[Commentary] On Heated Tobacco Products and the Importance of Science-Based Assessments and Product Classification

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Abstract

Proper assessment of heated tobacco products (HTPs), which are alternatives to cigarettes that heat rather than burn tobacco, is necessary to gain a full understanding of both the potential risks and benefits of these newer products. This includes understanding differences in HTP aerosol compared to cigarette smoke. Recent publications have attempted to characterize HTP emissions in order to provide guidance on relative risk and classification. However, improper representation of studies and misinterpretation of how products are designed and used has led to confusion about the relative risk of HTPs compared to cigarettes. This commentary provides clarification on these important issues with a focus on classification of emissions from the device.

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Commentary

It is well accepted that the primary health risks from smoking are not related to nicotine, but instead a consequence of chronic inhalation of the high level of toxicants generated from combustion when tobacco is burned [Benowitz, 2010; RCP 2016]. While the best way for people who smoke to reduce their risk of developing smoking-related disease is to quit tobacco and nicotine altogether, there remain people who do not. Following the principle of tobacco harm reduction [RCP, 2016], over the past two decades, alternative nicotine and tobacco products such as electronic cigarettes and heated tobacco products (HTPs) have been developed that aid and encourage those adult smokers who do not quit to completely switch to using a potentially lower-risk, non-combustible nicotine product. To evaluate the relative harms of these products, it is both essential to categorize them correctly and reasonable to compare their effects to those of the cigarettes that they aim to replace.

Recently, there has been much interest in the composition and classification of the aerosol of HTPs [Uguna and Snape 2022; Bekki *et al.* 2017; Auer *et al.* 2017; Davis, Williams, and Talbot 2019]. Extensive evidence indicates that emissions from HTPs are fundamentally different from those from a combustible cigarette and should be considered an aerosol rather than smoke [FDA 2019; VG Braunschweig 2021; Kärkelä *et al.* 2021; Kärkelä, Tapper, and Kajolinna 2022; Amorós-Pérez *et al.* 2021, 2022; Pratte, Cosandey, and Goujon 2017; Schaller *et al.* 2016; Haziza *et al.* 2020, 2017; Haziza, de La Bourdonnaye, Skiada, *et al.* 2016; Lüdicke *et al.* 2018; Haziza, de La Bourdonnaye, Merlet, *et al.* 2016]. Nevertheless, some authors are arguing that the HTP emissions can be considered smoke [Uguna and Snape 2022; Auer *et al.* 2017] and, further, that emissions from HTPs and cigarettes should be compared on a tobacco-weight rather than a unit-consumption basis [Uguna and Snape 2022]. These recent publications raise concerns about incorrect product classification and risk comparisons based on inaccurate scientific arguments.

The intention of this communication is not to describe in detail the generation and properties of emissions from combustible cigarettes and HTPs, which has been expertly covered by [Sussmann *et al.* 2023], but rather to comment on recent issues raised about aerosol categorization and product comparisons with a focus on PMI's HTP, which is marketed as *IQOS* in some countries.

Differentiating between cigarette smoke and HTP aerosol

To determine whether the emissions of a product should be classified as smoke, it is fundamental (1) to examine the physicochemical processes that generate the emissions; and (2) to characterize the aerosol composition in terms of its chemical and physical characteristics. The recent argument that HTP aerosol can be considered "smoke" is founded on the detection of "smoke" components in the emissions from the HeatStick [Uguna and Snape 2022; Auer *et al.* 2017] without considering their levels or whether these components are produced by chemical reactions, which would indicate creation of a unique substance, or transferred via physical phase-change processes during product operation, which not involve a change at the molecular level.

An analytical study (which has since faced concerns regarding the validity of the methods) [Maeder and Peitsch 2017; Caruso and Polosa 2017; Fujita, Cozzani, and Peitsch 2017; FDA, 2019]) of polycyclic aromatic hydrocarbons (PAHs) and volatile organic compounds (VOCs) reported that HTP emissions contain elements from pyrolysis and thermogenic degradation that are the same harmful constituents present in conventional tobacco smoke [Auer *et al.* 2017]. In the case of PAHs, small quantities are present in cured tobacco, and the very low levels observed in HTP emissions have been shown to be proportional to the PAH content of the tobacco materials in the HeatSticks, indicating direct transfer to the aerosol from the tobacco biomass [Goujon *et al.* 2020]. This contrasts with the large amounts of PAHs formed when tobacco burns in a cigarette, and which are the precursors of soot formation [Poget *et al.* 2021; Goujon *et al.* 2020; Pratte, Cosandey, and Goujon 2017; Bentley *et al.* 2020]. Without the production of PAHs at the high concentrations needed to initiate soot particle formation, smoke particles do not form in HTP emissions, and the aerosol produced is liquid-based.

A recent review also highlighted, in addition to PAHs, the presence of black carbon (suggesting soot) and appreciable

amounts of “tar” (also called nicotine-free dry particulate matter; NFDPM) as indicators that HTP emissions can be considered smoke [Uguna and Snape 2022]. Although an NFDPM value can be formally calculated for HTPs in the same way as for combustible cigarettes, the compositions of the two types of substance are fundamentally different [Mallock *et al.* 2018]. NFDPM is derived from total particular matter (TPM), defined as the portion of the smoke/aerosol that is trapped on the filter during standard smoke or aerosol analysis [ISO 4387:2000]. The majority of the TPM of cigarette smoke constitutes smoke-related toxicants, whereas that of HTP aerosol constitutes the humectants needed to generate the aerosol, with far lower levels of tobacco-related toxicants [Bentley, 2020]. Regarding the presence of black carbon in environmental HTP emissions, the cited study [Ruprecht *et al.* 2017] did not detect black carbon that is indicative of soot, but did detect 0.73%–0.79% of the level of 370nm black carbon that is present in cigarette smoke, concluding that the only carbon content in HTP emissions is derived from low levels of organic compounds.

For a full understanding of the vast difference in the physicochemical properties of emissions from combustible cigarettes, HTPs and e-cigarettes, we refer the reader to [Sussman *et al.* 2023]. In brief, tobacco smoke is a highly complex aerosol comprised of solid particles and liquid droplets generated through various processes that are initiated and sustained through ignition and combustion of the cigarette rod; HTP emissions are a complex vapour mixture derived by heating biomass at a temperature below the ignition point [Sussman *et al.* 2023].

Comparative analysis of HTP aerosol with cigarette smoke

In terms of evaluating the relative health implications of tobacco product emissions – irrespective of their classification as smoke or not – the product-use behaviour of the consumers must be factored in. [Uguna and Snape 2022] have stated that the yields of harmful and potentially harmful constituents (HPHCs) in HTP emissions have been underestimated by a factor of 3.2–3.6-fold because they have been compared with those in cigarette smoke on a per-unit rather than a tobacco-weight basis. However, a comparison based on the weight of tobacco in the products fails to account for the average daily consumption of HTP users versus smokers.

Heated tobacco products were developed as a potentially less harmful alternative to cigarettes. Data from numerous studies show that, when adult smokers switch from cigarettes to HTP, the number of HeatSticks that they use is comparable to the number of cigarettes that they smoked prior to switching [FDA 2019; Haziza *et al.* 2020, 2017; Haziza, de La Bourdonnaye, Skiada, *et al.* 2016]. A clinical study conducted over 90 days has further demonstrated that exposure to nicotine after using one HeatStick is comparable to that after smoking one cigarette [Haziza *et al.* 2020].

Research based on this ratio of use (i.e., 1 cigarette to 1 HeatStick) clearly and reproducibly shows that emissions of HPHCs in HTP aerosol that users are exposed to are significantly lower than those in combustible tobacco smoke [FDA 2019; Kärkelä, Tapper, and Kajolinna 2022; Mallock *et al.* 2018; Schaller *et al.* 2016]. Further, reductions in biomarkers of exposure to HPHCs measured in clinical studies are aligned with the reduction in formation of the respective compounds in the aerosol compared to the levels in cigarette smoke on a per-unit basis [FDA 2019; Znyk, Jurewicz, and Kaleta 2021; Haziza *et al.* 2020; Lüdicke *et al.* 2018; Haziza *et al.* 2017; Haziza, de La Bourdonnaye, Skiada, *et al.* 2016; Haziza, de La

Bourdonnaye, Merlet *et al.* 2016].

Conclusions

Based on our scientific assessment of HTPs, together with the results from several independent peer-reviewed studies and independent combustion and aerosol science experts, HTP aerosol is fundamentally different to cigarette smoke and does not fit the definition of smoke, being a liquid-droplet-based aerosol that lacks solid particles. Furthermore, HTP aerosol contains only 532 compounds at levels above 100 ng/HeatStick [Bentley *et al.* 2020], as compared approximately 4800 compounds that have been detected in cigarette smoke at the same threshold [Bentley *et al.* 2020, Rodgman and Green 2003, Rodgman and Perfetti 2013].

When assessing smoke-free products that may reduce the public health burden relative to continued cigarette smoking, it is important that the totality of evidence is taken into consideration, that individual studies are not misrepresented, and that products are evaluated in accordance with how they are used by consumers. Regarding the totality of evidence on THR aerosol, of which only a small portion has been cited herein, the conclusions are clear: it is not smoke, and while not risk-free, it contains only a fraction of the HPHCs found in cigarette smoke.

Statements and Declarations

The authors are employees of Philip Morris International.

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