PART 3 – SUPPORTING DATA

SUPPORTING DATA SUMMARY

This application refers to tobacco rather than nicotine as a pure chemical substance, and the requested change to Schedule 7 is a class exemption for tobacco prepared and packed for heating rather than a specific product.

That being the case, much of the information contained in this application is focused on comparing HTP products with conventional cigarettes.

Supporting data is by way of reference to published papers, regulatory decisions and policy statements, as noted in the bibliography. This includes peer reviewed journal papers relating to studies performed by the tobacco industry and other researchers.

The supporting data and references fall into four general categories

1) Published statistics and peer reviewed papers of independent research on the effects (including use, misuse and abuse) of nicotine and tobacco, in various forms.
2) Information on studies performed by industry such as Philip Morris International and British American Tobacco on HTP vs conventional cigarettes.
3) Regulatory opinions and decisions from comparable overseas regulators including, but not limited to, the U.S. FDA, New Zealand Ministry of Health, UK Committees on Toxicology, Carcinogenicity and Mutagenicity of Chemicals in Food, Consumer Products and the Environment, WHO and the Japanese National Fire Agency.
4) Policy statements and opinion pieces from other government agencies, UK Royal College of Physicians, Royal Australian College of General Practitioners and other peak bodies and stakeholders.

In particular, in the Risks and Benefits Section A, there is compelling evidence provided by independent researchers and the tobacco industry in relation to the reduced level of HPHCs in HTPs, relative to conventional cigarettes and how this may affect overall health outcomes and indoor air quality. These are illustrated in the following publications: (Schaller et al. 2016a; Schaller et al. 2016b; Li et al. 2018; Jaccard et al. 2017; Mallock et al. 2018; Forster et al. 2018, Bekki et al. 2017; Uchiyama et al. 2018; FDA TPL Report, 2019, PMI 2018, Pratte et al 2017, FDA 2019, FDA 2016, Royal College of Physicians 2016, WHO 2009, WHO 2000, Nordlund et al 2019). There is also supporting details on the impact of HTP aerosol on the environment and bystanders (Appendix 4).

Additional information on some current brands of HTPs, relevant to Section D of the application, is located in Appendix 2. PMI’s HTP is one of the most studied HTPs and Appendix 3 lists publications and reviews for the product.

The risks of abuse and misuse (including attractiveness to youth, never-smokers or former smokers) are summarised in Section A and thoroughly discussed in Section E. THS abuse liability was assessed based on the review of available information from various sources, including product design and content, aerosol chemistry, human clinical and behavioural data and an example comparison is provided between IQOS and conventional cigarettes using the methodology of Carter 2009.
Section C provides evidence on reduced toxicity of HTPs in comparison to CCs, as well as additional details on independent assessments by comparable regulators and agencies (Appendix 5).

An overview of recent independent studies giving insight into the use patterns and misuse/abuse potential of different tobacco products has been provided with reference to Queloz and Etter, 2019, Delgrande et al., 2019 and Osaki, 2019.

Section E also includes reference to Appendix 6 which provides the full abuse liability assessment provided by PMI to the U.S. FDA as part of PMI’s Modified Risk Tobacco Product application for THS.

Section F discusses the concept of tobacco harm reduction as well as the approach taken by comparable regulators.

Studies by PMI that are included in this application are peer reviewed publications or information in the public domain such as FDA submission dockets. Study reports are available for all studies relating to PMI’s HTP and can be supplied if required.

All references used within the body of the document are hyperlinked to the Bibliography for ease of readability.

SUPPORTING DATA DETAILS

Additional data to substantiate indicated data points in the submission has been included as addenda in the following appendices:

- Appendix 1: Countries that Regulate Heated Tobacco Products
- Appendix 2: Marketed HTP Devices and Consumable
- Appendix 3: List of independent studies and reviews of PMI’s HTP
- Appendix 4: Impact of HTP aerosol on the environment and on bystanders
- Appendix 5: Examples of research conducted by independent researchers or regulatory authorities on the mainstream aerosol of the HTPs and reference cigarette smoke
- Appendix 6: Abuse Liability

A Glossary of terms and abbreviations is also provided for ease of reference.

Data, including independent studies that have been conducted by medical institutions, have been provided by way of reference to peer reviewed journals and published papers, regulatory decisions and policy statements.

COPIES OF PAPERS REFERENCED

Copies of papers referenced are included as separate attachments and have been uploaded with the application.

All work referenced, copied and submitted for the purposes of this application, and used by the Commonwealth, can be taken to be authorised by the Commonwealth under section 183 of the Copyright Act 1968 (Cth).
PART 4 – BIBLIOGRAPHY


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Nicotine (in Tobacco Prepared and Packed for Heating)
Philip Morris Limited, 31 October 2019

available at: https://www.grandviewresearch.com/industry-analysis/heated-tobacco-products-htps-market


Osaki Y., Chief investigator, Professor, Division of Environmental and Preventive Medicine, Faculty of Medicine, Tottori University. http://researchers.adm.tottori-u.ac.jp/html/100000120_en.html


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Wald NJ, Watt HC. Prospective study of effect of switching from cigarettes to pipes or cigars on mortality from three smoking related diseases. BMJ. 1997; 314(7098):1860-3.


<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>3R4F</td>
<td>Reference cigarette produced by the University of Kentucky</td>
</tr>
<tr>
<td>ABS</td>
<td>Australian Bureau of Statistics</td>
</tr>
<tr>
<td>ANDS</td>
<td>Alternative Nicotine Delivery Systems</td>
</tr>
<tr>
<td>ANPRM</td>
<td>Advance Notice of Proposed Rulemaking, FDA (U.S.)</td>
</tr>
<tr>
<td>AUC</td>
<td>Area under the concentration-time curve</td>
</tr>
<tr>
<td>AUC(0-24 h)</td>
<td>Area under the concentration-time curve from 0 to 24 hours</td>
</tr>
<tr>
<td>AUC(0-last)</td>
<td>Area under plasma concentration-time curve from start of product use to time of last quantifiable concentration</td>
</tr>
<tr>
<td>AUC(0-t’)</td>
<td>Partial AUC, where t’ is the subject-specific time of maximum nicotine concentration</td>
</tr>
<tr>
<td>BAT</td>
<td>British American Tobacco</td>
</tr>
<tr>
<td>BfR</td>
<td>German Federal Institute for Risk Assessment</td>
</tr>
<tr>
<td>BoExp/ BoE</td>
<td>Biomarker(s) of exposure. A chemical, its metabolite, or the product of an interaction between a chemical and some target molecule or cell that is measured in the human body (e.g. cotinine in blood or urine for second-hand tobacco smoke, benzene metabolites in urine for traffic-related pollution)</td>
</tr>
<tr>
<td>CC</td>
<td>Conventional cigarette, Combustible cigarette</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence interval</td>
</tr>
<tr>
<td>CISPR</td>
<td>International Special Committee for Radio Protection</td>
</tr>
<tr>
<td>CLP</td>
<td>Classification, Labelling and Packaging (E.U.)</td>
</tr>
<tr>
<td>Cm</td>
<td>Maximum nicotine concentration</td>
</tr>
<tr>
<td>Cmax</td>
<td>Maximum plasma concentration</td>
</tr>
<tr>
<td>Cmin</td>
<td>Minimum plasma drug concentration</td>
</tr>
<tr>
<td>CNS</td>
<td>Central Nervous System</td>
</tr>
<tr>
<td>COAG</td>
<td>Council of Australian Government</td>
</tr>
<tr>
<td>COHb</td>
<td>Carboxyhemoglobin</td>
</tr>
<tr>
<td>COPD</td>
<td>Chronic obstructive pulmonary disease</td>
</tr>
<tr>
<td>COT</td>
<td>Committee of Toxicology (U.K.)</td>
</tr>
<tr>
<td>CROs</td>
<td>Contract Research Organisation</td>
</tr>
<tr>
<td>CTP</td>
<td>Center of Tobacco Products, FDA (U.S.)</td>
</tr>
<tr>
<td>CVD</td>
<td>Cardiovascular disease</td>
</tr>
<tr>
<td>DoH or DOH</td>
<td>Commonwealth Department of Health</td>
</tr>
<tr>
<td>Acronym</td>
<td>Description</td>
</tr>
<tr>
<td>---------</td>
<td>-------------</td>
</tr>
<tr>
<td>EAC</td>
<td>Eurasian Conformity standards</td>
</tr>
<tr>
<td>EHTP</td>
<td>Electrically Heated Tobacco Product. Typically consists of a consumable product (such as tobacco sticks or <em>HeatSticks</em>) that contains tobacco which is electrically heated</td>
</tr>
<tr>
<td>EHTS</td>
<td>Electrically Heated Tobacco Systems</td>
</tr>
<tr>
<td>EN</td>
<td>European Norm standards</td>
</tr>
<tr>
<td>ENDS</td>
<td>Electronic Nicotine Delivery Systems</td>
</tr>
<tr>
<td>ETS</td>
<td>Environmental tobacco smoke. Also known as secondhand smoke, it is a complex mixture of chemicals generated during the burning and smoking of tobacco products to which a person is unintentionally exposed, most commonly in the home, formerly in public places. It comes from both the smoke from the tip of the cigarette and the smoke that the smoker is exhaling</td>
</tr>
<tr>
<td>FCTC</td>
<td>Framework Convention of Tobacco Control (W.H.O.)</td>
</tr>
<tr>
<td>FDA</td>
<td>Food and Drug Administration (U.S.)</td>
</tr>
<tr>
<td>FDA-18</td>
<td>Abbreviated FDA list of 18 HPHCs in smoke/aerosol</td>
</tr>
<tr>
<td>FDA-18 + 6</td>
<td>Abbreviated FDA list of 18 HPHCs in smoke/aerosol + 6 tobacco constituents</td>
</tr>
<tr>
<td>FDA-93</td>
<td>Established FDA list of 93 HPHCs in tobacco products and tobacco smoke</td>
</tr>
<tr>
<td>FEV₁</td>
<td>Forced expiratory volume in 1 second</td>
</tr>
<tr>
<td>FFC</td>
<td>Federal Communications Commission (U.S.)</td>
</tr>
<tr>
<td>HC</td>
<td>Health Canada (including Health Canada list of 44 constituents in the mainstream smoke of tobacco products)</td>
</tr>
<tr>
<td>HCI</td>
<td>Health Canada Intense (puffing regime). First described by Health Canada, when taking one puff of 55 ml volume and 2 s duration every 30 s with 100% of the ventilation zone on the cigarette filter blocked</td>
</tr>
<tr>
<td>HD</td>
<td>Heart Disease</td>
</tr>
<tr>
<td>HDL-C</td>
<td>High Density lipoprotein-C</td>
</tr>
<tr>
<td><em>HeatSticks</em></td>
<td>Specially designed heated tobacco consumables that contain tobacco and is intended for exclusive use with the <em>IQOS</em> holder</td>
</tr>
<tr>
<td>HNB or HnB</td>
<td>Heat-not-burn. Refers to tobacco that is heated instead of lit or burnt. Also referred to as a Heated Tobacco Product (HTP)</td>
</tr>
<tr>
<td>HPHCs</td>
<td>Harmful and potentially harmful constituent(s). Chemical compounds in tobacco products or tobacco smoke that cause or could cause harm to smokers or nonsmokers</td>
</tr>
<tr>
<td>HTP</td>
<td>Heated Tobacco Product. The consumable product (such as tobacco sticks or <em>HeatSticks</em>) that contains tobacco for heating</td>
</tr>
<tr>
<td>IAQ</td>
<td>Indoor air quality</td>
</tr>
<tr>
<td>IARC</td>
<td>International Agency for Research on Cancer</td>
</tr>
<tr>
<td>IC</td>
<td>Integrated Circuit</td>
</tr>
<tr>
<td>Abbr</td>
<td>Description</td>
</tr>
<tr>
<td>-------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>IEC</td>
<td>International Electrotechnical Commission</td>
</tr>
<tr>
<td>IOM</td>
<td>Institute of Medicine</td>
</tr>
<tr>
<td>iQOS and IQOS</td>
<td>Commercial names (both registered trademarks) of PMI’s Tobacco Heating Device</td>
</tr>
<tr>
<td>ISO</td>
<td>International Organization for Standardization</td>
</tr>
<tr>
<td>JNFA</td>
<td>Japanese National Fire Authority</td>
</tr>
<tr>
<td>JTI</td>
<td>Japan Tobacco International</td>
</tr>
<tr>
<td>KT&amp;G</td>
<td>Korean Tobacco &amp; Ginseng</td>
</tr>
<tr>
<td>LOQ</td>
<td>Limit of Quantitation/ Quantification</td>
</tr>
<tr>
<td>MFDS</td>
<td>Ministry of Food and Drug Safety (Korea)</td>
</tr>
<tr>
<td>MLA</td>
<td>Mouse Lymphoma Assay</td>
</tr>
<tr>
<td>MRTP</td>
<td>Modified risk tobacco product</td>
</tr>
<tr>
<td>MRTPA</td>
<td>Modified risk tobacco product application</td>
</tr>
<tr>
<td>NFDPM</td>
<td>Nicotine-Free Dry Particulate Matter</td>
</tr>
<tr>
<td>NNAL</td>
<td>4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol</td>
</tr>
<tr>
<td>NNS</td>
<td>Nicotine Nasal Spray</td>
</tr>
<tr>
<td>NTDA</td>
<td>Non Targeted Differential Analysis</td>
</tr>
<tr>
<td>NRT</td>
<td>Nicotine replacement therapy</td>
</tr>
<tr>
<td>OECD</td>
<td>Organization for Economic Co-operation and Development</td>
</tr>
<tr>
<td>PHE</td>
<td>Public Health England</td>
</tr>
<tr>
<td>PK</td>
<td>Pharmacokinetics</td>
</tr>
<tr>
<td>PK/PD</td>
<td>The relationship between blood plasma nicotine (PK) concentration and suppressing the urge to smoke (PD) in adult smokers</td>
</tr>
<tr>
<td>PM USA</td>
<td>Philip Morris U.S.A.</td>
</tr>
<tr>
<td>PMI-58</td>
<td>List of constituents and analytes defined by PMI that are quantified in the THS aerosol</td>
</tr>
<tr>
<td>PML</td>
<td>Philip Morris Limited, the Australian Philip Morris International subsidiary</td>
</tr>
<tr>
<td>PMTA</td>
<td>Premarket tobacco product application</td>
</tr>
<tr>
<td>R&amp;D</td>
<td>Research and Development</td>
</tr>
<tr>
<td>RCP</td>
<td>Royal College of Physicians (U.K.)</td>
</tr>
<tr>
<td>REX</td>
<td>Reduced exposure studies</td>
</tr>
<tr>
<td>REXA</td>
<td>Reduced exposure studies in ambulatory settings</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>REXC</td>
<td>Reduced exposure studies in confinement settings</td>
</tr>
<tr>
<td>RACGP</td>
<td>Royal Australian College of General Practitioners</td>
</tr>
<tr>
<td>RRP</td>
<td>Reduced risk product(s)</td>
</tr>
<tr>
<td>SA</td>
<td>Smoking Abstinence</td>
</tr>
<tr>
<td>SmPC</td>
<td>Summary of Product Characteristics</td>
</tr>
<tr>
<td>To</td>
<td>Time point of first product use during study day</td>
</tr>
<tr>
<td>&quot;Tar&quot;</td>
<td>Nicotine-Free Dry Particulate Matter (NFDPM)</td>
</tr>
<tr>
<td>THD</td>
<td>Tobacco Heating Device (Holder and Charger)</td>
</tr>
<tr>
<td>THS</td>
<td>Tobacco Heating System (Tobacco Heating Device + HTP/Tobacco Sticks). Combination of consumable product (HTP) plus heating device. Also referred to as an EHTS (Electrically Heated Tobacco System) if the heat source is electronic.</td>
</tr>
<tr>
<td>Tobacco Sticks</td>
<td>Tobacco containing sticks (resembling cigarettes) manufactured to be used as part of the THS. May also be sometimes referred to as Heat Sticks.</td>
</tr>
<tr>
<td>Tmax</td>
<td>Time to the maximum concentration</td>
</tr>
<tr>
<td>TPM</td>
<td>Total particulate matter</td>
</tr>
<tr>
<td>TSNA</td>
<td>Tobacco-specific N-nitrosamines</td>
</tr>
<tr>
<td>Type II Error</td>
<td>A Type I error is the rejection of a true null hypothesis, whereas Type II error describes the error that occurs when one fails to reject a null hypothesis that is actually false. In other words, it produces a false positive. The error rejects the alternative hypothesis, even though it does not occur due to chance.</td>
</tr>
<tr>
<td>UL</td>
<td>Underwriters Laboratories standards</td>
</tr>
<tr>
<td>US SURG</td>
<td>United States Surgeon General</td>
</tr>
<tr>
<td>WBC</td>
<td>White blood cell (count)</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>
APPENDIX 2: MARKETED HTP DEVICES AND CONSUMABLES
## Appendix 2: Marketed HTP Devices and Consumables

<table>
<thead>
<tr>
<th>Company</th>
<th>Product</th>
<th>Brand</th>
<th>Markets available</th>
</tr>
</thead>
<tbody>
<tr>
<td>BAT</td>
<td>Consumable</td>
<td>Dunhill (for glo)</td>
<td>Bulgaria</td>
</tr>
<tr>
<td>BAT</td>
<td>Consumable</td>
<td>Kent (for glo)</td>
<td>Romania, Japan, Russia, Azerbaijan, Ukraine</td>
</tr>
<tr>
<td>BAT</td>
<td>Consumable</td>
<td>Kool (for glo)</td>
<td>Japan</td>
</tr>
<tr>
<td>BAT</td>
<td>Consumable</td>
<td>Neo (for glo)</td>
<td>Switzerland, Japan, Croatia, South Korea, Malaysia, Ukraine, Greece, Czech Republic, Kazakhstan, Poland, Serbia, Italy</td>
</tr>
<tr>
<td>BAT</td>
<td>Device</td>
<td>Glo Express</td>
<td>Italy, Romania</td>
</tr>
<tr>
<td>BAT</td>
<td>Device</td>
<td>Glo nano</td>
<td>Romania, Italy</td>
</tr>
<tr>
<td>BAT</td>
<td>Device</td>
<td>Glo series 1</td>
<td>Malaysia, Switzerland, Serbia</td>
</tr>
<tr>
<td>BAT</td>
<td>Device</td>
<td>Glo series 2</td>
<td>Poland, Romania, Malaysia, Japan, Croatia, Ukraine, Greece, Kazakhstan, Russia, Bulgaria, South Korea, Czech Republic, Azerbaijan</td>
</tr>
<tr>
<td>BAT</td>
<td>Device</td>
<td>Glo series 2 mini</td>
<td>Japan, Croatia, South Korea, Ukraine, Greece, Kazakhstan, Russia, Bulgaria,</td>
</tr>
<tr>
<td>CNTC</td>
<td>Consumable</td>
<td>COO (for MOK)</td>
<td>South Korea, Maldives</td>
</tr>
<tr>
<td>CNTC</td>
<td>Consumable</td>
<td>Kuanzhai (for KungFu)</td>
<td>South Korea</td>
</tr>
<tr>
<td>CNTC</td>
<td>Consumable</td>
<td>MC (for MC)</td>
<td>South Korea</td>
</tr>
<tr>
<td>CNTC</td>
<td>Device</td>
<td>MOK</td>
<td>South Korea, Maldives</td>
</tr>
<tr>
<td>CNTC</td>
<td>Device</td>
<td>MOK mini</td>
<td>South Korea, Maldives</td>
</tr>
<tr>
<td>CNTC</td>
<td>Device</td>
<td>KungFu</td>
<td>South Korea</td>
</tr>
<tr>
<td>CNTC</td>
<td>Device</td>
<td>MC 2.0 (Mate)</td>
<td>South Korea</td>
</tr>
<tr>
<td>Imperial</td>
<td>Consumable</td>
<td>iD (for Pulze)</td>
<td>Japan</td>
</tr>
<tr>
<td>Imperial</td>
<td>Device</td>
<td>Pulze</td>
<td>Japan</td>
</tr>
<tr>
<td>JTI</td>
<td>Consumable</td>
<td>Mevius (for Ploom S)</td>
<td>Japan</td>
</tr>
<tr>
<td>JTI</td>
<td>Device</td>
<td>Ploom S</td>
<td>Japan</td>
</tr>
<tr>
<td>KT&amp;G</td>
<td>Consumable</td>
<td>Fiit (for lil)</td>
<td>South Korea</td>
</tr>
<tr>
<td>KT&amp;G</td>
<td>Device</td>
<td>lil mini</td>
<td>South Korea</td>
</tr>
<tr>
<td>Device</td>
<td>Consumable</td>
<td>HEETS</td>
<td>Marlboro</td>
</tr>
<tr>
<td>-------</td>
<td>-----------</td>
<td>-------</td>
<td>---------</td>
</tr>
<tr>
<td>KT&amp;G</td>
<td>Lil Plus</td>
<td>South Korea</td>
<td>Japan, Korea, Malaysia, New Zealand, Albania, Armenia, Belarus, Bosnia &amp; Herz., Israel, Kazakhstan, Moldova, Russia, Serbia, Ukraine, Andorra, Azores, Bulgaria, Canary Islands, Corsica, Croatia, Cyprus, Czech Republic, Denmark, France, Germany, Greece, Hungary, Italy, Latvia, Lithuania, Madeira, Netherlands, Poland, Portugal, Romania, Slovak Republic, Slovenia, Spain Mainland, Sweden, Switzerland, United Kingdom, Canada, Caribbean Other, Colombia, Dominican Republic, Guatemala, PMIDF (PMI Duty Free), Palestine Auth. Area, Reunion, South Africa, Turkish Cyprus, UAE</td>
</tr>
<tr>
<td>PMI</td>
<td>Consumable</td>
<td>HEETS</td>
<td>Japan</td>
</tr>
<tr>
<td>PMI</td>
<td>Device</td>
<td>Marlboro</td>
<td>As per HEETS consumables</td>
</tr>
</tbody>
</table>

Note: As at September 2019
APPENDIX 3 – INDEPENDENT PUBLICATIONS
2019


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2018


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2017


2016


2015


2014

APPENDIX 5 – Examples of research conducted by independent researchers or regulatory authorities on the mainstream aerosol of the HTPs and reference cigarette smoke.
The Department of Environmental Health, National Institute of Public Health in Japan, one of the WHO Tobacco Laboratory Network (TobLabNet) laboratories analyzed nicotine, tar, carbon monoxide (CO) and tobacco-specific nitrosamines (TSNAs) in the mainstream aerosol and tobacco fillers of IQOS regular and IQOS menthol, and compared their concentrations with those from reference cigarettes (3R4F and 1R5F) using WHO TobLabNet methods. The authors conclude "In this study we could provide important information showing that the concentration levels of hazardous compounds in the mainstream smoke of IQOS are much lower than those in conventional combustion cigarettes." Although it is low concentration, toxic compounds are definitely included in the mainstream smoke of IQOS.

2. UK: Independent Scientific Advisory Committees on Toxicity (COT), Carcinogenicity (COC) and Mutagenicity (COM)
The UK Committee on Toxicity (COT), with support from the Committee on Carcinogenicity (COC) and Committee on Mutagenicity (COM) assessed the toxicological risks from novel heat-not-burn tobacco products and compared these risks to those from conventional cigarettes. The Committee has reviewed evidence on two heated tobacco products, IQOS (PMI) and iFUSE (BAT). The Committees stated “For both products, there were some HPHCs where the reduction was approximately 50%, but the reduction in a number of other HPHCs was greater than 90%, with many of the compounds being below the limits of detection or quantification for the assays used” and “Overall, the Committees conclude that while there is a likely reduction in risk for smokers switching to heat-not-burn tobacco products, there will be a residual risk and it would be more beneficial for smokers to quit smoking entirely.” Statement on the toxicological evaluation of novel heat-not-burn tobacco products published on the 12th of December 2017 by the UK Committee on Toxicity (COT): https://cot.food.gov.uk/sites/default/files/heat_not_burn_tobacco_statement.pdf

3. The China National Tobacco Quality Supervision and Test Centre (“CNTQSTC”), a member of the WHO Tobacco Laboratory Network (TobLabNet), published on the 8th of January 2018 an independent study in Nicotine & Tobacco Research comparing the HPHCs present in IQOS aerosol and 3R4F reference cigarette smoke (Li et al, 2018) This peer reviewed publication by Li et al (2018) “Chemical Analysis and Simulated Pyrolysis of Tobacco Heating System 2.2 Compared to Conventional Cigarettes” includes % reduction results of carbon monoxide and 25 Harmful and Potentially Harmful Constituents (HPHCs) in IQOS aerosol versus 3R4F reference cigarette smoke using the ISO and Health Canada intense testing regime. The authors stated “The majority of mainstream constituents of THS 2.2 were reduced compared to 3R4F [reference cigarette].” Specifically, they found that compared to the 3R4F reference cigarette, IQOS produced “more than 90% [lower levels of] HPHCs, except for carbonyls, ammonia, and NAB, which were about 50–80% lower.” The authors cautioned “that reduction of harmful constituent emissions cannot be interpreted as equivalent to a proportionate harm/risk reduction for smokers.”
4. Laboratory studies performed by The German Federal Institute for Risk Assessment (BfR)

On 5 May 2018, the German Federal Institute of Risk Assessment (BfR) published the results of their independent assessment of IQOS. The study, published in Archives of Toxicology, analysed the IQOS aerosol using the Health Canada Intense Smoking Regimen. In its report, BfR concludes:

*Our study confirms that levels of major carcinogens are markedly reduced in the emissions of the analysed HNB product in relation to the conventional tobacco cigarettes and that monitoring these emissions using standardized machine smoking procedures generates reliable and reproducible data which provide a useful basis to assess exposure and human health risks. Importantly, our data confirms absolute values for selected toxicants in the emissions of the analysed HNB that are in agreement with data published by the manufacturer (Schaller et al. 2016). The herein confirmed reductions of relevant toxicants by about 80%-99% are substantial, leading to the relevant question of putatively reduced health risks.*

Link to the report: [https://link.springer.com/epdf/10.1007/s00204-018-2215-y?author_access_token=m2gTAwzR8IIN1XHPyz2Egve4RwlQNchNByi7wbcMAY7B4pkXqsqfUkMAy](https://link.springer.com/epdf/10.1007/s00204-018-2215-y?author_access_token=m2gTAwzR8IIN1XHPyz2Egve4RwlQNchNByi7wbcMAY7B4pkXqsqfUkMAy)

5. Independent Testing by FDA

In order to verify chemical and physical data submitted to the U.S. FDA as part of PMI’s Modified Risk Tobacco Product Applications (MRTPAs) for IQOS, the U.S. FDA commissioned independent testing at the FDA’s Southeast Tobacco Laboratory (STL) in October 2017. The constituents tested were selected based on the characteristics of the EHTP. STL reported the value for NFDPM as “tar”. There were some differences between the applicant’s analytical and aerosol generation methods and those used by STL. Preliminary assessment of the data indicated that the levels of acrolein, formaldehyde and benzo[al]pyrene measured by STL were higher than the values reported by the applicant; however, these three HPHCs were still significantly lower than the levels in the mainstream smoke of the reference cigarette 3R4F. Greater than 90% reduction was observed for acrolein and benzo[al]pyrene, and greater than 80% reduction was observed for formaldehyde in the aerosol compared to 3R4F. The levels of NFDPM (quoted by STL as tar) and nicotine determined by STL were similar to the levels reported by the applicant. Finally, the levels of ammonia, NNN, and NNK in the EHTP measured by STL were similar to the levels reported by the applicant.


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