

Exhibit 9

Submission to Tobacco Products Scientific Advisory Committee

Caryn Cohen M.S.
Office of Science
Center for Tobacco Products
Food and Drug Administration
Document Control Center
Bldg. 71, Rm. G335, 10903
New Hampshire Ave.
Silver Spring, MD 20993-0002

To: Tobacco Products Scientific Advisory Committee (TPSAC)
For: TPSAC meeting 24-25th January 2018
Subject: Modified Risk Tobacco Product Applications: Applications for IQOS system with Marlboro Heatsticks, IQOS system with Marlboro Smooth Menthol Heatsticks, and IQOS system with Marlboro Fresh Menthol Heatsticks [\[link\]](#)
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Submission by:

David B. Abrams
Professor
Department of Social and Behavioral Sciences
NYU College of Global Public Health
New York University
United States

Frank Baeyens
Professor of Psychology
University of Leuven
Belgium

Scott D. Ballin, JD
Health Policy Consultant,
Former Vice President and Legislative Counsel,
American Heart Association
United States

Clive D. Bates
Director, Counterfactual, London, Former
Director Action on Smoking and Health,
London
United Kingdom

Brian L. Carter
Director of Scientific Communications
Consumer Advocates for Smoke-free
Alternatives Association
United States

Karl Fagerström
President Fagerström Consulting AB
Vaxholm
Sweden

Konstantinos Farsalinos, M.D.
Researcher
Onassis Cardiac Surgery Center, Athens
University of Patras,
Greece

Marewa Glover
Professor, School of Health Sciences
College of Health
Massey University
New Zealand

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the primary causes of disease and other harms listed in these warnings. It is essential that relevant warnings are used – these statutory default warnings are not applicable, and no evidence exists to support their use. They would be misleading and damaging.

We argue that, beyond reasonable doubt, the IQOS and Heatstick products under evaluation create substantially reduced toxic exposures to users than cigarette smoking, and that implausible and unknown mechanisms would be required for this substantial reduction in exposure *not* to translate into less risk of harm or reduced risks of tobacco-related diseases. Accordingly, we think that the three claims should be accepted as framed and tested by the applicant and the relevant orders made as soon as possible. A lengthy delay in deciding the application simply means more smoking, disease and death while smokers wait to have access to and proper information about a low-risk alternative to smoking.

Do the statements convey the magnitude of risk reduction? Our main concern is that the claims requested are too weak given the likely magnitude of exposure and risk reduction. For example, the phrase “presents less risk” could be understood as 5% less, 30% less, 70% less, or 90% less – and only the last of these is likely to be approximately correct. If consumers misperceive the extent of risk-reduction, then the result is likely to be more smoking than there otherwise would be.

2 Health impacts and relative risk of IQOS

We consider that the IQOS product is a reduced-risk tobacco product creating exposures substantially lower than equivalent cigarette smoking. The magnitude of reduction in exposures and results of cell studies and human clinical trials justifies a conclusion, again, that the product will create substantially reduced risk and harm in users who switch from cigarette smoking.

The basis for this is the extensive science base developed by the manufacturer and published in high quality peer-reviewed journals specializing in regulatory science. We consider the case rests on four main strands:

1. The physical and chemical processes involved are completely different to smoking.
2. The toxicity of the IQOS aerosol is far less than cigarette smoke.
3. Biomarkers of toxin exposure are substantially and rapidly reduced after switching from smoking to heated tobacco use.
4. Reduced exposure is expected to be translated to reduced harm and disease risk

2.1 The physical and chemical process involved are completely different

Heated tobacco products have an inherently different design to cigarettes and operate at much lower temperatures. According to data from the manufacturer, the heated product design allows for electrical heating of the tobacco stick to reach a maximum temperature of 350°C (660°F). This compares to the

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high combustion temperature of tobacco cigarettes, reaching up to 900°C (1650°F) during a puff,⁵ that create the mixture of solid and liquid particles and toxic gases. The lower temperature range is specifically designed to avoid combustion and the resulting toxic emissions. Several of the most harmful toxic chemicals in smoke are products of combustion,^{6,7,8} therefore, avoiding the combustion processes is expected to reduce the toxicity of the aerosol.

2.2 The chemical profile and toxicity of IQOS aerosol is different from cigarette smoke

Evidence published from the manufacturer has clearly shown that the potentially toxic emissions from IQOS are substantially lower compared to tobacco cigarettes.

Schaller et al⁹ evaluated IQOS aerosol for the presence of 59 compounds, including 54 priority toxicants in tobacco smoke that have been listed by authorities such as the World Health Organization, the U.S. Food and Drug Administration and Health Canada (Harmful and Potentially Harmful Chemicals – HPHCs).⁸ Different puffing regimes were tested, including ISO regime, Health Canada Intense regime and more intense puffing conditions, up to 110 mL puff volume and 4.5 seconds puff duration. Substantial reductions in toxic emissions, ranging from 60-99% for different compounds, compared to a standardized tobacco cigarette (3R4F) was observed.

Similar differences were observed recently in another study by the manufacturer comparing IQOS with commercial tobacco cigarettes.¹⁰ Additionally, cytotoxicity and mutagenicity studies identified an 85-95% reduction in the potencies of IQOS compared to 3R4F cigarettes. The levels of nicotine emitted to the aerosol of IQOS were approximately 30% lower compared to 3R4F cigarettes using Health Canada Intense puffing regime. The latter finding was recently verified in an independent study comparing IQOS with commercially-available tobacco cigarettes.¹¹ Additionally, it was found that the unused tobacco stick of IQOS contains similar concentration of nicotine as the tobacco of regular cigarettes, suggesting that nicotine is not added to the tobacco stick.

⁵ Baker RR. Smoke generation inside a burning cigarette: modifying combustion to develop cigarettes that may be less hazardous to health. *Prog. Energy Combust. Sci.* 2006;32:373-385. [\[link\]](#)

⁶ U.S.DHSS. How Tobacco Smoke Causes Disease The Biology and Behavioral Basis for Smoking-Attributable Disease A Report of the Surgeon General. Public Health. U.S. Dept. of Health and Human Services, Public Health Service, Office of the Surgeon General; 2010. 792 p. [\[link\]](#)

⁷ White JL, Conner BT, Perfetti TA, Bombick BR, Avalos JT, Fowler KW, et al. Effect of pyrolysis temperature on the mutagenicity smoke condensate of tobacco. *Food Chem Toxicol.* 2001;39:499-505. [\[link\]](#)

⁸ McGrath TE, Wooten JB, Geoffrey Chan W, Hajaligol MR. Formation of polycyclic aromatic hydrocarbons from tobacco: The link between low temperature residual solid (char) and PAH formation. *Food Chem Toxicol.* 2007 Jun;45(6):1039-50. [\[link\]](#)

⁹ Schaller J-P, Keller D, Poget L, Pratte P, Kaelin E, McHugh D, et al. Evaluation of the Tobacco Heating System 2.2. Part 2: Chemical composition, genotoxicity, cytotoxicity, and physical properties of the aerosol. *Regul Toxicol Pharmacol.* 2016 Nov 30;81 Suppl 2:S27-47. [\[link\]](#)

¹⁰ Jaccard G, Tabin Djoko D, Moennikes O, Jeannet C, Kondylis A, Belushkin M. Comparative assessment of HPHC yields in the Tobacco Heating System THS2.2 and commercial cigarettes. *Regul Toxicol Pharmacol.* 2017 Aug 14;90:1-8. [\[link\]](#)

¹¹ Farsalinos KE, Yannovits N, Sarri T, Voudris V, Poulas K. Nicotine delivery to the aerosol of a heat-not-burn tobacco product: comparison with a tobacco cigarette and e-cigarettes. *Nicotine Tob Res.* 2017 Jun 16. [\[link\]](#)