

Comments on the article entitled “Heat-Not-Burn Tobacco Cigarettes: Smoke by Any Other Name” by [Auer R, 2017](#).

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Philip Morris International (PMI) supports scientific data transparency, data sharing and actively encourages the conduct of independent studies on IQOS that are aimed at advancing scientific and medical knowledge or verifying the results we obtained through our assessment program described by [Smith MR, 2016](#). To date we have published over 30 peer-reviewed articles describing studies specifically conducted with IQOS [1]. We have also submitted a Modified Risk Tobacco Product (MRTP) application with the U.S. FDA [2]. It is important that independent studies are conducted with a high degree of scientific rigor, the same degree of rigor that is expected from our company. Key standards for scientific research are:

1. Studies should be conducted using fit-for-purpose and validated methods
2. Study results should be interpreted in an appropriate and non-misleading manner

As independent scientists are starting to analyze our products, it is perhaps not surprising that different methodologies are applied. We note, for example, that [Auer R, 2017](#) reporting on a chemical analysis of the IQOS aerosol used a “*smoking device designed and tested in [their] facility*”. Without further description of this system, it is hard to compare their analysis with those we have reported previously, using standard and validated smoking machine systems and procedures. While some of the reported results seem consistent with those that we have previously published, significant points of difference in the described methodologies may account for the disagreements in results obtained by Auer *et al.* in comparison to our peer-reviewed and published data.

3. Methodologies for smoke and aerosol generation have been amply described in the literature. We are therefore surprised that the authors did not use a recognized smoking regime, but rather used a hybrid between the ISO and the Health Canada Intense (HCI) regime [3], and then used this data to compare their results with those published using the ISO regime ([Vu AT, 2015](#)).
4. We were surprised by the measurement results the authors obtained for the volatile organic compounds. For instance, it is perplexing that they report yields of approximately 1 µg acrolein per stick for both IQOS and the cigarette they used in their study. It appears that the acrolein values reported by the authors for the cigarette are 50 times lower than those published by e.g. Health Canada ([Hammond D, 2008](#)). Similarly Auer *et al.* find 10 times lower levels of formaldehyde in cigarettes than Health Canada. Furthermore, the yields of acetone, crotonaldehyde and propionaldehyde are also underestimated.
5. It is generally established that the HCI regime is more relevant to how humans smoke than the ISO regime. Under HCI we find that the reference cigarette 3R4F yields 154±20 µg acrolein per stick ([Schaller JP, 2016](#)), which is similar to the 142±17 µg/stick reported by Health Canada. We have also reported that IQOS yields 11±2.36 µg acrolein per stick under HCI. Furthermore, under the ISO, IQOS yields 4.89±0.74 µg acrolein per stick ([Schaller JP, 2016](#)).
6. Regarding the polycyclic aromatic hydrocarbons, Auer *et al.* reported a level of acenaphthene for IQOS that is three fold higher than for cigarettes. Acenaphthene is not part of the list of 58 substances we routinely quantify, nor is it part of any regulatory lists (including the most extensive list, the FDA 93). It is, however, a compound we have measured in the smoke of 3R4F, but could not detect in the IQOS aerosol. Our method is based on mass spectrometry, which is a specific detector, as opposed to the non-specific detection system used by the authors. Their reported level for IQOS may therefore come from an artefact, not linked specifically to acenaphthene.
7. It is also surprising that for many analytes, the reported standard deviations are close to, or even larger than the mean values.
8. Taken together, the above-mentioned issues lead us to question the analytical methods that were used. For future studies we recommend that the authors should reduce the measurement variability between the replicas, validate their methods with a reference cigarette (e.g. 3R4F) and compare their results with those published by a recognized regulatory agency.
9. Unfortunately, the results for carbon monoxide (CO) measurements are reported in ppm (parts per million). We would recommend that they should have been converted to mg/stick. Reporting in the

way the authors do precludes a comparison of the measured levels with a standard reference cigarette. In addition, the level of CO for the cigarette was above the measurement range of the used instrument, which precludes a comparison between the IQOS and cigarette yields.

10. Contrary to the authors' suggestions, "Heat-not-burn" is not an advertising slogan but a shorthand for a product description. We have clearly demonstrated the absence of combustion in IQOS through robust scientific substantiation, which we summarized on [PMscience](#) [1] and in our MRTP application to the U.S. FDA [2]. This has been corroborated by several combustion experts. Furthermore, we have never claimed that IQOS is devoid of pyrolytic processes, which are well known to increase with temperature, and are responsible for much of the remaining HPHCs found in the IQOS aerosol.
11. The authors suggest that we are "dancing around the definition of smoke to avoid indoor-smoking bans". Unfortunately, the authors did not present any data regarding the impact of IQOS on indoor use. Due to the way in which IQOS functions and is used, its impact on air quality cannot be linearly extrapolated from mainstream aerosol chemistry data. Towards that end, proper indoor air quality studies, using validated methods are needed. One such example can be found in [Mitova MI, 2016](#).
12. PMI has consistently communicated that IQOS aerosol is not devoid of HPHCs, and has transparently published the relative yields of HPHCs in comparison with cigarette smoke. Chemical analysis of the IQOS aerosol shows that it contains on average >90% reduction in the levels of HPHCs when compared with the smoke of the 3R4F reference cigarette. This furthermore leads to a concomitant reduction in cytotoxicity and genotoxicity ([Schaller JP, 2016](#)).
13. Since we understand the skepticism around tobacco industry-generated data, we also commissioned an independent, recognized and accredited laboratory to quantify the 58 analytes we routinely measure in our studies [4]. The data was submitted as part of our MRTP application to the U.S. FDA [2].
14. The totality of the evidence collected to date, across a broad range on toxicology, systems toxicology and clinical studies, indicates that IQOS has the potential to present less risk of harm compared to continued smoking for adult smokers who switch to it completely [1].

[1] Smith M, Haziza C, Hoeng J, Lüdicke F, Maeder S, Vanscheeuwijck P and Peitsch MC (2017) The Science behind the Tobacco Heating System: a summary of published scientific articles. Available at: <https://www.pmiscience.com/library/pmi-science-ths-executive-summary>.

[2] U.S. Food and Drug Administration (FDA). Philip Morris Products S.A. Modified Risk Tobacco Product (MRTP) Applications. May 24, 2017. Available from: <https://www.fda.gov/TobaccoProducts/Labeling/MarketingandAdvertising/ucm546281.htm>.

[3] Health Canada (2000). Health Canada - Tobacco Products Information Regulations SOR/2000-273, Schedule 2. <http://laws-lois.justice.gc.ca/PDF/SOR-2000-273.pdf>.

[4] Available at: <https://www.pmiscience.com/platform-development/platform-development/aerosol-chemistry-physics/hphcs/levels-hphcs-measured>.