PHILIP MORRIS PRODUCTS S.A.

To: STOP: Stopping Tobacco Organizations & Products: [redacted]

December 11, 2020

STOP: Stopping Tobacco Organizations and Products Issue Brief—*FDA does not rule that IQOS reduces tobacco-related harm, yet PMI still claims victory*—published on ExposeTobacco.org accessed via TobaccoTactics.org

Dear [redacted],

We have been made aware of your issue brief, "FDA does not rule that IQOS reduces tobacco-related harm, yet PMI still claims victory" (the **Article**) and we are writing to put you on notice that there are significant factual errors and misleading statements contained throughout the Article. We request that you correct these immediately. To assist you in this matter, important contextual information for your consideration and guidance is provided in Annex 1, and a non-exhaustive list of examples of factual errors and misleading statements in the Article is provided in Annex 2.

We request that you revisit the Article in its totality and implement corrections immediately in line with your commitment to "collecting data and investing in comprehensive research" and drawing upon the expertise of your "investigative journalists, epidemiologists, former civil servants, advocates, storytellers and more."[1] We also note that Vital Strategies "is committed to conducting itself according to the highest standards of ethical conduct and seeks to avoid even the appearance of impropriety in its actions"[2]. Further, we note that Tobacco Tactics, which specifically references STOP and the Article on its website (via search), provides a guide to writing[3] and request that you revisit the Article in its totality and implement corrections forthwith, in line with Tobacco Tactics' commitment to provide information that is "objective, factual and well referenced, not subjective or judgemental"[4]. We look forward to hearing from you and seeing the Article updated in line with the stated commitments of the STOP partner organizations.

[1] https://exposetobacco.org/about/ accessed December 9, 2020
[2] https://www.vitalstrategies.org/privacy-policy/combatting-corruption-and-bribery%ef%bb%bf/ accessed December 10, 2020
[3] https://tobaccotactics.org/wiki/guide-to-writing/ accessed December 03, 2020
[4] https://tobaccotactics.org/wiki/guide-to-writing/ accessed December 03, 2020

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Please know that in keeping with PMI's commitment to fostering open and transparent dialogue, we will make all of our correspondence regarding the erroneous information you have published available to the public via our website and through our owned media channels.

If you are not the person in your organization who deals with matters of accuracy in published materials, please forward this letter and annexes to the most appropriate person as a matter of urgency.

Sincerely,

Dr. Moira Gilchrist

VP Strategic and Scientific Communications

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Annex 1

Contextual Information Regarding the Subject Matter of the Article

On July 7, 2020, the U.S. Food and Drug Administration (FDA; the **Agency**) authorized the marketing of Philip Morris Products S.A.'s *IQOS* Tobacco Heating System as modified risk tobacco products (MRTPs)[5]. In their accompanying press release[6], FDA stated that these were *"the first tobacco products to receive "exposure modification" orders, which permits the marketing of a product as containing a reduced level of or presenting a reduced exposure to a substance or as being free of a substance when the issuance of the order is expected to benefit the health of the population."* FDA's press release also notes that *"There are two types of MRTP orders the FDA may issue: a "risk modification" order or an "exposure modification" order. The company had requested both types of orders for the IQOS Tobacco Heating System. After reviewing the available scientific evidence, public comments and recommendations from the Tobacco Products Scientific Advisory Committee, the FDA determined that the evidence did not support issuing risk modification orders at this time but that it did support issuing exposure modification orders for these products. This determination included a finding that issuance of the exposure modifications orders is expected to benefit the health of the population as a whole."*

FDA's authorization[7] states 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 (section 911(g)(2)(A) of the FD&C Act)."* The authorization explains why *IQOS* is fundamentally different from cigarettes. FDA is clear that reduced exposure to harmful chemicals does not render the *IQOS* Tobacco Heating System harmless. Nevertheless, reduced exposure statements are permitted for products authorized under the MRTP pathway and FDA has now allowed use of reduced exposure statements related to our *IQOS* tobacco heating system—the first and only electronic nicotine product to be granted marketing orders through the FDA's MRTP process. With this authorization, FDA has explicitly permitted that exposure reduction information be made available to consumers.

PMI makes clear that *IQOS* is not risk free; it is addictive; it is not a cessation aid and we do not present or market it as such; the best choice any smoker can make is to quit tobacco and nicotine altogether. Those adult smokers who do not quit deserve access to and accurate information about better alternatives, such as *IQOS*. Governments, regulators, scientists and the public health community deserve to hear the truth about U.S. FDA's historic decision in order that they can decide for themselves how best to modernize tobacco regulation and leverage innovations like *IQOS* in the interests of public health.

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[5] https://www.fda.gov/tobacco-products/advertising-and-promotion/modified-risk-orders accessed December 08, 2020.
[6] https://www.fda.gov/news-events/press-announcements/fda-authorizes-marketing-iqos-tobacco-heatingsystem-reduced-exposure-information accessed December 09, 2020.
[7] https://www.fda.gov/media/139796/download accessed December 09, 2020.

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Annex 2

Non-Exhaustive List of Factual Errors and Misleading Statements in the Article

Of the Article's numerous inaccuracies, the most serious and misleading are detailed below. In addition to addressing these points, we respectfully request that the authors of the Article review it in its entirety and correct any additional factual errors or misleading statements.

(1) The Article states *"The FDA has two standards for assessing modified risk. It agreed that the data submitted by PMI showed that IQOS **may reduce exposure** to harmful substances, but that IQOS **does not reduce risk** of disease and death when compared to cigarette smoking." **(emphasis by STOP)***

FDA does not have two standards for assessing modified risk. Rather, the Federal Food, Drug, and Cosmetic Act ("FDCA"), as amended by the Family Smoking Prevention and Tobacco Control Act ("TCA") provides that a tobacco product may be authorized as a modified risk tobacco product under FDCA Section 911(g)(1) or FDCA Section 911(g)(2). A product authorized under either section is a modified risk tobacco product by virtue of the application, as well as the definition of the term in FDCA Section 911(b)(1).

Please clarify that FDCA (as opposed to FDA) provides for authorization of modified risk tobacco products under two different statutory provisions (i.e., Section 911(g)(1) and Section 911(g)(2)).

(2) FDA did not find that *IQOS "**may reduce exposure** to harmful substances, but that IQOS **does not reduce risk** of disease and death when compared to cigarette smoking." **(emphasis by STOP)***

IQOS received an exposure modification order under FDCA Section 911(g)(2), which authorized *IQOS* to be sold in the United States with the following information: "*the IQOS system heats tobacco but does not burn it,*" "*this significantly reduces the production of harmful and potentially harmful chemicals*," and "*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*." Thus, it is simply inaccurate to state that FDA *"agreed that data submitted by PMI showed that IQOS **may reduce exposure** to harmful substances, but that IQOS **does not reduce risk** of disease and death when compared to smoking." **(emphasis by STOP)***. FDA's determination was based on the substantial reductions across the constituents on FDA's HPHC list, which demonstrates that, on the whole, as compared to cigarette smoke, the process used to heat tobacco in the *IQOS* system significantly reduces the production of harmful and potentially harmful chemicals compared to cigarette smoke. Indeed, this is why FDA authorized the claim that *"scientific studies have shown that switching completely from conventional*

cigarettes to the IQOS system significantly reduces your body's exposure to harmful and potentially harmful chemicals."

While the FDA concluded that the evidence did not support issuing risk modification orders at this time, FDA did conclude that the evidence supported issuing exposure modification orders. This determination included a finding that issuance of the exposure modifications orders is appropriate to promote public health and 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. Further, FDA found that the 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 to be established in subsequent studies.

Please adopt the following corrections:

(a) **Clarify that the FDA authorized the reduced exposure claim *"switching completely from conventional cigarettes to the IQOS system significantly reduces your body's exposure to harmful or potentially harmful chemicals."* Thus, FDA found that switching completely to *IQOS* does, in fact, reduce exposure to harmful (or potentially harmful) substances. Note, the distinction between the Article's statement that *IQOS* "may" reduce exposure to harmful substances.**

(b) **Remove the sentence that suggests FDA agreed that *IQOS* does not reduce risk of disease and death when compared to cigarette smoking. AND/OR**

(c) **Correct the sentence to state, *"FDA concluded evidence did not support issuing risk modification orders at this time. However, FDA also found that 'the 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 to be established in subsequent studies.'"***

(3) The Article states *"[e]ven though IQOS failed to meet an important standard for assessing MRTP status, PMI lost no time in proclaiming victory."*

Presumably, this is a reference to the fact that the FDA concluded that the evidence submitted did not support issuing risk modification orders at this time, but that such evidence did support issuing exposure modification orders. *IQOS* is a "modified risk tobacco product" as that term is defined by statute and received authorization to be marketed with reduced exposure information to U.S. consumers. Thus, it is inaccurate to state that *IQOS* failed to meet an important standard for *assessing MRTP status* because FDA could not have issued an exposure modification order under FDCA Section 911(g)(2) if *IQOS* did not satisfy the criteria for being classified as a "modified risk tobacco product" and issuing an exposure modification order.

Please remove the statement, *"[e]ven though IQOS failed to meet an important standard for assessing MRTP status . . ."*

(4) The Article states, *"In short, there is currently no evidence that IQOS is safer than cigarettes."*

The statement inaccurately portrays the state of the scientific evidence regarding *IQOS*, as well as FDA's evaluation of it.

(a) FDA does not use the "safe" or "safer" standard: it is clear that FDA would not utilize this language to describe the marketing authorization. Indeed, where it comes to the standard of safe, FDA clearly states in its release that *"[e]ven with this action, these products are not safe nor 'FDA approved.' The exposure modification orders also do not permit the company to make any other modified risk claims or any express or implied statements that convey or could mislead consumers into believing that the products are endorsed or approved by the FDA, or that the FDA deems the products to be safe for use by consumers."*[8]

(b) The requisite statutory findings under Section 911(g)(2) include findings that, among other things, issuing a marketing order would be appropriate to promote the public health, that the magnitude of the overall reduction in harmful substances is substantial, and that the 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. While the FDA concluded that the evidence did not support issuing risk modification orders at this time, FDA did conclude that the evidence supported issuing exposure modification orders. This determination included a finding that issuance of the exposure modifications orders is appropriate to promote public health and 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. Further, the totality of evidence suggests that a measurable and substantial reduction in morbidity or mortality among individual tobacco users is reasonably likely to be established in subsequent studies. To be clear, *IQOS* is not "risk-free," it delivers nicotine, which is addictive. However, the FDA's decision clarifies that *IQOS* is a modified risk tobacco product and that is why the Agency issued an authorization for the product that allows it to be marketed in the United States with reduced exposure information.

Please remove the statement, *"In short, there is currently no evidence that IQOS is safer than cigarettes."*

(5) The Article states *"independent analyses of PMI's own data submitted to the FDA suggest IQOS may be as harmful as smoking*". The Article mentions selected statements and analyses by individuals with well-known opinions about PMI and *IQOS*. However, it fails to mention PMI's

[8] FDA Authorizes Marketing of IQOS Tobacco Heating System with 'Reduced Exposure' Information | FDA

public responses and positions on these matters (e.g., PMI's response to a study by Stanton Glantz), and the growing body of other independent studies related to *IQOS*. Regrettably, it also misleadingly portrays the state of the scientific evidence regarding *IQOS*, as well as FDA's evaluation of that evidence.

Please adopt the following corrections:

(a) **Remove sentence and/or all information related to the sentence *"independent analyses of PMI's own data submitted to FDA suggest IQOS may be as harmful as smoking,"* including the reference to the cited Stanton Glantz paper. OR**

(b) **Add that PMI has noted that the description in this Article misleadingly portrays the state of scientific evidence regarding *IQOS*, as well as FDA's evaluation of it. FDA's press release can be found [here] while other documents relating to the authorization can be found [here].**

(6) The Article states *"Even PMI quietly acknowledged this: In its MRTP application to the FDA, PMI gave an 'important warning' (Figure 1): "it has not been demonstrated that switching to the IQOS system reduces the risk of developing tobacco-related diseases compared to smoking cigarettes."*

Our findings to date regarding *IQOS* are a matter of public record.[9] Based on these findings, we sought FDA's authorization of *IQOS* as an MRTP with modified risk claims, including exposure modification and risk modification messages. You have taken this statement completely out of context to create a misleading impression. The correct context is that statement referenced above was tested in conjunction with PMI's reduced exposure message to demonstrate consumer understanding of the reduced exposure information with a variety of different pieces of contextual information. However, FDA stated in its Technical Project Lead review document that *"…the currently available evidence suggests that, in general, disclaimers on tobacco products are often limited in their effectiveness. Accordingly, I do not expect that the disclaimer would improve consumer understanding. As noted above, testing of actual consumer perception shows that as the applicant proposes to label and market the product (without a disclaimer), consumers will not be misled about the current state of the evidence regarding the relative health risks of the product. Overall, the available evidence demonstrates that consumers generally understand the relative health risks of the product that are reasonably likely, which would be expected to impact behavior in a way that promotes public health."*[10] As such, the disclaimer was not required in the marketing order.

[9] https://www.fda.gov/tobacco-products/advertising-and-promotion/philip-morris-products-sa-modified-risk-tobacco-product-mrtp-applications

[10] See MRTPA TPL Summary, at 13

Please adopt the following corrections:

To provide the correct context, clarify that the cited PMI "important warning" was one of several warnings tested in conjunction with the authorized reduced exposure message to demonstrate consumer understanding of the reduced exposure information with a variety of different pieces of contextual information. Please also note in your article that FDA did not require the application of this warning in the Marketing Order for *IQOS*.

(7) The Article states, *"Because PMI could not demonstrate **risk** modification, the FDA instead considered, and subsequently granted, an **exposure** modification order. For this order, PMI had to demonstrate IQOS has the **potential** to benefit overall population health by proving it substantially reduced **exposure** of harmful substances to users and those around them."* ***(emphasis by STOP)***

The Article misstates the statutory standard under FDCA Section 911(g)(2). In particular, under Section 911(g)(2), to issue an exposure modification order, FDA must find, among other things, that the applicant has demonstrated that issuance of an order with respect to the application is *"appropriate to promote the public health"* and *"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."* [FDCA Section 911(g)(2)(A)(i), (B)(iv)]. Note, the distinction between "expected," which dictionaries define as "to consider probable or certain," and "potential," which dictionaries define as "existing in possibility." Accordingly, the article suggests that FDA could have issued its authorization on the basis of mere possibility, as opposed to probability.

Please clarify that PMI's MRTP application for *IQOS* requested authorization under both g(1) and g(2) and that to issue an exposure modification order PMI had to demonstrate that issuing an exposure modification order for *IQOS* would be "appropriate to promote the public health" and "is expected the population as a whole, taking into account both users of tobacco products and persons who do not currently use tobacco products." [FDCA Section 911(g)(2)(A)(i), (B)(iv)].

(8) The Article states *"when assessing IQOS aerosol PMI typically only analyses 40 of the 93 harmful or potentially harmful substances recognized by FDA. It further states, "more comprehensive data from PMI's analysis show that up to 56 other substances are in fact higher in IQOS aerosol than in cigarette smoke, some more than 1000% higher. It is not certain that all these data have been seen by the FDA."*

(a) STOP appears to be referencing the Tobacco Control article, "IQOS: examination of Philip Morris International's claim of reduced exposure" by Gideon St. Helen *et al*.[11] However, STOP fails to reference PMI's public response to the referenced article where the first part of the above statement is sourced. Further, it fails to reference that, at the time the article was

[11] St Helen G., Jacob Iii P, Nardone N, Benowitz NL. IQOS: examination of Philip Morris International's claim of reduced exposure. Tob Control. 2018;27(Suppl 1):s30-s6.

written, well-established analytical protocols to measure these HPHCS were not available, leading to the FDA recommendation of the abbreviated list of 18 HPHCs. In addition, since the time of publication, validated analytical protocols have been developed, which allowed PMI to test for all HPHCs listed in the extended FDA list. These data were submitted to FDA in September 2018.[12] The total reduction of the levels of HPHCs was found to be fully aligned with the previous measurement made using the PMI-58 list. Both PMI's and independent assessments of the *IQOS* aerosol have consistently found that the product emits levels of harmful and potentially harmful chemicals that are on average more than 90 percent reduced compared with the levels emitted in cigarette smoke.

(b) Further, the Article omits important contextual information and misleadingly suggests that FDA did not see the above-referenced data. In the Scientific Review of Modified Risk Tobacco Product Application (MRTPA) Under Section 911(d) of the FD&C Act – Technical Project Lead [hereinafter, "MRTPA TPL Summary"], FDA stated "*In the non-targeted differential screening study, the applicant identified 53-61 compounds across Heatstick variants (80 unique compounds) that are either present exclusively or are found in higher quantities in the aerosol of the IQOS system with Heatsticks compared to the mainstream smoke in the 3R4F reference cigarette."*[13] As background, PMI submitted two different aerosol assessments (1) the targeted assessment which included the quantification of the known harmful and potentially harmful constituents (HPHCs) and (2) the non-targeted assessment which is an extensive evaluation of the aerosol of *IQOS* and the smoke of a 3R4F reference cigarette to identify compounds that might be unique or in higher concentration in the aerosol of *IQOS*. As a result of the non-targeted assessment, PMI identified and assessed 80 compounds in the *IQOS* aerosol that are unique or are present in higher concentrations than in cigarette smoke. From this, PMI identified four of the 80 compounds as potentially carcinogenic to humans during PMI's toxicology evaluation, but determined that the levels were below the levels of toxicological concern. In the PMTA Technical Project Lead Review (TPL) [hereinafter, the "PMTA TPL Summary"], FDA stated in their toxicological risk assessment of *IQOS* that *"the levels of exposure to these possible carcinogens appear low and when considered with other data does not preclude a conclusion the products are appropriate for the protection of public health."*[14]]. FDA also stated in the MRTPA TPL that, *"[d]espite the increase in some constituents of concern, the substantial reduction across constituents on FDA's HPHC list demonstrates that, on the whole, the process used to heat tobacco in the IQOS system significantly reduces the production of harmful and potentially harmful chemicals compared*

[12] https://digitalmedia.hhs.gov/tobacco/static/mrtpa/PMP/September%2021%2C%202018.zip
[13] MRTPA TPL Summary, at 24: Technical Project Lead (TPL) Review: MR0000059-MR0000061, MR0000133 (fda.gov)
[14] *IQOS* PMTA TPL Summary, at 32: Technical Project Lead (TPL) Review: MR0000059-MR0000061, MR0000133 (fda.gov)]

to cigarette smoke."[15] FDA reviewed this data as part of its review of the *IQOS* application and requested additional information be submitted as part of the postmarket surveillance and studies program that FDA required PMI to submit as a condition of its issuance of an exposure modification order. As such, it is inaccurate and misleading to suggest that FDA did not see the data regarding the presence of substances in *IQOS* aerosol that are higher than in cigarette smoke.

Please adopt the following corrections:

(a) **Remove all information and references derived from the Gideon St. Helen et al. Tobacco Control paper. OR**

(b) **Include the following statement from PMI: *"With respect to the referenced findings, PMI has prepared a point-by-point assessment of the cited paper, which can be found here."* AND**

(c) **Clarify that FDA stated that PMI's non-targeted differential screening *"identified 53-61 compounds across Heatstick variants (80 unique compounds) that are either present exclusively or are found in higher quantities in the aerosol of the IQOS system with Heatsticks compared to the mainstream smoke in the 3R4F reference cigarette."* AND**

(d) **Include discussion of contextual information that only four of the 80 unique compounds were identified by PMI as potentially carcinogenic. Further, clarify that FDA stated in their toxicological risk assessment of *IQOS* that *"the levels of exposure to these possible carcinogens appear low and when considered with other data does not preclude a conclusion the products are appropriate for the protection of public health."* [*IQOS* PMTA TPL Summary, at 32]. FDA also stated in the MRTPA TPL that, *"[d]espite the increase in some constituents of concern, the substantial reduction across constituents on FDA's HPHC list demonstrates that, on the whole, the process used to heat tobacco in the IQOS system significantly reduces the production of harmful and potentially harmful chemicals compared to cigarette smoke."* [MRTPA TPL Summary, at 26]. AND**

(e) **Remove the statement *"it is not certain that all these data have been seen by the FDA."***

(9) The Article states, *"[e]ven though the FDA has instructed PMI that it cannot tell or mislead consumers to believe that IQOS is FDA-approved, there is a risk that PMI's spin of the FDA decision may have done exactly that."*

U.S. law expressly prohibits any manufacturer of MRTPs from making any claim that a tobacco product is "FDA approved" or "endorsed" by the FDA for use by consumers [See FDCA § 301(tt)(1), (3)]. Consistent with U.S. law, and the MRTP marketing order, PMI does not make claims that FDA endorses or approves *IQOS*.

[15] MRTPA TPL Summary, at 26: Technical Project Lead (TPL) Review: MR0000059-MR0000061, MR0000133 (fda.gov).

Please clarify that PMI does not convey, mislead, or mislead consumers into believing that *IQOS* is FDA "approved" or "endorsed" by FDA for use by consumers. PMI is very clear: FDA authorized *IQOS* as a modified risk tobacco product (MRTP), with reduced exposure messages, under the MRTP regulatory pathway. The Company has also clearly communicated and distinguished FDA authorization from FDA "approval".

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