extended periods. Clinical studies in the review also indicated reductions in biomarkers of exposure to harmful and potentially harmful constituents (HPHCs) by 47% to 96% among smokers who switched to IQOS, alongside

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[1] Hatsukami, D. K., & Carroll, D. M. (2020). Tobacco harm reduction: Past history, current controversies and a proposed approach for the future. Preventive Medicine, 140, 106099. https://www.sciencedirect.com/science/article/pii/S0091743520301237

[2] U.S. Food and Drug Administration. (2025). The relative risks of tobacco products. Retrieved from https://www.fda.gov/tobacco-products/health-effects-tobacco-use/relative-risks-tobacco-products

[3] National Academies of Sciences, Engineering, and Medicine. (2018). Public health consequences of e-cigarettes. The National Academies Press. https://nap.nationalacademies.org/catalog/24952/public-health-consequences-of-e-cigarettes

[4] Başaran, R., Güven, N. M., & Eke, B. C. (2019). An overview of iQOS® as a new heat-not-burn tobacco product and its potential effects on human health and the environment. Turkish Journal of Pharmaceutical Sciences, 16(3), 371–374. https://pmc.ncbi.nlm.nih.gov/articles/PMC7227951/

[5] Ghazi, S., Song, M.-A., & El-Hellani, A. (2024). A scoping review of the toxicity and health impact of IQOS. Tobacco Induced Diseases, 22, Article 188867. https://pmc.ncbi.nlm.nih.gov/articles/PMC11145630/

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Washington, D.C. 20005
202-525-5717

Free Markets. Real Solutions.
www.rstreet.org

October 7, 2025

Dr. Bret Koplow
Acting Director
Center for Tobacco Products (CTP)
United States Food and Drug Administration
Rockville, MD 20852

Re: Docket No. **FDA-2025-N-2030**

Dear Dr. Koplow and members of the Tobacco Products Scientific Advisory Committee,

The R Street Institute (R Street) respectfully submits the following comments in response to the public meeting on the modified risk tobacco product (MRTP) application for IQOS products submitted by Philip Morris Products S.A. R Street is a nonprofit, nonpartisan public policy organization focused on advancing free markets and limited, effective government in various areas, including Integrated Harm Reduction. Our work is based on the belief that health policy rooted in harm reduction can significantly reduce the adverse outcomes of harmful behaviors and alleviate the burdens of healthcare costs. Decades of research show that abstinence-only methods are ineffective at a population level for risky behaviors. Policies that criminalize behaviors like smoking lead to unintended negative consequences.

We are writing this letter to express our strong support for the renewal of the MRTPA for the IQOS product line, including the Marlboro Amber HeatSticks, Marlboro Green Menthol HeatSticks, Marlboro Blue Menthol HeatSticks, IQOS 2.4 System Holder and Charger, and IQOS 3.0 System Holder and Charger. As advocates for public health and evidence-based tobacco regulation, we believe that renewing this MRTPA aligns with the principles of tobacco harm reduction and the continuum of risk framework, which are essential for reducing tobacco-related diseases in the United States. The IQOS system, a heat-not-burn tobacco product developed by Philip Morris International, represents a scientifically supported alternative for adult smokers who are unable or unwilling to quit nicotine use entirely. By heating tobacco rather than combusting it, IQOS significantly reduces exposure to harmful and potentially harmful chemicals compared to traditional combustible cigarettes, thereby offering a pathway to mitigate the health risks associated with smoking.

Tobacco use remains one of the leading preventable causes of death in the United States, with combustible cigarettes accounting for the vast majority of tobacco-related morbidity and mortality. According to the U.S. Surgeon General, cigarette smoking causes over 480,000 deaths annually, primarily due to exposure to toxicants produced by combustion, such as tar, carbon monoxide, and numerous carcinogens. In this context, the concept of tobacco harm reduction (providing less harmful alternatives to smokers) has emerged as a pragmatic public health strategy. Harm reduction recognizes that while complete abstinence from nicotine is ideal, many smokers face significant barriers to quitting. Instead of insisting on an all-or-nothing approach, harm reduction encourages transitioning users to products lower

on the continuum of risk, where combusted tobacco products like cigarettes occupy the highest risk position, and non-combusted alternatives, including heated tobacco products (HTPs) like IQOS, offer substantially reduced harm.[1]

The continuum of risk is a well-established framework in tobacco control, endorsed by scientific consensus and regulatory bodies. It posits that tobacco and nicotine products exist on a spectrum of harm, with the level of risk determined primarily by the delivery method and the presence of combustion. Combusted products, such as cigarettes, are at the most harmful end because burning tobacco at high temperatures (over 600°C) generates thousands of toxic chemicals, including over 70 known carcinogens. In contrast, non-combusted products, like smokeless tobacco or medicinal nicotine, are at the lower end. Heated tobacco products, which heat tobacco to around 350°C without burning it, fall in between, producing an aerosol with significantly fewer and lower levels of harmful constituents.[2] This framework is not merely theoretical; it is grounded in extensive research demonstrating that switching to lower-risk products can reduce individual and population-level health risks. For instance, the National Academies of Sciences, Engineering, and Medicine have acknowledged that e-cigarettes, another non-combusted product, likely expose users to fewer toxicants than combustible cigarettes, supporting the harm reduction potential of such alternatives.[3] Extending this logic to HTPs like IQOS is consistent with promoting public health by encouraging smokers to migrate down the risk continuum.

Scientific evidence specifically on IQOS underscores its position on the lower end of the risk continuum compared to cigarettes. Studies have shown that IQOS produces vapor containing nearly 90% fewer toxic substances than cigarette smoke, including reduced levels of volatile organic compounds, polycyclic aromatic hydrocarbons, and other harmful chemicals.[4] For example, nicotine levels in IQOS aerosol are comparable to those in cigarettes, ensuring satisfaction for smokers, but concentrations of nitrosamines and carbon monoxide are dramatically lower—approximately one-fifth and 1% of cigarette levels, respectively. This reduction in toxicants translates to lower environmental and second-hand exposure risks, as IQOS emissions contain fewer submicron particles that linger in the air compared to cigarette smoke. Such findings align with the harm reduction paradigm, where the goal is to minimize exposure to combustion byproducts without necessarily eliminating nicotine use.

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[1] Hatsukami, D. K., & Carroll, D. M. (2020). Tobacco harm reduction: Past history, current controversies and a proposed approach for the future. Preventive Medicine, 140, 106099. https://www.sciencedirect.com/science/article/pii/S0091743520301237

[2] U.S. Food and Drug Administration. (2025). The relative risks of tobacco products. Retrieved from https://www.fda.gov/tobacco-products/health-effects-tobacco-use/relative-risks-tobacco-products

[3] National Academies of Sciences, Engineering, and Medicine. (2018). Public health consequences of e-cigarettes. The National Academies Press. https://nap.nationalacademies.org/catalog/24952/public-health-consequences-of-e-cigarettes

[4] Başaran, R., Güven, N. M., & Eke, B. C. (2019). An overview of iQOS® as a new heat-not-burn tobacco product and its potential effects on human health and the environment. Turkish Journal of Pharmaceutical Sciences, 16(3), 371–374. https://pmc.ncbi.nlm.nih.gov/articles/PMC7227951/

[5] Ghazi, S., Song, M.-A., & El-Hellani, A. (2024). A scoping review of the toxicity and health impact of IQOS. Tobacco Induced Diseases, 22, Article 188867. https://pmc.ncbi.nlm.nih.gov/articles/PMC11145630/

improvements in health effect biomarkers such as high-density lipoprotein cholesterol and lung function. Even independent studies, while sometimes reporting mixed results, have noted that IQOS induces less cytotoxicity in lung epithelial cells (90–95% reduction) and impairs endothelial function to a lesser degree than cigarettes. These outcomes reinforce the continuum of risk, positioning IQOS as a less harmful option that can facilitate harm reduction for persistent smokers.

Biomarkers of potential harm (BoPH) provide objective measures of the health benefits associated with switching to IQOS. A systematic review and meta-analysis of HTPs, including IQOS, examined effects on BoPH such as those related to cardiovascular function, oxidative stress, and inflammation.[6] Under controlled conditions, HTPs demonstrated largely beneficial effects on biomarkers of endothelial dysfunction, oxidative stress, and platelet function compared to cigarettes. In ambulatory settings, similar benefits were observed for respiratory function and metabolic syndrome markers, with mixed but predominantly positive outcomes for inflammation. Although the review highlights the need for longer-term independent studies, the existing data suggest that short-term use of HTPs like IQOS can mitigate some of the harms inflicted by continued cigarette smoking. This evidence supports renewing the MRTPA, as it indicates that IQOS can play a role in reducing the overall risk profile for adult smokers within the harm reduction framework.

Pulmonary health, a primary concern in tobacco use, also benefits from switching to IQOS. Research investigating the impact of transitioning from cigarettes to HTPs on lung infection outcomes found that such a switch results in modest reductions in endothelial damage and improved bacterial clearance in the lungs compared to continued cigarette exposure.[7] In mouse models pre-exposed to cigarette smoke and then switched to IQOS, plasma markers of lung damage decreased, and inflammatory responses were less severe during acute challenges. While complete cessation yielded the best results, the study underscores that switching to IQOS offers partial protection against pulmonary complications, aligning with the continuum of risk where partial harm reduction is preferable to none. This is particularly relevant for smokers at high risk for respiratory diseases, as IQOS reduces exposure to irritants that exacerbate conditions like chronic obstructive pulmonary disease (COPD).

Real-world evidence from natural experiments further validates the harm reduction potential of IQOS. In a study examining tobacco behaviors before and after IQOS availability in the U.S. market, adult users reported a significant decrease in cigarette consumption upon adopting IQOS, with the proportion of cigarette users dropping from 89.9% to 63.0% and weekly cigarette intake falling from 106.3 to 39.0.[8] Notably, following market removal, cigarette use rebounded, highlighting IQOS's role in sustaining reduced smoking. Regression analyses showed that IQOS use was associated with 86% higher odds of quitting cigarettes entirely. This demonstrates how IQOS facilitates movement down the risk continuum, reducing combustible tobacco use and associated harms.

The FDA has already recognized these benefits through its authorization of reduced-exposure claims for IQOS. In 2022, the agency granted a modified risk order allowing marketing claims that switching completely to IQOS significantly reduces exposure to harmful chemicals, based on evidence that the

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[6] Braznell, S., Dance, S., Hartmann-Boyce, J., & Gilmore, A. (2025). Impact of heated tobacco products on biomarkers of potential harm and adverse events: A systematic review and meta-analysis. Tobacco Control. Advance online publication. https://tobaccocontrol.bmj.com/content/early/2025/04/16/tc-2024-059000.abstract

[7] Bhat, T. A., Kalathil, S. G., Leigh, N. J., et al. (2024). Can switching from cigarettes to heated tobacco products reduce consequences of pulmonary infection? Respiratory Research, 25, 381. https://link.springer.com/article/10.1186/s12931-024-02992-y

[8] Noggle, B., Ball, K. M., & Vansickel, A. R. (2024). A reduced exposure heated tobacco product was introduced then abruptly taken off United States shelves: Results from a tobacco harm reduction natural experiment. Harm Reduction Journal, 21, 84. https://link.springer.com/article/10.1186/s12954-024-01000-2

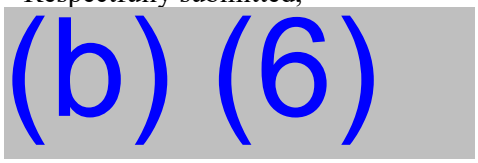
system heats tobacco without burning it, thereby lowering HPHC production.[9] This decision was informed by scientific studies showing substantial reductions in bodily exposure to toxicants. Renewing the MRTPA would build on this precedent, ensuring continued access to a product that supports harm reduction while maintaining regulatory oversight to prevent youth initiation and monitor long-term effects.

Critics may argue that HTPs like IQOS could renormalize tobacco use or appeal to non-smokers, but evidence suggests otherwise. Risk perception studies indicate that users view IQOS as less harmful than cigarettes but not risk-free, encouraging switches among smokers rather than new uptake.[10] Moreover, the FDA's continuum of risk framework emphasizes regulating products based on their relative harm, with safeguards like age restrictions and marketing limitations to protect vulnerable populations. By renewing the MRTPA, the agency can enforce these measures, ensuring IQOS contributes positively to public health.

In conclusion, renewing the MRTPA for the IQOS product line is a science-driven decision that advances tobacco harm reduction and respects the continuum of risk. The evidence from peer-reviewed literature and FDA evaluations demonstrates that IQOS offers adult smokers a less harmful alternative, reducing exposure to toxicants and potentially lowering disease risks. Denying renewal could drive users back to more harmful combustible cigarettes, undermining public health goals. We urge the FDA to prioritize this renewal to save lives and reduce the societal burden of tobacco use.

Thank you for considering this letter as part of the public comment process.

Respectfully submitted,



Jeffrey S. Smith, Ph.D.
Resident Senior Fellow
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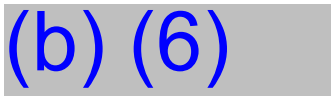

[9] U.S. Food and Drug Administration. (2022). FDA authorizes reduced exposure claim for IQOS 3 system holder and charger. Retrieved from https://www.fda.gov/tobacco-products/ctp-newsroom/fda-authorizes-reduced-exposure-claim-iqos-3-system-holder-and-charger

[10] Hatsukami, D. K., & Carroll, D. M. (2020). Tobacco harm reduction: Past history, current controversies and a proposed approach for the future. Preventive Medicine, 140, 106099. https://www.sciencedirect.com/science/article/pii/S0091743520301237

Food and Drug Administration
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In The Matter of 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.

The American Consumer Institute is an independent 501(c)(3) education and research organization. Its mission is to identify, analyze, and protect the interests of consumers in selected legislative and rulemaking proceedings in information technology, health care, insurance, and other matters.

We are writing in support of re-authorizing Philip Morris Products S.A.'s modified risk tobacco products.[1] According to the CDC, "smoking kills more than 480,000 Americans each year."[2] Evidence shows that heated tobacco products (HTPs) reduce smokers' exposure to harmful toxins compared to cigarettes.[3] HTPs—like other harm reduction and smoking cessation tools—are useful tools for reducing suffering from smoking-related disease and lowering healthcare expenditures for patients, as well as Medicare and Medicaid. Re-authorizing these products would advance the Food and Drug Administration's (FDA's) public-health mandate by continuing to provide adult smokers with a less harmful alternative.

1. Marlboro Amber HeatSticks, Marlboro Green Menthol HeatSticks, Marlboro Blue Menthol HeatSticks, IQOS 2.4 System Holder and Charger, and IQOS 3.0 System Holder and Charger
2. "Burden of Cigarette Use in the U.S.," Center for Disease Control, Reviewed October 8, 2024, https://www.cdc.gov/tobacco/campaign/tips/resources/data/cigarette-smoking-in-united-states.html.
3. Haziza, et al., "Reduction in Exposure to Selected Harmful and Potentially Harmful Constituents Approaching Those Observed Upon Smoking Abstinence in Smokers Switching to the Menthol Tobacco Heating System 2.2 for 3 Months (Part 1)," Nicotine and Tobacco Research, Vol. 22, Issue 4, Pages 539–548, April 2020, https://pmc.ncbi.nlm.nih.gov/articles/PMC7164581/; Gale, et al., "Changes in Biomarkers of Exposure on Switching From a Conventional Cigarette to Tobacco Heating Products: A Randomized, Controlled Study in Healthy Japanese Subjects," Nicotine and Tobacco Research, Vol. 21, Issue 9, Pages 1220–1227, September 2019, https://pmc.ncbi.nlm.nih.gov/articles/PMC6698948/.

When these products were first authorized in 2019 the FDA specifically noted the substantial reduction in harmful and potentially harmful chemicals (HPHCs):

> "In particular, through the FDA's scientific evaluation of the company's applications, peer-reviewed published literature and other sources, the agency found that the aerosol produced by the IQOS Tobacco Heating System contains fewer toxic chemicals than cigarette smoke, and many of the toxins identified are present at lower levels than in cigarette smoke. For example, the carbon monoxide exposure from IQOS aerosol is comparable to environmental exposure, and levels of acrolein and formaldehyde are 89% to 95% and 66% to 91% lower than from combustible cigarettes, respectively."[4]

The evidence that HTPs reduce risk compared to cigarettes has grown stronger since the FDA first authorized these products for sale. A review of the health effects of HTPs reports HPHC levels were 90 percent lower, and levels of Group 1 carcinogens—as defined by the International Agency for Research on Cancer[5]—were 95 percent lower compared to smoking.[6] Smokers who switched show reduced exposure to HPHCs across 15 biomarkers. There is evidence of reduced impact from in vitro[7] and in vivo (mice) studies,[8] as well as studies of smokers.[9]

A randomly controlled study on the effectiveness of HTPs as a smoking-cessation tool found that among smokers who did not intend to quit, HTPs had smoking-reduction rates to comparable to vaping,[10] which has been shown to be an effective means for quitting. [11]

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4. "FDA permits sale of IQOS Tobacco Heating System through premarket tobacco product application pathway," United States Food and Drug Administration, April 30, 2019, https://www.fda.gov/news-events/press-announcements/fda-permits-sale-iqos-tobacco-heating-system-through-premarket-tobacco-product-application-pathway.
5. "Agents Classified by the IARC Monographs, Volumes 1–139," International Agency for Research on Cancer, Updated June 27, 2025, https://monographs.iarc.who.int/agents-classified-by-the-iarc/.
6. Reuven Zimlichman, Elena Scotti, and Giuseppe Plebani, "Heated Tobacco Products and Cardiovascular Disease: A Narrative Review of Peer-Reviewed Publications," American Medical Journal, September 15, 2022, https://www.emjreviews.com/en-us/amj/cardiology/symposium/heated-tobacco-products-and-cardiovascular-disease-a-narrative-review-of-peer-reviewed-publications-s02622/.
7. Schaller, et al., "Evaluation of the Tobacco Heating System 2.2. Part 2: Chemical composition, genotoxicity, cytotoxicity, and physical properties of the aerosol," Regulatory Toxicology and Pharmacology, Vol. 81, Supplement 2, Pages S27–S47, November 30, 2016, https://www.sciencedirect.com/science/article/pii/S0273230016302902.
8. Phillips, et al., "An 8-Month Systems Toxicology Inhalation/Cessation Study in Apoe-/- Mice to Investigate Cardiovascular and Respiratory Exposure Effects of a Candidate Modified Risk Tobacco Product, THS 2.2, Compared With Conventional Cigarettes," Toxicological Sciences, Vol 149, Issue 2, Pages 41–432, February 2016, https://pubmed.ncbi.nlm.nih.gov/26609137/.
9. Lüdicke, et al., "Effects of Switching to a Heat-Not-Burn Tobacco Product on Biologically Relevant Biomarkers to Assess a Candidate Modified Risk Tobacco Product: A Randomized Trial," Cancer Epidemiology Biomarkers and Prevention, Vol. 28, Issue 11, Pages 1934–1943, 2019, https://pubmed.ncbi.nlm.nih.gov/31270101/.
10. Caponnetto, et al., "Comparing the Effectiveness, Tolerability, and Acceptability of Heated Tobacco Products and Refillable Electronic Cigarettes for Cigarette Substitution (CEASEFIRE): Randomized Controlled Trial," JMIR Public Health and Surveillance, Vol. 9, 2023, https://pubmed.ncbi.nlm.nih.gov/37014673/.
11. "Vaping to quit smoking," United Kingdom National Health Service, accessed September 18, 2025, https://www.nhs.uk/better-health/quit-smoking/ready-to-quit-smoking/vaping-to-quit-smoking/.

Smokers are a diverse population and need different tools when they choose to quit. Yet the FDA currently offers far more choice to people who continue to smoke than those trying to stop. Between 2018 and 2022 the FDA approved 892 new cigarette products, giving consumers a wide array of more harmful options.[12] By comparison, the FDA has approved 45 reduced-risk products in total—only eight of which are heated tobacco products (formerly "noncombusted cigarettes").[13] Smokers need options when attempting to quit, and there are very few authorized alternatives relative to the number of cigarette products the FDA has authorized.

While there are no risk-free ways to consume nicotine, some methods are far less harmful than others. HTPs significantly reduce the risks associated with tobacco use. These products can help ensure fewer people suffer from smoking-related illnesses and can reduce avoidable costs borne by patients and by Medicare and Medicaid. Re-authorizing these products will help ensure Americans have viable, less harmful options when trying to quit smoking.

Respectfully,

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12. "FDA Approves More Than 1200 Combustibles and 900 New Cigarettes," Vapor Technology Association, March 2023, https://vaportechnology.org/wp-content/uploads/2023/04/VTA-Report-%E2%80%93-FDA-Approves-Combustibles.pdf.
13. "Premarket Tobacco Product Marketing Granted Orders," United States Food and Drug Administration, Updated March 28, 2024, https://www.fda.gov/tobacco-products/premarket-tobacco-product-applications/premarket-tobacco-product-marketing-granted-orders.

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September 24, 2025

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Submitted via e-mail

RE: Docket No. FDA-2025-N-2030, Tobacco Products Scientific Advisory Committee; Notice of Meeting re Renewal of Modified Risk Granted Orders for IQOS 2.4, IQOS 3.0, and Certain HeatSticks

The Campaign for Tobacco-Free Kids ("CTFK") submits these comments in connection with the October 7, 2025 meeting of the Tobacco Products Scientific Advisory Committee ("TPSAC") to discuss the renewal of the modified risk granted orders ("MRGOs") issued to Philip Morris Products S.A., an affiliate of Philip Morris International (PMI and its affiliates hereinafter referred to as "PMI"), for the following products: MR0000059: Marlboro Amber HeatSticks, MR0000060: Marlboro Green Menthol HeatSticks, MR0000061: Marlboro Blue Menthol HeatSticks, MR0000133: IQOS 2.4 System Holder and Charger, and MR0000192: IQOS 3.0 System Holder and Charger. 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]

[1] Under the 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).

INTRODUCTION

As detailed below, PMI has failed to meet the statutory standard for renewal of its 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.

These comments expand upon a letter that CTFK and other public health organizations sent to FDA in June 2024 outlining key developments related to IQOS. That letter ("June 2024 Letter") is attached herein and incorporated by reference.[2]

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"

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

[2] 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.

showing that consumers make the leap between claims of "reduced exposure" to mean claims of lowering risk.[3] Studies published since then have only reiterated these findings.

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."[4] These findings are reinforced by other recent studies showing that consumers, including youth,[5] do not distinguish between reduced exposure and reduced risk messages; instead, they interpret and respond to both types of statements similarly.[6]

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.[7] 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."[8] Consistent with other research, this finding indicates that consumers continue to misinterpret the authorized claims to mean that IQOS use reduces consumers' disease risk.

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[3] 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.

[4] 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/.

[5] 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.

[6] 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.

[7] 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.

[8] 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.

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 statute requires applicants seeking a modified exposure order to submit "actual consumer perception" data showing 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 USC 387k(g)(2)(B)(iii). The research discussed above, as well as PMI's misleading statements discussed in Part II, create a heavy presumption that IQOS has failed to meet this statutory requirement.

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."[9] 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."[10] FDA thus required postmarket 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."[11]

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.[12] Some consumers, including youth,[13] do not fully understand what is meant

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[9] 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").

[10] *Id.* at 52.

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

[12] 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.

[13] 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.

by "switching completely."[14] Researchers have suggested including explicit language in modified risk messages to convey that partial switching does not reduce risk or exposure[15] or adding an explanation of "switching completely."[16]

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."[17] The MRGO specifically instructed PMI that it "may not market these products with reduced risk claims."[18] Notably, PMI has since abandoned its efforts to secure authorization to make modified risk claims, which at the least appears to be a recognition that it cannot meet the statutory standard for such claims.

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[14] 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.

[15] 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.

[16] 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.

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

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

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."[19]

- 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.[20]

- 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."[21]

Additional misrepresentations of the modified exposure order 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 order is particularly troubling given consumers' well-documented tendency to interpret reduced exposure claims to mean reduced risk, as discussed earlier in these comments.

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,

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

[20] 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).

[21] 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).

research on the health impacts of HTPs, including IQOS, which is the dominant brand on the market,[22] 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.[23] 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,[24] and then in Fort Lauderdale, Florida in mid-2025.[25] 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).[26]

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

In its MRTP renewal application, 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."[27] As mentioned in a previous letter from public health groups to FDA about PMI's global

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[22] 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.

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

[24] *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.

[25] 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.

[26] *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.

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

IQOS marketing targeted to youth, PMI did not adequately explain how the experience in these two countries would apply to the U.S. setting.[28] The sweeping redactions in this renewal application 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."[29] Independent research from some of the countries that PMI references in its application, 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.[30] 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.[31] Other studies from Japan showed that 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.[32] The

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

[29] 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.

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

[31] 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.

[32] 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.

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."[33]

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,[34] 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.[35] 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.[36] Similarly, several studies of dual users of cigarettes and HTPs in other data sources have found declines in visits to smoking cessation clinics,[37] lower likelihood of making quit attempts,[38] and no significant difference in intention to quit smoking compared to exclusive cigarette smokers.[39] Further, three studies of South Korean youth showed high rates of

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[33] 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.

[34] 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.

[35] 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.

[36] 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.

[37] 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.

[38] 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.

[39] 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

dual use of HTPs and cigarettes and negative or no association between HTP uptake and smoking cessation or quit attempts.[40]

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.[41] 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,[42] reinforcing the concern that the novelty of these products attracts youth and can lead to addiction and dual use.

Thus, the available independent research fails to substantiate PMI's claims that IQOS benefits individual or population health and is, in fact, contradictory to 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 application.

OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH 8471 (2020), http://dx.doi.org/10.3390/ijerph17228471.

[40] 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.

[41] 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.

[42] 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.

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[43] and what flavors were tested,[44] 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[45] – 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.[46] In particular, real-life conditions, in which substances deposited in the device during use are reheated repeatedly, can generate more HPHCs and particles.[47] One study stated, "When compared with an array of cigarettes, IQOS did not have consistently reduced emission of toxicants."[48] FDA should take these newer studies into consideration when deciding on whether or not to renew this application. At the very least, FDA should require additional independent research to determine the potential for harm from these chemicals before re-authorizing the claims.

While not the subject of this application, 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.

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[43] 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.

[44] 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.

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

[46] 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.

[47] *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.

[48] 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.

Reviews of available research have found "a considerable body of evidence indicating that HTP use has adverse cardiovascular and respiratory effects"[49] 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."[50] 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."[51]

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."[52]

Finally, given the unreliability of research funded and produced by tobacco companies, including PMI, it is critical that FDA and TPSAC consult independent studies to decide this renewal application, 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.[53] 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

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[49] 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.

[50] 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.

[51] 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.

[52] 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.

[53] 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.

by tobacco companies generally produce more favorable findings for HTPs.[54] 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.[55] 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.[56]

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 between 35-64 years old.[57] PMI's marketing tactics for IQOS clearly show that the company is targeting a much broader audience than just adult smokers.

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[54] 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.

[55] 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.

[56] 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.

[57] 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.

As we have highlighted for FDA in previous comments[58] and letters,[59] 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.[60]

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.[61] PMI joined with Rolling Stone UK for a Future of Music concert, described as "a night filled with music from cutting-edge artists, showcasing the trends and sounds

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[58] 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.

[59] 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.

[60] 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.

[61] *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), https://seatca.org/dmdocuments/DTI%20Complaint%20PMFTC-Aoki%20event%2015Apr2025.pdf.

that are shaping the future."[62] 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[63] and artists in Egypt who designed IQOS-branded items like t-shirts, tote bags, and towels in what is described as a "lifestyle campaign."[64] 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.[65] PMI launched a marketing campaign in Fort Lauderdale, FL, with an exclusive concert featuring Grammy-winning artists Lauryn Hill and Wyclef Jean.[66] 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.[67]

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[62] *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/.

[63] 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.

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

[65] 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/.

[66] 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/.

[67] 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 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

V. FDA's Conclusions Supporting a Rule Prohibiting Menthol Cigarettes Undercut Any Justification for Renewal of the MRGO 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.[68] 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.[69]

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."[70] 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."[71] 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

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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.

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

[69] 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.

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

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

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."[72] 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.

CONCLUSION

We urge TPSAC to take account of the developments discussed above and recommend the denial of the renewal application.

Respectfully submitted,

Campaign for Tobacco-Free Kids

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

June 2024 Letter

June 27, 2024

Dr. Brian King
Director, Center for Tobacco Products
U.S. Food and Drug Administration
10903 New Hampshire Ave.
Silver Spring, MD 20993-0002

Sent by e-mail

Dear Dr. King:

As you are aware, within the last several years, the U.S. Food and Drug Administration (FDA) has granted various marketing granted orders (MGOs) and modified risk orders (MROs) to affiliates of Philip Morris International (PMI and its affiliates hereinafter referred to as PMI) for its IQOS heated tobacco system and its Heatstick components (hereinafter referred to as IQOS). PMI now has applied for renewal of its "exposure modification order" for IQOS 3,[1] as well as filing for premarket authorization of ILUMA, its next-generation IQOS product, and for a modified exposure order for ILUMA that seeks to make the same "reduced exposure" claim it was authorized to make for IQOS 3. We write to ensure that FDA consider various developments since these orders were granted for IQOS that bear on whether the previously granted modified exposure orders should be renewed and whether the marketing order and modified exposure applications for ILUMA should be granted. Those developments fall into three categories:

(1) Recent independent studies of IQOS in other countries fail to show a population-wide public health benefit;

(2) PMI repeatedly has made misleading and deceptive statements wrongly suggesting that FDA has found that IQOS reduces the risk of disease; and

(3) FDA's own conclusions supporting a prohibition of menthol cigarettes contradict any justification for continued or future authorization of menthol-flavored IQOS.

Background

Following the grant of the MGO on April 30, 2019, Altria, the exclusive distributor of IQOS in the United States, began selling IQOS in September 2019 in Atlanta, GA, before expanding its sales to Richmond, VA in November 2019 and to Charlotte, NC in July 2020. By late 2021, IQOS and Heatsticks were available throughout Georgia, Virginia, North Carolina, and

[1] Under Section 911 of the FDCA, such exposure modification orders are a type of "modified risk" order. *See* 21 U.S.C §387k(b)(1) and (2)(A)(i).

South Carolina.[2] However, in September 2021, the U.S. International Trade Commission ruled against PMI in a patent infringement action brought by British American Tobacco and imposed a ban on imports of IQOS into the U.S.[3] Altria announced that it would stop selling IQOS and Heatsticks in the U.S. on November 29, 2021[4] and, in January 2022, the company announced that it did "not expect to have access to IQOS devices or Marlboro Heatsticks in 2022."[5] Thus, IQOS was available in the U.S. for approximately two years (2019-2021). PMI has announced that it plans to reintroduce early versions of IQOS in four cities in two states in the second quarter of 2024, using the distribution system of Swedish Match, its newly acquired subsidiary.[6] In July 2023, PMI filed for renewal of its "exposure modification order" for IQOS 3.[7]

In October 2023, PMI filed for premarket authorization of ILUMA, its next-generation IQOS product, and also filed a modified risk application for ILUMA that seeks to make the same "reduced exposure" claim it was authorized to make for IQOS 2.4 and 3. The company has stated it plans a national roll-out of ILUMA following the grant of a marketing order, reaching ten states in the first year, and using the distribution system of Swedish Match.[8]

Various public health organizations have submitted multiple filings with FDA opposing the marketing and modified risk orders granted to PMI for its IQOS products on several grounds,[9] including the following:

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[2] Campaign for Tobacco-Free Kids (Tobacco-Free Kids), *Heated Tobacco Products: Philip Morris International's IQOS*, at 2 (Mar. 28, 2022), https://assets.tobaccofreekids.org/factsheets/0404.pdf.

[3] *Certain Tobacco Heating Articles & Components Thereof,* Inv. No. 337-TA-1199, Notice of the Commission's Final Determination Finding A Violation of Section 337; Issuance of a Limited Exclusion Order and Cease and Desist Orders; Termination of the Investigation, 2021 WL 4520945 (U.S. Int'l Trade Comm'n Sep. 29, 2021).

[4] Altria, *IQOS and the ITC Decision*, Dec. 31, 2021 archive accessed from Wayback Machine, https://web.archive.org/web/20211231035553/https://www.altria.com/about-altria/our-voice-and-actions/iqos-and-the-itc-decision.

[5] Seeking Alpha, Altria Group, Inc. (MO) CEO Billy Gifford on Q4 2021 Results - Earnings Call Transcript (Jan. 27, 2022), https://seekingalpha.com/article/4482171-altria-group-inc-mo-ceo-billy-gifford-on-q4-2021-results-earnings-call-transcript.

[6] PMI, Philip Morris International's 2023 Investor Day Transcript, at 68 (Sep. 28, 2023), https://philipmorrisinternational.gcs-web.com/static-files/539f900e-e06e-469d-8851-934a5c0bf334.

[7] *Id.* at 51.

[8] *Id.* at 68.

[9] The undersigned here incorporate those filings by reference. *See* Comments of Tobacco-Free Kids to TPSAC, Docket No. FDA-2017-N-5994 (January 3, 2018), https://assets.tobaccofreekids.org/images/content/2018_01_03_CTFK_IQOS_comments.pdf; Letter from Matthew Myers to CTP Director Mitch Zeller re Global Marketing of IQOS by PMI (March 23, 2018), https://assets.tobaccofreekids.org/press_office/2018/2018_03_28_IQOS_global_marketing.pdf; Letter from Matthew Myers to CTP Director Mitch Zeller re Social Media Marketing of IQOS in the United States by PMI (August 13, 2018), https://assets.tobaccofreekids.org/content/what_we_do/federal_issues/fda/2018_08_13_IQOS_FDA_Social_Media_Marketing.pdf; Comments of Public Health Groups in Docket No. FDA-2017-D-3001 (February 11, 2019), https://assets.tobaccofreekids.org/content/what_we_do/federal_issues/fda/regulatory/2019_02_11_Public_Health_Groups_Comments_IQOS_MRPTAs.pdf; Letter of Public Health Groups to CTP Director Mitch Zeller re Marketing Order for IQOS (May 14, 2019), https://assets.tobaccofreekids.org/content/what_we_do/federal_issues/fda/2019_05_14_youth_marketing_iqos.pdf; Comments of Public Health Groups in Docket No. FDA-2021-N-0408 (December 10, 2021), https://assets.tobaccofreekids.org/content/what_we_do/federal_issues/fda/regulatory/2021_12_10_IQOS-3-MRTPA-Comments.pdf.

- PMI presented insufficient evidence on the impact of the marketing of IQOS with modified risk claims on non-users of tobacco products, including youth.
- PMI presented insufficient evidence that its marketing will target only adult smokers, particularly in light of its marketing of IQOS abroad, which reaches youth, and its social media marketing,[10] which reached youth in the U.S. prior to the issuance of a marketing order.
- PMI did not provide information on the impact of marketing menthol IQOS products with modified risk claims on the Black population and youth.
- The evidence indicates that the marketing of IQOS with modified risk claims will lead to greater dual use with cigarettes instead of leading substantial numbers of smokers to switch completely to IQOS.
- There is substantial scientific uncertainty about the extent of individual health benefits from complete switching from cigarettes to IQOS.

New Developments Bearing on IQOS Marketing and Modified Risk Orders

New developments since the issuance of the marketing and modified risk orders for IQOS indicate that the reintroduction of the IQOS products as modified risk products, and the marketing of ILUMA as a modified risk product, will fail to meet the "appropriate for the protection of the public health" statutory standard. First, recent independent studies of IQOS in other countries fail to identify any population-wide benefit from this product. Second, PMI has shown that if its reduced exposure claims are permitted, the company will convert FDA's authorization into claims that IQOS products are reduced risk products. After FDA authorized specific reduced exposure statements in July, 2020, PMI officials repeatedly made misleading and deceptive public statements suggesting that the FDA found IQOS to be less harmful or to present less of a risk of disease than one or more other tobacco products, when FDA has found the evidence insufficient to establish a lower risk of disease from IQOS. Third, FDA's own conclusions supporting a rule prohibiting menthol cigarettes undercut any justification for the authorization of menthol-flavored IQOS.

I. RECENT INDEPENDENT STUDIES OF IQOS IN OTHER COUNTRIES FAIL TO SHOW A POPULATION-WIDE PUBLIC HEALTH BENEFIT

Recent research on the impact of IQOS in other countries fails to demonstrate a public health benefit from the introduction of IQOS, indicating that marketing and modified risk orders sought by PMI may not be appropriate for the protection of public health.

In January 2022, Cochrane Library issued *Heated tobacco products for smoking cessation and reducing smoking prevalence*, reviewing the available studies of these products, of which the majority were produced by tobacco companies and were determined by Cochrane reviewers to be at unclear or high risk of bias. The review concluded, "No studies reported on the

[10] PMI's global social media marketing of IQOS is discussed in Tobacco Free Kids' Report *#SponsoredByBigTobacco: Tobacco & Nicotine Marketing on Social Media* (Dec. 2023). https://assets.tobaccofreekids.org/content/what_we_do/industry_watch/social-media-marketing-tactics/2023_12_08_SponsoredByBigTobacco.pdf.

use of heated tobacco for cigarette smoking cessation, so their effectiveness for this purpose remains uncertain."[11]

Because PMI first introduced IQOS in Japan in 2014, it often points to that country as a model example of its success, showing high rates of "conversion" from cigarettes to IQOS and declines in cigarette sales paired with increases in IQOS sales.[12] Importantly, Japan regulates tobacco products very differently from the U.S.; for instance, nicotine e-cigarettes can only be sold in Japan if they have received approval as medicinal products, and no such products have been approved.[13] In Japan, therefore, e-cigarettes do not compete in a legal market with heated tobacco products (HTPs). As the Cochrane Library report commented about the experience in Japan, "The rate of decline in cigarette sales accelerated after the introduction of heated tobacco to market in Japan but, as data were observational, it is possible other factors caused these changes. Moreover, falls in cigarette sales may not translate to declining smoking prevalence, and changes in Japan may not generalize elsewhere."[14] For comparison, an analysis of sales data in Poland, where both e-cigarettes and HTPs are available, showed that HTP sales added to the steady conventional cigarette sales,[15] rather than coinciding with a decline in those sales.

Analysis of data from the International Tobacco Control Policy Evaluation Project (ITC Project), presented in a session at the 2023 Society for Research on Nicotine and Tobacco Annual Conference, showed not only that PMI's claims about complete switching rates in Japan are inaccurate, but that most smokers become dual users and actually increase their overall tobacco consumption as a result. Gravely, et al., found that only 17% of IQOS users had "completely transitioned" to IQOS in 2020, compared to the 73% that PMI claimed in its Shareholder report.[16]

Fong, et al.,[17] found a higher likelihood of transitioning from exclusive smoking to long-term dual use of cigarettes and HTPs compared to transitioning to exclusive HTP use. They did not find an association between long-term HTP use and greater likelihood of quitting cigarettes. Finally, they determined that smokers who had ever used HTPs were less likely to quit all tobacco compared to those who had never used HTPs. The researchers concluded, "The dramatic

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[11] 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.

[12] *See, e.g.*, PMI, *Can innovative products like IQOS accelerate the decline of smoking?* (last accessed Dec. 13, 2023), https://www.pmi.com/sustainability/case-studies-and-market-stories/can-innovative-products-like-iqos-accelerate-the-decline-of-smoking.

[13] https://globaltobaccocontrol.org/en/policy-scan/e-cigarettes/countries?country=101.

[14] Tattan-Birch et al., *supra* at 11.

[15] Alex C. Liber et al., *Poland is not replicating the HTP experience in Japan: a cautionary note*, 32 TOBACCO CONTROL 524 (2023), https://pubmed.ncbi.nlm.nih.gov/34876532/.

[16] The analysis was conducted using PMI's characterization of "completely transitioned," defined as at least 95% of respondents' total tobacco consumption coming from HTPs. Gravely, S, et al. An Examination of Philip Morris International's Estimate of IQOS Consumers Who Have "Completely Transitioned" From Cigarettes: Findings From the 2018/19 and 2020 ITC Japan Surveys. Presentation at 2023 Society for Research on Nicotine and Tobacco Annual Meeting. March 3, 2023 (attached as Exhibit 1).

[17] Fong, GT, et al. Transitions of Tobacco Product Use Among Adults Who Smoke Cigarettes and Adults Who Use Heated Tobacco Products (HTPs) in Japan: Initial Findings from Three Waves of the ITC Japan Cohort Survey (2018-20). Presentation at 2023 Society for Research on Nicotine and Tobacco Annual Meeting. March 3, 2023 (attached as Exhibit 2).

decrease in cigarette sales and the increase in HTP sales in Japan is likely due (nearly) entirely to partial substitution among smokers who are now duals, and likely to become long-term duals rather than due to smokers quitting or transitioning to using neither product."

In looking at cigarette and HTP stick consumption among those who transitioned between various stages of use in Japan, Xu, et al.,[18] found that dual users added more HTP sticks than they reduced cigarettes, resulting in an increase in overall tobacco consumption. Along with those from a small preliminary study, where switchers had higher IQOS consumption,[19] these findings may indicate a possible new pattern of use about which the health consequences are unknown. Even if IQOS or HTPs provide lower exposure to toxicants than cigarette smoking, if consumption is higher, this may not translate into a reduction of a user's risk.

The ITC Project's data from South Korea, presented at the 2024 Society for Research on Nicotine and Tobacco Annual Conference, showed similar results to those for Japan. Analysis found substantially lower rates of complete switching among cigarette and IQOS users, indicating that PMI exaggerated its claims of switching.[20] A separate study found high rates of dual use among cigarette smokers who took up HTPs and very low rates of complete switching among cigarette smokers, leading to the conclusion that "HTP use was not associated with smoking cessation but with a very high percentage of HTP-cigarette dual use (>95%)."[21] A third study found increases in total tobacco consumption among dual users, due to added HTP stick use that outweighed the slight reduction in cigarettes smoked.[22] Of note, South Korea allows the sale of e-cigarettes, like in the U.S., but in the ITC Project's analysis, e-cigarette use did not have a measurable impact on the results.

Thus, analyses of the IQOS experiences in Japan and South Korea demonstrate that dual use is the most common use pattern, leads to increased tobacco consumption, and tends to be long-term and not associated with complete quitting of all tobacco products. The available independent research, therefore, does not indicate that IQOS produces any real benefits for individual or population health.

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[18] Xu, SS, et al. Changes in Cigarette and Total Tobacco Consumption Among People Who Smoke Who Did and Did Not Initiate Heated Tobacco Products: Findings from the 2018-2021 ITC Japan Surveys. Presentation at 2023 Society for Research on Nicotine and Tobacco Annual Meeting. March 3, 2023 (attached as Exhibit 3).

[19] Matthew D. Stone et al*., Switching from cigarettes to IQOS: A pilot examination of IQOS-associated reward, reinforcement, and abstinence relief*, 238 DRUG & ALCOHOL DEPENDENCE (2022), https://www.sciencedirect.com/science/article/abs/pii/S0376871622003064?via%3Dihub.

[20] Gravely, S, et al. An Examination of Philip Morris International's Estimate of Korean Adults Who Have "Completely Transitioned" from Cigarettes to IQOS: Findings from the 2020 and 2021 ITC Korea Surveys. Presentation at 2024 Society for Research on Nicotine and Tobacco Annual Meeting. March 23, 2024 (attached as Exhibit 4).

[21] The study found that only 0.3% of exclusive cigarette smokers transitioned to exclusive HTP use. Fong, GT, et al. Transitions between Cigarettes and Heated Tobacco Products among Adults Who Use Vs Do Not Use Nicotine Vaping Products in the Republic of Korea: Findings from the 2020, 2021, and 2023 ITC Korea Surveys. Poster Presentation at 2024 Society for Research on Nicotine and Tobacco Annual Meeting. March 22, 2024 (attached as Exhibit 5).

[22] Xu, SS, et al. Changes in Total Tobacco Consumption among Korean Adults When Transitioning Between Exclusive Cigarette Smoking and Dual Use of Cigarette and Heated Tobacco Products: Findings from the 2020-2023 ITC Korea Surveys. Presentation at 2024 Society for Research on Nicotine and Tobacco Annual Meeting. March 23, 2024 (attached as Exhibit 6).

II. PMI REPEATEDLY HAS MADE MISLEADING AND DECEPTIVE STATEMENTS WRONGLY SUGGESTING THAT FDA HAS FOUND THAT IQOS REDUCES THE RISK OF DISEASE

The MGO granted for IQOS 2.4 in 2019 was followed by the grant of PMI's modified risk application on July 7, 2020. It is critical to understand that PMI's application sought to make two kinds of modified risk claims in marketing IQOS: (1) under Section 911(g)(1) of the FDCA, a "reduced risk" claim that switching completely from conventional cigarettes to IQOS "can reduce the risks of tobacco-related diseases," and (2) under Section 911(g)(2)(A) and (B), a "reduced exposure" claim that switching completely from conventional cigarettes to IQOS "significantly reduces your body's exposure to harmful or potentially harmful chemicals."

FDA denied PMI's request for authorization to make a "reduced risk" claim (a "risk modification order") because the Technical Project Lead Scientific Review (TPL)[23] found that "the applicant **has not demonstrated** 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." TPL at 8 (emphasis in original). FDA issued only an "exposure modification order," authorizing only the following "reduced exposure" claim:

> 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.[24]

The July 7 exposure modification order specifically instructs PMI that "because these products have not been authorized under section 911(g)(1) (risk modification order) you may not market these products with reduced risk claims." In addition, FDA stated that it would monitor PMI's marketing of the product.[25]

The importance of this instruction to PMI follows from the provisions of the FDCA governing modified risk applications. The authorization to make "reduced exposure" claims under Section 911(g)(2) requires companies to refrain from marketing the authorized tobacco product as a reduced risk product under Section 911(g)(1). Moreover, the authorization to make "reduced exposure" claims requires a showing that:

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[23] https://www.fda.gov/media/139796/download?attachment.
[24] Modified Risk Granted Orders – Exposure Modification, at 1 (July 7, 2020), https://www.fda.gov/media/139797/download?attachment.
[25] *Id.* at 2 (emphasis in original).

(iii) testing of actual consumer perception shows that, as the applicant proposes to label and market the product, 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.[26]

Thus, the July 7 exposure modification order limited the statements that PMI could make so that consumers will not be misled by the "reduced exposure" claims into believing that IQOS had been demonstrated to be less harmful or to reduce the risk of tobacco-related disease. The World Health Organization (WHO), after the FDA order was issued, warned against misleading representations of the FDA action, noting that "[t]he US FDA authorization rejected claims that the use of the product is less harmful than another tobacco product or reduces risks to health," and "[t]he exposure modification orders . . . do not permit the company to make any other modified risk claims . . . ."[27]

Statements made by PMI about IQOS since FDA authorized the "reduced exposure" claim have been calculated to associate IQOS with a reduction in disease risk, in violation of the statute and FDA's instruction to PMI to avoid reduced risk claims. For example, on the day FDA authorized the marketing of IQOS with a "reduced exposure" message, a PMI press release repeatedly referred to IQOS as a "better choice" for smokers than continuing to smoke:

- "Today's decision demonstrates that IQOS is a fundamentally different tobacco product and a better choice for adults who would otherwise continue smoking."
- "The FDA's decision further builds on the emerging independent international scientific consensus that IQOS is a better choice than continuing to smoke . . . ."
- "Today's decision makes it possible to inform these adults that switching completely to IQOS is a better choice than continuing to smoke."[28]

Other statements in the press release provide added context, making it clear that the phrase "better choice" is meant to convey that IQOS is a healthier choice that reduces the risk of disease:

- "The best choice **for health** is to never start smoking or to quit altogether. For those who don't quit, the best thing they can do is switch to a scientifically substantiated smoke-free product." (emphasis added)[29]

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[26] Section 911(g)(2)(B)(iii) of the Tobacco Control Act.

[27] WHO statement on heated tobacco products and the US FDA decision regarding IQOS (July 27, 2020) (WHO statement) https://www.who.int/news/item/27-07-2020-who-statement-on-heated-tobacco-products-and-the-us-fda-decision-regarding-iqos.

[28] PMI, *FDA Authorizes Marketing of IQOS as a Modified Risk Tobacco Product* (July 7, 2020) (statement by PMI CEO Andre Calantzopoulos), https://www.pmi.com/media-center/press-releases/press-details/?newsId=22631.

[29] This identical statement also was posted on the PMI website. *See* PMI, *U.S. FDA authorizes PMI's IQOS as a modified risk tobacco product (MRTP)* (July 7, 2020) https://www.pmi.com/media-center/news/fda-authorizes-pmi-iqos-as-modified-risk-tobacco-product.

- "PMI is building a future on a new category of smoke-free products that, while not risk-free, are a much better choice than continuing to smoke."

These statements from PMI convey the message that switching from conventional cigarettes to IQOS is a "better choice" because IQOS reduces the risk of harmful health effects. This is precisely the kind of "reduced risk" claim that PMI was instructed by FDA not to make in its marketing of IQOS because the science does not support such a claim.

PMI repeatedly has made similar "reduced risk" statements to support its efforts to use the FDA exposure modification order to promote IQOS globally and, particularly, to lobby foreign governments to create a legislative and regulatory environment favorable to IQOS:

- In September of 2020 during a webinar in the Philippines, Stacey Kennedy of PMI Asia Pacific operations, said, "**IQOS, our leading flagship brand in the reduced risk portfolio**, **was granted the modified risk tobacco claim in the United States**." According to a news article covering the webinar, Ms. Kennedy also "explained [that] the US FDA decision has effectively differentiated IQOS from combustible products **when it comes to health risk**."[30]

- An ad in Mexico mentions that IQOS has "been authorized by the U.S. Food and Drug Administration (FDA) as a product of 'modified risk'" and then later includes a quote from a PMI official that PMI wants to inform smokers "about the **lower risk alternatives**" that exist in Mexico.[31]

- In an April 2022 letter to the Prime Minister of Kazakhstan referencing the FDA modified risk order, PMI threatened to pull back investments in Kazakhstan if the country didn't share "the same views on the **reduced risk potential** of our next generation products and an appropriate regulatory framework."[32]

Thus, PMI has repeatedly misrepresented its FDA exposure modification order—in violation of that order—to create a favorable environment for the sale of IQOS in multiple countries.

In evaluating these misleading statements, FDA should recognize that the term "modified risk tobacco product" in the TCA is not limited to products with claims of reduced risk made in advertising for the product. Rather, the term is broadly defined to include a tobacco product "the manufacturer of which has taken any action directed to consumers through the media or otherwise, other than by means of the tobacco product's label, labeling or advertising . . . that would be reasonably expected to result in consumers believing that the tobacco product . . . may present a lower risk of disease . . . or presents a reduced exposure to . . . a substance or substances."[33] The PMI statements quoted above, in press releases, webinars, advertisements and

[30] https://mb.com.ph/2020/09/07/philip-morris-urges-ph-to-adopt-us-fda-finding/ (September 7, 2020) (emphasis added).
[31] https://lifeandstyle.expansion.mx/bespoke-ad/2021/08/19/iqos-y-el-proceso-de-cambio-para-evolucionar (June 21, 2021) (emphasis added) (certified English translation attached as Exhibit 7).
[32] Exhibit 8, at 1 (emphasis added).
[33] 21 U.S.C. §387k(b)(2)(A)(iii).

letters to public officials and legislative bodies, arguably are, either directly or indirectly, directed at consumers and can be expected to result in consumer misunderstanding of what FDA actually found. These types of promotional statements still fall within FDA's obligation to monitor PMI's marketing of IQOS, even if they are not advertising in the traditional sense.

Nor should the fact that some of the statements were made in other countries render them irrelevant to FDA's evaluation of whether PMI's pending applications should be granted. First, nothing in the TCA limits the restrictions on modified risk claims to statements made in the United States. Second, FDA has a strong interest in protecting the integrity of its orders against misrepresentation wherever it occurs. The TCA permits certain claims to be made about products in order to facilitate the communication of truthful information to consumers, not the communication of false or misleading information designed to promote the product in foreign markets. Third, in this online age, it is fanciful to imagine that the impact of a misleading statement about a product made in another country will be limited to that country, with no effect on U.S. consumers. Indeed, the notion that a statement has a single "location" has become an anachronism. For instance, as mentioned previously, PMI's paid social media marketing for IQOS from other countries still reaches young audiences in the U.S. Finally, the fact that PMI repeatedly has misrepresented the FDA orders suggests a serious risk that it will do so again in connection with any newly authorized IQOS products and claims in the U.S.

PMI's misuse of the FDA exposure modification order is particularly concerning because it exploits, and likely exacerbates, the tendency of consumers to interpret reduced exposure claims as indicating reduced risk. One recent study examined the impact of IQOS advertising with reduced exposure versus reduced risk messaging among 2,222 US and Israeli adults.[34] It found that reduced exposure (vs. control) messaging resulted in lower perceived relative harm, exposure and disease risk. According to the study, "These results suggest that consumers do not clearly disentangle the differences in the reduced risk versus reduced exposure messaging, as noted in prior research."[35] The authors cite prior research showing that "[m]any consumers misinterpret the authorized IQOS messaging regarding reduced exposure claims as indicating reduced risk."[36] They also note that since July 2020, media reports in several countries cite PMI as "mischaracterizing FDA's MRTP decision as evidence that IQOS is a reduced harm product . . . ."[37] In sum, "Current findings show 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 – and that [PMI] further exploits this potential to unduly influence consumers by misrepresenting FDA authorization in other countries."[38]

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[34] 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*, TOBACCO CONTROL (published online ahead of print, 2022 Nov. 25), https://tobaccocontrol.bmj.com/content/early/2022/11/24/tc-2022-057639.
[35] *Id.* at 7.
[36] *Id.* at 2. Indeed, PMI's own qualitative and quantitative studies, submitted to FDA in support of its modified risk application, showed that "reduced exposure claims are likely to be perceived as reduced risk claims and will, therefore, mislead the public." Lucy Popova et al., *Light and mild redux: heated tobacco products' reduced exposure claims are likely to be is understood as reduced risk claims*, 27 (Suppl. 1) TOBACCO CONTROL s87, s91-92 (2018), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6202239/.
[37] Berg et al., *supra*, at 2.
[38] *Id.* at 7.

Another recent study shows that PMI's misleading messaging is reflected in news coverage of the FDA exposure modification order in low- and middle-income countries. A survey of news articles mentioning the FDA order appearing in the months following its issuance found that 52% of them incorrectly stated that FDA has determined IQOS to be a reduced risk product or that IQOS is a reduced harm product, while 38% of the articles correctly described the FDA order by using only reduced exposure language.[39] According to the authors, these results suggest that "reduced exposure is sometimes misreported as reduced risk in the news media," which is "consistent with findings from independent experimental studies and studies of consumer understanding submitted by PMI as part of their MRTP application, which found that consumers who viewed reduced exposure claims reported lower risk perceptions."[40] For example, a May 2023 Greek news article covering a presentation by the head of PMI Europe incorrectly reported that the FDA "has approved IQOS . . . as a **differentiated risk tobacco product** . . . ." in an article discussing "harm reduction" achieved through tobacco products of "differentiated risk."[41]

This research raises serious questions as to whether PMI's IQOS products can satisfy the requirements of Section 911(g)(2) that, with regard to authorization of a reduced exposure product, there must be a finding that "consumers will not be misled into believing that the product" is "less harmful" or presents "less of a risk of disease than 1 or more other commercially marketed tobacco products." In light of PMI's statements, and public perceptions, following the 2020 exposure modification order, there should be a heavy presumption that FDA cannot make such a finding for IQOS.

III. FDA'S OWN CONCLUSIONS SUPPORTING A PROHIBITION OF MENTHOL CIGARETTES UNDERCUT ANY JUSTIFICATION FOR CONTINUED OR FUTURE AUTHORIZATION OF MENTHOL-FLAVORED IQOS

The marketing orders granted by FDA for IQOS include "Smooth Menthol" and "Fresh Menthol" Heatsticks (which have been renamed "Green Menthol and "Blue Menthol" respectively). FDA also has authorized modified exposure claims for these menthol IQOS products. The marketing and modified risk applications for ILUMA also include the brands TEREA BLUE and TEREA GREEN, which presumably are menthol-flavored as well. Since FDA issued the marketing orders and modified risk orders for IQOS products, including the menthol-flavored products, the agency has proposed a Rule prohibiting menthol as a characterizing flavor in cigarettes, which has been transmitted as a Final Rule for review by the Office of Information and Regulatory Affairs at the Office of Management and Budget. In the preamble to the Proposed Rule, FDA requested comment on possible exceptions to the menthol Rule for certain products that meet the definition of "cigarette" in the Rule including "noncombusted" products.[42] In comments on the Proposed Rule, over 100 public health, medical,

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[39] Meagan O. Robichaud et al., *How Media Stories in Low- and Middle-Income Countries (LMICs) Discussed the US Food and Drug Administration's (FDA's) Modified Risk Tobacco Product (MRTP) Order for IQOS*, 25 NICOTINE & TOBACCO RESEARCH 1659, 1661 (2023), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10445252/.
[40] *Id.* at 1663.
[41] https://www.protagon.gr/epikairotita/to-mellon-xwris-tsigaro-pernaei-apo-tin-ellada-44342719064 (May 11, 2023) (emphasis added) (certified English translation attached as Exhibit 9).
[42] FDA, Proposed Rule, Tobacco Product Standard for Menthol in Cigarettes, 87 Fed. Reg. 26,454, 26,487 (May 4, 2022) ("Proposed Menthol Rule").

education, civil rights and community organizations argued that no such exception for IQOS or other heated products would be appropriate for the protection of the public health.[43]

In the Preamble to the Proposed Rule on Menthol Cigarettes, FDA concluded that "menthol in cigarettes increases smoking initiation."[44] By producing "a minty taste and cooling sensation when inhaled" menthol makes cigarettes more palatable for new users and facilitates "experimentation and regular use, particularly among younger smokers."[45] These findings, premised on menthol's sensory effects, likely would also apply to heated cigarettes that contain menthol, such as menthol-flavored IQOS products, including ILUMA.

FDA also found that the interaction of menthol and nicotine in the brain enhances nicotine addiction, particularly among young people.[46] According to FDA, "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.[47] 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 all IQOS products. Thus, all menthol-flavored IQOS products would be expected to have a similar impact.

Finally, as FDA has established, due to the industry's decades of targeting Black communities, and other underserved populations, with marketing for menthol cigarettes, their continued presence on the market substantially contributes to disparities in cigarette use and the resulting disparities in health outcomes. In proposing the Rule to prohibit menthol as a characterizing flavor in cigarettes, FDA determined that "[m]embers of underserved communities, such as African American and other racial and ethnic populations, individuals who identify as LGBTQ+, pregnant persons, those with lower household income or educational attainment, and individuals with behavioral health disorders are more likely to report smoking menthol cigarettes than other population groups" and thus "bear a disproportionate burden of tobacco-related morbidity and mortality."[48] 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.

Indeed, IQOS menthol products may significantly undermine achievement of the smoking cessation goals set by the *HHS Framework to Support and Accelerate Smoking Cessation 2024,* particularly as to Black communities and other underserved populations that are the focus of the *Framework.*[49] As FDA has found, "The totality of scientific evidence on menthol

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[43] Comments filed in Docket No. FDA-2021-N-1349 (August 2, 2022), at 29-30, https://assets.tobaccofreekids.org/content/what_we_do/federal_issues/fda/Support_Prohibiting_Menthol_Cigarettes_8_2_2022.pdf.
[44] Proposed Menthol Rule, 87 Fed. Reg. at 26,463.
[45] *Id*.
[46] *Id*. at 26,468.
[47] *Id*. at 26,465.
[48] *Id*. at 26,458.
[49] https://www.hhs.gov/sites/default/files/hhs-framework-support-accelerate-smoking-cessation-2024.pdf.

and cessation supports the conclusion that menthol cigarettes contribute to reduced cessation success, particularly among Black smokers."[50]

Thus, FDA's conclusions supporting a prohibition of menthol cigarettes contradict any justification for continued or future authorization of menthol-flavored IQOS.

Conclusion

The undersigned urge FDA, in considering PMI's marketing and modified risk applications for IQOS, to take into account these recent developments, as they directly bear on whether PMI should be permitted to market IQOS in the U.S. and whether it should be permitted to make modified risk claims in connection with IQOS.

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

[50] Proposed Menthol Rule, 87 Fed. Reg. at 26,468.

EXHIBIT 1

An Examination of Philip Morris International's Estimate of IQOS Consumers Who Have "Completely Transitioned" From Cigarettes: Findings From the 2018/19 and 2020 ITC Japan Surveys

Shannon Gravely[1], Gang Meng[1], Steve Shaowei Xu[1], Christian Boudreau[1], Mary Thompson[1], Takahiro Tabuchi[2], Kota Katanoda[3], Itsuro Yoshimi[4], K. Michael Cummings[5], Andrew Hyland[6], and Geoffrey T. Fong[1,7]

[1] University of Waterloo, Canada; [2] Cancer Control Center, Osaka International Cancer Institute, Japan; [3]Japan National Cancer Center, Japan; [4] National Cancer Center Japan; [5] Medical University of South Carolina, USA; [6] Roswell Park Comprehensive Cancer Center, USA; [7]Ontario Institute for Cancer Research

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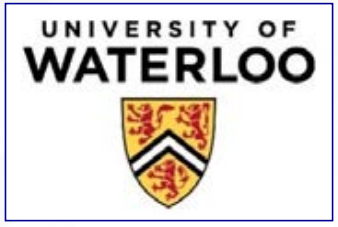

Disclosures and Funding

International Tobacco Control Policy Evaluation Project

The authors have no relationships with industry to disclose

Disclosures of Interests:

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- Geoffrey T. Fong has served as an expert witness or consultant for governments defending their country's policies or regulations in litigation.
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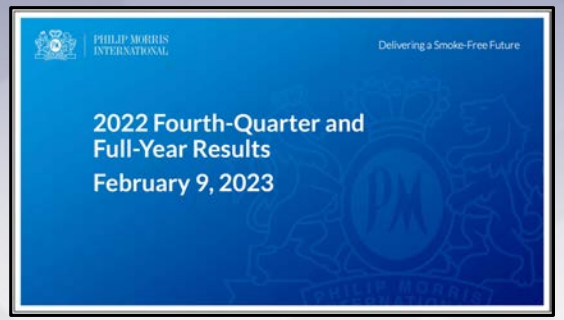
- K. Michael Cummings has served as a paid expert witness in litigation against cigarette manufacturers in the United States.
- All other authors including the presenter have no conflict of interests to declare.

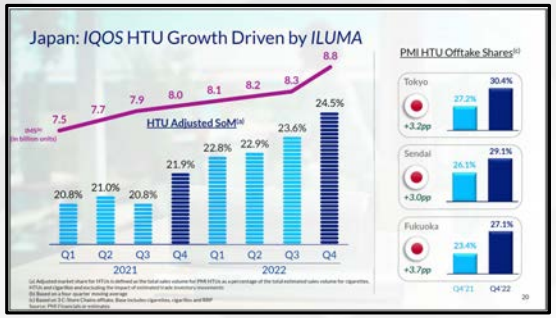
Funding:

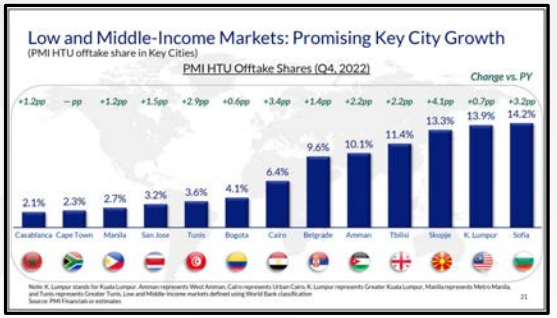
The ITC Japan Project was supported by the Japan National Cancer Center and Research Development Fund (28-A-24) and the Canadian Institutes of Health Research Foundation Grant (FDN-148477). Additional support to GTF is provided by a Senior Investigator Grant from the Ontario Institute for Cancer Research (IA-004). The funding agencies did not have any role in study design, collection, analysis, and interpretation of the data.

Background

- Philip Morris International (PMI) quarterly reports include information about the performance and growth of IQOS
- As of 2022, IQOS was being sold in nearly 70 countries
- 2021: 28% of PMIs net revenues
- Volume, growth, success in converting people who smoke to IQOS





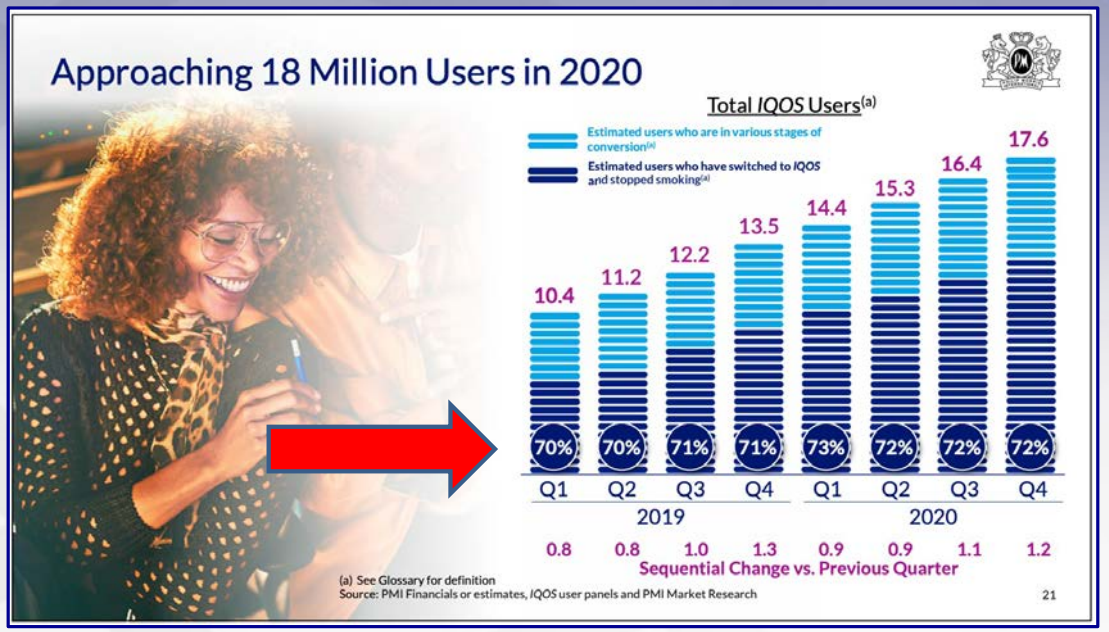


Have IQOS consumers stopped smoking?

PMI Definition:

"Completely Transitioned"

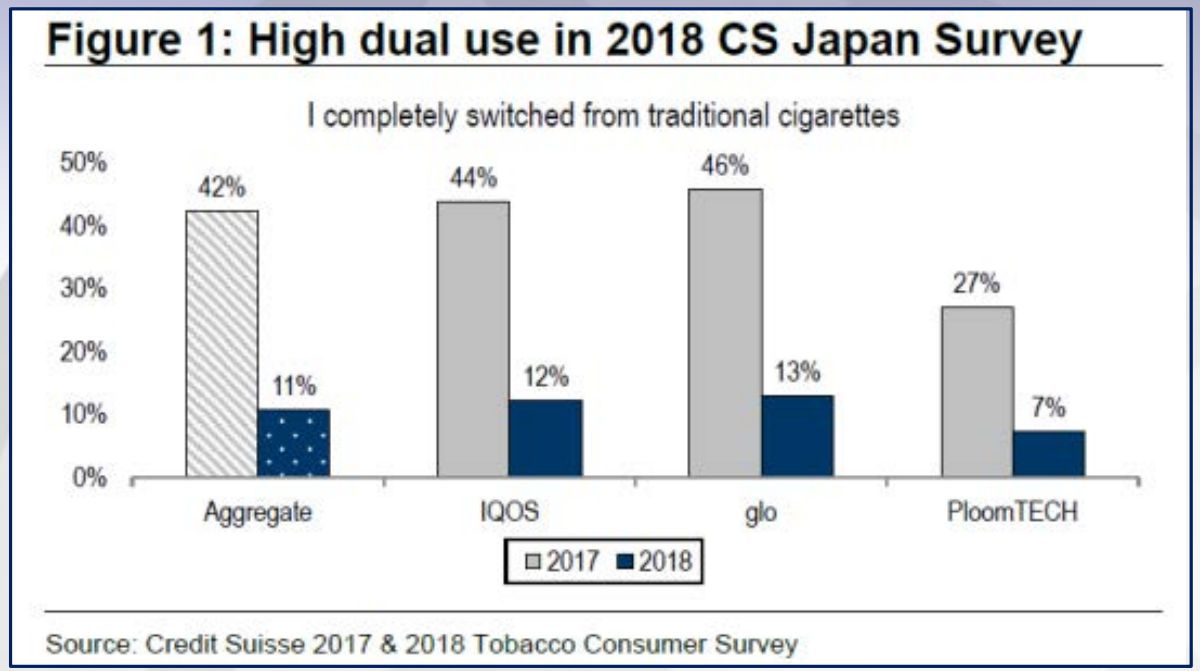
At least 95% of total tobacco consumption is from HTPs



PMI reports that in their IQOS Customer Survey, the percentage of IQOS consumers who had completely transitioned from cigarettes was:

- 70% in Q1 2019
- 72% in Q2 2020

What do non-industry studies say?



Industry-independent studies in Japan using nationally representative data have shown that about **2/3 of HTP consumers are continuing to smoke cigarettes**.

That is, **only about 1/3 of HTP consumers have "completely transitioned."**

(Tabuchi et al. 2018; Santos et al. 2019)

Important for industry-independent studies to test PMI's reports that 70-72% of IQOS consumers have "completely transitioned" from cigarettes to IQOS (and other HTPs)

Study Objectives

- Cross-sectional study using national data from the ITC Japan Surveys at:
  - ➢ Wave 2 (Dec 2018-Feb 2019) and
  - ➢ Wave 3 (May-Jun 2020) to calculate:
    - – The proportion of HTP consumers who have "completely transitioned" (≥ 95% HTPs) for:
      (1) IQOS
      (2) All HTPs (leading brands: IQOS, Ploom TECH & glo)
    - – Compare ITC proportions to PMI's

ITC Japan Survey & PMI Japan IQOS Customer Survey

	ITC	PMI
Survey type	Online	Online
Survey design	Cohort sample with replenishment	Cross-sectional
Respondent Source	Rakuten Insight (survey firm)	IQOS users registered on the PMI IQOS User Database
Data source	Wave 2 (Dec 2018-Feb 2019) Wave 3 (May-Jun 2020)	Year 3 (2019). Source: Q1 2019 report Year 4 (2020-2021). Source: Q2 2020 report
Eligibility criteria	Use HTPs ≥ weekly	Past 30-day IQOS consumers
	Aged 20+ years	Aged 20+ years
	Used ≥ 100 HTP sticks/lifetime	Used ≥ 100 HTP sticks/lifetime
HTPs	HTPs: IQOS, glo, Ploom TECH	IQOS and other HTPs (brands not stated)
Sample size	W2: N=520 IQOS, 543 other HTPs W3: N=854 IQOS, 656 other HTPs	Year 3: N=2013 IQOS users Year 4: N=2000 IQOS users

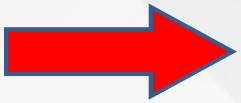
*ITC: people who currently and formerly smoked (<weekly cigarette use and former smoking, consumption of cigs = 0)

Analyses of the ITC Japan Survey data

- Cross-sectional weights were original ITC weights (using JASTIS* surveys as the benchmark) recalibrated to PMI's sex * age distribution.
- We did this to adjust the ITC data so that it was more comparable to the PMI data.
- Each Ploom TECH capsule x 4 to get number of equivalent HTP sticks

Cigarettes (CPD)+ HTPs (HPD) = total consumption (TPD)

HPD/TPD = proportion of total consumption from HTPs

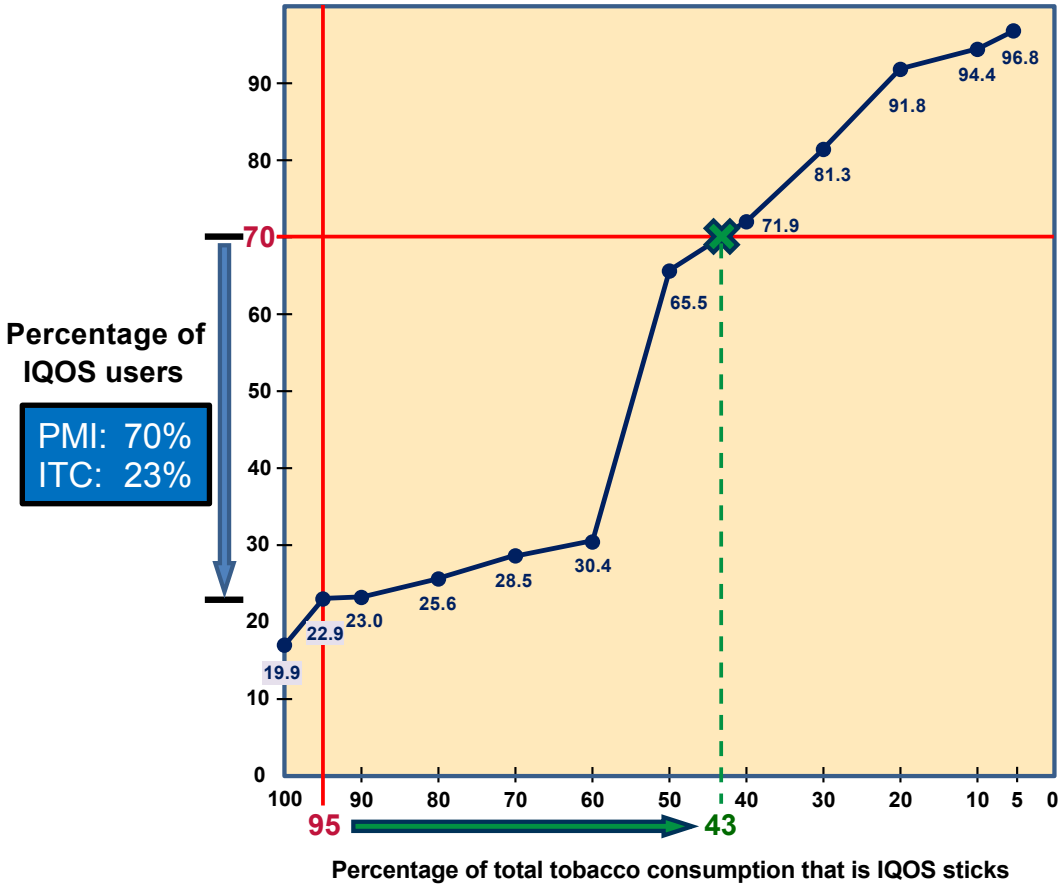


Construct the cumulative distribution of the HPD/TPD ratio from **highest** (100% and 95%: "completely transitioned") to **lowest** (5% and 0%: exclusive smoking)

***Japan** "Society and New **Tobacco**" Internet Survey (**JASTIS**); HPD: HeatSticks per day; CPD: cigarettes per day

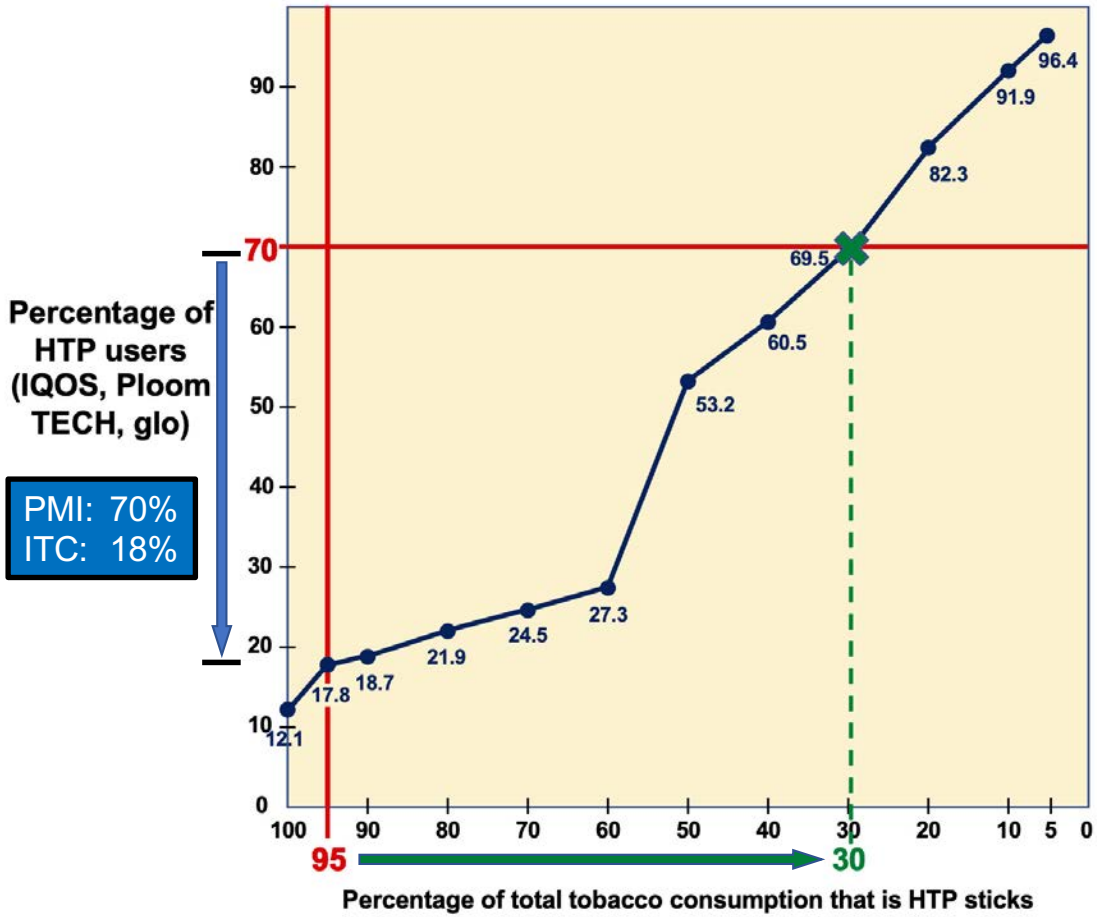

RESULTS

ITC Japan W2 (2018/19) vs. PMI (Q1 2019): ITC IQOS Consumers (N=520)



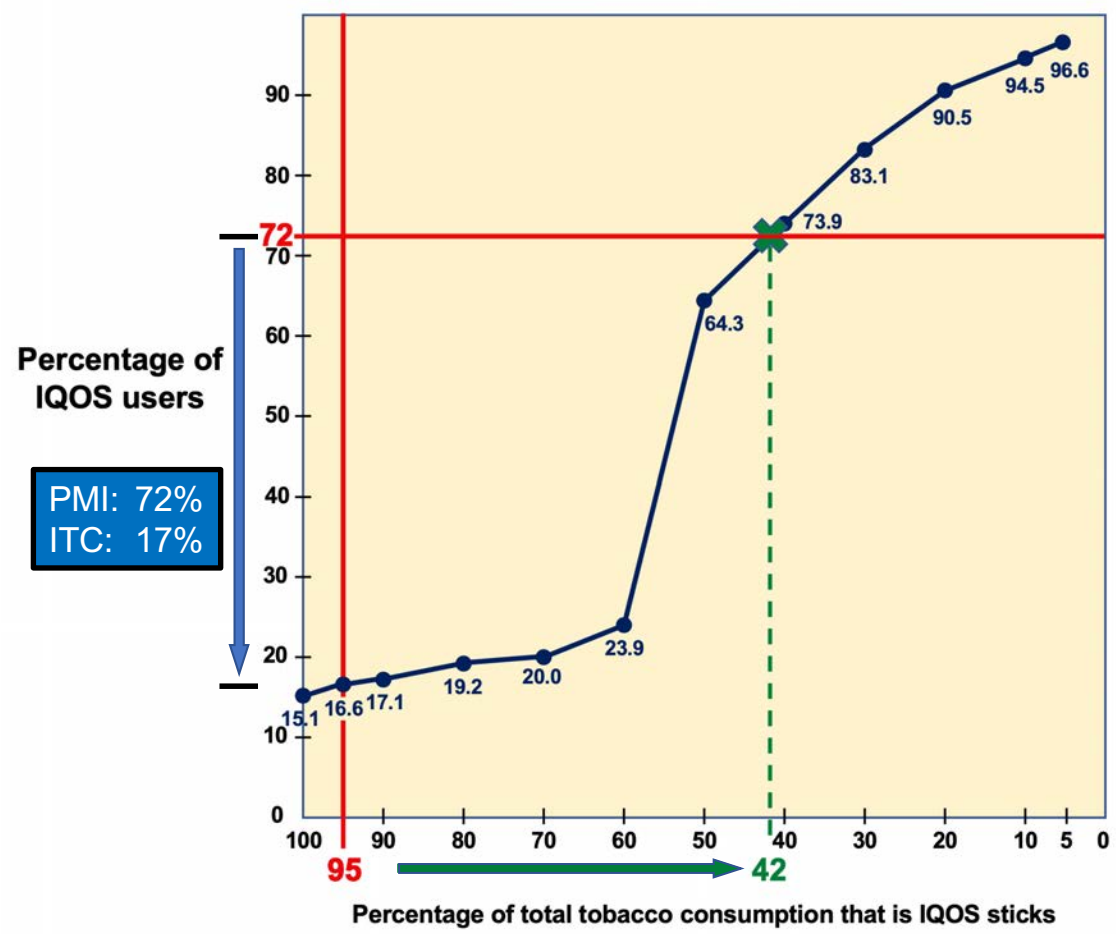
* Weighted to PMI age x sex distribution

ITC Japan W2 (2018/19) vs. PMI (Q1 2019): ITC All HTP Consumers (N=1063)



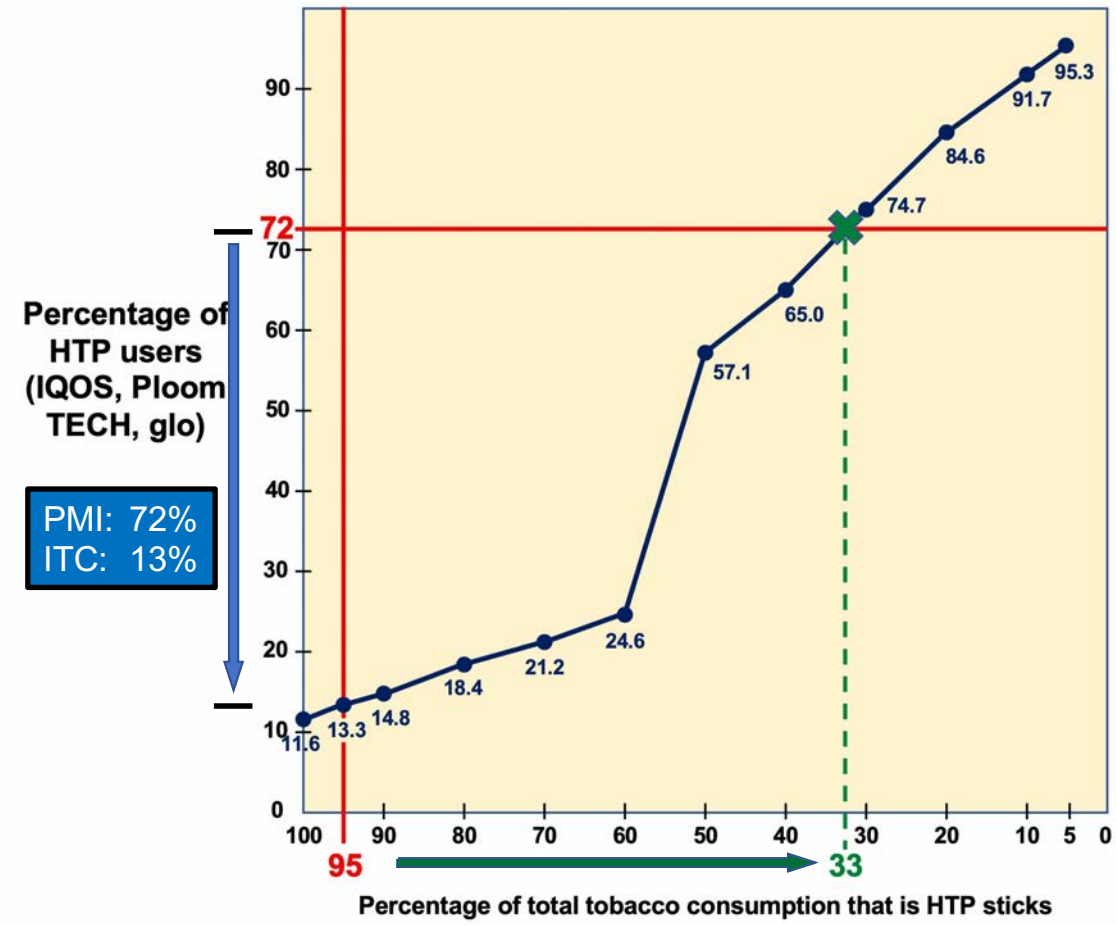
* Weighted to PMI age x sex distribution

ITC Japan W3 (2020) vs. PMI (Q2 2020): IQOS Consumers (N=854)



* Weighted to PMI age x sex distribution

ITC Japan W3 (2020) vs. PMI (Q2 2020): All HTP Consumers (N=1510)



* Weighted to PMI age x sex distribution

Summary

	% Completely Transitioned	
Data Source	2019	2020
PMI Shareholder Report from IQOS User Survey: % of IQOS Users who were completely transitioned	70%	73%
ITC: IQOS Users	23%	17%
ITC: All HTP Users	18%	13%

Summary and Conclusion

- Large discrepancy between the ITC data and the PMI data on the percentage of IQOS consumers who have “completely transitioned” from cigarettes: ITC percentages were much lower.
- Dual use is by far the dominant use pattern of those who use IQOS and other HTPs.
- IQOS customers in the survey may be more likely to be those who have completely transitioned: satisfaction with product is higher, which is strongly linked to having quit cigarettes (Xu et al.–reasons for using HTPs: 55% use HTPs because HTPs might help them quit).
- **These findings highlight the importance of non-industry research on use patterns of HTPs, particularly how HTPs interact with cigarettes.**

Major Support for the ITC Project

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International Tobacco Control Policy Evaluation Project

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P01 CA200512

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FDN-148477

Ontario Institute for Cancer Research
Senior Investigator Award (2007-2027)

ITC Project Research Organizations

ITC Project Research Support

EXHIBIT 2

International Tobacco Control Policy Evaluation Project

Transitions of Tobacco Product Use Among Adults Who Smoke Cigarettes and Adults Who Use Heated Tobacco Products (HTPs) in Japan: Initial Findings from Three Waves of the ITC Japan Cohort Survey (2018-20)

Geoffrey T. Fong[1,2]*, Gang Meng[1], Shannon Gravely[1], Mary E. Thompson[1], Steve Shaowei Xu[1], Anne C. K. Quah[1], Janine Ouimet[1], Itsuro Yoshimi[3], Kota Katanoda[3], Takahiro Tabuchi[4], K. Michael Cummings[5], Andrew Hyland[6]

[1]University of Waterloo, Canada; [2]Ontario Institute for Cancer Research, Canada; [3]Japan National Cancer Center, Japan; [4]Osaka International Cancer Institute, Japan; [5]Medical University of South Carolina, USA; [6]Roswell Park Comprehensive Cancer Center, USA;

大阪国際がんセンター がん対策センター

国立研究開発法人 国立がん研究センター National Cancer Center Japan

Presented at Society for Research on Nicotine and Tobacco 29th Annual Meeting, March 3, 2023 St Antonio, Texas

***Contact: s4xu@uwaterloo.ca**

UNIVERSITY OF WATERLOO

OICR Ontario Institute for Cancer Research

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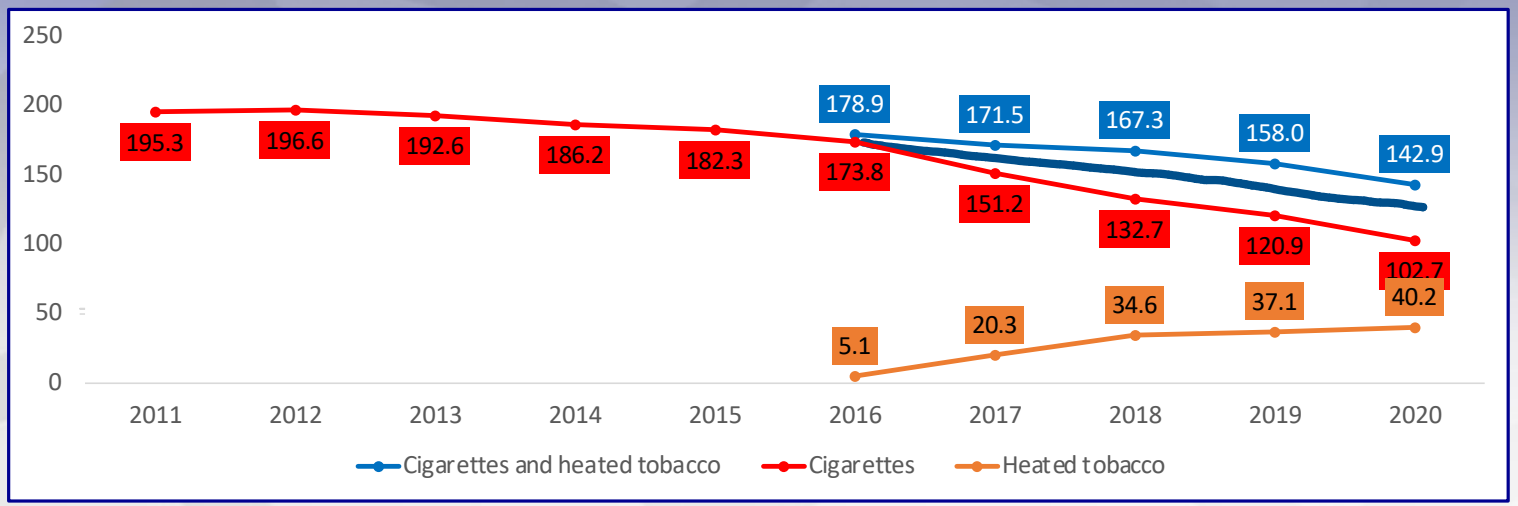
Introduction: The emergence of HTPs in Japan and the decline of cigarettes



- Japan's tobacco landscape has changed significantly with the introduction of HTPs
- Before HTPs came on the market, cigarette sales were slowly decreasing.
- After HTPs were introduced nationally in September 2015:
  - Cigarette sales have decreased more rapidly.
  - HTP consumption continued to increase.
  - Cigarettes have been partially replaced by HTPs.

Article

What Is Accounting for the Rapid Decline in Cigarette Sales in Japan?

K. Michael Cummings [1,*], Georges J. Nahhas [1] and David T. Sweanor [2]

Digging deeper: what is the interaction between cigarettes and HTPs at the individual level?

- We know that there are enormous changes taking place in Japan's tobacco market.
- The sales data are **consistent** with the idea that cigarettes are being substituted for HTPs, but these are **aggregate data**.
- It is important to understand the interplay between cigarettes and HTPs at the **individual level:**
  - To what extent are people who smoke taking up HTPs, and when they do, does this lead to quitting cigarettes, quitting HTPs and going back to cigarettes only, or quitting both cigarettes and HTPs?
  - The proportions of these transitions are critically important for making assessments of the population-level effects.
  - Are patterns of use stabilizing over time? For example: What are the expected long-term tobacco use patterns for HTP users: long-term dual use or long-term exclusive HTP use?
  - By examining transitions at the individual level, it is also possible to identify the factors associated with each kind of transition.
  - These individual-level analyses are only possible with a longitudinal cohort design.

The ITC Japan Cohort Surveys

- 4 waves conducted: JP1 in 2018, JP2 in 2018-19, JP3 in 2020, JP4 in 2021
- Recruitment from high quality national web panel (Rakuten Insight)
- Survey design: Longitudinal with replenishment, with quotas each wave on:
  - Cig-only: cigarettes only at least monthly (cig-only), those who use HTPs only at least weekly, those who use both products (dual), and non-users.
- Survey weights calibrated to results from the JASTIS survey make the data representative of the adult population at each wave.
- Retention between waves: 66%

Table 3: JP3 target and valid sample with retention and replenishment numbers by subsample

Subsample group	JP2 final N	JP3 target N	JP3 recontacted N	JP3 replenished N	JP3 final N
Current exclusive smokers (including recontact cigarette quitters)	1,911	2,000	1,205	643	1,848
Current exclusive HTP-users (including recontact HTP-only quitters)	931	1,000	468	501	969
Current cigarette-HTP dual users (including recontact cigarette-HTP quitters)	895	1,000	660	249	909
Never or non-users	491	500	462	294	756
Total	**4,228**	**4,500**	**2,795**	**1,687**	**4,482**

Basic table of transitions in product use between waves

Wave 1		Wave 2				Total
		Cig only	Dual	HTP only	Neither Product	
Cig only	N	**1478**	483	41	100	2102
	%	**69.6**	22.5	1.8	6.1	
Dual	N	41	**198**	19	10	268
	%	18.7	**71.7**	6.4	3.3	
HTP only	N	2	14	**42**	4	62
	%	5.0	26.1	**62.8**	6.1	
Recent Quitter	N	11	4	1	**25**	41
	%	31.8	10.4	0.7	**57.2**	
Total		**1532**	**699**	**103**	**139**	2473

Wave 2		Wave 3				Total
		Cig only	Dual	HTP only	Neither Product	
Cig only	N	**974**	134	38	80	1226
	%	**77.7**	12.4	3.3	6.7	
Dual	N	209	**352**	68	17	646
	%	30.0	**56.1**	11.7	2.3	
HTP only	N	10	183	**329**	42	565
	%	5.3	32.5	**45.4**	16.7	
Recent Quitter	N	16	8	4	**17**	61
	%	44.0	6.8	3.4	**45.9**	
Total		**1209**	**677**	**439**	**173**	2498

Percentages are weighted and adjusted by sex, age group, and time in sample • Cig only: those who smoke at least monthly • HTP only: those who use HTPs at least weekly
- Recent Quitters at baseline are short term quitters (<2y) and people who smoke very occasionally (< monthly).

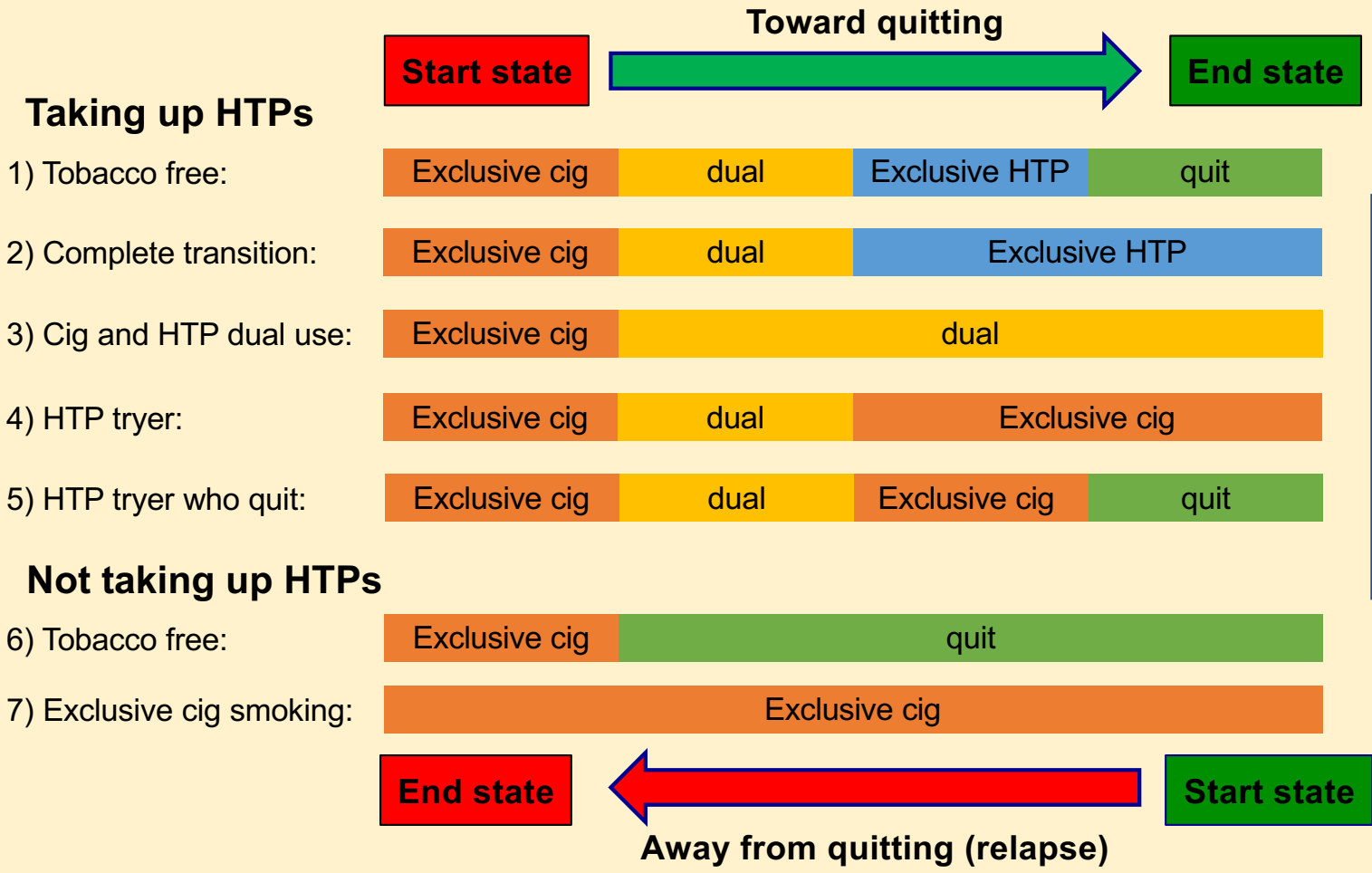
It's not so simple—challenges in drawing conclusions from the transition tables

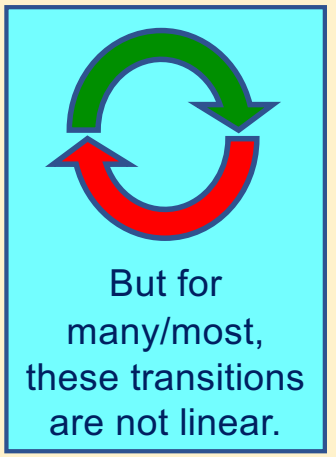
- Transition tables provide initial information about how each of the four user groups changed or didn't change between waves (W1 to W2 = 10-11 months).
- The simple transition tables capture population movement but may be misleading with respect to individual histories: they over-represent the experience of individuals who have occupied initial Dual or HTP-only states for a longer period of time (**length biased sampling**).
- Another challenge: who were dual using who quit smoking prior to the recruitment into the survey are not included, but those who are dual using who haven't yet quit smoking (or have tried to quit but failed) are included. **("treatment failure" issue**)
- Any survey (longitudinal or not) is taking a **snapshot of a movie**: the flow of individuals through a journey of product use, with some staying in a particular state for a long time, others for a short time.
- What can we do to do better measure and understand this process?

Possibilities for improving our snapshots of a movie

- Don’t start with those who dual use. Instead start with those who only smoke cigarettes and then follow them through their transition states. This deals with the “failed quitters” challenge.
- Distinguish between more transient, short-term states of use and more stable, longer-term states of use. That extends the timeframe of the snapshots that we are taking in our surveys. (iPhone “live” photo option)
- Examine transitions over more than 2 waves: enabling some inferences about whether the transitions between products and use states is changing as HTPs have become more established in the Japan tobacco marketplace.

Theoretical transition stages for exclusive cigarette smokers who initiate/do not initiate HTPs





Population cross-section proportions of different states of product use

	Wave 1	Wave 2	Wave 3
Cig only & never regular HTP use	84.8%	53.5%	52.6%
Cig only & ever regular HTP use	4.9%	9.8%	20.6%
Short term dual (< 6 months)	2.9%	14.2%	4.6%
Long term dual (6 months or more)	2.5%	17.4%	19.9%
HTP only	4.8%	5.0%	2.3%
Total	100.0%	100.0%	100.0%

Evidence of the possible emergence of a stable class of people who are engaging in long-term dual use

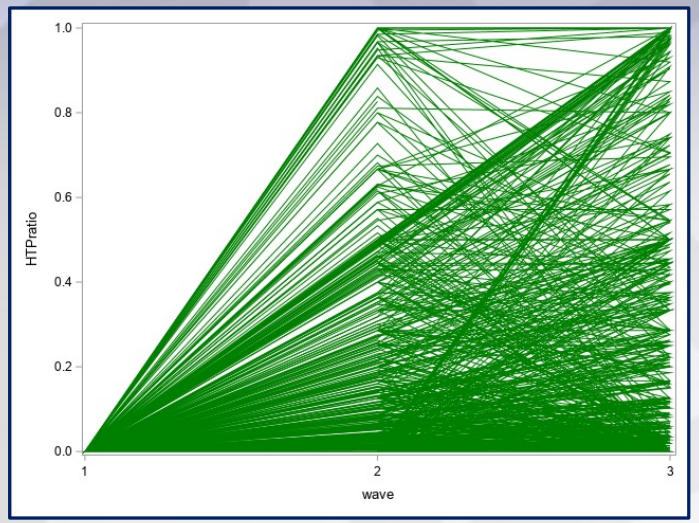
Expanded Transition Matrix for Cig-Only at Baseline

Baseline survey		Follow-up survey									
		Cig only		Dual		HTP only		Quitters			
		never used HTP regularly	ever used HTP regularly	Short-term	Long-term	Short-term	Long-term	ever used HTP regularly		never used HTP regularly	
								Short-term	Long-term	Short-term	Long-term
Cig only	never used HTP regularly	X	X	X	X	X	X	X	X	X	X
	ever used HTP regularly		X	X	X	X	X	X	X		
Dual	Short-term		X	X	X	X	X	X	X		
	Long-term		X	X	X	X	X	X	X		

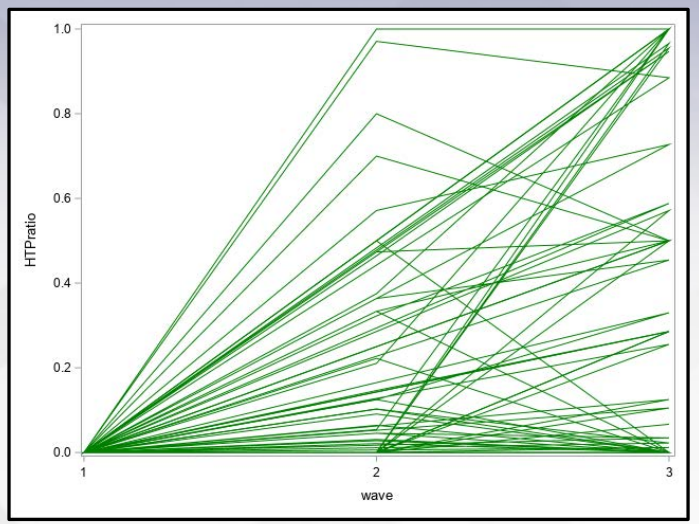
- The table decomposes each group into **stable/long-term**: those who report having been in the state that they are in at the time of the survey for at least 6 months vs **transient/short-term**: those who have not been in the state for less than 6 months. We use this expanded table in the analyses that follow
- This expanded transition matrix addresses length-bias at baseline: short-term dual use is a transient stage; long-term dual use is a relatively stable stage.
- Enables us to estimate long-term tobacco use patterns at follow up.
- Avoids “treatment failure” problem. Including just exclusive smokers who never used HTP regularly at baseline would provide a clean start point where samples with “no treatment” were included. Eliminating fluctuations at follow-up would compare those who are “affected” by HTP use with those who are “not affected” by HTP use.

Individual-Level Transitions at a Glance

Wave 1 cig only smokers who had NEVER used HTP



Wave 1 cig only smokers who HAD ever used HTP



- A lot of dual use (the points between the top and bottom)
- Transitions from dual use to exclusive smoking are more frequent (bottom) than to HTP only (top)
- A majority of respondents who picked up HTPs remained using a relatively lower amount of HTPs compared to cigarettes (greater density in the lower regions of the figure than the upper regions)
- Not many straight lines from Waves 2 to 3: not much stability over time. Lot of experimentation with HTPs.

Expanding the transition matrix: W1 to W2 and to W3

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wave 1 (2018)	wave 2 (2019)																		
	cig only & never regular HTP use		cig only & ever regular HTP use		short term dual		long term dual		short term HTP only		long term HTP only		quitter ever used HTP		short term quitter never used HTP		long term quitter never used HTP		Total
	N=	%	N=	%	N=	%	N=	%	N=	%	N=	%	N=	%	N=	%	N=	%	N=
cig only & never regular HTP use	907	66.9	67	6.1	275	18.3	73	4.5	14	0.9	5	0.5	3	0.5	17	1.8	8	0.5	1369
cig only & ever regular HTP use			49	62.8	14	17.6	14	16.4	2	1.5	0	.	1	1.6					80
short-term dual (<6m)			15	19.2	11	16.3	64	62.2	0	.	2	2.3	0	.					92
long-term dual (6m+)			8	8.3	4	8.8	63	76.9	0	.	4	3.2	2	2.9					81
Total	907		139		304		214		16		11		6		17		8		1622

wave 1 (2018)	wave 3 (2020)																		
	cig only & never regular HTP use		cig only & ever regular HTP use		short term dual		long term dual		short term HTP only		long term HTP only		quitter ever used HTP		short term quitter never used HTP		long term quitter never used HTP		Total
	N=	%	N=	%	N=	%	N=	%	N=	%	N=	%	N=	%	N=	%	N=	%	N=
cig only & never regular HTP use	733	53.5	240	17.5	72	5.8	214	14.8	8	0.4	22	1.4	25	1.8	19	1.3	39	3.6	1372
cig only & ever regular HTP use			44	51.8	5	8.4	19	23.2	1	2.7	6	7.2	5	6.8					80
short-term dual (<6m)			28	31.0	6	5.8	47	52.5	2	1.7	7	8.6	1	0.5					91
long-term dual (6m+)			11	14.3	2	3.5	54	70.5	0	.	10	7.2	4	4.5					81
Total	733		323		85		334		11		45		35		19		39		1624

- Data are weighted but unadjusted. The difference in n for baseline cig only % never regular HTP user between the two tables is dual to missing HTP use durations.

- About half of the never HTP users in 2018 tried HTPs between 2018 and 2020: HTPs increased dramatically in popularity
- Transitioning from exclusive smoking to long-term dual was MUCH more likely (14.8%) than transitioning to HTP only (1.4%)
- Those who were long-term duals in 2018 stayed in that state (70.5%); more than half (52.5%) of short-term duals became long-term duals, showing that starting off in dual use leads to dual use as a stable state.

1. Is Long-Term HTP use associated with a greater likelihood of quitting cigarettes?

wave 1 (2018)	wave 3 (2020)													
	cig only & never regular HTP use		long-term quitter never used HTP		Long-term quit among never HTP users	long-term dual		long-term HTP only		Long-term quitter who ever long-term used HTP		Long-term quit among long-term HTP users	Difference (P-value)
	N=	%	N=	%	%	N=	%	N=	%	N=	%	%	
cig only & never regular HTP use	733	53.5	39	3.6	3.6/(3.6+53.5) =6.3	214	14.8	22	1.4	1	0.1	1.4+0.1/(1.4+0.1+14.8) =9.2	Diff=2.9% (p=0.34)

NO, it is not–a non-significant (p=.34) trend

Long-term HTP users (N=237) = 9.2%

Never HTP users (N=772) = 6.3%

2. Is Long-Term HTP use associated with a greater likelihood of quitting cigarettes among daily smokers vs. non-dailys?

wave 1 (2018)		wave 3 (2020)													
		cig only & never regular HTP use		long-term quitter never used HTP		long-term quit among never HTP users	long-term dual		long-term HTP only		Long-term quitter who ever long-term used HTP		long-term quit among long-term HTP users	Difference (P-value)
		N=	%	N=	%	%	N=	%	N=	%	N=	%	%	
cig only & never regular HTP use	Daily smoker	704	53.4	35	3.5	3.5/(3.5+53.4) = 6.2	204	14.7	21	1.4	1	0.1	(1.4+0.1)/(1.4+0.1+14.7) = 9.3	Diff=3.1% (p=0.31)
	Non-daily smoker	29	53.8	4	5.9	5.9/(5.9+53.8)= 9.9	10	15.2	1	1.1	0	0	1.1/(1.1+15.2)= 6.6	Diff=-3.3% (p=0.70)

NO, it is not–a (p=.31) trend for daily and no difference for non-daily (p=.70)

Daily

Long-term HTP (N=226) = 9.3%

Never HTP (N=739) = 6.2%

Non-Daily

Long-term HTP (N=11) = 6.6%

Never HTP (N=33) = 9.9%

3. Is Long-Term HTP use associated with a greater likelihood of daily smokers transitioning to non-daily smoking?

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Non-daily smoking is a precursor for future quitting

wave 1 (2018)	wave 3 (2020)									
	daily cig only & never regular HTP		non-daily cig only & never regular HTP use		cig reduction among never HTP users	daily cig long-term dual		non-daily cig long-term dual		cig reduction among long-term HTP users	Difference (P-value)
	N=	%	N=	%	%	N=	%	N=	%	%	
ily cig only & never regular HTP use	684	52.3	18	1.0	1.0/(1.0+52.3) = 1.9	186	13.5	11	0.8	0.8/(0.8+13.5) = 5.4	Diff=3.5% (p=0.08)

Maybe: A trend (p=.08) toward transitioning to non-daily smoking

Long-term HTP users (N=197) = 5.4%

Never HTP users (N=702) = 1.9%

4. Association between ever-using HTPs and: (a) not smoking cigarettes, (b) using neither cigarettes nor HTPs

wave 1 (2018)	cig only & never regular HTP use		cig only & ever regular HTP use		short term dual		long term dual		short term HTP only		long term HTP only		quitter ever used HTP		short term quitter never used HTP		long term quitter never used HTP		Total
	N=	%	N=	%	N=	%	N=	%	N=	%	N=	%	N=	%	N=	%	N=	%	N=
cig only & never regular HTP use	733	53.5	240	17.5	72	5.8	214	14.8	8	0.4	22	1.4	25	1.8	19	1.3	39	3.6	1372

Cigarette free

	Denominator (%)	Numerator (%)	Not using any nicotine product at Wave 3(%)	Difference (P-value)
Ever-used HTPs	All groups that ever-used HTPs: 17.5 + 5.8 + 14.8 + 0.4 + 1.4 + 1.8 = 41.7	cig quitter ever used HTPs: 1.8 + 1.4 + 0.4 = 3.6	3.6/41.7 = 8.6%	Diff = 0.2% (p=0.92)
Never used HTPs	cig only & never regular HTP use + quitter never used HTPs: 53.5 + 1.3 + 3.6 = 58.4	cig quitter never used HTPs: 1.3 + 3.6 = 4.9	4.9/58.4 = 8.4%	

Tobacco free: Neither cigarettes nor HTPs

	Denominator (%)	Numerator (%)	Not using any nicotine product at Wave 3(%)	Difference (P-value)
Ever-used HTPs	All groups that ever-used HTPs: 17.5 + 5.8 + 14.8 + 0.4 + 1.4 + 1.8 = 41.7	quitter ever used HTP: 1.8	1.8/41.7 = 4.3%	Diff = -4.1% (p=0.02)
Never used HTPs	cig only & never regular HTP use + quitter never used HTPs: 53.5 + 1.3 + 3.6 = 58.4	quitter never used HTPs: 1.3+3.6 = 4.9	4.9/58.4 = 8.4%	

- **Cigarette Free:** no difference between ever-used HTPs (8.4%) and never-used HTPs (8.6%)
- **Tobacco Free:** those who ever-used HTPs from W1 to W3 were significantly less likely (4.3%) than those who never-used HTPs (8.4%)

The journey of those who exclusively smoke at W1 (2018) over two years (W2: 2018-19 and W3: 2020)

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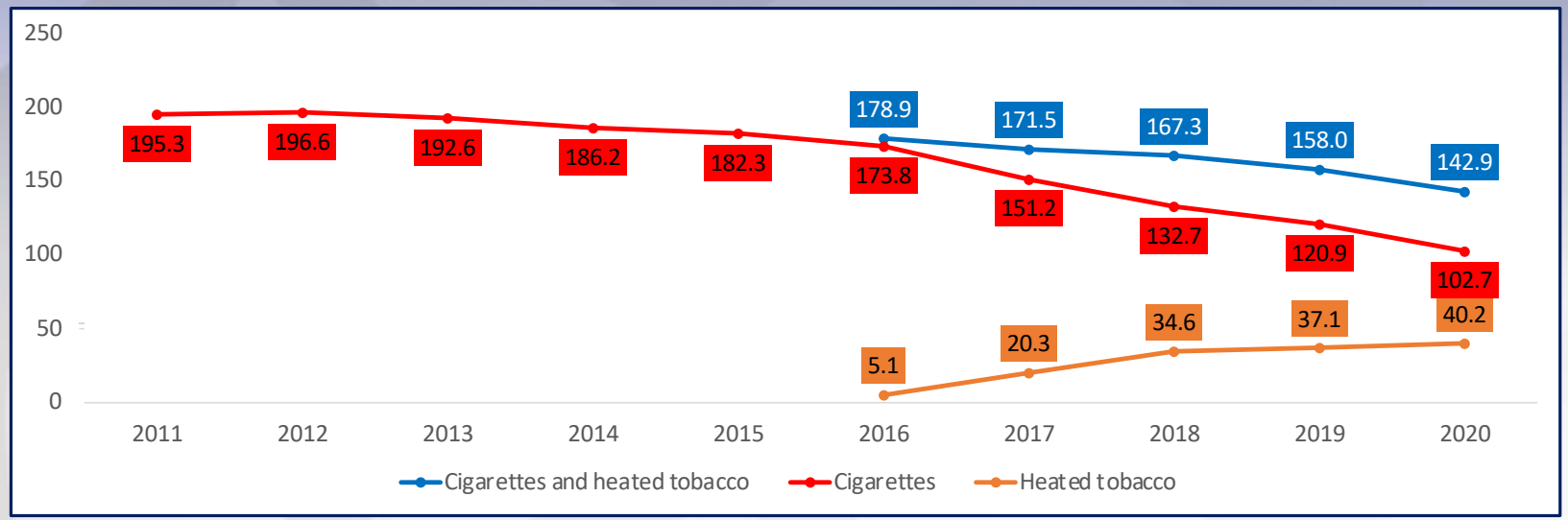
- The Wave 1 to Wave 3 period (2018-2020) was a period of change for the market in Japan: this was not a period when wave-to-wave transitions are “stationary”.
- By Wave 3 (2020), there was greater stationarity: toward long-term dual use.
- While only 10.8% of those who smoked at Wave 1 had used HTP regularly by that time, by Wave 3, this increased to close to half.
- **Quitting cigarettes among daily smoking** at W1: no diff—long-term HTPs (9.3%) vs. nevers (6.2%)
- **Quitting cigarettes among <daily smoking** at W1: no diff—long-term HTPs (6.6%) vs. nevers (9.9%)
- **Transition from daily smoking to non-daily**: positive trend—long-term HTPs (5.4%) vs. nevers (1.9%)
- **Transition to quit cigarettes**: no diff between ever-tried HTPs (8.6%) vs. never-tried (8.4%)
- **Transition to no tobacco use**: those ever-tried HTPs were less likely (4.3%) vs. nevers (8.4%)

Neither ever-trying HTPs nor using HTPs for a longer period (≥6M) was associated with quitting cigarettes, and both were negatively associated with transitioning to using neither product.

How can we best interpret the trends in sales of cigarettes and HTPs in Japan?



The dramatic decrease in cigarette sales and the increase in HTP sales in Japan is likely due (nearly) entirely to partial substitution among smokers who are now duals, and likely to become long-term duals rather than due to smokers quitting or transitioning to using neither product.

Next steps in our explorations

- Controlling for covariates and applying regression adjustments to the results of this analysis.
- Questionnaire additions: questions about details of the process of initiating HTPs, length and amount of use, timing of HTP cessation vs cigarette cessation.
- More advanced statistical methods: event history models applied to transitions through relatively stable states: cigarette smoking, long-term dual use, long-term exclusive HTP use, tobacco-free

Major Support for the ITC Project

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US National Cancer Institute
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Canadian Institutes of Health Research
FDN-148477

Ontario Institute for Cancer Research
Senior Investigator Award (2007-2027)

ITC Project Research Organizations

ITC Project Research Support

EXHIBIT 3

International Tobacco Control Policy Evaluation Project

Changes in Cigarette and Total Tobacco Consumption Among People Who Smoke Who Did and Did Not Initiate Heated Tobacco Products: Findings from the 2018-2021 ITC Japan Surveys

Steve S. Xu[1]*, Gang Meng[1], Shannon Gravely[1], Anne C. K. Quah[1], Janine Ouimet[1], Itsuro Yoshimi[2], Kota Katanoda[2], Takahiro Tabuchi[3], K. Michael Cummings[4], Andrew Hyland[5], Geoffrey T. Fong[1, 6]

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大阪国際がんセンター がん対策センター

国立研究開発法人 国立がん研究センター National Cancer Center Japan

Presented at Society for Research on Nicotine and Tobacco 29th Annual Meeting, March 3, 2023 San Antonio, Texas
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OICR Ontario Institute for Cancer Research

Disclosures and Funding

Disclosures of Interest:

- Kota Katanoda received a JMWH Bayer Grant from Sep. 1, 2017 to Aug. 31, 2019 via the Japan Society for Menopause and Women's Health.
- Geoffrey T. Fong has served as an expert witness or consultant for governments defending their country's policies or regulations in litigation.
- Geoffrey T. Fong and Shannon Gravely served as paid expert consultants to the Ministry of Health of Singapore in reviewing the evidence on plain/standardized packaging.
- K. Michael Cummings has served as a paid expert witness in litigation against cigarette manufacturers in the United States.
- All other authors including the presenter have no conflict of interests to declare.

Funding sources:

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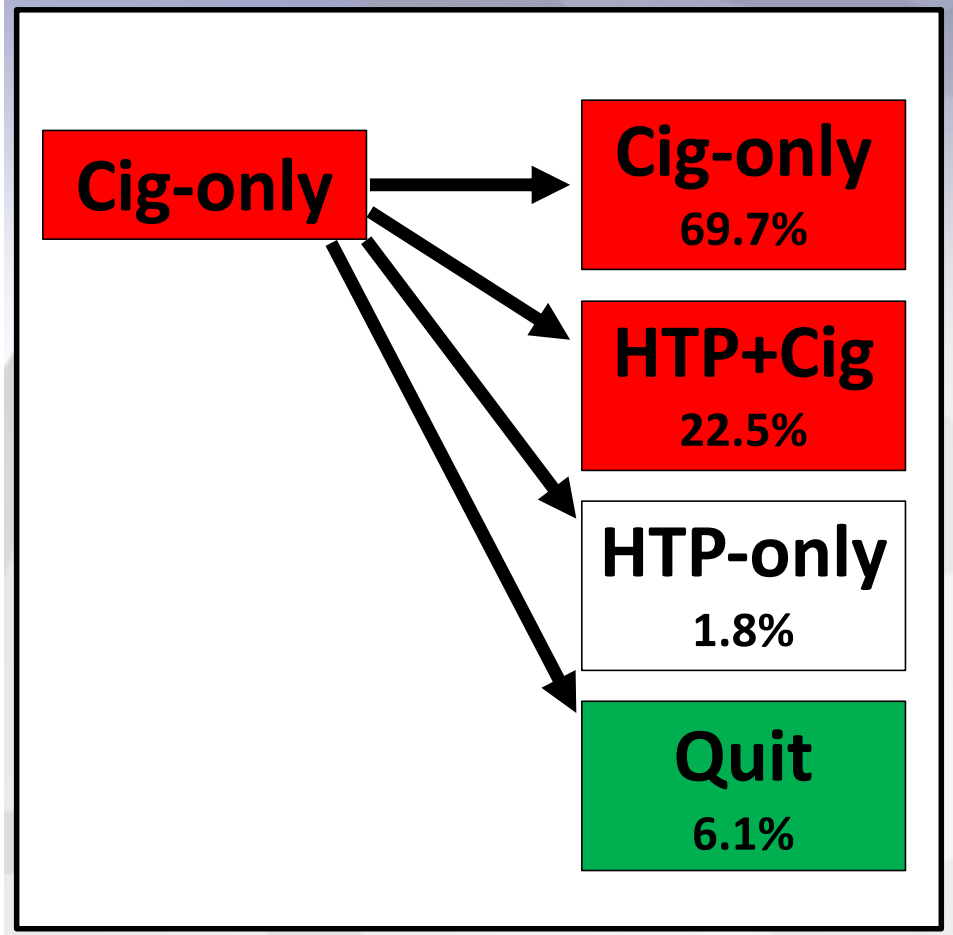
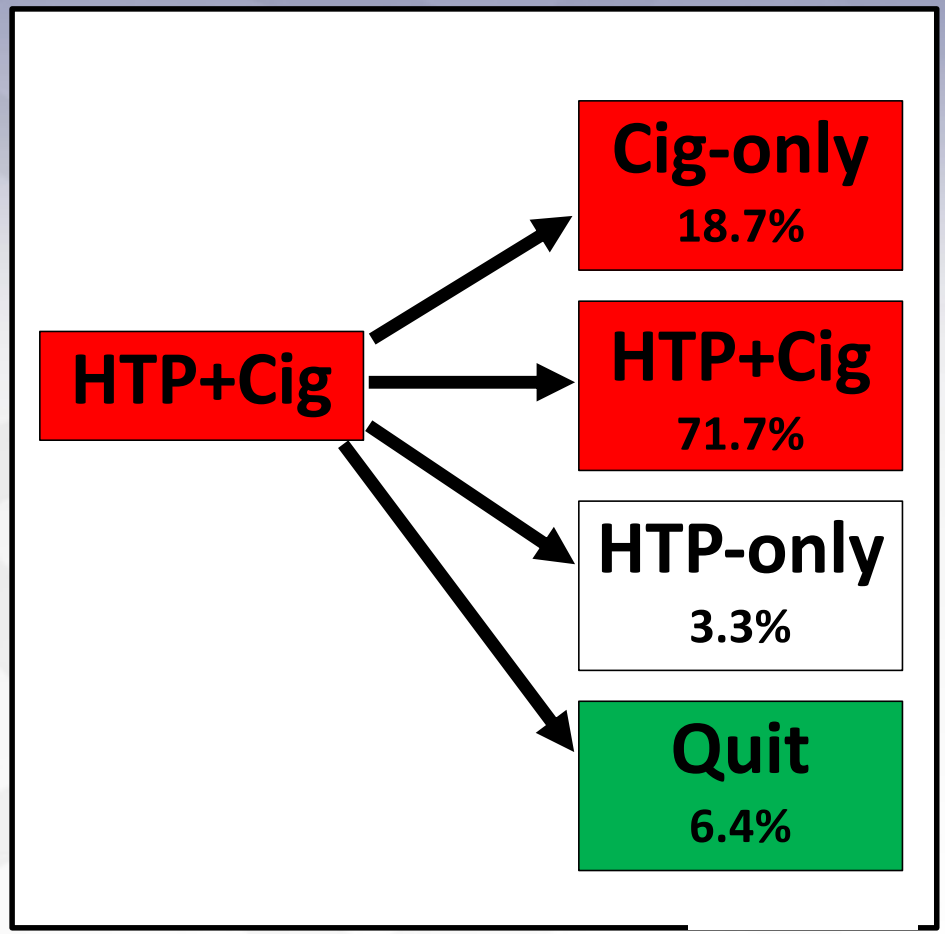
ITC Japan: Transitions of people who smoke cigarettes only and people who dual use HTPs-cigarettes (2018-19)





How does consumption change when people transition from (1) cig-only to dual, and (2) dual to cig-only & HTP-only?

- Will focus on **consumption,** but will talk about the distinction between business implications and possible public health implications.
- Key definitions for examining changes in tobacco consumption:

  Cigarettes: Cigarettes per day **(CPD)**

  Heated Tobacco Products: HTP sticks per day **(HPD)***

  Total Tobacco: CPD + HPD = **TPD**

* For those who use Ploom TECH, one capsule = 4 HTP sticks

Possible directions and extent of changes in cigarette and HTP consumption over time

Tobacco Use Transition	Consumption		
	CPD	HPD	TPD (CPD+HPD)
Cig-only →Cig-only	+ or −		
Cig-only → HTP+Cig	+ or −	+	+ or −
HTP+Cig → HTP+Cig	+ or −	+ or −	+ or −
HTP+Cig → Cig-only	+ or −	−	+ or −
HTP+Cig→ HTP	−	+ or −	+ or −

CPD: Cigarettes per day HPD: Heated Tobacco sticks per day TPD: Total Tobacco (Cig+HTP) sticks per day

Study Sample and Analytic Methods

Study Sample

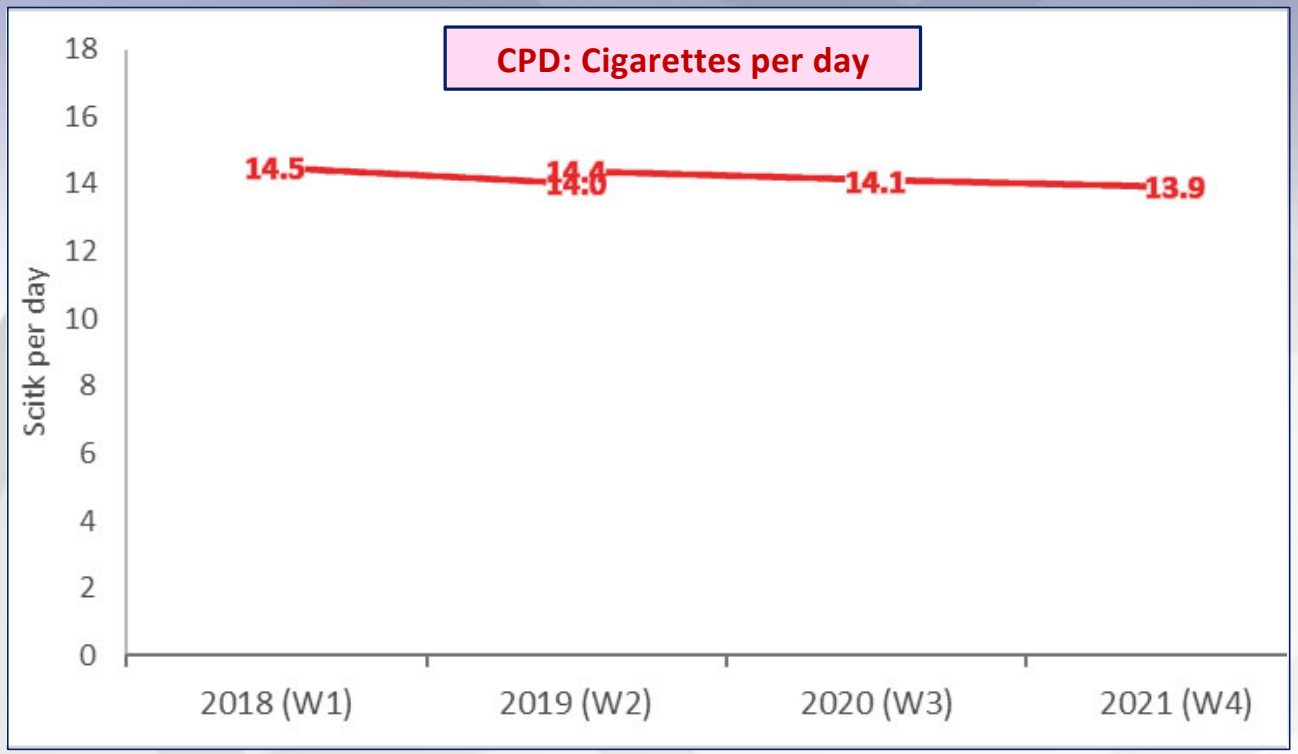
- Adults (aged ≥20) in 4 waves of the ITC Japan Surveys (2018-21)
- Baseline of people who smoke cigarettes only (≥weekly)
- Baseline of people who dual use HTPs-cigarettes (≥weekly for both products)
- Participated in two **consecutive** waves

Year	Cigarette-only	Dual HTP-Cigarette
2018-2019	1051	134
2019-2020	613	323
2020-2021	660	301

Analytic Methods

- Weighted longitudinal linear regression analyses examined changes in average daily tobacco consumption (cigarettes—**CPD**; HTPs—**HPD**; and TOTAL—**TPD**)

Cig-only → Cig-only

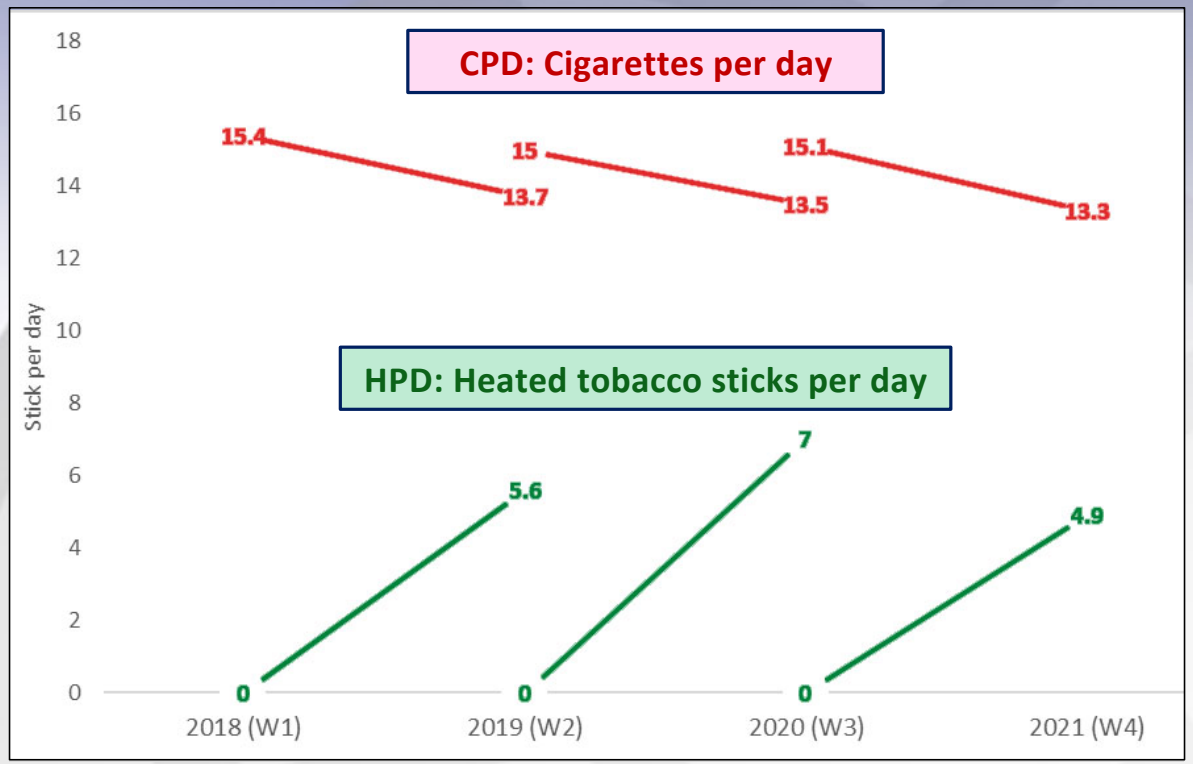


Year	Product	Difference (stick/%)
2018-2019	Cig	–0.5 (–3.4%)
	HTP	0
	Total	**–0.5 (–3.4%)**
2019-2020	Cig	–0.3 (–2.1%)
	HTP	0
	Total	–0.3 (–2.1%)
2020-2021	Cig	–0.2 (–1.4%)
	HTP	0
	Total	–0.2 (–1.4%)

Those who continued to exclusively smoke cigarettes:

- No change in CPD (and thus no change in TPD)

Cig-only → HTP+Cig



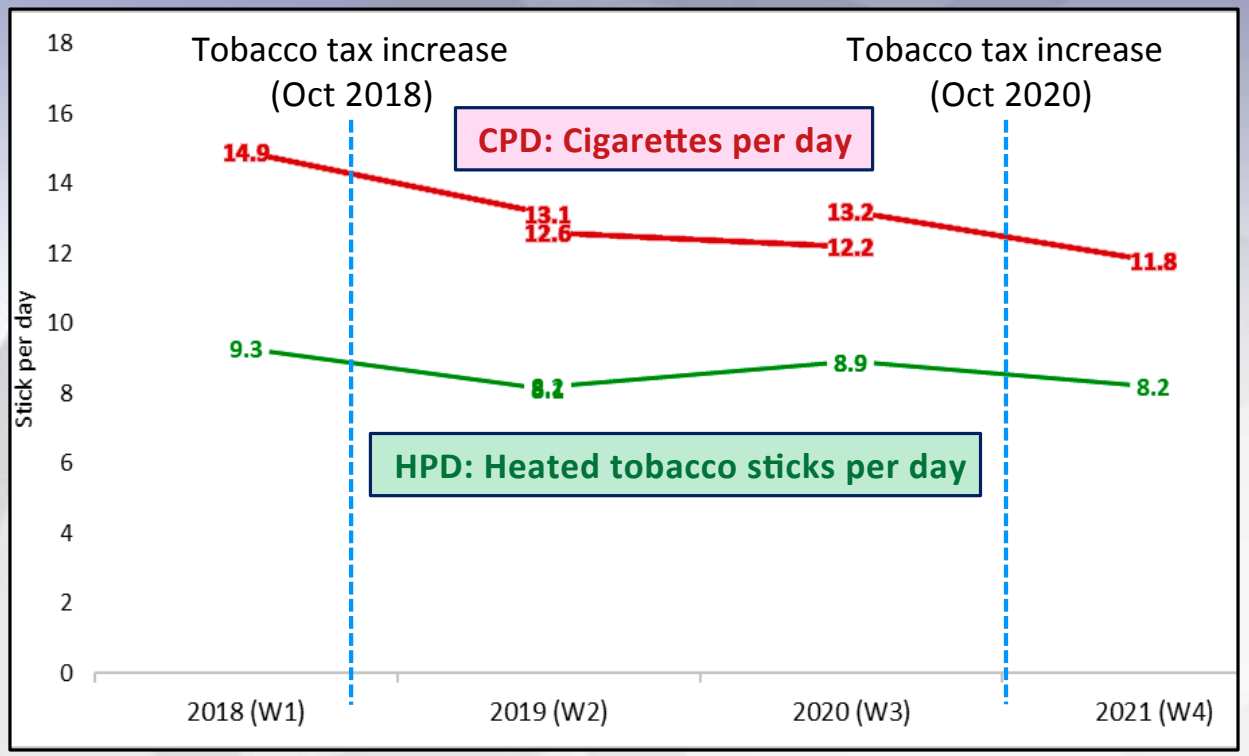
Year	Product	Difference (stick/%)
2018-2019	Cig	–1.7 (–11.0%) ***
	HTP	+5.6
	Total	**+3.9 (+25.3%)**
2019-2020	Cig	–1.5 (–10.0%) *
	HTP	+7.0
	Total	**+5.5 (+33.3%)**
2020-2021	Cig	–1.8 (–11.9%) ***
	HTP	+4.9
	Total	**+3.1 (+20.5%)**

* p<0.05	*** p<0.001

Those who switched from exclusive cigarette smoking to using both cigarettes and HTPs:

- Reduced their cigarette consumption by 10-12% (-1.5 to -1.8 sticks) but added 2-4 times more HTP sticks.
- Net change = 20-33% higher total stick consumption

HTP+Cig → HTP+Cig



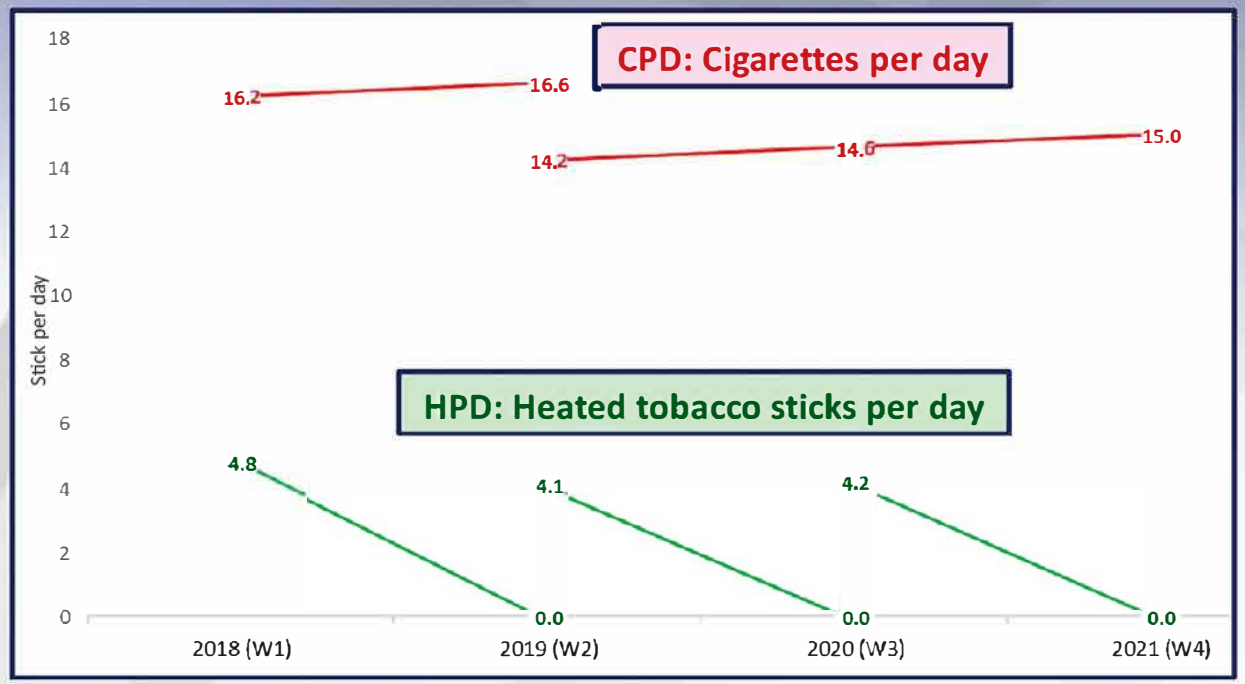
Year	Product	Difference (stick/%)
2018-2019	Cig	–1.8 (–12.1%) **
	HTP	–1.2 (–12.9%)
	Total	**–3.0 (–12.4%) **
2019-2020	Cig	–0.4 (–3.1%)
	HTP	+0.7 (+8.5%)
	Total	**+0.3 (+3.3%)**
2020-2021	Cig	–1.4 (–10.6%) *
	HTP	–0.7 (–7.9%)
	Total	**–2.3 (–10.3%) **

* p<0.05	** p<0.01

Those who continued to use both cigarettes and HTPs:

- Reduced both cigarettes and HTPs consumption in 2018-19 and 2020-21 (when there was a tobacco tax increase).
- But little change between 2019-20, when there was no tobacco tax increase.

HTP+Cig → Cig-only



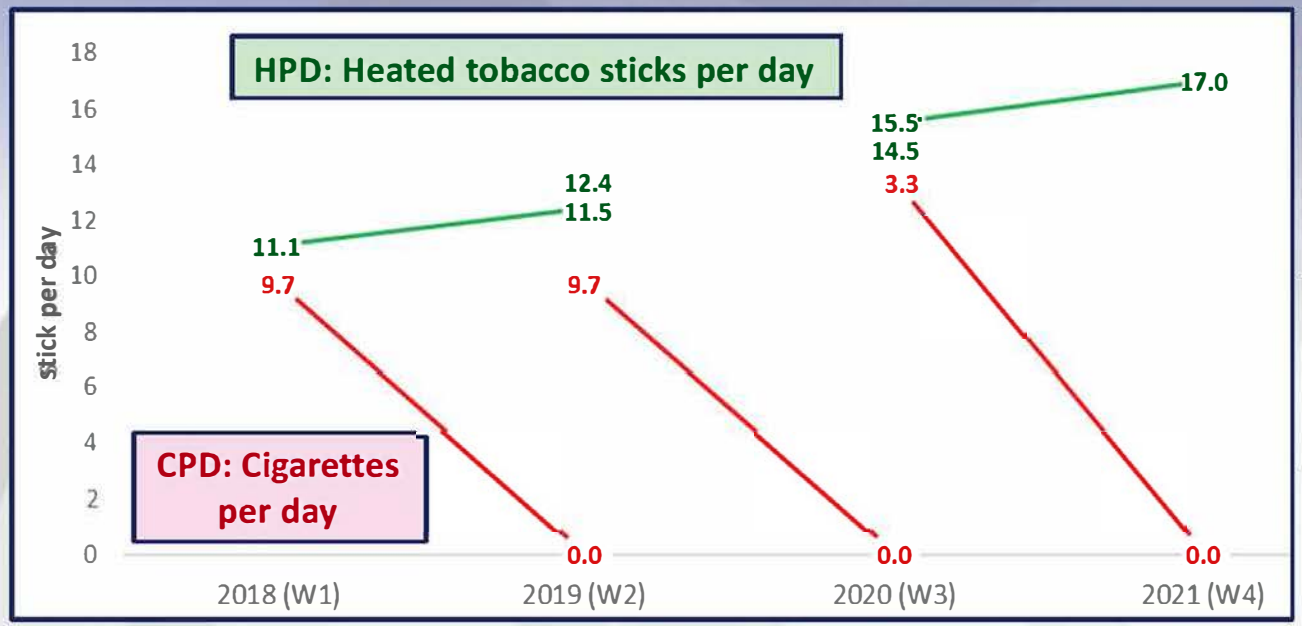
Year	Product	Difference (stick/%)
2018-2019	Cig	+0.4 (+2.4%)
	HTP	−4.8
	Total	**−4.4 (−21.0%) ****
2019-2020	Cig	+0.4 (+2.8%)
	HTP	−4.1
	Total	**−3.7 (−20.2%)****
2020-2021	Cig	+0.4 (+2.7%)
	HTP	−4.2
	Total	**−3.8 (−20.8%) ****

* p<0.05 ** p<0.01

Those who used both cigarettes and HTPs then went (back) to cigarette-only:

- Did not increase their cigarette consumption.
- Net effect: reduction of 20% of total stick consumption

HTP+Cig → HTP-only



Year	Product	Difference (stick/%)
2018-2019	Cig	–9.7
	HTP	+1.3 (+11.7%) *
	Total	**–8.4 (–40.4%) *** **
2019-2020	Cig	–9.7
	HTP	+3.7 (+20.2%) ***
	Total	**–6.9 (–31.1%) *** **
2020-2021	Cig	–13.3
	HTP	+1.5 (+9.7%) ***
	Total	**–11.6 (–40.3%) *** **

* p<0.05	*** p<0.001

Those who used both cigarettes and HTPs then transitioned to HTP-only :

- Increased their HTP consumption by 10-20%
- Net effect: reduction of 30-40% of total stick consumption

Directions and extent of changes in tobacco consumption

Tobacco Use Transition	Consumption		
	CPD	HPD	TPD (CPD+HPD)
Cig-only → Cig-only	0		
Cig-only → HTP+Cig	–(10-12%)	++	++ (by 20-33%)
HTP+Cig → HTP+Cig	0 / –	0 / –	0 / –
HTP+Cig → Cig-only	0	– –	– – (by 20-21%)
HTP+Cig → HTP-only	– – –	+ (10-20%)	– – – (by 31-40%)

CPD: Cigarettes per day HPD: Heated Tobacco sticks per day TPD: Total Tobacco (Cig+HTP) sticks per day

Comparison of total tobacco consumption by user group from 4 cross-sectional surveys

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Study	Cig-only	HTP+Cig	HTP-only
ITC Japan Survey Wave 2 (Dec 2018-Jan 2019)	14.1	**20.8**	16.0
Japan TMCS (Apr 2018-Jun 2019)	16.6	**23.4**	15.7
PMI IQOS User Survey Year 1 (Dec 2016-July 2017)	NA	**24.8**	16.8
JT Ploom TECH User Survey (Dec 2018)	16.2 *	**20.1**	18.8

* Reported CPD before taking up Ploom TECH (PT); 1 Ploom TECH tobacco capsule = 4 HTP sticks

Summary and Conclusion

When people transition from cigarettes TO dual use:

…They add HTP sticks by a much greater number than they reduce cigarettes, resulting in an average of **26% increase in total consumption.**

When people transition AWAY from dual use:

…**Back to cigarettes only (common)**: they add cigarette sticks by a lower number than they reduce HTP sticks, resulting in an average of **21% decrease in total consumption.**

…To HTPs only (rare): they add HTPs by a lower number than they reduce cigarettes, resulting in an average of **37% decrease in total consumption.**

Business conclusion: Dual use is a substantial benefit for companies who produce both cigarettes and HTPs.

Potential public health consequences?

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- Not clear because we are missing a key element: **the relative harmfulness of HTP sticks vs. cigarettes**.
- Consider the average consumption change for those transitioning from cig-only to cig+HTP:
  - Cigs: –1.7 sticks
  - HTPs: +5.8 sticks
  - HTP/cig ratio = 5.8/1.7 = 3.4

Year	Product	Difference (stick/%)
2018-2019	Cig	–1.7 (–11.0%) ***
	HTP	+5.6
	Total	**+3.9 (+25.3%)**
2019-2020	Cig	–1.5 (–10.0%) *
	HTP	+7.0
	Total	**+5.5 (+33.3%)**
2020-2021	Cig	–1.8 (–11.9%) ***
	HTP	+4.9
	Total	**+3.1 (+20.5%)**

* p<0.05 | *** p<0.001

- Simple heuristic**: if the harmfulness of cigarettes relative to HTPs exceeds 3.4, then the decrease of 1.7 cigs may decrease risk more than the increase of 5.8 HTP sticks increases risk. The net effect would be a reduction in risk.

Public Health Conclusion: Transitioning from Cig-Only to Dual use may or may not constitute a less harmful state, depending on the relative harmfulness of HTPs vs. cigarettes.

** Simple because there is certainly a non-linear (log) relationship between consumption and harmfulness.

Major Support for the ITC Project

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US National Cancer Institute
P01 CA200512

Canadian Institutes of Health Research
FDN-148477

Ontario Institute for Cancer Research
Senior Investigator Award (2007-2027)

ITC Project Research Organizations

ITC Project Research Support

EXHIBIT 4

AN EXAMINATION OF PHILIP MORRIS INTERNATIONAL'S ESTIMATE OF KOREAN ADULTS WHO HAVE "COMPLETELY TRANSITIONED" FROM CIGARETTES TO IQOS: FINDINGS FROM THE 2020 AND 2021 ITC KOREA SURVEYS

Shannon Gravely[1], Gang Meng[1], Mi Yan[1], Steve S. Xu[1], Hong Gwan Seo[2], Sungkyu Lee[3], Sung-il Cho[4], Yeol Kim[2], Gil-yong Kim[5], Sujin Lim[5], Su Young Kim[5], Anne C.K. Quah[1], K. Michael Cummings[6], Andrew Hyland[7], Geoffrey T. Fong[1,8]

[1]University of Waterloo, Canada; [2]National Cancer Center, Republic of Korea; [3]Korea Center for Tobacco Control Research and Education, Republic of Korea; [4]Seoul National University, Republic of Korea; [5]National Tobacco Control Center, Korean Health Promotion Institute, Republic of Korea; [6]Medical University of South Carolina, USA; [7]Roswell Park Comprehensive Cancer Center, USA ; [8]Ontario Institute of Cancer Research, Canada

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Society for Research on Nicotine and Tobacco Annual Meeting
March 20-23, 2024, Edinburgh Scotland
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Presenter's affiliation(s) and disclosures

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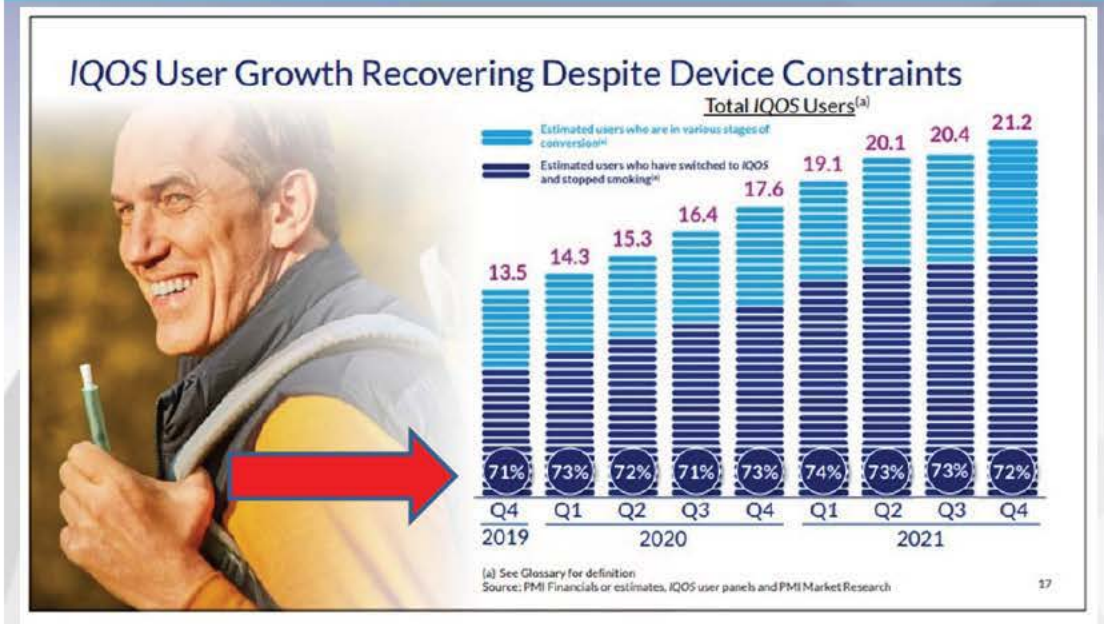
Disclosures of Interests:

- SG, SSX, GM, GTF, ACKQ, MY are supported by grants from the US National Cancer Institute (P01 CA200512) and the Canadian Institutes of Health Research (FDN-148477).
- Geoffrey T. Fong has served as an expert witness or consultant for governments defending their country's policies or regulations in litigation.
- Geoffrey T. Fong and Shannon Gravely served as paid expert consultants to the Ministry of Health of Singapore in reviewing the evidence on plain/standardized packaging.
- K. Michael Cummings has served as a paid expert witness in litigation against cigarette manufacturers in the United States.
- All other authors including the presenter have no conflict of interests to declare.

Funding:

- The ITC Korea Survey was supported by grants from the Korean Health Promotion Fund and the Canadian Institutes of Health Research Foundation Grant (FDN-148477).
- Core support for the overall ITC Seven Country Nicotine Product Survey was provided by the US National Cancer Institute (P01 CA200512) and the Canadian Institutes of Health Research (FDN-148477).
- Additional support to GTF is provided by a Senior Investigator Grant from the Ontario Institute for Cancer Research and the Canadian Cancer Society O. Harold Warwick Prize.

Have IQOS consumers stopped smoking?



PMI Definition:

Quit smoking and switched to IQOS: ≥95% of daily tobacco consumption is IQOS

Data source: IQOS user panels and PMI Market Research

PMI reports that in their ***IQOS user sample*** panels, the percentage of customers who had quit smoking and switched to IQOS:

➡ 71-74% in 2020 & 2021

METHODS: PMI IQOS user panel in Japan

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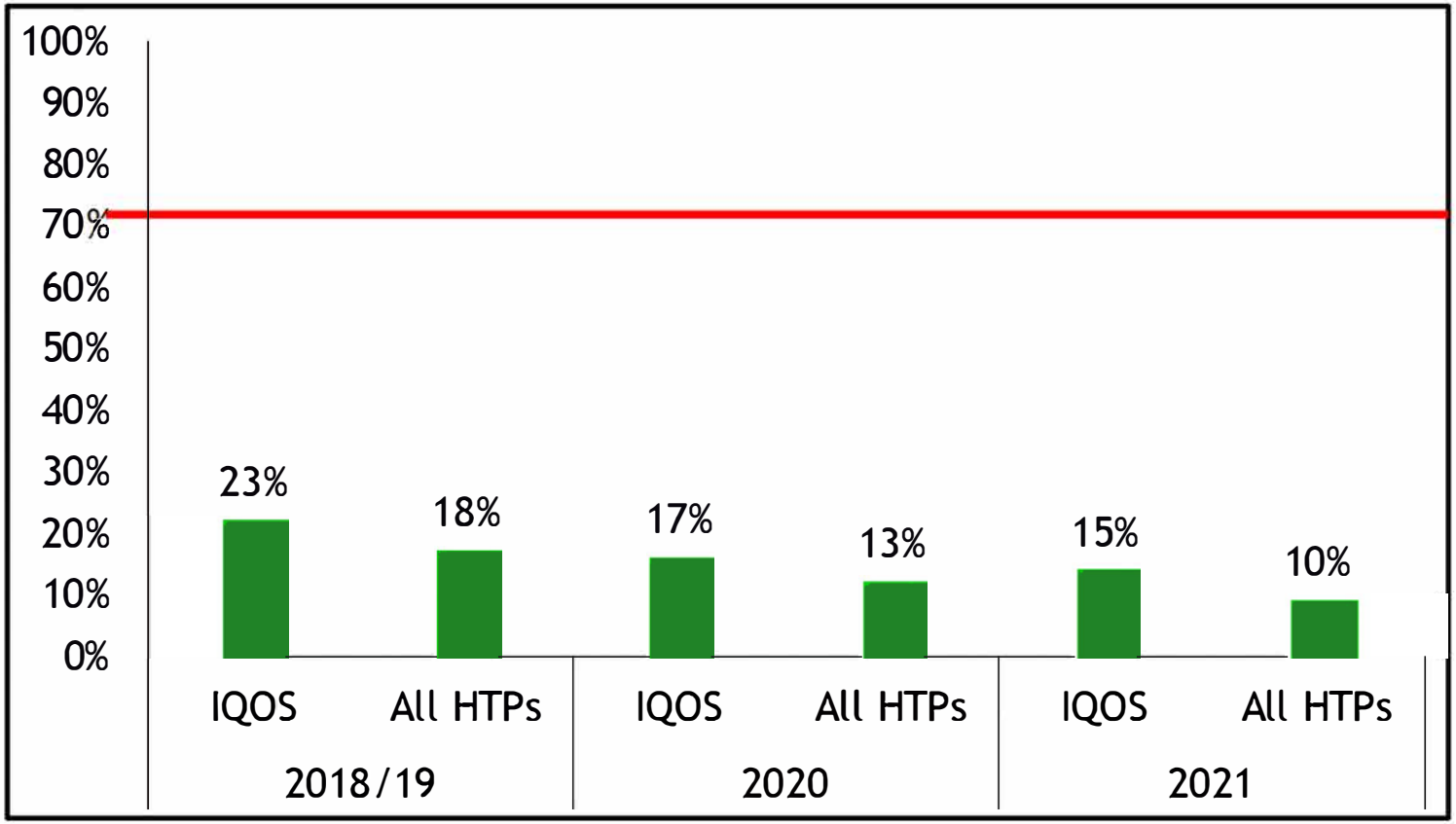
- Online (cross-sectional) survey of IQOS customers in Japan
- Purchased IQOS and agreed to participate in research
- Used IQOS in the past 30 days
- Aged 20+ years
- 100 HTP sticks in their lifetime
- 98% had a smoking history at the time of purchase
- ~2000 respondents each year (500/quarter)

Fischer et al., Trends in prevalence and patterns of use of a heated tobacco product (IQOS™) in Japan: A three-year repeated cross-sectional study, F1000Research 2022, 11:720)

Percentage of Japanese adults using HTPs who have quit smoking cigarettes: 2018-2021 ITC Japan Surveys



PMI IQOS users: 70-74% have quit smoking

Republic of Korea

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- We extended our study to the Republic of Korea:
  - 4th largest global HTP market
  - HTPs used by those with similar sociodemographics to Japan
  - Both HTPs and e-cigarettes are legal
- IQOS most commonly used HTP among adults (56%: ITC Japan Survey data)

Study Objectives

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1. Using cross-sectional national data from two waves of the ITC Korea Surveys, we estimated the % of adults who regularly use HTPs and who have quit smoking cigarettes:
   - Among those using IQOS
   - Among those using the leading HTP brands: IQOS, lil, Ploom, & glo
2. Compare ITC % of HTP users who have quit smoking to those of PMI's IQOS user sample (panel surveys)

METHODS: ITC Korea Survey

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In 2020, 1099 respondents (ages 19+) were using HTPs ≥weekly (IQOS: n = 609)

In 2021,1220 were using HTPs at least weekly (IQOS: n = 652)

All were smoking cigarettes or had quit smoking at the time of the survey

Used 100 HTP sticks (or equivalent) in their lifetime

Daily tobacco consumption was adopted from PMI's Stakeholder reports: IQOS account for ≥95% of daily tobacco consumption (HTPs + cigarettes per day)*

**Calculated using ITC KRA weighted data based on the age*sex distribution of PMI's Japan IQOS User Surveys (PMI Korea data are not available), thus aligning our weighted estimates with PMI's own estimates as closely as possible with publicly available information*

Corresponding survey dates used for this study: ITC Korea Surveys and PMI IQOS user sample surveys

ITC Korea Surveys	PMI Reports Year: Quarter
Wave 1: June 19 to 28, 2020	2020: Q2 IQOS user sample
Wave 2: Nov 3 to Dec 13, 2021	2021: Q4 IQOS user sample

Analyses of the ITC Korea Survey data

- Cross-sectional weights were original ITC weights (Korea Community Health Survey as the benchmark) recalibrated to PMI's sex* age distribution.
- This adjusts the ITC data so that matches the sex * age distribution of the PMI surveys

Daily tobacco consumption† =
Cigarettes + HTPs* =

HTPs/Cigarettes + HTPs

Cumulative distribution from 5% to 100%

Quit smoking = ≥95% HTPs

HTPs: Heat sticks or equivalent # capsules; † daily tobacco consumption did not include other nicotine/tobacco products

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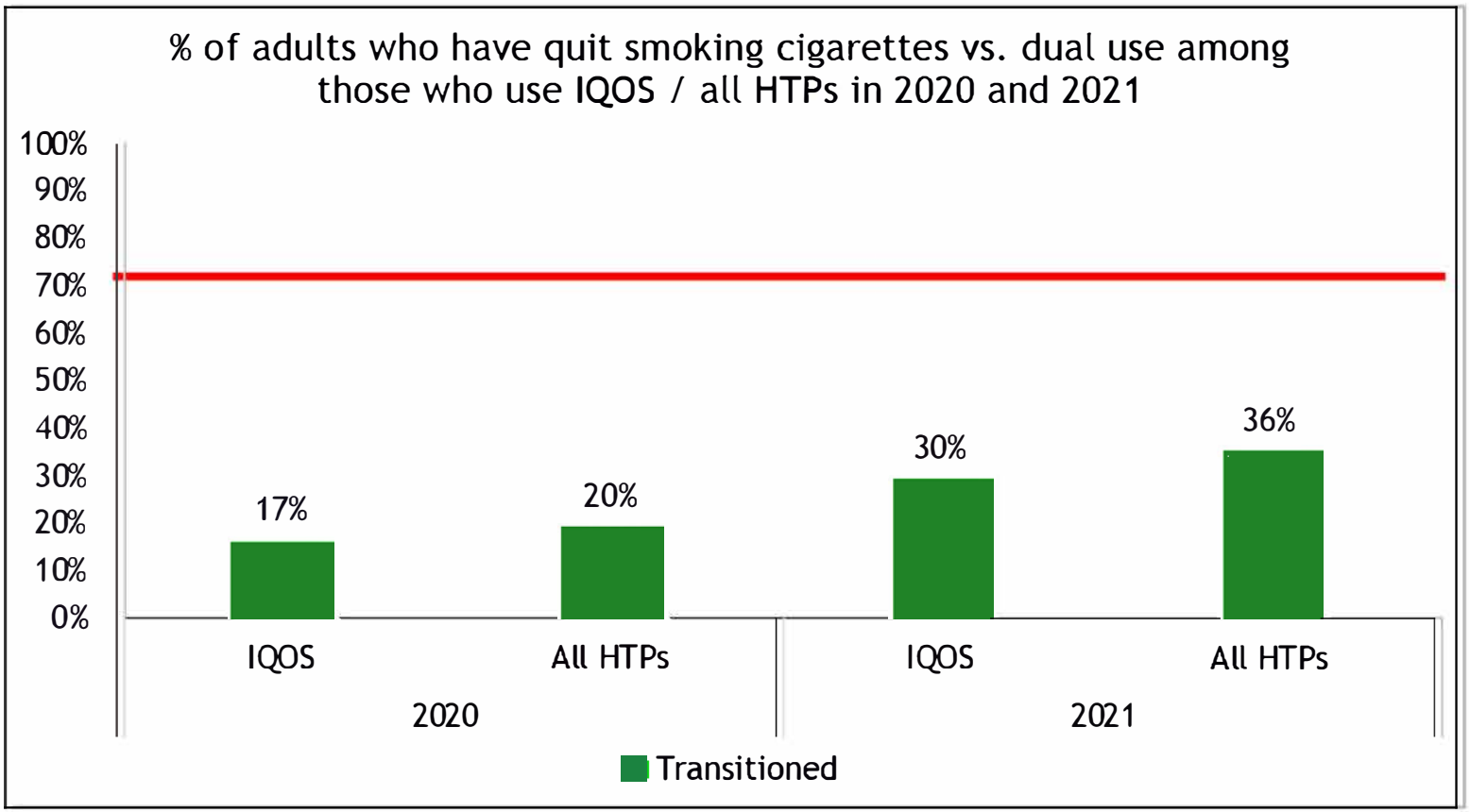
International Tobacco Control
Policy Evaluation Project

Transition rates did not differ between people who vaped nicotine vs. those who did not (all p>0.5).



PMI IQOS users: 70-74% have quit smoking

Quit smoking = the proportion of HTP consumers who's daily HTP and cigarette tobacco consumption was ≥ 95% HTPs

Summary and Conclusion

- Most Korean adults regularly using IQOS and/or other HTPs did not quit smoking; rather, they had high rates of dual use.
- These results in Korea replicate our findings in Japan in 2020; but higher in 2021 in Korea
- Large discrepancy between the ITC data and the PMI data on the percentage of IQOS consumers who have quit smoking and switched to IQOS: ITC percentages were much lower.
- Are HTP consumers using HTPs to quit?
  - Seo et al. ITC publication: reasons for using HTPs: 35.4% Korean adults use HTPs because HTPs might help them quit. 49.7% for other reasons besides quitting or reducing smoking (Seo et al. IJERPH, 2023, 11;20(6):4963).
- **These findings highlight the importance of non-industry research on measuring and understanding use patterns of HTPs, particularly how HTPs interact with cigarettes.**

Major Support for the ITC 7 Country Nicotine Product Adult Survey

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International Tobacco Control Policy Evaluation Project

US National Cancer Institute:
P01 CA200512

Canadian Institutes of Health Research:
FDN-148477

National Health and Medical Research Council of Australia: APP1106451, GTN1198301

Ontario Institute for Cancer Research:
Senior Investigator Award (2007-2027)

Korea Health Promotion Fund — Main support for Korea Surveys

New Zealand Health Research Council
(19/641)

ITC Project Research Organizations

ITC Project Research Support

EXHIBIT 5

Funding: This study was supported by a grant from the Korean Ministry of Health and Welfare and the Canadian Institutes of Health Research (FDN 148477). Additional support to GTF was provided by a Senior Investigator Award from the Ontario Institute for Cancer Research. The funders had no role in the design and conduct of the study; data collection/management, analysis, interpretation of the data, or the preparation of this presentation.

Disclosures: GTF has served as an expert witness or consultant for governments defending their country's policies or regulations in litigation. KMC has in the past and continues to serve as a paid expert witness in litigation filed against cigarette manufacturers. All other authors have no conflicts of interest to declare.

TRANSITIONS BETWEEN CIGARETTES AND HEATED TOBACCO PRODUCTS AMONG ADULTS WHO USE VS DO NOT USE NICOTINE VAPING PRODUCTS IN THE REPUBLIC OF KOREA: FINDINGS FROM THE 2020, 2021, AND 2023 ITC KOREA SURVEYS

Geoffrey T. Fong[1,2], Gang Meng[1], Shannon Gravely[1], Mary E. Thompson[1], Steve S. Xu[1], Anne C.K. Quah[1], Hong Gwan Seo[3,4], Sungkyu Lee[5], Su Young Kim[6], Gil-yong Kim[6], Sujin Lim[6], Sung-Il Cho[7,8], K. Michael Cummings[9], Andrew Hyland[10]

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Number: POS04-121
Date: Fri 3/22/2024
Time: 5:30-7:00pm

BACKGROUND

- The Republic of Korea is the world's 4th largest market for heated tobacco products (HTPs). In Korea, HTPs are regulated at the same level as cigarettes. It is important to understand how HTPs interact with cigarettes.
- We previously examined transitions of HTPs to/from cigarettes in Japan, the world's largest HTP market, finding that HTPs were not associated with smoking cessation but instead with long-term dual use.
- Korea differs from Japan in that nicotine vaping products (NVPs) are legal. The nicotine market in Korea is thus more similar to the nicotine market in the United States and other countries. It is important to understand interactions among the three products.

OBJECTIVES

- Among a national sample of Korean adults—to examine transitions between states of tobacco product use (cigarette only, HTP only, dual use, former smokers who do not use HTPs) across consecutive waves.
- To examine specifically if HTP use is associated with transitions away from smoking.
- To examine whether transitions differed for those who also used NVPs vs. those who did not use NVPs. This can be tested in Korea but not in Japan, where NVPs are banned.

METHODS

- Data came from Waves 1-3 (2020, 2021, 2023) of the ITC Korea Surveys, national cohort surveys of adults (19+ years). The dataset consisted of respondents who participated in at least 2 of the 3 waves. Wave 1 cohort: N = 1696; Wave 2 cohort: N = 1073
- We employed a Markov multi-state (MSM) model to examine transitions in use of cigarettes and HTPs over each wave. MSM treats time as a continuous variable—more realistic since there were interwave interval differences; other modeling approaches treat time as discrete.
- Four states of tobacco product use:
  1. Those who smoked cigarettes but did not use HTPs ≥weekly (Cig only)
  2. Those who used HTPs but did not smoke ≥weekly (HTP only)
  3. Those who smoked and used HTPs ≥weekly (Cig+HTP Dual)
  4. Those who quit cigarettes and who did not use HTPs or used HTPs <weekly (No Cig/HTP)
- Analyses were weighted. Sex, age, and initial NVP status were covariates.
- We also examined whether vaping was associated with different transition patterns:
  1. Those who also vaped: N=385
  2. Those who did not also vape: N=2384

RESULTS

Transition Tables

- In these tables, we present the MSM estimates of one-year cumulative transition probabilities for each pre-transition state. MSM takes into account the actual time interval between waves.
- In the top transition table (All Respondents), sex, age, and initial NVP status were covariates.
- The bottom two transition tables present the transitions by whether they were or were not vaping at the initial wave. The transitions for the HTP only and No Cig/HTP groups did not include sex and age as covariates due to low sample size.
- Statistical tests employed standard errors estimated by bootstrapping.

All Respondents

Pre-Transition State	Post-Transition State %				
	Cig Only	Dual	HTP only	No Cig/HTP	Non-smoking
Cig only N=2155	86.1 (85.0, 87.2)	8.2 (7.4, 9.1)	0.3 (0.2, 0.3)	5.4 (4.5, 6.3)	5.7
Cig+HTP dual N=1467	11.4 (9.4, 13.5)	85.0 (81.8, 88.1)	3.0 (1.9, 4.2)	0.6 (-1.3, 2.5)	3.6
HTP only N=128	5.0 (3.8, 6.3)	58.9 (49.1, 68.7)	30.8 (20.8, 40.8)	5.3 (1.5, 9.2)	36.1
No Cig/HTP N=188	11.0 (6.3, 15.7)	2.4 (1.3, 3.5)	2.9 (1.0, 4.7)	83.8 (78.1, 89.5)	86.7

- For three groups, >80% did not transition over time. The exception was HTP only: only 31% stayed in that state, and they were much more likely to transition (back) to smoking.
- Cig only: 8.5% of them initiated HTPs, but nearly all of them (8.2/8.5 = 96.5%) were still smoking at the next wave (i.e., they were dual using).
- Dual use: they were not less likely than Cig only to have quit cigarettes: 3.6% vs. 5.7% (p=0.10), but they were much less likely than Cig only to have quit both cigarettes and HTPs: 0.6% vs. 5.4%. (p<0.001).
- Future transition analyses will be conducted starting with those who exclusively smoke at Wave 1, and then start the analysis of transitions at Wave 2.

Those using HTPs who vaped at initial wave

Pre-Transition State	Post-Transition State %				
	Cig Only	Dual	HTP only	No Cig/HTP	Non-smoking
Cig only + NVP N=133	79.0 (73.4, 84.6)	12.8 (9.6, 16.9)	0.4 (0.2, 0.6)	7.8 (4.3, 11.4)	8.2
Cig+HTP dual + NVP N=342	6.4 (4.4, 8.3)	90.1 (87.1, 93.0)	3.1 (1.4, 4.8)	0.5 (-0.6, 1.6)	3.6
HTP only + NVP N=22	3.8 (1.6, 4.1)	39.1 (23.9, 54.3)	37.9 (19.6, 56.2)	19.2 (4.9, 33.5)	57.1
No Cig/HTP + NVP N=43	17.6 (10.7, 24.5)	2.1 (1.1, 3.2)	1.0 (-0.3, 2.3)	79.2 (71.2, 87.2)	80.2

- For those using HTPs who vaped at initial wave: Similar transition pattern
- Cig only who took up HTPs (13.2%): 12.8/13.2 = 97% dual use
- Dual use: less likely to have quit smoking than cig only (3.6% vs. 8.2%) (p = 0.01)

Those using HTPs who did NOT vape at initial wave

Pre-Transition State	Post-Transition State %				
	Cig Only	Dual	HTP only	No Cig/HTP	Non-smoking
Cig only & No NVP N=2022	86.8 (85.7, 87.9)	7.7 (6.8, 8.5)	0.3 (0.2, 0.3)	5.3 (4.4, 6.2)	5.6
Cig+HTP dual & No NVP N=1125	12.2 (9.8, 14.5)	84.2 (80.8, 87.7)	3.0 (1.8, 4.2)	0.6 (-1.4, 2.6)	3.6
HTP only & No NVP N=106	5.3 (3.8, 6.7)	59.3 (49.1, 69.5)	31.3 (20.3, 42.3)	4.1 (1.6, 6.6)	35.4
No Cig/HTP & No NVP N=145	10.8 (5.9, 15.7)	2.3 (1.2, 3.4)	2.8 (0.8, 4.7)	84.1 (78.3, 89.9)	86.9

- For those using HTPs who did NOT vape at initial wave: Similar transition pattern
- Cig only who took up HTPs (8.0%): 7.7/8.0 = 96% dual use
- Dual use: no more likely to have quit smoking than cig only (3.6% vs. 5.6%) (p = 0.14)

CONCLUSIONS

- Transitions to/from cigarettes and HTPs in Korea were similar to transitions we previously found in Japan: when those who smoke took up HTPs, there were low rates of transitioning away from cigarettes.
- HTP use was not associated with smoking cessation but with a very high percentage of HTP-cigarette dual use (>95%).
- NVP use was a partial moderator: although cig only who also vaped were more likely to transition to HTPs overall (p = 0.02), NVPs did not moderate transitions to not smoking. In other words, NVPs and HTPs were substitutes, but neither was associated with transitions away from smoking.
- Studies of HTP emissions and biomarkers of exposure show that although HTPs are not harmless, they expose consumers to lower levels of most toxicants than cigarettes, but higher than NVPs (e-cigarettes).
- The impact of HTPs on public health depends on the extent to which HTPs increase smoking cessation.
- This ITC Korea study is consistent with the ITC Japan study: suggesting that HTPs may not help increase transitions towards quitting smoking.

Society for Research on Nicotine and Tobacco Annual Meeting
March 20-23, 2024, Edinburgh, Scotland
Contact: Geoffrey T. Fong (gfong@uwaterloo.ca)
Website: https://itcproject.org/

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Core Support provided by the U.S. National Cancer Institute (P01 CA200512)
Core Support provided by a Canadian Institutes of Health Research Foundation Grant (FDN-148477)

EXHIBIT 6

Changes in Cigarette and Total Tobacco Consumption among Korean Adults When Transitioning between Exclusive Cigarette Smoking and Dual Use of Cigarette and Heated Tobacco Products: Findings from the 2020-2023 ITC Korea Surveys

Steve S. Xu[1]*, Gang Meng[1], Mi Yan[1], Shannon Gravely[1], Hong Gwan Seo[2], Sungkyu Lee[3], Sung-il Cho[4], Yeol Kim[2], Su Young Kim[5], Gil-yong Kim[5], Sujin Lim[5], Anne C. K. Quah[1], K. Michael Cummings[6], Andrew Hyland[7], Geoffrey T. Fong[1, 8]

[1]University of Waterloo, Canada; [2]National Cancer Center, Republic of Korea; [3] Korea Center for Tobacco Control Research and Education; [4]Seoul National University, Republic of Korea;[5]Korea Health Promotion Institute; [6]Medical University of South Carolina, USA; [7]Roswell Park Comprehensive Cancer Center, USA; [8]Ontario Institute for Cancer Research, Canada

Presented at Society for Research on Nicotine and Tobacco 30th Annual Meeting, March 23, 2024
Edinburgh, Scotland
***Contact: s4xu@uwaterloo.ca**

None of the authors report any support from tobacco, nicotine, or pharmaceutical companies in the past 5 years, and this study was not funded by such companies

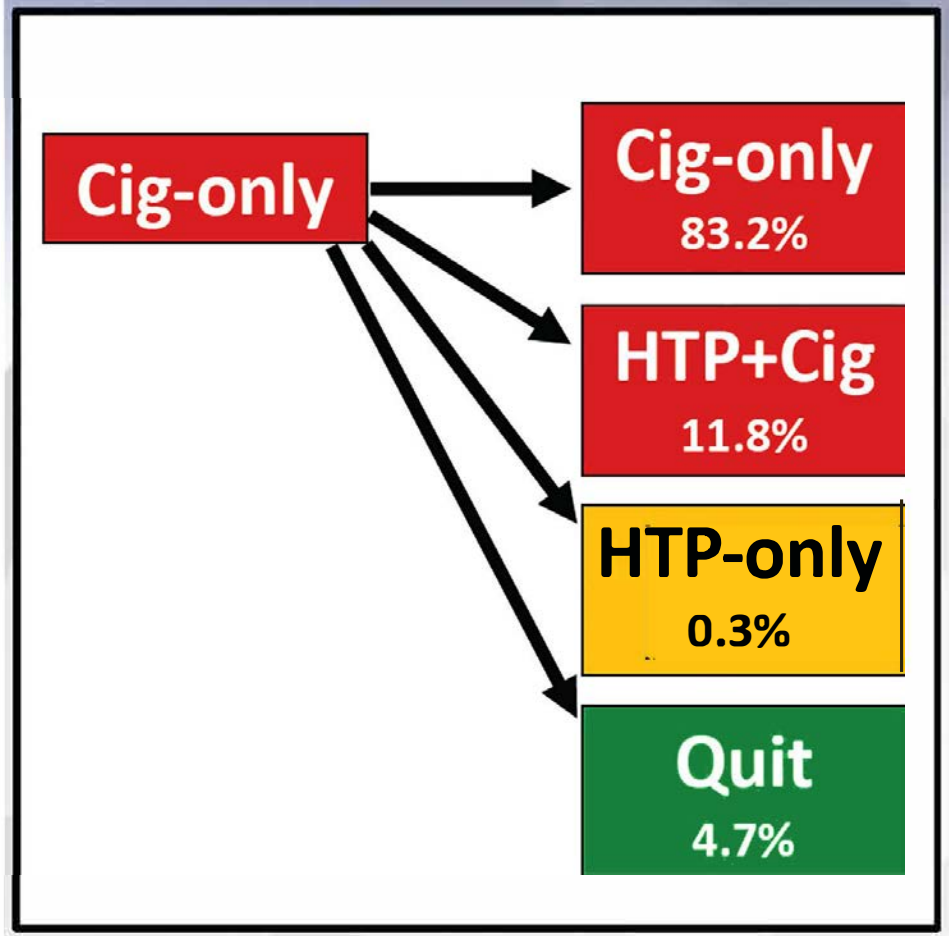
Disclosures of Interests:

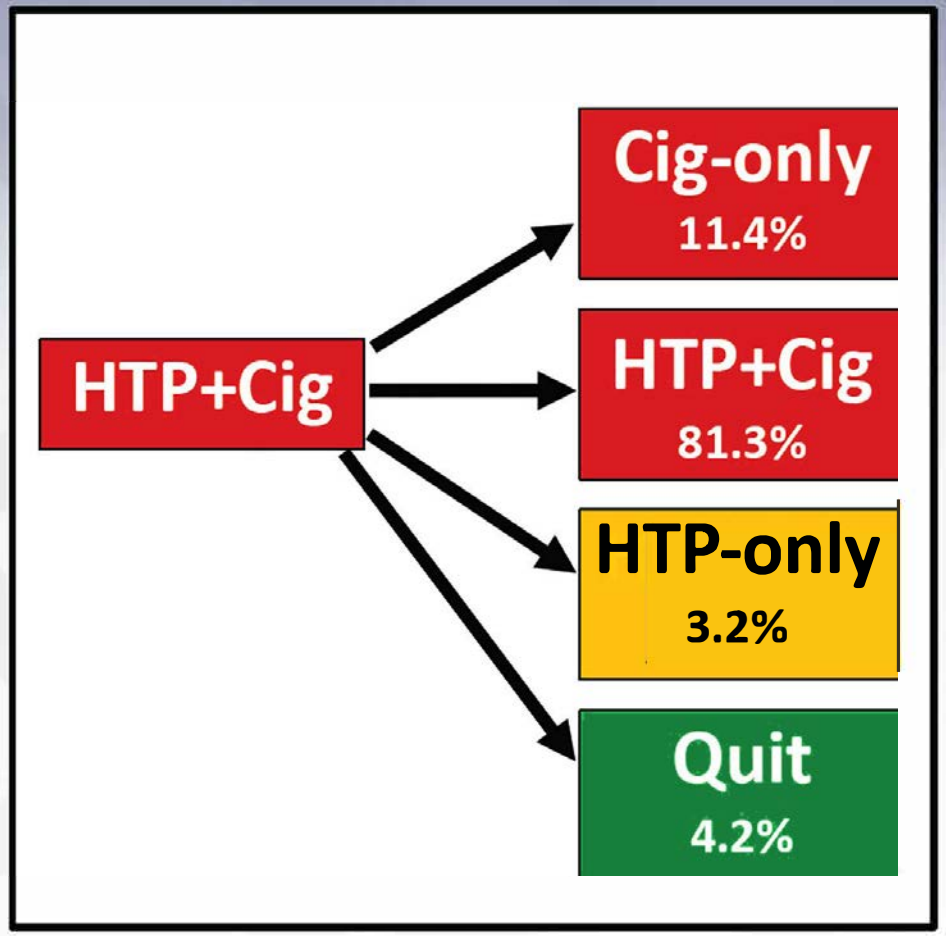
- Geoffrey T. Fong has served as an expert witness or consultant for governments defending their country's policies in litigation.
- Geoffrey T. Fong and Shannon Gravely served as paid expert consultants to the Ministry of Health of Singapore in reviewing the evidence on plain/standardized packaging.
- K. Michael Cummings has served as a paid expert witness in litigation against cigarette manufacturers in the United States.

Funding:

- The **ITC Korea Survey** was supported by grants from the Korean Health Promotion Fund and the Canadian Institutes of Health Research (FDN-148477).
- Core support for the **overall ITC Seven Country Nicotine Product Survey** was provided by the US National Cancer Institute (P01 CA200512) and the Canadian Institutes of Health Research (FDN-148477)
- Additional support to GTF was provided by a Senior Investigator Grant from the Ontario Institute for Cancer Research, Senior Prevention Scientist Award from the Canadian Cancer Society Research Institute, and the Canadian Cancer Society O. Harold Warwick Prize.

ITC Korea: Transitions of people who smoke cigarettes only and people who dual use HTPs-cigarettes (2020-21)





Research questions

1. How does tobacco consumption change when people transition from (1) cig-only to dual (cig+HTP); (2) dual to cig-only; (3) dual to HTP-only

Measures of consumption	
Cigarettes:	Cigarettes per day **(CPD)**
HTPs:	Heated tobacco sticks per day **(HPD)***
Total Tobacco:	CPD + HPD = **TPD**

* For those who use Ploom TECH, one capsule = 4 heated tobacco sticks
* For those who use glo sens, one capsule = 6.3 heated tobacco sticks

2. In Korea, unlike in Japan, nicotine vaping products (NVPs; e-cigarettes) are legal. Does vaping change the pattern of consumption change when people transition to/from dual use?

Study Sample and Analytic Methods

- **Study Source and Sample:**
  - ITC Korea Survey, national web panel cohort survey (total N~4700).
  - Adults (≥19 yrs) who smoke and/or recently quit, and/or use HTPs and/or NVPs
  - Wave 1: 2020 (N=4740), Wave 2: 2021 (N=4467), Wave 3: 2023 (N=4769)
- Followed two groups from baseline wave to followup (2020 to 2021; 2021 to 2023)
  - Those who smoke cigarettes only (≥weekly)
  - Those who dual use cigarettes & HTPs (≥weekly)
- Measured the consumption of cigarettes and HTPs before/after transitions

Baseline-Followup	**Cigarette Only**	**Dual HTP-Cigarette**
2020 – 2021	975	604
2021 – 2023	1184	865

- **Analytic Methods:** Weighted longitudinal linear regression analyses of changes in average daily tobacco consumption: CPD, HPD, TPD

Cigarettes only → Cigarettes + HTPs (dual use)(12%)

Tobacco Consumption	Baseline	Followup	Diff	% Diff	Test of diffs
Cigarettes/day (CPD)	13.3	12.7	-0.6	-6.0%	W1-W2: n.s. W2-W3: n.s.
Heat sticks/day (HPD)	0	6.4	+6.4		
Total sticks/day (TPD)	13.3	19.1	+5.8	+43.6%	W1-W2: p<0.001 W2-W3: p<0.001

- Very slight reduction in cigarettes, but large addition of HTP sticks
- When those who only smoke cigarettes add HTPs to dual use, their total tobacco stick consumption increases by 44%.

Does vaping change the consumption pattern from exclusive smoking to dual use?

All who changed from exclusive smoking to dual use

Tobacco	Baseline	Followup	Diff
Cigs/day	13.3	12.7	-0.6
HTPs/day	0	6.4	+6.4
Total/day	13.3	19.1	+5.8

- Those who also vaped: much lower stick consumption (getting nicotine from vaping)
- Vaping does not change the basic pattern of changes in consumption.

Those who vaped at baseline and/or followup

Tobacco	Baseline	Followup	Diff
Cigs/day	9.8	9.3	-0.5
HTPs/day	0	5.0	+5.0
Total/day	9.8	14.3	+4.5

Those who did NOT vape

Tobacco	Baseline	Followup	Diff
Cigs/day	14.4	13.7	-0.7
HTPs/day	0	6.6	+6.6
Total/day	14.4	20.3	+5.9

HTP+Cigarette Dual use → Cigarette only (11%)

Tobacco Consumption	Baseline	Followup	Diff	% Diff	Test of diffs
Cigarettes/day (CPD)	13.7	11.2	-2.5	-18.2%	W1-W2: p=.02 W2-W3: p=.02
Heat sticks/day (HPD)	6.0	0	-6.0	-100%	
Total sticks/day (TPD)	19.7	11.2	-8.5	-43.1%	W1-W2: p<.001 W2-W3: p<.001

- Cigarettes do NOT increase; rather they also decrease (significantly)
- This was consistent for both wave transitions (W1-W2 and W2-W3)
- When those who dual use cigarettes and HTPs go back to cigarettes only, their total tobacco stick consumption decreases by 43%.

Does vaping change the consumption pattern from dual use back to exclusive smoking?

We could not examine the impact of vaping for consumption changes for dual use to exclusive smoking since there were only 8 respondents who made this transition who also vaped.

Cigarette-HTP dual use → HTP only (3%)

Tobacco Consumption	Baseline	Followup	Diff	% Diff	Test of diffs
Cigarettes/day (CPD)	9.2	0	-9.2	-100%	
Heat sticks/day (HPD)	10.0	15.0	+5.0	+50%	W1-W2: n.s. (low n) W2-W3: n.s. (low n)
Total sticks/day (TPD)	19.2	15.2	-4.2	-21.8%	W1-W2: n.s. (low n) W2-W3: n.s. (low n)

- HTP sticks increased, but not as much as cigarettes decreased
- Net effect: Total consumption decreased by 22%
- Low sample size so low power for statistical tests.

Summary and Conclusions

1. When people transition from **cigarette-only** to **cigarette-HTP dual use**:
   44% increase in total consumption
2. When people transition AWAY from dual use:
   – **Dual to cigarette only** (11% of duals): 43% decrease in total consumption
   – **Dual to HTP only** (3% of duals): 22% decrease in total consumption.
3. Dual use is an **apex state**: much higher total consumption than exclusive use (of cigarettes or of HTPs)
4. Same pattern of results as in Japan, but more pronounced in Korea
5. Using NVPs does not alter the basic pattern of changes in consumption.

Dual use is a substantial benefit for companies who produce both cigarettes and HTPs.

Major Support for the ITC Seven Country Nicotine Product Survey of which the ITC Korea Survey is a component

itc International Tobacco Control Policy Evaluation Project

US National Cancer Institute:
P01 CA200512

Canadian Institutes of Health Research:
FDN-148477

National Health and Medical Research Council of Australia: APP1106451, GTN1198301

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Senior Investigator Award (2007-2027)

Korea Health Promotion Fund — Main support for Korea Surveys

New Zealand Health Research Council
(19/641)

ITC Project Research Organizations

ITC Project Research Support

Thank you very much!

매우 감사합니다

EXHIBIT 7

IQOS and the Process of Changing to Evolve

Ever think about all the times you looked for a different way of doing things and ended up discovering something much better? #TheChallenge

Mon June 21, 2021 08:55 AM

Message paid for by Phillip Morris

Recent times have challenged us to transform ourselves in a few short weeks: more technology, new habits, fast adaptations. It's an era of new starts, with all the opportunities that involves.

One inspirational example of change is Philip Morris. This 173-year-old company, the leader of the tobacco market, is revolutionizing its production to the point of creating a device that lays the foundations for a smoke-free future.

IQOS is an electronic device created with HeatControl™ technology that heats **real tobacco** instead of burning it. In short, it's a milestone for the industry—such that it has already been authorized by the US Food and Drug Administration (FDA) as a product of “modified risk.”

And the fact that natural tobacco is not burnt means that fewer toxic chemicals are emitted than with a traditional cigarette. This device is less bothersome to non-smokers:

- ☐ No smoke
- ☐ No Fire
- ☐ No ash
- ☐ With real tobacco.

What's more, IQOS comes with a variety of cases, holders, and accessories in many colors.

We would like to inform the adult population that has decided not to quit cigarettes about the lower-risk

alternatives that are available in the country. This way, they will have enough information to freely and responsibly decide whether to use them.

Catalina Betancourt, Vice President of Corporate Affairs at Philip Morris Mexico.

Because in this free search for something better, the company is also promoting another important principle:

If you don't smoke, don't start. If you do smoke, quit. If you don't want to quit but want to make a change, #ChooseTheChange.

Philip Morris is offering a total transformation that will revolutionize smokers' worlds: a smoke-free future. IQOS' challenge is to live the change.

Want to learn more? Visit IQOS on Instagram @IQOS_MX and Twitter @iqos_mx

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I, (b) (6), hereby certify that the document(s) included in this delivery, to the best of my knowledge and belief, are true, accurate and complete translations from **Spanish (US)** into **English (US)** of the content from the following file(s):

- IQOS y el proceso de cambio para evolucionar

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EXHIBIT 8

PHILIP MORRIS PRODUCTS S.A.

His Excellency Alikhan Smailov
Prime Minister of the Republic of Kazakhstan

April 5, 2022

Dear Prime Minister Smailov,

I was honored to have the opportunity to meet you on March 31, 2022, and share our company's perspective on investments to localize production of next generation of innovative portfolio – our heated tobacco products in Kazakhstan. Thanks for your honest feedback and considering to provide tax incentives for the project.

At the same time I was surprised to notice that ideology seems to prevail over science and evidence when assessing these novel products. At the same time, a growing number of governments around the world recognized the health benefits of heated tobacco products, such as their reduced exposure, and the decision of the U.S. Food Drug and Administration that authorized these products as benefitting public health.

I would like to express my sincere gratitude to your proposal to establish a working group consisting of Ministries of Health, Finance, Economy, Foreign Affairs, and Philip Morris International. We stand ready to share scientific evidence proving that heated tobacco products can promote public health. We are happy to invite a delegation of your Cabinet and leading Kazakh scientists to visit our R&D center in Neuchatel, Switzerland, or alternatively bring our scientists over to Nursultan. I just ask for an objective review of the science behind our products, so that you can take an informed decision whether to have millions of Kazakhs to continue smoking or move to better alternatives.

We have expressed serious consideration of bringing investments to Kazakhstan to locally manufacture our innovative products, also with the objective to develop a hub to export them to other countries. Undoubtedly, such investment will bring diversified technological innovation to Kazakhstan, generate additional economic benefits across the entire supply chain and reaffirm our trust and intention to sustain long-term commitment to the country. Without sharing the same views on the reduced risk potential of next generation of our products and an appropriate regulatory framework investing into a manufacturing hub may not be a win-win solution for both parties.

We look forward to cooperation with the Government of Kazakhstan to make this investment happen and look forward to meet you again, as we discussed.

Sincerely (b) (6)

Marco Mariotti
President Eastern Europe Region

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EXHIBIT 9

Massimo Adolina, PMI: Greece's key role for a cigarette-free future

In addressing the Delphi Economic Forum, Massimo Andolina, President for Europe of Philip Morris International, spoke about the company's radical transformation, driven by science and the vision of the end of cigarettes. Source:

Protagon.gr Protagon Team MAY 11, 2023, 12:30 PM Source: Protagon.gr

"Nowadays there are alternatives. We need to evolve our thinking about tobacco, just as we have evolved our thinking in other areas of our lives."

In addressing the Delphi Economic Forum, Massimo Andolina, President for Europe of Philip Morris International, spoke about the company's radical transformation, driven by science and the vision of the end of cigarettes.

Philip Morris International has invested over 10.5 billion dollars in the last 15 years in research and development of new products, designing and developing better alternatives to cigarettes. Mr. Andolina explained that this radical transformation instilled a tremendous sense of purpose in everyone in the company. Employing around 1,000 world-class scientists, engineers and technicians, Philip Morris International now offers options to adult smokers who refuse to quit.

These new products that are being developed can change the lives of these individuals. The US Food and Drug Administration (FDA) has approved IQOS, Philip Morris International's innovative tobacco heating product, as a differentiated risk tobacco product, concluding that the available scientific evidence demonstrates that IQOS is expected to benefit the health of the population overall, taking into account both smokers and non-smokers.

The Beginning of a New Solution

"We had to transform our products and convey the story and the mission of what we are trying to do to the world," explained Massimo Andolina, an exercise that had not been always easy over the years. "Without a sense of purpose internally it would be impossible, but it is this sense that drives every single person working in the company nowadays. After all, at Philip Morris International, when something is difficult, it pushes us to go that extra mile. The existence of challenges can be the beginning of a new solution," he said.

Source: Protagon.gr The President of Europe of Philip Morris International - Massimo Andolina

Reducing Risk with Real Benefits

He spoke in detail about the importance of "harm reduction" achieved through differentiated risk tobacco products and the importance of a regulatory framework in this area. "We need to accelerate cooperation between stakeholders - we all have a role to play in this. It is important to look at the science, the technology, and the data to decide on what is convincing."

He also cited the example of Sweden, whose government was the first to adopt a positive attitude towards alternative tobacco products. As a result, Swedes now smoke far less than other Europeans, which has a significant and measurable impact on the health of the population. He also cited the example of Japan, one of the first countries to launch IQOS, thanks to which 1/3 of smokers have so far given up cigarettes.

Papastratos is a key piece of the puzzle

Mr. Andolina also referred to the important role Papastratos, a subsidiary of Philip Morris International, plays in Greece, with particular emphasis on what our country has to offer. “We believe in the potential of the people we have here,” he said.

Besides, Papastratos is a “key piece of the puzzle” for Philip Morris International’s big shift. Already in 2017, a difficult time for the country, the company made an investment of 300 million euro, which transformed the Papastratos factory in Aspropyrgos into a unit for the exclusive production of heated tobacco rods for IQOS.

A major new investment of 200 million euro was also recently announced, with the addition of four new production lines at the Aspropyrgos plant, the creation of 300 new jobs and exports worth a total of 300 million euro, bringing the total investment since 2017 to date to 700 million euro.

The continuous investments in the company’s factory, in addition to increasing its production capacity, make the industry of the future a reality today, and support the extrovert orientation of the Greek economy. It is worth mentioning that 83% of Papastratos’ production is now exported to foreign markets.

A Future Without Cigarettes

How close might a cigarette-free future be? Massimo Andolina shared his own prediction: “It will happen in our lifetime. Greece could be one of the first cigarette-free countries in Europe, probably as early as 2030.”

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NEW YORK CITY DEPARTMENT OF
HEALTH AND MENTAL HYGIENE
Michelle Morse, MD
Acting Commissioner

September 24, 2025

Michelle Morse, MD, MPH
Acting Health Commissioner

Gotham Center
42-09 28th St.
Long Island City, NY 11101

Via Electronic Submission

http://www.regulations.gov

Re: Renewal of the Modified Risk Granted Orders Issued to Philip Morris Products S.A. for three types of Marlboro HeatSticks and two versions of IQOS System Holder and Charger.

To Whom It May Concern:

The New York City Department of Health and Mental Hygiene (NYC Health Department) appreciates the opportunity to provide comments to the Tobacco Products Scientific Advisory Committee (the Committee) regarding Renewal of the Modified Risk Granted Orders Issued to Philip Morris Products S.A. for Marlboro HeatSticks and IQOS System Holders and Chargers.

The NYC Health Department believes the statutory standards for granting the exposure Modification Order under section 911(g)(2) of the Federal Food, Drug, and Cosmetic Act were never met during their initial application, and the additional information and data now available, further weakens IQOS's ability to meet the required standard of protecting public health. Now that IQOS is being reintroduced into the United States (U.S.) market, the Committee and the U.S. Food and Drug Administration (FDA) have an obligation to consider newer data from worldwide studies suggesting that this designation is inappropriate. Likewise, the Committee and FDA should take into account evidence demonstrating that Philip Morris International (PMI) used the order to make unauthorized reduced risk claims in multiple other countries.[1] For example, reporting in the *Manila Bulletin*, a widely circulated English language newspaper in the Philippines, said a PMI official "explained the U.S. FDA decision has effectively differentiated IQOS from combustible cigarettes when it comes to health risk"[2] - which is an overt claim of reduced health harm despite the FDA's clear rejection of a reduced risk claim for IQOS. While the exposure modification order did not result in significant adoption of IQOS in the U.S., this was likely due to limited availability, given that IQOS was taken off the market in 2020 due to a patent infringement claim and only recently reintroduced in specific cities in Texas and Florida. In fact, although IQOS was not readily available in New York City (NYC), a 2019 NYC Health Department poll found that 20% of New Yorkers ages 18-24 polled had already heard of the product at that time.[3]

Research from parts of the world where IQOS is more readily available continue to demonstrate that caution is warranted and is outlined in further detail below. This growing body of evidence indicates that Modified Risk Granted order should not be renewed.

The availability of IQOS Does Not Promote Public Health

As the NYC Health Department has noted in previous comments regarding these products, the FDA must take into account several additional factors when evaluating the benefit to health of individuals and of the population as a whole: (1) the likelihood that existing tobacco product users will stop using them completely and switch to using IQOS; (2) the likelihood that persons who do not use tobacco products will start using IQOS; and (3) the

risks and benefits to persons from the use of IQOS compared to the use of medications approved by the FDA to treat nicotine dependence.[4]

(1) Existing Tobacco Users May Not Fully Switch to IQOS, Undermining Potential Reduced Exposure

Evidence suggests that many existing tobacco users who try IQOS will not stop using combustible tobacco products completely and will become dual users. Supporting this concern, a cohort study in Japan found that among non-smokers and former smokers, using heated tobacco products predicted increased likelihood of relapse to or initiation of combustible cigarettes one year later.[5] Similarly, PMI data from Germany found that only half (53%) of IQOS users use IQOS exclusively, while the remainder also smoke cigarettes.[6] Other data from PMI, following people who used IQOS during 2022 in four countries, found that more than one third of people used cigarettes in addition to IQOS and that proportion did not decrease over time in any of the country panels studied.[7] Recent studies from the International Tobacco Control Project (ITC) at Canada's University of Waterloo found that even fewer people in Japan and Korea quit smoking when using IQOS than suggested in PMI data.[8]

Further, a 2019 NYC Health Department poll found that among New Yorkers who had heard of IQOS, 69% of those who smoke every day had tried IQOS, without giving up cigarettes.[9] If dual use of IQOS and traditional cigarettes becomes a norm, it would likely erode any anticipated harm reduction benefits and eliminate PMI's justification for IQOS's modified risk claim.

(2) Youth and Adults Who Have Never Smoked May Start with IQOS, Especially Given IQOS Marketing in the US to Date

Heated tobacco products (HTPs) like IQOS pose more risk for youth uptake than cigarettes or other combustible tobacco products, due to their novelty, product design, and marketing (high tech, clean, lower harm, etc.), which are all similar to e-cigarettes.[10,11,12] Like e-cigarettes, IQOS may be used by youth (and adults) who never would have smoked conventional tobacco products, leading to an overall increase in the segment of the population with a nicotine addiction.[13,14] In fact, there is evidence from around the globe substantiating this concern. One study found that almost half (46%) of Italians who have tried IQOS products had never previously smoked cigarettes.[15] In Greece, prevalence of use is highest in younger adults (21%), the majority of whom started using them before age 25, compared to adults aged 40 and above (11%).[16] In Japan, while younger people are less likely to use tobacco overall, they are more likely to use HTPs than other age groups.[17] A study analyzing data from 11 European countries among those ages 15 and older found that the 15–24 year-old age group was most likely to have tried HTPs, compared to other age groups.[18] And in South Korea, adolescents began using HTPs at a rate three times higher than the rate at which they had previously adopted e-cigarette use.[19]

In NYC, among those who had heard of IQOS, nearly half (48%) of 25-44-year-olds reported having tried the product.[20] Although IQOS has had limited availability in the U.S., the product was launched in Atlanta in 2019. There, the product was marketed as 'clean' and 'high-tech,' and marketing included promotion of $1 'personal IQOS trials' in stores, technical assistance, and chances to socialize with IQOS representatives.[21] The effect of that marketing is clear: in 2020, although IQOS was not available in NYC, nearly one in five New Yorkers had heard of the product.[22] The recent IQOS relaunch in Texas and Florida again offers pop-up stores, mobile units, and flagship stores featuring modern, minimalistic décor, similar to technology retailers.[23,24] These marketing strategies position IQOS as a high-tech product, which may appeal to youth and young adults who have never used tobacco products.

(3) IQOS Is Not a Proven Cessation Device

It is not known how these devices perform relative to FDA-approved tobacco treatment medications and other evidence-based cessation approaches. A 2022 Cochrane review of 13 randomized control trials and time series studies attempting to evaluate this issue found that all studies were industry funded, that none reported on smoking cessation outcomes, and there was insufficient evidence to assess for adverse events.[25] In China, secondary analysis of a randomized clinical trial evaluating the effectiveness of brief advice and referral for smoking cessation found that using heated tobacco product was not associated with cigarette abstinence at 6 months in a community-based cohort of smoking adults with intentions to quit or reduce smoking.[26]

These new analyses reveal that the use case presented by PMI—adults who smoke completely switching to IQOS to stop smoking—is not what happens in the real world. Given these findings and the dearth of data available on population level effects, the Modified Risk Granted Orders should not be renewed.

IQOS May Pose Additional Harm For the Population As a Whole, Due to Secondhand Exposures and Impacts on Smoke-Free Policies

There is evidence to suggest that IQOS exposes others in the vicinity of use to the deleterious effects of secondhand and side stream toxic aerosols. A systematic review of studies analyzing IQOS emissions found that while IQOS emits lower levels of some substances compared to cigarettes, it has greater emissions of other harmful and potentially harmful constituents (HPHC), some of which are not included on the list of HPHCs considered by the FDA.[27] These emissions include volatile organic compounds and fine particulate matter, exposing those nearby to potentially harmful effects. [28,29,30] In fact, a national survey in Japan found that nearly half of non-tobacco users who were exposed to secondhand aerosol from HTPs reported symptoms, including asthma attacks and chest pain. [31,32] HTPs also produce aldehydes, nanoparticle and particulate matter[33] in quantities that negatively affect indoor air quality.[34,35] The systematic review also found that while PMI-funded studies reported immediate returns to baseline air quality, independent studies concluded that HPHCs lingered in the air after IQOS use.[36]

Moreover, because smoke-free air laws in many jurisdictions were drafted to cover conventional, combustible tobacco products, IQOS use is not covered by some existing smoke-free air laws. This is because many smoke-free air laws define "smoking" narrowly and require material to be burned or combusted.[37] A 2019 study from Japan demonstrated that heated tobacco products, like IQOS, were being used in smoke-free locations, including workplaces and restaurants.[38] A more recent study found that people who use HTPs were more likely to use the products in their homes (52% daily and 78% more than once a month) than people who smoked cigarettes (38% and 58%).[39] Such use erodes existing protections and changes norms surrounding smoke-free spaces.

Conclusion

For these reasons, and because there is insufficient evidence to indicate it has reduced harm to either individuals or at the population level, the **Modified Risk Granted Orders should not be renewed.** In addition, the FDA should provide aggressive oversight and enforcement of IQOS marketing. Thank you for allowing public comment on this critically important issue.

Sincerely,

(b) (6)

Michelle Morse, MD, MPH
Acting Commissioner
New York City Department of
Health and Mental Hygiene

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October 7, 2025

FDA Tobacco Product Scientific Advisory Committee Public Advisory Meeting
Consumer Choice Center Testimony

As a consumer advocacy group that fights for lifestyle freedom, innovative technologies, and smart policy, we appreciate the Food and Drug Administration's Tobacco Product Scientific Advisory Committee's open call for public comment on the Modified Risk Tobacco Products (MRTP) program and current products seeking MRTP renewal.

According to the FDA, an MRTP application generally must demonstrate that the product will significantly reduce harm and the risk of tobacco-related disease to individual tobacco users and benefit the health of the population as a whole. In order to reach a decision to authorize marketing of a proposed MRTP, FDA must consider a variety of factors under section 911(g)(4).

As staunch advocates for consumer choice, we outline and expand on key points we think are crucial to consider for this issue:

1. **An appropriate and scientifically minded reduced-risk protocol for nicotine products is both necessary and vital if we want to protect the next generation.**

The combustion from traditional cigarettes produces smoke containing more than 6,000 chemicals, among those are some that have been associated with known smoking-related illnesses such as lung cancer and heart disease. Considering that heated tobacco products (HTPs), like the IQOS system, heats the tobacco but does not burn it, HTPs are a less harmful alternative to combustible tobacco.

As of February 2022, the FDA has authorized IQOS and three of its Heatstick products to be marketed as modified risk tobacco products with legitimate claims that a person who uses regular cigarettes and fully switches to IQOS can reduce their exposure to harmful chemicals. This greatly benefits consumers as more of those who smoke will be made aware of the fact that there are products available which are less harmful than consuming combustible tobacco and could prompt them to switch.

FDA's website lists the 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.

Since the original MRTP authorization, there has not been any evidence contradicting the

science presented in 2022. With that in mind, we hope that the current products up for renewal are granted reauthorization, in addition to the FDA looking at additional smokeless tobacco or nicotine products which deserve a modified risk authorization as well to provide further options for consumers to choose from within the regulated market.

Reducing the barriers of receiving MRTP authorization will help more smokeless tobacco and nicotine products achieve this status and allow consumers to use the pertinent information to make more informed decisions about their health, potentially encouraging consumers to switch to a less harmful choice when consuming nicotine.

2. **We must spread awareness of other less harmful nicotine alternatives to combustible tobacco such as nicotine pouches, snus, gums, and lozenges, and our national health regulator should be empowered to do so.**

While IQOS is the specific product being focused on for this TPSAC matter, it's crucial that other nicotine alternative products are also being considered and promoted as less harmful options than combustible tobacco for consumers.

E-cigarettes or nicotine vapes are the most popular and effective technology to move consumers away from combustible tobacco, but other nicotine alternative products exist including nicotine pouches, snus, nicotine gums and lozenges, and more.

The United Kingdom was one of the first countries to embrace vaping as a harm reduction tool when Public Health England announced in 2015 that studies showed it to be 95% less harmful than smoking. Since 2015, the UK government continues to study the effects that vaping has had on public health and produces their findings annually. The latest report from 2022 shows that flavored vaping products, specifically fruit and menthol/mint flavors, remain the most common aid used by people to help them stop smoking combustible tobacco. When analyzing the stop smoking service data from 2020 to 2021, it was noted that vaping devices produced the highest success rates for attempts at quitting.

The UK government then doubled down on its harm reduction strategy through vaping by encouraging one million smokers to swap their cigarettes for a free vape starter kit, providing financial incentives to pregnant women to quit smoking, as well as introducing mandatory information sheet inserts about vaping into packages of cigarettes.

New Zealand has also embraced groundbreaking evidence-based regulation of vaping and HTPs which was supplemented by a government-led mass media campaign called 'Vape To Quit Strong' and included an informational website aimed to 'support smokers to switch to regulated products that are less harmful than smoking.' The result of this campaign was an incredible drop in smoking prevalence from 16.4% to 6.8% between 2011 and 2023.

It is our belief that MRTPs should be quickly granted to any nicotine alternative that has scientific evidence indicating it is less harmful than combustible cigarettes to ensure consumers are aware of as many less harmful alternatives to combustible tobacco as possible.

3. **Approval of additional reduced-risk products, and renewal of risk modification orders, would be beneficial for millions of Americans and public health.**

Modified Risk Tobacco Product classification should encourage innovation of nicotine alternatives to combustible tobacco that have the potential to drastically reduce smoking-related death and disease. In its current form, the MRTP process lacks clarity and discourages innovators from pursuing it to begin with. This unclear and burdensome process harms consumers as it prevents less harmful nicotine products from being effectively marketed, meaning the consumers who are ready to move away from combustible tobacco products but aren't sure what to switch to could miss the opportunity to understand what the less harmful products available to them are.

As the Reagan-Udall Evaluation Report noted, FDA's Center for Tobacco Products has an opportunity to develop a more concise and understandable framework for MRTP applications to follow. Some of these recommendations include prioritizing timely development and completion of policies and scientific standards necessary for high-quality MRTP applications and simplifying, standardizing, documenting, and publicly sharing review procedures.

In general, more transparency from the FDA's Center for Tobacco Products in regard to the regulatory process and scientific foundation from which they are operating off of would be prudent. Ideally, CTP would openly support the importance of MRTP authorized products and create an effective communication strategy to educate adult consumers of combustible tobacco products as to what other options they have for FDA-approved less harmful nicotine alternatives.

Although not the focus of this TPSAC meeting, we would be remiss not to mention the importance of also reforming the PMTA process in addition to the MRTP pathway. While over 26 million applications were submitted to the FDA's Center for Tobacco Products seeking approval to sell their products on the legal market, to date only 39 e-cigarette products have been approved, including only 9 separate devices, and only in tobacco and menthol flavors. All PMTAs for flavored nicotine products were originally rejected, and of the estimated remaining 560,000 pending applications, the CTP has continually missed their agreed upon 180-day timeline for review.

We appreciate the agency's recent announcement of a new pilot program that aims to increase efficiency and streamline the review process for PMTAs for nicotine pouch products, but believe that all nicotine alternative products should be included to ensure a vibrant marketplace of less harmful options to combustible tobacco are available for consumers who currently smoke and are looking to reduce their risk.

We also commend the agency for approving some flavored products (outside of tobacco and menthol) for this first time ever when the FDA issued marketing granted orders for ZYN nicotine pouches in flavors including: chill, cinnamon, citrus, coffee, mint, menthol, peppermint, smooth, spearmint, and wintergreen. This is a step in the right direction to help consumers as studies show that those who use flavored nicotine alternative products are 2.3x more likely to stop smoking combustible tobacco.

It's clear that these regulatory pathways for product authorization were created with the intention of ensuring that any products reaching the marketplace meet the required standards for consumer use. However, it is also clear that these FDA regulatory pathways are still broken and have created an extremely complex illicit market that meets consumer demand in a way that the current pathway does not allow the regulated marketplace to compete with. The illicit market presents dangerous conditions for consumers, considering the products are unregulated, age verifications are not performed, and points of sale could present additional safety concerns.

Streamlining the PMTA process to ensure more nicotine alternative products come to market is crucial to combat the illicit market, help consumers stop smoking combustible tobacco, and improve public health.

4. **Low-risk nicotine alternatives have the potential to completely supplant combustible tobacco use in the United States, which would continue to save lives, empower consumers, and strengthen our public health.**

The FDA can look to other global public health counterparts and follow in their successful footsteps, like Sweden. The World Health Organization recently announced that Sweden will likely become the first smoke-free country. Sweden has embraced the concept of tobacco harm reduction and supports its citizens to switch from combustible cigarettes to less harmful alternatives including vaping, nicotine pouches, and snus.

Consequently, Sweden has reduced its smoking rates two times faster than any other country in the European Union and smoking rates have declined by 55% in the last decade. Additionally, smoking-related deaths are 22% lower in Sweden than the European Union average and cancer incidence is 41% lower than in the rest of Europe, with total deaths from cancer being 38% lower.

Nicotine pouches became available in Sweden in 2018 and the smoking rates dropped by more than 20% since then. Interestingly, snus has been used mostly by men in Sweden as means to stop smoking combustible tobacco and nicotine pouches have become the preferred option for female smokers.

Nicotine pouches and snus are gaining popularity and provide consumers with additional options and choices to move away from combustible tobacco. While gums and lozenges are less popular among consumers, they still pose a versatile contribution to ending smoking.

In conclusion, MRTP authorizations play a crucial role in educating consumers on the less harmful nicotine alternatives available on the regulated market. Products with existing MRTP authorizations should keep their clearance due to the scientific evidence showing they are less harmful than combustible tobacco. Additionally, the MRTP application and authorization process should be reformed and streamlined to ensure that even less harmful nicotine alternatives are promoted to the consumers who need them most and public health can drastically improve as a result.

Thank you for your time and consideration on this matter.

Respectfully,

Elizabeth Hicks
US Affairs Analyst

712 H St NE PMB 94982
Washington, DC 20002

consumerchoicecenter.org

info@consumerchoicecenter.org

September 25, 2025

Attn: Rachel Jang, PharmD, DFO

Office of Regulations, Center for Tobacco Products
Food and Drug Administration
10903 New Hampshire Ave.
Bldg. 71, Rm. G335
Silver Spring, MD 20993-0002

Re: Public comment on the MRTPA renewal for IQOS heated tobacco product system, submitted by Philip Morris Products S.A.

The Pelican Institute for Public Policy is a non-profit, non-partisan organization that researches and develops policy solutions to address the most significant barriers to opportunity in Louisiana and across the United States. We educate the public about the benefits of individual liberty and free enterprise, turning great ideas into powerful policy solutions that make a meaningful difference in people's lives. We also routinely address cases of significant government overreach that present barriers to opportunity.

With the above goals in mind, we offer this letter in support of the modified risk grant orders authorizing Philip Morris Products S.A. to market IQOS heated tobacco products. Over the past several years, evidence has shown that use of the IQOS system, which heats tobacco instead of burning it, offers significantly less harm to consumers when compared to conventional cigarette use. We believe the scientific standards continue to be met to market these products as modified risk tobacco products, giving the public access to additional options that lessen their body's exposure to harmful or potentially harmful chemicals.

We urge the FDA and CTP to meet its harm reduction goals and enhance the availability of safer consumer options by approving this request.

Sincerely,

(b) (6)

Daniel J. Erspamer
Chief Executive Officer
Pelican Institute for Public Policy

AMERICANS for TAX REFORM

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September 24, 2025

To: Tobacco Products Scientific Advisory Committee Office of Science, Center for Tobacco Product

c/o Food and Drug Administration
Document Control Center
Building 71, Room G335
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Re: [Docket No. FDA-2025-N-2030]
Advisory Committee Meeting Scheduled On Modified Risk Tobacco Product Renewal Applications For IQOS Products scheduled for October 7th, 2025

Dear Committee,

On behalf of Americans for Tax Reform, we thank the committee's willingness to accept public comment regarding renewal of Modified Risk Tobacco Product (MRTP) authorizations for:

- Marlboro Amber HeatSticks
- Marlboro Green Menthol HeatSticks
- Marlboro Blue Menthol HeatSticks
- IQOS 2.4 System Holder & Charger
- IQOS 3.0 System Holder & Charger

Americans for Tax Reform (ATR)is a non-profit, non-partisan, non-governmental organization representing taxpayers and consumers throughout these United States, with a long-standing interest in advocating sound, evidenced based public policy. ATR has long supported evidence based, risk-proportionate tobacco policy—moving people who would otherwise smoke away from combustion and toward meaningfully less harmful alternatives. Our submissions and commentary to U.S. international bodies consistently argue the evidence that demonstrate how prohibitionist approaches backfire, while harm reduction saves lives and protects consumers.

As such, ATR urges the Tobacco Products Scientific Advisory Committee (TPSAC) to recommend renewal of the existing reduced-exposure MRTP orders for IQOS and its corresponding HeatSticks. The FDA's prior decisions (July 7, 2020, and March 10, 2022) were based on a robust scientific record demonstrating that heating tobacco—rather than burning it—significantly reduces the formation of harmful and potentially harmful constituents and that complete switching to IQOS significantly reduces users' exposure to toxic chemicals. Nothing material has emerged since those orders to undermine that conclusion; if anything, subsequent systematic reviews and FDA's own technical assessments have reinforced it.

Our research affiliate, the Tholos Foundation (formerly ATR Foundation), conducts global harm-reduction analysis and case studies. In 2023 Tholos released Safer Nicotine Works, a white paper analyzing Sweden and Japan that documents substantial declines in smoking when safer alternatives—including heated tobacco—are available and acceptable to adult smokers. ATR also highlighted Tholos' 2023 harm-reduction compilation (vaping, HTP, snus, pouches), emphasizing the overwhelming evidence that non-combustibles are significantly less harmful than cigarettes. In 2025, the Tholos Foundation was a key founding partner of the international "Prohibition Does Not Work" platform, which has issued three reports on the failures of nicotine prohibition in Germany, Australia, and Brazil, which issue dire cautionary tales if their lessons are not learned here.

In 2020 the FDA authorized reduced-exposure messaging for IQOS; in 2022 FDA extended the same findings to the IQOS 3 holder/charger, stating that the device heats rather than burns tobacco, producing significantly fewer HPHCs and that complete switching significantly reduces a user's exposure to those chemicals. FDA's Technical Project Lead (TPL) memo also reported no evidence of increased youth risk for IQOS 3 versus 2.4, and low interest among never-smokers—important population-level safeguards. There is no reason to think this has changed. Similarly, meta analysis of all studies on the impact of such products on biomarkets are in line with FDA's earlier findings as to the lower risk exposures.

Those conclusions remain well-founded and consistent with the current evidence base, so the legally relevant question—whether the exposure claims are still accurate and beneficial—should can *only* be answered in the affirmative.

In addition to the clear scientific basis upon which MRTP's would be justified according to the statutory requirements, real world experience in other jurisdictions adds further weight to this.

Japan is the best natural experiment for heated tobacco. Tholos' analysis, drawing on government and market data, shows that after nationwide introduction of tobacco heating products (2016), cigarette sales dropped by roughly a third in five years, with declines proceeding far faster than in the preceding decade-plus. Adult uptake of HTPs concentrated among smokers; youth experimentation remained comparatively low. While HTPs are not risk-free, the displacement of combustible cigarette sales is consistent with population-level harm reduction. External sources corroborate the overall pattern: multiple studies document marked acceleration in cigarette sales decline post-HTP introduction in Japan. These outcomes are precisely the kind of behavioral substitution the MRTP framework seeks to facilitate: when adults who would otherwise smoke switch completely to a lower-exposure product.

It is also important to note that concerns issued by abstinence-only supporters of prohibition, such as on youth or non-smoker uptake, are clearly not supported by the data. FDA's own TPL review for IQOS 3 found no evidence of increased youth initiation relative to 2.4 and low interest among adult never-smokers. Similarly, concerns about dual use are not only a poor argument against extending the MRTP, they are an argument in it's favour: The solution to dual use is clear, accurate communication – exactly what the MRTP entails.

Finally, persistent misinformation about reduced-risk products continues to circulate among the public, leading many smokers to wrongly believe that switching provides no health benefit. FDA has acknowledged this widespread misperception, noting the urgent need for clear, accurate communication about the continuum of risk. Renewing the MRTP orders is therefore not just a regulatory formality but a public health necessity. These authorizations give consumers confidence in the science and help correct false narratives, empowering smokers to make informed decisions that could dramatically reduce harm at the population level.

In conclusion, the statutory question for TPSAC is whether renewing these reduced-exposure orders remains appropriate for the protection of public health. It is overwhelmingly clear on the basis of all available evidence that this is the case. Firstly, the core scientific facts relied upon in 2020 and 2022 remain not only true, but have been reinforced by more recent systematic and meta-analysis reviews. Secondly, real world experiences show adult smokers successfully making the switch to such products with corresponding declines in cigarette sales. Finally, harm reduction works. Where governments enable safer alternatives, and consumers have the right to choose such products with accurate informational messaging, smoking falls faster; where they suppress them, illicit markets and worse outcomes proliferate. In the wake of significant misinformation about reduced risk products, this renewal is a vital step in ensuring accurate information is available to smokers that will help them switch to safer products, saving countless lives in the process.

We strongly urge the Committee therefore to follow the science, and the statutory responsibilities entrusted to it. and advise for a renewal. Millions of lives quite literally depend upon it.

Tim Andrews
Director of Consumer Issues
Americans for Tax Reform

TAXPAYERS PROTECTION ALLIANCE

September 25, 2025

Rachel Jang, PharmD
Center for Tobacco Products
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Dr. Jang:

On behalf of the millions of taxpayers and consumers we represent, the Taxpayers Protection Alliance is pleased to present the following comments before the Tobacco Products Scientific Advisory Committee.

For the roughly 30 million American adults addicted to cigarettes, quitting is no easy feat. Even relatively effective quit-smoking aids such as nicotine patches have a six-month success rate of approximately 20 percent.[1] Fortunately, reduced-risk products such as IQOS allow users the sensation of smoking cigarettes without the significant health risks that accompany smoking.

Five years ago, the Food and Drug Administration (FDA) recognized this and took the commendable step of allowing the marketing of IQOS as a "modified risk tobacco product" (MRTP). As a result of this designation, Philip Morris International, the manufacturer, has been able to provide information to consumers on IQOS' reduced exposure to harmful, cancer-causing substances. The FDA decided after the producer demonstrated that, "because the IQOS Tobacco Heating System heats tobacco and does not burn it, it significantly reduces the production of harmful and potentially harmful chemicals compared to cigarette smoke."[2]

That decision was supported by volumes of data submitted by PMI[3] and corroborated by independent research. In 2017, a research team led by Dr. Reto Auer of the University of Bern in Switzerland examined the level of carcinogens emitted from an IQOS puff, compared to the traditional cigarette brand Lucky Strike. The team found that amounts of harmful polycyclic aromatic hydrocarbons (PAH) found in IQOS smoke were far lower than for cigarette smoke.[4]

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[1] https://pmc.ncbi.nlm.nih.gov/articles/PMC4410859/.
[2] https://www.prnewswire.com/news-releases/fda-authorizes-marketing-of-iqos-tobacco-heating-system-with-reduced-exposure-information-301089261.html#:~:text=The%20IQOS%20system%20heats%20tobacco,modification%20orders%20for%20these%20products.
[3] https://www.fda.gov/tobacco-products/advertising-and-promotion/philip-morris-products-sa-modified-risk-tobacco-product-mrtp-applications.
[4] https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2628970.

In the time since the FDA allowed for IQOS to be marketed as an MRTP, additional evidence has been released affirming the relative safety of IQOS for smokers looking to make healthier choices. According to a comprehensive review of the evidence published in 2024 by health researchers at The Ohio State University, the use of IQOS is associated with significant decreases in exposure to harmful gases and chemicals, such as carbon monoxide, benzene, and acrolein.[5] The researchers also noted that studies using high-quality systems toxicology showed minimal harmful impacts from using IQOS. The evidence is vast and the conclusions clear: IQOS is a reduced-risk product that can save and improve millions of lives.

As the Tobacco Products Scientific Advisory Committee convenes to consider the renewal of the FDA's modified risk granted orders, we urge the committee and FDA to consider the significant evidence that IQOS is a far safer option for consumers than cigarettes. We also encourage the FDA, more generally, to adopt a more flexible regulatory framework that allows consumers access to harm-reduction products. We thank you for your time and attention to this important issue.

Sincerely,

(b) (6)

Ross Marchand
Senior Fellow

[5] https://pubmed.ncbi.nlm.nih.gov/38832049/.

From: (b) (6)
To: TPSAC
Subject: [EXTERNAL] Our Concern
Date: Friday, September 26, 2025 2:08:00 AM

Dear Rachel Jang, PharmD, DFO:

We sincerely hope that the Tobacco Products Scientific Advisory Committee continues to thrive.

Tobacco is generally considered a recreational product, but among all recreational products, tobacco is considered the only one that only has harmful effects on our health of all of lives with diseases and environmental pollutions on our planet, the Earth.

This document addresses the health and environmental concerns surrounding the FDA's approval of Philip Morris International's IQOS, heated tobacco cartridge, from a medical and scientific perspective.

The first concern is the high possibility that children may accidentally ingest or inhale the tobacco leaves potentially damaging the mouth, esophagus, stomach, other organs, and microbiota as well as acute nicotine poisoning. The second concern is that the products' toxicants, such as benzo[a]pyrene, polycyclic aromatic hydrocarbons, contained in first-hand and second-hand smoke, will be as health risks and environmental pollutants.

In addition, in recent years, there has been a growing trend among both adult women and non-adults to use heated tobacco products for convenience and as fashion. It has also been reported that pregnant women who have used heated tobacco products are at increased risk of low birth weight and birth defects. The heated tobacco cartridges produce tobacco-specific nitrosamines in aerosol, which can induce a state of anesthetic overload. It has long been known that tobacco contains heavy metals such as lead and zinc, and surprisingly, the radioactive isotopes 210 lead and 210 polonium have also been found to be present. These heavy metals accumulate in the body and can be onset of their poisoning and internal exposure (irradiation).

We appreciate your understanding of our concerns.

(b) (6)

e-mail: (b) (6)

Tel: (b) (6) ; Fax: (b) (6)

From:	Geoffrey Fong
To:	TPSAC
Cc:	Rudolph, Karin; Geoffrey Fong
Subject:	[EXTERNAL] Re: TPSAC Public Comment submission
Date:	Monday, October 6, 2025 10:57:58 AM

As a quick clarification for the first paragraph: the data are from the ITC Project multi-wave prospective cohort study in Japan...
Best regards,
Geoffrey T. Fong

From: Geoffrey Fong <geoffrey.fong@uwaterloo.ca>
Date: Monday, October 6, 2025 at 10:56 AM
To: TPSAC@fda.hhs.gov <TPSAC@fda.hhs.gov>
Cc: Geoffrey Fong <geoffrey.fong@uwaterloo.ca>, Rudolph, Karin <karin.rudolph@fda.hhs.gov>
Subject: TPSAC Public Comment submission

To Whom It May Concern:

I am submitting the following presentation, which was given at the World Conference on Tobacco Control, Dublin, Ireland, in June 2025. It presents data from the International Tobacco Control Policy Evaluation Project (the ITC Project), which conducted a multi-wave prospective cohort study among those who use cigarettes, heated tobacco products (HTPs), either exclusively or those who used both products.

These data are relevant to two important questions about the **real-world use** of HTPs, cigarettes, and both (dual users): to what extent have current IQOS users (and more generally HTP users) in Japan quit smoking? And how do transitions from exclusive smoking to dual use, and dual use to exclusive smoking affect changes in consumption: of cigarettes, of HTP heat sticks, and total consumption.

These data from the ITC Japan Survey are, we believe, an important source of evidence regarding the real-world use of IQOS and of HTPs, and would be of interest to FDA and TPSAC.

Please let me know if there is any additional information, or need for clarification. Please

note that the ITC Project website has information about the ITC Japan Project at the following website:

https://itcproject.org/countries/japan/

Best regards,
Geoffrey T. Fong

Geoffrey T. Fong, OC, PhD, FRSC, FCAHS
University Professor of Psychology and Public Health Sciences
University of Waterloo
Senior Investigator, Ontario Institute for Cancer Research
https://uwaterloo.ca/psychology/people-profiles/geoffrey-fong
Principal Investigator, International Tobacco Control Policy Evaluation Project (ITC Project)
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