Because PMI has not demonstrated that IQOS is associated with lower risks, FDA should not permit modified exposure claims, because such claims are likely to be misunderstood as modified risk claims

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Philip Morris International (PMI) proposes to market IQOS with reduced exposure and reduced risk claims. The tobacco industry has a long history of using reduced exposure claims to mislead consumers, including adolescents,[1] into believing that the products in question have reduced risk, most notably through the use of "light" and "mild" cigarette claims. ***Therefore, it is particularly important that the FDA take care not to give legal sanction for PMI to market their IQOS product to mislead the public in the same way that it has done with earlier products. In particular, the FDA should not allow marketing of IQOS that claims or implies modified exposure.***

The inherently deceptive nature of reduced exposure and reduced risk marketing claims were at the core of the U.S. Department of Justice's Racketeer Influenced and Corrupt Organization (RICO) Act lawsuit against the major cigarette companies for defrauding the public about the dangers of smoking. In August 2006 Judge Gladys Kessler held[2] that the tobacco companies, including Philip Morris, were liable for violating RICO by fraudulently covering up the health risks associated with smoking and for marketing their products to children. Judge Kessler found that the companies "have engaged in and executed – and *continue to engage in and execute* -- a massive 50-year scheme to defraud the public, including consumers of cigarettes, in violation of RICO [emphasis added]." In her 1,683 page opinion with extensive Findings of Fact, Judge Kessler found, among other fraudulent acts, that Philip Morris and other tobacco companies deceptively marketed cigarettes characterized as "light" or "low tar," while knowing that those cigarettes were at least as hazardous as "full flavored" cigarettes; misled smokers, former smokers, and non-smokers to believe that these cigarettes were safer; and deliberately targeted the youth market. Importantly, the court found that there was a reasonable likelihood that defendants would continue to violate RICO in the future.

[1] Kropp, RY & Halpern-Felsher, BL. Adolescents' beliefs about the risks involved in smoking 'light' cigarettes. Pediatrics. 2004 Oct. 114(4): e445-e451. PMID: 15466070.
[2] *United States v. Philip Morris USA Inc*., 449 F.Supp.2d 1 (D.D.C. 2006), available at http://www.publichealthlawcenter.org/sites/default/files/resources/doj-final-opinion.pdf.

Among many relevant Findings, paragraph 2402 on page 888 of the opinion states: "According to [Brand Manager of Marlboro from 1969 to 1972, James] Morgan, Philip Morris made a calculated decision to use the phrase "lower tar and nicotine" even though its own marketing research indicated that consumers interpreted that phrase as meaning that the cigarettes not only contained comparatively less tar and nicotine, but also that they were a healthier option."[3]

Paragraph 2403 on page 888 states: "Morgan, who later became CEO of Philip Morris, further explained in 2002 that rather than relying on the tar and nicotine numbers from the FTC Method, 'the major influence in people's perceptions in the tar of a cigarette would have come from the marketing positioning of a brand as opposed to people literally reading the FTC [tar and nicotine figures].'"[4]

Based on these and other Findings, the court concluded at paragraph 2627 on page 971 that Philip Morris and the other tobacco companies knew that "many smokers who were concerned and anxious about the health risks from smoking would rely on the health claims made for low tar cigarettes as a reason, or excuse, for not quitting smoking."[5]

PMI's modified risk tobacco product (MRTP) application for IQOS makes reduced risk claims about IQOS that, like its earlier "light" and "mild" claims that were deemed fraudulent in the RICO case, are not substantiated by PMI's own internal research reported in its application (Section 1 below). And PMI's reduced exposure claims in its labeling and marketing are likely to be misunderstood as reduced risk claims (Sections 2 and 3 below). Therefore, FDA should not permit PMI to market IQOS with either reduced risk or reduced exposure claims.

Following the 2006 RICO decision, in 2009 Congress recognized and described the tobacco companies' use of reduced exposure claims to mislead the public and Judge Kessler's findings in 14 of the 49 Findings for the Family Smoking Prevention and Tobacco Control Act.[6] Of particular relevance, Finding 46 states:

> If manufacturers state or imply in communications directed to consumers through the media or through a label, labeling, or advertising, that a tobacco product is approved or inspected by the Food and Drug Administration or complies with Food and Drug Administration standards, *consumers are likely to be confused and misled.* Depending upon the particular language used and its context, *such a statement could result in consumers being misled into believing that the product is endorsed by the Food and Drug Administration for use or in consumers being misled about the harmfulness of the product because of such regulation, inspection, approval, or compliance.*

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[3] *United States v. Philip Morris USA Inc*., 449 F.Supp.2d 1 (D.D.C. 2006), available at http://www.publichealthlawcenter.org/sites/default/files/resources/doj-final-opinion.pdf.
[4] *United States v. Philip Morris USA Inc*., 449 F.Supp.2d 1 (D.D.C. 2006), available at http://www.publichealthlawcenter.org/sites/default/files/resources/doj-final-opinion.pdf.
[5] *United States v. Philip Morris USA Inc*., 449 F.Supp.2d 1 (D.D.C. 2006), available at http://www.publichealthlawcenter.org/sites/default/files/resources/doj-final-opinion.pdf.
[6] Family Smoking Prevention and Tobacco Control Act, Public Law 111-31 (June 22, 2009).

If FDA authorizes PMI to make confusing (if not deliberately deceptive) claims in its labeling and/or advertising, it could result in consumers being misled into believing IQOS is endorsed by FDA or into misunderstanding IQOS's harmfulness. Indeed, FDA would be complicit in perpetuating PMI's engagement and execution in a decades-long scheme to mislead, if not defraud, the public, and in discouraging smokers from not quitting smoking.

1. PMI's own data presented in its application do not support any claim of modified risk in human users

As detailed in another public comment,[7] in its application PMI presents data on 24 biomarkers of potential harm in American human users, including measures of inflammation, oxidative stress, cholesterol and triglycerides, blood pressure, and lung function. These human data are the most important information in the application because they represent direct evidence on how IQOS affects people. Based on details in section 6.1.4.4 of the PMI MRTP application, there is no statistically detectable difference between IQOS and conventional cigarettes for 23 of these 24 biomarkers in Americans in PMI's studies. This is indicated by the fact that 23 of the 95% confidence intervals include zero (i.e., no statistically significant difference).

Moreover, when using the conventional 95% confidence standard for statistical hypothesis testing, one would expect 5% of the tests to yield false positives. Five percent of 24 tests is 1.2 tests, which means that one would expect 1 or 2 false positive results. PMI had one positive result, which is what one would expect by chance.

In addition, as detailed in other public comments, PMI has not provided compelling evidence that IQOS HeatSticks are less dangerous than conventional cigarettes in terms of cardiovascular,[8] pulmonary,[9] hepatic,[10] and other risks.[11]

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[7]Glantz S. PMI's Own Data on Biomarkers of Potential Harm in Americans Show that IQOS is Not Detectably Different from Conventional Cigarettes, so FDA Must Deny PMI's Modified Risk Claims. Docket Number: FDA-2017-D-3001. November 13, 2017. Tracking number:1k1-8zrx-juh9.

[8] Springer ML, Nabavizadeh P, Mohammadi L. The evidence PMI presents in its MRTP application for IQOS is misleading and does not support the conclusion that IQOS will not harm endothelial function; independent research done in a more relevant physiological model shows that IQOS harms endothelial function as much as conventional cigarettes. Docket Number: FDA-2017-D-3001. November 20, 2017. Tracking number: 1k1-8zxa-mq9v.

[9] Chun LF, Moazed F, Matthay MA, Calfee CS, Gotts JE. IQOS emissions create risks of immunosuppression and pulmonary toxicity, so FDA should not issue an order permitting IQOS to be labeled or marketed with reduced risk claims. Docket Number: FDA-2017-D-3001. November 30, 2017. Tracking number: 1k1-903a-mnpl

[10] Chun LF, Moazed F, Matthay MA, Calfee CS, Gotts JE. PMI's MRTP application for IQOS does not adequately evaluate potential for hepatotoxicity risk. Docket Number: FDA-2017-D-3001. November 30, 2017. Tracking number: 1k1-9039-d91g.

[11] St.Helen G, Jacob P III, Nardone N, Benowitz NL. Because PMI application did not report the full range of HPHCs in IQOS aerosol, characterize HPHCs in sidestream emissions, include a non-targeted analysis of chemicals in emissions, or conduct clinical studies to describe exposure

Overall, PMI's own data support the conclusion that IQOS is no different from conventional cigarettes in terms of effects on these biomarkers of potential harm in American people; any marketing claims of modified risk are fundamentally misleading and should not be permitted.

2. A modified exposure claim is likely to be misunderstood as a modified risk claim, so PMI should not be permitted to market IQOS with a modified exposure claim.

To issue a modified exposure order, section 911(g)(2)(B)(iii) requires the applicant to demonstrate that "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." ***PMI's own data submitted in the application show that consumers will be misled, so FDA should not grant it a modified exposure order.***

PMI's qualitative studies (THS-PBA-02-US and THS-PBA-04-US) demonstrate that consumers perceive reduced exposure claims as reduced risk claims. In particular, participants' comments on the "Reduced exposure claim" in PMI's qualitative studies demonstrate that they equated reduced exposure with reduced risk. Participants stated:

- "It does look nice and it seems like It's going to be less harmful ... (what makes you say It seems like It could be less harmful?) Just the kind of wording: get the flavor and taste satisfaction you expect from a cigarette so it seems like it wants to substitute. It's an innovation of product that maybe is trying to replace the harmful risks that a regular cigarette contains ... " (AS Hale 36-50 Menthol LTN/ SLTN Chicago P2)"
- "It reduces your body's exposure to the chemicals ... that would be my biggest take-away .. .it suggests that it is better for you than a traditional cigarette. (Better - In what way?) It's the lesser of two evils; it's a better bad choice ... It reduces harmful chemicals which is likely to reduce your chances of getting a tobacco-related disease." (AS Female 21-34 LTN/ SLTN Phoenix P2)

In evaluating all claims, PMI summarizes (in THS-PBA-02-US Study report) that all messages (including reduced exposure claims) were perceived by smokers as statements about lower harm. The fact that PMI's report does not distinguish perception of reduced risk and reduced exposure provides additional evidence that reduced exposure claims are viewed as reduced risk claims. For example, this statement appears several times related to evaluation of reduced exposure claims:

"After reading Product Message L, all participants perceive THS 2.2 to be:
• a lower risk of exposure to harmful compounds than conventional cigarettes, but a

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to toxicants during dual use with other tobacco products, FDA must deny PMI's application. Docket Number: FDA-2017-D-3001. November 29, 2017. Tracking number:1k1-902j-m8kv.

higher risk than e-cigarettes, NRTs and cessation
• a lower risk of developing tobacco-related diseases than conventional cigarettes, but a higher risk than e-cigarettes, NRTs and cessation."

In short, despite PMI's contradictory statements, the actual reports, transcripts, and data submitted by PMI provide substantial evidence that consumers perceive reduced exposure claims as reduced risk claims. FDA must make its determination based on objective scientific evidence, not on subjective and unsubstantiated assertions.

3. PMI's proposed advertising and labeling do not accurately describe the conditions of use and PMI failed to demonstrate that consumers comprehend these messages

For a modified risk order, section 911(h)(1) requires any advertising or labeling to "enable the public to comprehend the information concerning modified risk and to understand the relative significance of such information in the context of total health and in relation to all of the diseases and health-related conditions associated with the use of tobacco products." However, PMI has not demonstrated that the public comprehends IQOS's labeling or advertising messages. Instead, as detailed in another public comment,[12] the evidence cited in PMI's MRTP application indicates that *the proposed labeling and warnings for IQOS will mislead consumers*, particularly youth, about the product. Moreover, as detailed in another public comment,[13] despite the explicit requirements of section 911 and the recommendations of FDA's Guidance on MRTP applications, PMI's IQOS application does not adequately consider IQOS's appeal to or impact on youth or adolescents, and does not provide the necessary scientific evidence to support its MRTP claims of reduced risk or reduced exposure, especially as these claims affect youth and adolescents. In particular, PMI did not address the likelihood that adolescents who otherwise would not have used any tobacco product might find IQOS appealing and will initiate using IQOS as their first tobacco product. This outcome can be expected because adolescents, in addition to the public at large, are likely to be confused by and misinterpret reduced harm and reduced exposure claims.

As described in detail above, the evidence in PMI's application does not demonstrate that IQOS – even used alone – is less dangerous that conventional cigarette smoking. PMI also fails to address the combined risks of using IQOS while continuing to smoke conventional cigarettes (dual use), even though PMI's own data in the application show substantial levels of dual use

[12] Halpern-Felsher B, McKelvey K, Popova L, Kim M, Chaffee B, Vijayaraghavan M, Ling P, Lempert LK, Glantz SA. The evidence cited in PMI's MRTP Application indicates that the proposed labeling and warnings for IQOS will mislead consumers, particularly youth, about the product. Docket Number: FDA-2017-D-3001. December 8, 2017. Tracking number: 1k1-908n-holz

[13] Halpern-Felsher B, McKelvey K, Kim M, Chaffee B, Vijayaraghavan M, Popova L, Ling P, Lempert LK, Glantz SA. PMI's MRTP Application for IQOS Does Not Consider IQOS's Appeal to Youth or Adolescents, or the Likelihood that Youth and Adolescents will Initiate Tobacco Use with IQOS or Use IQOS with Other Tobacco Products. Docket Number: FDA-2017-D-3001. December 7, 2017. Tracking number: 1k1-9087-458e.

(e,g. PMI's study THS-PBA-08-US shows that over 6 weeks, only 5-8% of participants used HeatSticks exclusively, and most people used HeatSticks and conventional cigarettes together; Table 15.2.6.2.2).

Indeed, to be granted an MRTP order under section 911(g), PMI must demonstrate that the marketing of its IQOS product will or 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." For its modified exposure claim, PMI must further demonstrate that issuance of an exposure modification order would be "appropriate to promote the public health." Therefore, in its Guidance, FDA recommends that an MRTP application should contain *"an overall assessment of the potential effect that the marketing of the product as proposed may have on tobacco-related morbidity and mortality in the population as a whole."* In an effort to meet this requirement, PMI created its "Population Health Impact Model" (PHIM) that purports to estimate the potential impact on public health of marketing its IQOS as an MRTP. However, as described in detail in another public comment,[14] PMI failed to meets its burden to demonstrate that a MRTP order would "benefit the health of the population as a whole" or "promote the public health" because its PHIM makes several questionable assumptions and leaves out some important measures of health impact. Importantly, the PHIM completely ignores the possible health impacts of IQOS use on young adults and nonusers, and the PHIM assumes cigarette users will switch to IQOS use exclusively.

Even if one grants PMI's unsubstantiated assertion that switching completely to IQOS reduces risk, PMI failed to demonstrate that the public comprehends these health issues. Importantly, PMI failed to demonstrate that consumers understand that the risks of using its IQOS product are reduced *only if they do not use other products concurrently with IQOS*, and failed to demonstrate that consumers understand the meaning of the words "switch completely" used in IQOS labeling. Section 911(h)(3)(B) provides that FDA may require the labeling of "conditions of use" if the "conditions of use of the product may affect the risk of the product to human health." ***PMI's proposed advertising and labeling do not adequately describe the conditions of use – namely, that to (allegedly) reduce their risk of tobacco-related diseases, consumers must use IQOS exclusively, and may not use it with any other tobacco product – and PMI has not demonstrated that consumers understand these conditions of use.***

Indirect persuasion using metaphors and implicit claims is widely used in advertisements to make consumers receptive to multiple positive inferences about the promoted product and lead the audience to a conclusion that would be considered misleading if stated directly.[15] Comparative claims have been shown to mislead consumers to form (erroneous) favorable

[14] Max W, Lempert L, Sung H-Y, Lightwood J, Wang Y, PhD, and Yao T. Philip Morris's Population Health Impact Model Based on Questionable Assumptions and Insufficient Health Impact Measures Does Not Adequately Support its MRTP Application. Docket Number: FDA-2017-D-3001. November 22, 2017. Tracking number: 1k1-8zy0-6rfg.

[15] McQuarrie EF, Phillips BJ. Indirect Persuasion in Advertising: How Consumers Process Metaphors Presented in Pictures and Words. Journal of Advertising. 2005;34(2):7-20.

generalizations on promoted products.[16] ***That is exactly what the tobacco companies did with "light" and "mild" cigarettes and what it seeks FDA permission to do with IQOS.***

Conclusion

Because PMI has not demonstrated that IQOS is associated with lower risks to humans, FDA should not permit modified exposure claims, because such claims are likely to be misunderstood as modified risk claims. FDA should not put its imprimatur on PMI's claims and thereby implicitly, if not explicitly, participate in and continue PMI's deceptive practices.

[16] Andrews JC, Burton S, Netemeyer RG. Are Some Comparative Nutrition Claims Misleading? The Role of Nutrition Knowledge, Ad Claim Type and Disclosure Conditions. Journal of Advertising. 2000;29(3):29-42.