PHILIP MORRIS INTERNATIONAL

December 17, 2024

A Perspective on the Royal College of Physicians' report, *E-cigarettes and harm reduction, an evidence review*

Dear [redacted]

I write regarding the Royal College of Physicians (RCP) report—*E-cigarettes and harm reduction, an evidence review*—for two purposes. The first is to express gratitude for the thorough set of science-based recommendations to reduce the global health burden of smoking espoused in the report. Secondly, and unfortunately, I must also draw your attention to serious biases in chapter nine, which represent a significant departure from the rest of the report.

Regarding my first purpose, your report concludes that: "*a risk-based approach to harm reduction is ethically and scientifically sounder than a precautionary approach, especially given the known serious harms of tobacco and the known difficulties in driving tobacco smoking and its associated harms down further without new tools to assist*." My company agrees with this; moreover, many independent public health experts also share similar views.

With respect to my second purpose, enclosed for your consideration are two items:

- A response to selected claims made in chapter nine of the report, in which scientists from my company have provided rebuttals to various claims that are false, misleading or lacking necessary context; and

- Correspondence I have sent to members of the Tobacco Control Research Group (TCRG) at the University of Bath who are named as contributors to your report and who are heavily cited in chapter nine. As you will see, Philip Morris International has identified numerous inaccurate and misleading claims directly affiliated with TCRG.

With the advent of smoke-free alternatives to cigarettes, reducing the global burden of tobacco-related disease could be accomplished faster than anyone ever thought possible. However, this can only happen when public discourse about the products, and the companies that are marketing and selling them, is fact-based and free from unwarranted bias.

I would welcome the opportunity to discuss the opportunities that exist to make your proposed risk-based approach to harm reduction a reality.

Sincerely,

MDGilchrist

Dr. Moira Gilchrist
Chief Communications Officer
Philip Morris International

A Response from Philip Morris International to Selected Claims

From Chapter 9.4.6: "Tobacco Industry Science as a Further Threat to Tobacco Control"

In the Report:

"E-cigarettes and Harm Reduction: An Evidence Review"

by Royal College of Physicians (RCP), April 2024

Claim
"Major TTCs have also sought to obfuscate information and create confusion[144] about the harms of their products, including HTPs.[33,47,136–138]"

Response
Regarding Philip Morris International (PMI), this statement is false and represents an unsubstantiated dismissal of our scientific research based purely on a well-used narrative that major TTCs cannot be trusted – it is not supported by fact. More than a decade ago, PMI made a deliberate choice to embrace scientific transparency and openness, ensuring that our scientific studies are published, and data is shared in a proactive manner. This approach empowers individuals to engage directly with the data, enabling them to independently analyze and interpret the findings. By committing to open science and transparent disclosure of our scientific data, PMI fosters an environment where scientific integrity is paramount. PMI's commitment to openness and transparency is evident in several key practices. Clinical studies are registered on widely recognized platforms like clinicaltrials.gov, and data, study designs, and methods are shared in publicly accessible repositories.

Our practices are inspired by the pharmaceutical industry and are aligned to the 2012 draft guidance for modified risk tobacco product (MRTP) application issued by the U.S. Food and Drug Administration's (FDA's) Center for Tobacco Products. On July 7th, 2020, after thoroughly reviewing PMI's scientific data, the FDA granted authorization for the commercialization of *IQOS* in the U.S. as a modified risk tobacco product with reduced exposure claims. This decision highlights how robust the scientific evidence provided to the Agency is, and ultimately, the potential of *IQOS* to reduce harm compared with continued smoking. Although the request for modified risk claims was not accepted, FDA acknowledged the substantial potential for public health benefits and concluded that "*the applicant has demonstrated that the products sold or distributed with the proposed modified risk information meet the standard under section 911(g)(2) of the FD&C Act, including that a measurable and substantial reduction in morbidity or mortality among individual tobacco users is reasonably likely in subsequent studies, and issuance of an order is expected to benefit the health of the population as a whole, taking into account both users of tobacco products and persons who do not currently use tobacco products*" (TPL page 11).

Moreover, the number of independent studies on *IQOS* and other heated tobacco products (HTPs) has significantly increased over the past years, as shown on PMIScience.com. These studies often reinforce key findings from our own research efforts. However, it is important to acknowledge that variations may exist between studies, including differing results, data interpretations, methodological approaches, and conclusions drawn. It is essential to recognize that individual studies, regardless of their quality, only provide a fragment of the overall picture. A comprehensive understanding of the harm reduction potential of our smoke-free products emerges from the accumulation of evidence over time.

Supporting references:

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3. **Haziza C.** Assessing the effects of switching from cigarettes to the tobacco heating system relative to smoking cessation on biomarkers of potential harm—additional evidence on the potential to reduce the risk of smoking-related diseases. Presented at: Society for Research on Nicotine & Tobacco Annual Meeting; February 24, 2021; Virtual Meeting. https://www.pmiscience.com/en/research/publications-

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8. **PMI Science.** Clinical studies. https://www.pmiscience.com/en/research/product-assessment-approach/clinical-assessment/. Accessed August 29, 2024.
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11. **Reduced exposure study using THS 2.2 menthol with 5 days in a confinement setting and 85 days in an ambulatory setting.** ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT01970995. Accessed August 29, 2024.
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13. **U.S. Food and Drug Administration.** Premarket tobacco product marketing order TPL (Technical Project Lead Review); PM0000424-79. Section 6 – Summary of toxicological findings. *FDA Document.* April 29, 2019:42. https://www.fda.gov/media/124247/download. Accessed August 29, 2024.
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15. **A 26-week extension of the ZRHR-ERS-09-US study evaluating biological and functional changes in healthy smokers after switching to THS 2.2.** ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT02649556. Accessed August 29, 2024.

Claim

"A growing number of studies demonstrate that PMI's claims around the reduced-risk potential of IQOS are not entirely substantiated by its own scientific research.[123,139–143]"

Response

Our claims about *IQOS* are based on a rigorous, multi-step scientific assessment, which includes product design and control principles, aerosol chemistry, physics, and indoor air quality studies, as well as non-clinical and clinical assessment, perception and behaviour research, and post-market studies and surveillance. To accurately assess the risk of diseases that develop over decades and determine the potential for risk reduction with a modified risk tobacco product, it is essential to consider the full body of evidence rather than isolated studies or endpoints. The totality of evidence available on *IQOS* clearly shows that it poses less risk of harm compared with continued smoking and can reduce the risk of smoking-related diseases compared with continued smoking, and therefore has a different risk profile. Although not risk-free, switching completely to *IQOS* is a much better choice for adults who smoke compared with continued smoking. Our research demonstrates that, by eliminating combustion, the levels of harmful and potentially harmful constituents (HPHCs) are reduced on average by 90-95% in *IQOS* aerosol compared with cigarette smoke.

We have further demonstrated that this substantial reduction translates into a reduction in toxicity in laboratory models and multiple clinical studies show reduced exposure to HPHCs approaching levels observed with smoking cessation. In our one-year exposure response study, which involved a 6-month study followed by a six-month extension study, we measured eight biomarkers of potential harm (BoPH) involved in pathomechanistic pathways relevant for diseases associated with smoking. Study results showed that smokers who switched from cigarettes to *IQOS* for 12 months had favorable changes in all eight BoPH, in the same direction as smoking cessation. Moreover, recent findings from a cross-sectional risk marker study further substantiate the benefits of switching to *IQOS* compared with continued smoking by showing favorable differences in nine BoPH after at least 2 years of *IQOS* use while providing real-life data on *IQOS* users who chose to switch to it without intervention (study not yet published).

PMI's scientific assessment extends beyond aerosol chemistry, toxicology, and clinical studies. It also includes systems toxicology, an approach that examines the comparative biological impact of *IQOS* aerosol and cigarette smoke on large networks of molecular and functional changes occurring across multiple levels of biological organization (e.g., molecular, cellular, tissue, organ, whole organism) that, if disrupted, can lead to disease.

Overall, the findings from every line of evidence converge on a single conclusion: switching to *IQOS* has the potential to reduce the risk of smoking-related diseases compared with continued smoking.

PMI has shared its scientific data on *IQOS* publicly through PMIScience.com, scientific conferences as well as in peer-reviewed journals. In particular, a number of public health agencies have reviewed the available evidence. For example, FDA concluded, through its scientific evaluation of PMI's applications, peer-reviewed published literature, and other sources, 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. Public Health England noted in 2018 that the available evidence suggests that heated tobacco products may be considerably less harmful than tobacco cigarettes and more harmful than e-cigarettes. The German Federal Institute for Risk Assessment (BfR) confirmed that levels of major carcinogens are markedly reduced in the emissions of the analysed HNB product in relation to conventional tobacco cigarettes and that monitoring these emissions using standardized machine smoking procedures generates reliable and reproducible data which provide a useful basis to assess exposure and human health risks.

In conclusion, PMI has provided extensive evidence of the potential reduced risk of *IQOS* compared with continued smoking. While *IQOS* is not risk free, the evidence supports our claims, and we welcome further independent review on our smoke-free products.

Supporting references:

1. **A 26-week extension of the ZRHR-ERS-09-US study evaluating biological and functional changes in healthy smokers after switching to THS 2.2.** ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT02649556. Accessed August 29, 2024.
2. **Ansari SM, Hession PS, David M, et al**. Impact of switching from cigarette smoking to tobacco heating system use on biomarkers of potential harm in a randomized trial. Biomarkers. 2024;29:298-314. doi:10.1080/1354750X.2024.2358318.

3. **Bentley MC, Almstetter M, Arndt D, et al.** Comprehensive chemical characterization of the aerosol generated by a heated tobacco product by untargeted screening. *Analytical and Bioanalytical Chemistry*. 2020;412(11):2675-2685. doi:10.1007/s00216-020-02502-1.
4. **Evaluation of biological and functional changes in healthy smokers after switching to THS 2.2 for 26 weeks.** https://clinicaltrials.gov/study/NCT02396381. Accessed August 29, 2024.
5. **Haziza C.** Assessing the effects of switching from cigarettes to the tobacco heating system relative to smoking cessation on biomarkers of potential harm—additional evidence on the potential to reduce the risk of smoking-related diseases. Presented at: Society for Research on Nicotine & Tobacco Annual Meeting; February 24, 2021; Virtual Meeting. https://www.pmiscience.com/en/research/publications-library/christelle-haziza-srnt-2021-effects-switching-cessation-biomarkers-potential-harm/. Accessed August 29, 2024.
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17. **U.S. Food and Drug Administration.** Harmful and potentially harmful constituents in tobacco products and tobacco smoke: Established list. U.S. Food and Drug Administration. https://www.fda.gov/tobacco-products/rules-regulations-and-guidance/harmful-and-potentially-harmful-constituents-tobacco-products-and-tobacco-smoke-established-list. Accessed August 29, 2024.
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20. **World Health Organization.** The scientific basis of tobacco product regulation: Second report of a WHO study group. *WHO Technical Report Series 951*. https://www.who.int/publications/i/item/9789241209519. Published 2008. Accessed August 29, 2024.

Claim

"Recent research that critically appraised interventional clinical trials on HTPs also found that industry-affiliated studies were of poor quality and limited to investigating the impacts of their short-term use.[33]"

Response

The critique in the referenced study focuses on selective endpoints without considering the totality of evidence or the broader context. It fails to acknowledge that not all HPHCs in cigarette smoke have corresponding biomarkers of exposure. Our reduced exposure and exposure response studies have selected biomarkers based on rigorous criteria, including established links to smoking-related diseases and sensitivity to smoking status. The FDA has recognized that although biomarkers of exposure for every HPHC are not available, comparative aerosol data show significant reductions in many HPHCs compared with cigarette smoke. Additionally, our clinical studies follow FDA's guidelines for testing modified risk tobacco products and include short-term reduced exposure studies and 12-month exposure response studies. The integrity of FDA's review process ensures that all submitted studies are thoroughly evaluated. Additionally, recent findings from a cross-sectional risk marker study, conducted on adult participants who have transitioned from cigarettes to *IQOS* over the past 2 years and recruited across 37 healthcare institutions in Asia and Europe, strengthens the findings from previous reduced exposure and exposure response studies and provides real-life data on *IQOS* users who chose to switch without intervention (study not yet published).

Supporting references:

1. **Ansari SM, Hession PS, David M, et al.** Impact of Switching from Cigarette Smoking to Tobacco Heating System Use on Biomarkers of Potential Harm in a Randomized Trial. *Biomarkers*. 2024;29(5):298-314. doi:10.1080/1354750x.2024.2358318
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Claim

"PMI has also misrepresented the science on smoke and aerosol, claiming that IQOS is smoke-free, safer than conventional cigarettes, and even less harmful than e-cigarettes.[47,145]"

Response

This statement is inaccurate and misleading. PMI's claims about *IQOS* are based on scientific evidence demonstrating that it operates without combustion. This is supported by temperature measurements, the absence of exothermic reactions, the absence of solid-based particles arising from combustion, and no involvement of oxygen (required for combustion to start) during the heating process. This is further confirmed by aerosol chemistry studies indicating that HPHCs in *IQOS* aerosol are on average 90-95% lower than in cigarette smoke. Untargeted screenings reveal that *IQOS* aerosol is less complex than cigarette smoke, containing only four elevated compounds, all of which are below toxicological concern thresholds. The FDA's 2020 MRTP decision supports the claim that *IQOS* heats tobacco without burning it, acknowledging the absence of combustion and *IQOS*'s reduced emissions compared with combusted cigarettes. The FDA also noted that *IQOS* is unlikely to generate significant interest among never smokers, youth, or former smokers. *IQOS* is not risk free and we do not claim that *IQOS* is "safe" but assert it is less harmful than continuing to smoke combustible cigarettes. Moreover, we aim to provide clear, accurate information to adult consumers without making direct comparisons between different smoke-free products.

Supporting references:

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Claim
"Simultaneously, TTCs have promoted the 'benefits' of nicotine while downplaying its addictiveness and health harms.[138]"

Response
Our position is clear: nicotine is addictive and not risk free. However there is a scientific consensus that nicotine is not the primary cause of smoking-related diseases; instead it is the high levels of HPHCs generated by tobacco combustion. Our smoke-free products contain nicotine, which is one of the reasons why people continue to smoke along with ritual, taste, social and sensorial experience. These factors also play an important role in making smoke-free products acceptable for adults who would otherwise continue to smoke. Our communication is consistent and clear that nicotine is addictive and carries its own risks.

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1. **Philip Morris International.** Integrated Report 2023. Philip Morris International. https://www.pmi.com/resources/docs/default-source/ir2023-documents/pmi-integrated-report-2023.pdf. Published 2023:162. Accessed August 29, 2024.
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PHILIP MORRIS INTERNATIONAL

December 17, 2024

Tobacco Control Research Group's contributions to recent Royal College of Physicians report, *E-cigarettes and harm reduction, an evidence review*

Dear [redacted]

In April 2024, The Royal College of Physicians (RCP) issued a report—*E-cigarettes and harm reduction, an evidence review*—detailing strategies for reducing global combustible cigarette use. Encouragingly, the report concludes that e-cigarettes can be an effective means to help people stop smoking. Real-world evidence demonstrates that innovative nicotine-containing products that do not burn tobacco are already accelerating the decline of cigarette smoking beyond what traditional tobacco control measures can achieve alone.

Despite the well-known risks of cigarette use, the report notes that "*tobacco is currently used by an estimated 1.1 billion people*," concluding that the role of non-combusted alternatives in reducing smoking-related harms is underutilized due to "*lack of awareness of the efficacy of these products for smoking cessation and harm reduction, and public perceptions of the risks of vaping relative to smoking which do not reflect current evidence*." Because more than 1 billion people smoke, the RCP concluded that "*a risk-based approach to harm reduction is ethically and scientifically sounder than a precautionary approach, especially given the known serious harms of tobacco and the known difficulties in driving tobacco smoking and its associated harms down further without new tools to assist*." My company, Philip Morris International (PMI), agrees with that recommendation; moreover, many independent public health experts also share this view.

Though the RCP report provides a thorough set of science-based recommendations to reduce the global health burden of smoking, it takes a sharp and notable detour in chapter nine: *Tobacco industry interests, recent conduct and claims around harm reduction*. This chapter abandons the evidence-based approach to assessing alternatives to continued smoking contained in the rest of the report and instead makes inaccurate, misleading statements, and recycles antiquated criticisms of the tobacco industry and PMI in particular. I am writing to you because you are listed as contributors to the RCP report and, in addition, the Tobacco Control Research Group (TCRG) at the University of Bath is widely referenced throughout chapter nine—in fact, almost half of the total citations supporting this chapter are to sources authored by TCRG members.

I have written to several of you and your colleagues on 13 occasions requesting corrections to false and misleading statements you have made about PMI, our products and science in the media, scientific literature and on your websites. However, almost all these requests were ignored. PMI has, both privately and publicly, asked that you correct at least 22 false and misleading claims (here and here), of which only one erroneous claim has been corrected to date. More disturbing is that your invalid claims have been repeated in chapter nine of the RCP report (as detailed in this letter's conclusion).

Given your collective lack of response over the last years, I had not intended to write to you on this occasion. However, I note the recent letter to Nicotine and Tobacco Research wherein an independent public health researcher also pointed to serious inaccuracies in one of your publications. It seems I am not the only stakeholder questioning the veracity of your communications. Indeed, I also note that in 2021 the BBC upheld a complaint about a radio podcast in which they acknowledged that Professor Gilmore had made false and misleading statements about PMI's corporate practices and removed the interview with her from its website.

The RCP report finds it "*difficult to comprehend why tobacco has been allowed to burden global health so extensively for so long*." However, it is not that difficult to comprehend at all given the lack of fact-based debate on potential solutions and the companies who bring them to market. The RCP report states that *"[if] potential public health benefits from e-cigarettes are to be realised, it is essential to take account of the conduct of TTCs [Transnational Tobacco Companies]."* Given this, it would appear to be more important than ever that stakeholders with loud and well-funded voices—such as your institution—embrace a complete and factual debate, one free from biases and instead focused on how to effectively deploy smoke-free alternatives to accelerate the decline in smoking, irrespective of who brings them to market.

I invite you to consider a selection of the inaccurate and misleading claims related to PMI that are outlined below. The lack of action to correct factual inaccuracies and biased, misleading claims gives the impression that your work is simply subjective commentary, rather than an objective scientific examination and discussion. A truly serious attempt on your part to reduce and eliminate smoking requires an approach rooted in objectivity—even if the results of such an endeavor do not align with your ideology. Continuing to deploy your playbook of repeating outdated—and often factually inaccurate—grievances against my company will not lead to a single adult stopping smoking.

Respectfully, I request that you communicate to the RCP report's author group that many of your resources cited in the report do not reflect the substantial correction requests you have received from PMI over the last years.

In the interest of full disclosure, I will write publicly to RCP and provide PMI's perspective on their complete report and will draw their attention to your continued inaction on correspondence sent to you by PMI. Additionally, please be aware that this letter will also be made public.

I of course would welcome the opportunity to discuss this matter with you at any time. An absence of dialogue yields only the absence of a complete, reality-based plan to end smoking.

Sincerely,

Dr. Moira Gilchrist
Chief Communications Officer
Philip Morris International

A SELECTION OF FACTUAL ERRORS AND CONTEXTUAL MISDIRECTIONS CONTAINED IN CHAPTER NINE OF THE ROYAL COLLEGE OF PHYSICIANS REPORT "E-CIGARETTES AND HARM REDUCTION, AN EVIDENCE REVIEW"

Below is a selection of specific claims in chapter nine (marked in ***bold***) that appear to be derived, in whole or in part, from references authored by the Tobacco Control Research Group at the University of Bath. Over the last several years we have repeatedly asked for these to be corrected.

"TTCs made very public claims of commitment to what they called 'harm reduction',"[3,4] despite continuing to heavily invest in and market their tobacco product lines."[5-7]

PMI is clear on our commitment to tobacco harm reduction and mission to end smoking. We are proud to be fulfilling this commitment, and our progress is undisputedly demonstrated and supported by the facts. Publicly available data from our Securities and Exchange Commission filings bears this out:

- 37% of PMI's total net revenues came from our smoke-free business as of year-end 2023.
- 33 million estimated total adult users of PMI's smoke-free products.
- 20.8 million adults are estimated to have switched to *IQOS,* our heated tobacco system, and stopped smoking.
- 84 markets where our smoke-free products are available.
- *IQOS* net revenues surpassed Marlboro to become the number one international nicotine brand on this measure in Q4 2023.

We are proud to have reached 25 markets where smoke-free products exceed 50% of our top-line revenue for both Q4 2023 and the full year. We aim to reach 60 markets by 2030, driving our ambition for smoke-free revenues to exceed two-thirds of group net revenues. In markets where PMI smoke-free products were available for sale as of the end of 2023, the company's combustible tobacco product shipment volume decreased by more than 33% versus 2015. If this trajectory continues, PMI expects that the growth of smoke-free products and consequent replacement of cigarettes will translate into a more than 50% decline of the company's combustible tobacco product shipment volume in these markets by 2030.

We have also progressed on our 2025 aspiration to have low- and middle-income markets represent at least half of the markets where we commercialize our smoke-free products—which, as of the end of 2023, represent 47% of the markets where we commercialize them globally.

A smoke-free future—for our consumers and for our company—is attainable. The benefits this can bring to adults who would otherwise continue to smoke, and hence to global public health, are enormous. Accelerating progress requires all stakeholders to take an evidence-based approach that encourages proper government oversight and regulation of smoke-free alternatives in order that they can play their part in contemporary tobacco control policy.

"[Weakens tobacco control] Promotes harm reduction policies that focus on minimising harm at the individual level, rather than evidence based, population-level measures."

In relation to PMI, this is false. Take, for instance, what the U.S. Food and Drug Administration (FDA) concluded: On July 7, 2020, FDA issued modified risk tobacco product (MRTP) authorizations for the *IQOS* tobacco heating system. In doing so, the agency found that issuing reduced exposure modification orders for *IQOS* is "*appropriate to promote the public health*" and "*is expected to benefit the health of the population as a whole*."

Furthermore, an improvement at the population level cannot be achieved without reducing harm at the individual level. To that end, FDA concluded in its *IQOS* MRTP authorizations that *"[t]he scientific evidence that is available without conducting long-term epidemiological studies demonstrates that a measurable and substantial reduction in morbidity or mortality among individual tobacco users is reasonably likely in subsequent studies*."

"PMI's 'harm reduction equation' misleadingly equates individual smokers switching to lower-risk products to population harm reduction, regardless of whether any smokers quit, the extent of dual use, or what happens in the wider population. The latter, of course, includes the children who it targets with its new product marketing."

This is a misleading characterization of the harm reduction equation, a model developed by well-known health experts. As explained here, the harm reduction equation describes the criteria for making a significant impact on public health by converting the greatest number of existing adult smokers who would otherwise continue smoking to less-harmful alternatives and further reducing initiation of combustible cigarettes.

A few important steps are needed to make this commonsense approach a reality for millions of adults who smoke. First, less harmful alternatives to cigarettes must be developed. Second, these alternatives must be appealing to those adults—in other words, they should deliver a taste and sensory experience that leads adults who would otherwise continue to smoke to change completely to the better alternative. When this occurs a population-level health benefit can be realized.

PMI is clear that minors should not use any tobacco or nicotine products. We design and market our products for adults who currently consume nicotine and wish to continue doing so. Suggestions otherwise are baseless.

"PMI offered the NHS £1 billion to help smokers switch to alternatives, under the condition that the U.K. relax regulation on e-cigarettes and HTPs following Brexit, an offer that the U.K. government rejected."[8,38]

This claim is inaccurate and misleading. As we explained when we wrote to you in February 2021, PMI had proposed a comprehensive approach to establish a regulatory framework with the objective of enabling adults who smoke to have access to, and accurate information about, smoke-free alternatives. Simultaneously, the framework would have pushed tobacco companies to phase out cigarettes through a tobacco transition fund paid for by the industry—not £1 billion from PMI but apportioned based on the tobacco companies' respective market share of combustible tobacco sales.

The United Kingdom's government has repeatedly endorsed the principle of tobacco harm reduction and encouraged men and women who smoke to switch to less harmful alternatives, such as e-cigarettes, if they do not quit altogether. Unfortunately, the regulations governing tobacco and nicotine products are outdated and inconsistent, with improvements needed to achieve the government's goals as quickly as possible. We supported the creation of a new product category that is future-proofed and for which any communication of the products would be restricted to specifically targeting adults who smoke.

"PMI has also misrepresented the science on smoke and aerosol, claiming that IQOS is smoke-free, safer than conventional cigarettes and even less harmful than e-cigarettes."[47, 155]

As we have told you on numerous occasions, this statement is misleading and inaccurate. Multiple independent studies have concluded that *IQOS* does not produce smoke because it does not burn tobacco. For example, the FDA determined that PMI has "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."

We have sound scientific data demonstrating that *IQOS* operates without combustion (neither incomplete, nor complete), including temperature measurements, experiments demonstrating the absence of net exothermic processes, the exclusion of oxygen (a catalyzer of a combustion reaction) during the heating process, and measurements of constituents that represent typical markers of combustion.

Aerosol chemistry studies show the level of emissions of harmful and potentially harmful constituents (HPHCs) generated by *IQOS* are on average 90 to 95% lower than those found in cigarette smoke. Furthermore, our untargeted screening of the *IQOS* aerosol demonstrated that the it is significantly less complex than cigarette smoke, and that exposure to the four compounds of potential toxicological concern elevated in the *IQOS* aerosol compared with cigarette smoke are below the level of toxicological concern. Moreover, and in contrast to cigarette smoke, we have demonstrated that *IQOS* aerosol does not contain solid particles originating from a combustion process as described by Pratte et al. 2017.

All of this evidence was reviewed by FDA who concluded in their 2020 MRTP decision that "*The low temperature in the IQOS system, the lack of an exothermic process, the similar levels of HPHCs in the presence and absence of oxygen, and the low level of nitrogen oxides in the aerosol of the IQOS system with Heatsticks suggest that combustion does not occur in the IQOS system with Heatsticks when it is used as intended. There is sufficient evidence to support the following statement: The IQOS system heats tobacco but does not burn it*."

Please also take note that PMI has never marketed our smoke-free products as "*safe*." While *IQOS* is less harmful than combustible cigarettes, it is not risk free and is not a cessation device—and has never been marketed as such.