INTRODUCTION

Indonesia is a home to 65 million smokers and one of the countries with the highest number of smokers in the world. A recent study of 2018 Basic Health Research by the Ministry of Health showed that the prevalence of smoking in Indonesia showed no sign of decline despite highly aggressive tobacco control policies in Indonesia. The astronomically high number of smokers in Indonesia calls for a new approach in dealing with the issue.

Smoking has long been associated scientifically with increased morbidity and premature mortality. most of health hazards due to smoking comes from exposure to cigarette smoke (smoke aerosol), formed from the burning process of tobacco in conventional cigarettes. According to World Health Organization (WHO), most of health hazards due to smoking comes from exposure to cigarette smoke (smoke aerosol), formed from the burning process of tobacco in conventional cigarettes. This propels the implementation of the concept of tobacco harm reduction by striving for products for those still craving for tobacco can still consume, but at a lower risk. This study aims to determine the difference in HPHC content between conventional cigarettes and HTP. The research method used was literature review. In the preliminary stage, the researchers carried out a process of screening titles and abstracts from studies and then independently filtered the text papers completely according to the objectives of this study. The review yielded 22 journals meeting with the rules and regulations in this research. The results showed that all 9 HPHCs recommended for reduction (nine TobReg priority constituent) were shown to be 90% lower in HTP compared to conventional cigarettes. The conclusion was that there were differences in the HPHC content between conventional cigarettes and HTP.

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Keywords: HPHC; HTP; Conventional Cigarettes

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2. RESEARCH METHOD

The type of data used was secondary data in the form of quantitative data, qualitative data or a combination thereof. Textbooks underling the theory in this study was also used. Study search and selection were performed using Medline, Scopus, PubMed and Database Web of Science, limited to studies conducted until July 2020 with a search period up to September 2020. The search included terms related to HnB in general ('Heat not burn', 'Tobacco Heating System', 'Electronic Nicotine Delivery System', 'Novel Tobacco Product') and brand names ('IQOS', 'Ploom', 'Heets', 'glo', 'PNV'), and were limited to studies published from 2010, thereby excluding obsolete or outdated papers on HnB devices. Prior to further discussion of papers to be used as reference, at the preliminary stage the researchers carried out a process of screening titles and abstracts from the study then independently filtered the papers completely in accordance with the objectives of this study.

The method used for this literature review was tradition review, that is a method of literature review on a topic selected based on the knowledge and experience possessed by the researcher. Systematic Literature Review is a literature review method that is used using predetermined stages. It identified, assessed, and interpreted the whole findings of a study topic, to answer predetermined research questions. The selection of papers was also not carried out subjectively by researchers, but using predetermined protocols and filters.

The use of publications in this study referred to inclusion and exclusion criteria. The inclusion criteria included literatures and publication journals focusing on the discussion of the use of heated tobacco technology and publications that have been peer-reviewed. Textbooks on basic theories of toxicology and disease risk assessment were also utilized. The publications that were directly related to studies on HPHCs in heated tobacco products were limited to those published after 2010. However, publications prior to 2010 were still used for supporting references. The exclusion criteria included publications that have not been peer-reviewed, did not focus on heated tobacco products, were not published in English and could no longer be downloaded or documented. Sources used in this study included publications containing subjects on HPHC emission both in HTPs or conventional cigarettes.

3. RESULTS AND DISCUSSIONS

The process of searching and filtering databases from journals or scientific publications on either heated tobacco products (HTP) or e-cigarettes were performed from July 2020 to September 2020. There were 248 publications from the initial searching which would be then narrowed to 22 scientific publications and become a reference in this study (Figure 1).
3.1. HPHC Content in HTPs

The main driver of the conception of heated tobacco products is the need for an alternative for people who desire nicotine at lower risks. Health risks to smokers are caused more by exposure to HPHCs arising from the combustion process, not due to nicotine exposure. There was not enough evidence showing that nicotine is carcinogenic. Several heated tobacco products, both ready-to-market or just prototypes, can be seen in Table 1.

Table 1: Heated Tobacco Products That Are Ready to Market or Just Prototypes

| Heated Tobacco Products (HTP) and Manufacturers | Marketing (Year and Region) | Product Description |
|-------------------------------------------------|----------------------------|---------------------|
| IQOS®/THS 2.2 from PMI                           | 2014, Japan, Italy and Switzerland | IQOS® consists of a holder, charger and tobacco plug (HEETS). The tobacco plug (about 320mg) is put into the holder and heated with an electronically-controlled heating knife inserted into the part of the tobacco plug. Operating heating temperature <350 °C. Single use for 6 minutes or up to 14 puffs. |
| iFuse® from BAT                                  | 2015, Romania                | iFuse® includes electronic vapor device with a rechargeable Li-ion battery and integrated circuit power controller, on which Cartomizer (Neopod) is installed. This disposable Neopod® consists of an atomizer, liquid tank with 1.15 ml of unflavoured nicotine liquid and chamber containing a 130mg tobacco plug. When the user presses the button, a nicotine-containing vapor is generated, which is then pulled through the tobacco plug to absorb the flavour. Before reaching the tobacco plug, the aerosol reaches an average maximum temperature of <35 °C. |
| Glo®/THP 1.0 from BAT                            | 2016, Japan                  | Glo® includes electronic devices with a rechargeable Li-ion battery and heating chamber and tobacco plug. A tobacco plug (about 260mg) is heated in the heating chamber from the periphery. Operating heating temperature <250°C. Reaches operating temperature after 30-40 seconds and a single use lasts 3 minutes. |
| Ploom Tech®/PNTV from JTI                       | 2016, Japan                  | PNTV consists of a power supply, cartridges with heating and liquids, and capsules with a mixture of tobacco. Generates nicotine-free vapor by heating an unflavoured liquid; The steam then passes through the tobacco capsules to absorb the taste and nicotine. |
| Carbon-heated tobacco product (CHTP) from PMI     | Not marketed                 | A specially designed electric lighter induces a carbon heating source which then heats up the tobacco plug. |

Source: Simonavicius E. et al., 2018

The studies included in this literature review were reviewed with impartial view toward sources of funding. However, manufacturers who financed and report their own product findings were inherently bound by conflicts of interest. Table 2 is a summary of both independent or sponsor manufacturer studies.

Table 2: Summary of Independent and Sponsor Manufacturer Studies

| Researcher, Year of Publication | Type of Research, Country | Study Design | Heated Tobacco Product and Reference Product | Objective |
|--------------------------------|--------------------------|-------------|----------------------------------------------|-----------|
| HTP Studies on Mainstream Smoke|                          |             |                                              |           |
| Auer et al., 2017 7            | Independent, Switzerland | Comparative laboratory study using a smoking machine | IQOS® and Cigarettes | To compare HPHC levels in IQOS® mainstream aerosol emissions with mainstream smoke. |
| Farsalinos et al., 2018 8      | Independent, Switzerland |              | IQOS®, Cigarettes, E-Cigarettes: (i) Ciga-like (ii) eGo-style, Second Generation (pen-style tank) (iii) Variable wattage (tank model) | To compare nicotine levels in the emission of IQOS® mainstream aerosol from the regular and menthol tobacco plug with nicotine in various types of e-cigarette aerosols and mainstream cigarette smoke. |
| Study | Country | Study Design | Type | Objective |
|-------|---------|--------------|------|-----------|
| Bekki et al., 2017 | Independent, Japan | IQOS® and Cigarettes | To compare nicotine and HPHC levels in the IQOS® emission from a regular and menthol tobacco plug with mainstream cigarette smoke. |
| Schaller et al., 2016 | PMI, Switzerland | THS 2.2/IQOS® and Cigarettes | To compare HPHC levels in IQOS® (mainstream) emissions with mainstream cigarette smoke. |
| Schaller et al., 2016 | PMI, Switzerland | THS 2.2/IQOS® and Cigarettes | To compare HPHC levels in IQOS® emission (mainstream) from regular and menthol tobacco plugs (HEETS) with mainstream cigarette smoke. |
| HTP Studies on Mainstream Smoke | | | |
| Jaccard et al., 2017 | PMI, Switzerland | Comparative laboratory study using a smoking machine | THS 2.2/IQOS® and Cigarettes | To compare HPHC levels in IQOS® (mainstream) emissions with mainstream cigarette smoke. |
| Pratte et al., 2017 | PMI, Switzerland | | THS 2.2/IQOS® and Cigarettes | To compare the number of solid particles in IQOS® emission (mainstream) with mainstream cigarette smoke. |
| Eaton et al., 2016 | BAT, UK | | THP 1.0/Glo® and Cigarettes | To compare HPHC levels of Glo® emission (mainstream) with mainstream cigarette smoke. |
| Forster et al., 2016 | BAT, UK | | THP 1.0/Glo® and Cigarettes | To compare HPHC levels of Glo® emission with IQOS emission and cigarette smoke. |
| Poynton et al., 2017 | BAT, UK | | iFuse® Pen-style e-cigarette | To compare HPHC levels of iFuse® emission (mainstream) with Vype ePen emission and cigarette smoke. |
| HTP Studies for clinical trials | | | |
| Kamada et al., 2016 | Independent, Japan | Case report | IQOS® | To report cases of acute eosinophilic pneumonia after use. |
| Lopez et al., 2016 | Independent, US | Randomised crossover experimental trial | Pax LLTV Cigarette eGo e-cigarette (pen-style tank) | To compare nicotine delivery, airborne CO concentration (expired), and suppression of symptoms due to cessation. |
| Brossard et al., 2017 | PMI, Japan | Randomised crossover experimental trial | THS 2.2/IQOS®, Cigarettes and Nicotine gum | To compare nicotine delivery and effects on urge to smoke. |
| Haziza et al., 2016 | PMI, Japan | RCT | THS 2.2/IQOS® and Cigarettes | To compare HPHC exposure over 5 days of use. |
| Haziza et al., 2016 | PMI, Poland | RCT | THS 2.2/IQOS® and Cigarettes | To compare HPHC exposure over 5 days of use. |
| Lüdicke et al., 2017 | PMI, Poland | RCT | THS 2.1 and Cigarettes | To compare HPHC exposure over 5 days of use. |
| Lüdicke et al., 2016 | PMI, Poland | RCT | CHTP and Cigarettes | To compare HPHC exposure over 5 days of use. |
| Lüdicke et al., 2018 | PMI, Japan | RCT | THS 2.2/IQOS® and Cigarettes | To compare HPHC exposure over 5 days of use in confinement and subsequent 85 days of use in outpatient setting. |
| Lüdicke et al., 2018 | PMI, Japan | RCT | THS 2.2/IQOS® and Cigarettes | To compare the effects of biologically and clinically relevant risk markers over 90 days of use. |
| Picavet et al., 2016 | PMI, UK | Randomised crossover experimental | THS 2.1 and Cigarettes | To compare nicotine delivery and effects on urge to smoke. |
CO\(_2\), CO\(_2\), and NO\(_x\) gases are markers of combustion. By eliminating the combustion process, the levels of CO, CO\(_2\), and NO\(_x\) in HTP decreased significantly compared to conventional cigarette smoke\(^{12,13}\).

Table 3: Mean Levels ± SD (Standard Deviation) of Combustion Marker Gases in Conventional Cigarettes Compared to HTPs

| Marker (per stick) | HTP | Conventional Cigarette |
|-------------------|-----|------------------------|
| CO, mg            | NQ  | 32                     |
| CO\(_2\), mg      | 2.35| 85.1                   |
| NO\(_x\), \(\mu\)g | 10.1| 496                    |
| NO\(_x\), \(\mu\)g | 12.0| 553                    |

Source: Eaton, 2018\(^{12}\)

The data in table 3 shows that in the use of heated tobacco products, no combustion occurs, only heating. It is shown by the low levels of combustion markers namely CO, CO\(_2\), and NO\(_x\) in HTPs. Low exposure to CO was also demonstrated by Caponneto et al. (2018) where the level of CO exhalation—as a biomarker of CO exposure in HTP users—was significantly lower compared to conventional cigarette consumers\(^{25}\).

Mitoya et al. (2016), in their study showed a difference in HPHC levels of office space, residential air exposed to HTPs and conventional cigarettes\(^{26}\). In general, spaces exposed to HTP aerosols showed lower levels of HPHC compared to those exposed to cigarette smoke, except for a few compounds such as nicotine and acetaldehyde, which were similar to conventional cigarettes. In addition, it was shown that H\(_2\)O\(_2\)—one of free radical compounds in the ROS (reactive oxygen species) group—is 5 times lower in HTP aerosols than conventional cigarettes\(^{27}\). These studies corroborated existing studies concluding that the level of chemical compounds of mainstream smoke of conventional cigarettes largely is 90% higher than heated tobacco products\(^{13,5,10,28,29}\).

Table 5 shows a decrease in the concentration of most of HPHCs in HTPs compared to conventional cigarettes\(^{13}\).

Table 4: Content of HPHC Compounds in HTP Aerosols and Conventional Cigarettes and Their Decrease

| Parameter          | Unit     | Burnt Cigarette Mean ± SD | HTP Mean ± SD | Decrease (%) |
|--------------------|----------|---------------------------|---------------|--------------|
| TPM                | mg/stick | 46.9 ± 2.8                | 26.1 ± 1.1    | 44.3         |
| Water              | mg/stick | 15.1 ± 1.4                | 12.1 ± 1.1    | 20.1         |
| NFDPM              | mg/stick | 29.8 ± 1.4                | 13.6 ± 1.2    | 54.4         |
| CO                 | mg/stick | 32.0 ± 1.0                | NQ (0.223)    | 99.8         |
| CO\(_2\)            | mg/stick | 85.1 ± 4.0                | 2.05 ± 0.10   | 97.6         |
| Ammonia            | \(\mu\)g/stick | 32.5 ± 3.5              | 4.01 ± 0.99   | 87.7         |
| Hydrogen cyanide   | \(\mu\)g/stick | 343 ± 62                | BDL (0.525)   | 99.9         |
| Mercury            | ng/stick | 4.26 ± 0.50               | 1.28 ± 0.13   | 69.8         |
| Cadmium            | ng/stick | 105.5 ± 5                 | BDL (0.162)   | 99.9         |
| Black lead         | ng/stick | 28.7 ± 0.8                | 11.6 ± 8.7    | 59.5         |
| Chromium           | ng/stick | NQ (4.51)                 | 4.34 ± 1.14   | -22.7        |
| Nickel             | ng/stick | NQ (9.49)                 | NQ (0.878)    | NC           |

Source: Eaton, 2018\(^{12}\)
| Substance          | Unit  | Value       | % RSD     | % RSD     | % Recovery |
|--------------------|-------|-------------|-----------|-----------|------------|
| Arsenic            | ng/stick | 8.01 ± 0.56 | NQ (0.576) | 94.6      |
| Selenium           | ng/stick | NQ (2.63)   | NQ (0.731) | NC        |
| Copper             | ng/stick | 24.8 ± 2.1  | NQ (2.19)  | 91.5      |
| Cobalt             | ng/stick | BDL (0.893) | NQ (0.878) | NC        |
| Beryllium          | ng/stick | BDL (0.936) | NQ (0.024) | NC        |
| Iron               | ng/stick | 38.1 ± 10.0 | 19.3 ± 5.4 | 49.3      |
| Zinc               | ng/stick | 273 ± 17    | 21.5 ± 15.7 | 92.1      |
| Lead               | ng/stick | BDL (6.04)  | NQ (0.876) | NC        |
| NO                 | µg/stick | 495 ± 16    | 9.60 ± 0.79 | 98.1      |
| NOx                | µg/stick | 555 ± 19    | 12.9 ± 0.8  | 97.2      |
| Pyridine           | µg/stick | 28.6 ± 2.8  | 2.21 ± 0.29 | 92.3      |
| Quinoline          | µg/stick | 0.389 ± 0.028 | NQ (0.011) | 98.5      |
| Styrene            | µg/stick | 16.1 ± 2.0  | NQ (0.039)  | 99.8      |
| Nitrobenzene       | µg/stick | BDL (0.038) | BDL (0.011) | NC        |
| Benzo(b)furran     | µg/stick | 0.627 ± 0.067 | NQ (0.016) | 98.3      |
| Hydroquinone       | µg/stick | 84.2 ± 1.8  | 0.347 ± 0.035 | 99.6      |
| Resorcinol         | µg/stick | 1.57 ± 0.22 | BDL (0.016) | 99.5      |
| Catechol           | µg/stick | 87.4 ± 3.4  | 3.11 ± 0.49  | 96.4      |
| Phenol             | µg/stick | 13.5 ± 0.8  | 0.174 ± 0.022 | 98.7      |
| p-Cresol           | µg/stick | 8.72 ± 0.38 | BDL (0.010) | 99.9      |
| m-Cresol           | µg/stick | 3.48 ± 0.18 | NQ (0.019)  | 99.6      |
| o-Cresol           | µg/stick | 3.94 ± 0.16 | NQ (0.026)  | 99.6      |
| Propylene glycol   | mg/stick | 0.021 ± 0.005 | 0.390 ± 0.023 | - 1724    |
| Ethylene glycol    | mg/stick | 0.035 ± 0.001 | 0.011 ± 0.00 | 69.3      |
| Diethillin glycol  | mg/stick | BDL (0.004) | BDL (0.002) | NC        |
| Glycerol           | mg/stick | NQ (0.006)  | 0.044 ± 0.003 | - 883     |
| Naphthalene        | ng/stick | 2.35 ± 0.05  | 3.02 ± 0.26  | -28.4     |
| Pyrene             | ng/stick | 994 ± 94    | 2.2 ± 0.42   | 99.8      |
| Benzo(a)anthracene | ng/stick | 79.4 ± 7.5  | 8.97 ± 0.82  | 88.7      |
| Chrysene           | ng/stick | 24.2 ± 2.4  | 1.54 ± 0.11  | 93.7      |
| Benzo(a)pyrene     | ng/stick | 34.7 ± 3.2  | 2.61 ± 0.27  | 92.5      |
| Indeno(1,2,3-cd)pyrene | ng/stick | 12.9 ± 1.3  | NQ (0.354)  | 97.7      |
| Benzo(c)phenanthrene | ng/stick | 4.19 ± 0.37 | NQ (0.337)  | 97.2      |
| Cyclopentane(c,d)pyrene | ng/stick | 8.32 ± 0.81 | 0.874 ± 0.171 | 89.5      |
| Benzo(j)fluoranthelin | ng/stick | 7.82 ± 1.12 | 0.515 ± 0.036 | 93.4      |
| 1,3 Butadiene      | µg/stick | 108 ± 4     | BDL (0.029) | >99.9      |
| Isoprene           | µg/stick | 887 ± 49    | NQ (0.135)  | >99.9      |
| Acrylonitrile      | µg/stick | 19.5 ± 1.6  | BDL (0.032) | 99.9      |
| Benene             | µg/stick | 78.6 ± 4.6  | NQ (0.056)  | >99.9      |
| Toluene            | µg/stick | 131 ± 5     | NQ (0.204)  | 99.9      |
| Ethylbenzene       | µg/stick | 13.4 ± 0.9  | NQ (0.048)  | 99.8      |
| Ethylene oxide     | µg/stick | 19.3 ± 2.0  | BDL (0.036) | 99.9      |
| Substance                  | Unit       | Quantity      | Detection Limit | Recovery |
|----------------------------|------------|---------------|-----------------|----------|
| Vinyl chloride             | ng/stick   | 95.6 ± 9.2    | BDL (0.657)     | 99.7     |
| Propylene oxide            | ng/stick   | 903 ± 308     | BDL (15.6)      | 99.1     |
| Furan                     | µg/stick   | 61.9 ± 3.5    | 1.16 ± 0.01     | 98.1     |
| Vinyl acetate              | ng/stick   | 617 ± 20      | BDL (11.0)      | 99.1     |
| Nitromethane               | ng/stick   | 690 ± 58      | 42.4 ± 1.5      | 93.9     |
| 2-Nitropropane             | ng/stick   | 58.7 ± 6.1    | BDL (1.45)      | 98.8     |
| 5-Methylchrysene           | ng/stick   | 0.744 ± 0.205 | BDL (0.028)     | 98.1     |
| Benz(b)fluoranthenone      | ng/stick   | 12.3 ± 1.5    | 0.548 ± 0.091   | 95.5     |
| Benz(k) fluoranthene       | ng/stick   | 3.70 ± 0.49   | 0.225 ± 0.046   | 93.1     |
| Dibenz(a,h)anthracene      | ng/stick   | 0.915 ± 0.124 | BDL (0.046)     | 95.8     |
| Dibenz(a)pyrene            | ng/stick   | BDL (0.423)   | BDL (0.254)     | NC       |
| Dibenz(a,e)pyrene          | ng/stick   | NQ (0.696)    | BDL (0.125)     | NC       |
| Dibenz(a,j)pyrene          | ng/stick   | 1.66 ± 0.41   | BDL (0.132)     | 96.0     |
| Dibenz(a,h)pyrene          | ng/stick   | BDL (0.236)   | BDL (0.141)     | NC       |
| 1-Aminonaphthalene         | ng/stick   | 17.6 ± 0.6    | NQ (0.027)      | 99.8     |
| 2-Aminonaphthalene         | ng/stick   | 13.2 ± 0.8    | NQ (0.012)      | >99.8    |
| 3-Aminonaphthalene         | ng/stick   | 3.49 ± 0.27   | NQ (0.004)      | >99.9    |
| 4-Aminobiphenyl            | ng/stick   | 2.29 ± 0.12   | NQ (0.005)      | 99.8     |
| 2,6-Dimethylaniline        | ng/stick   | 6.11 ± 0.65   | 0.040 ± 0.004   | 99.4     |
| Benzidine                  | ng/stick   | BDL (0.010)   | BDL (0.003)     | NC       |
| o-Anisidine                | ng/stick   | 4.18 ± 0.23   | 0.244 ± 0.031   | 94.2     |
| o-Toluidine                | ng/stick   | 83.3 ± 2.1    | 0.371 ± 0.045   | 99.6     |
| N-Nitrosornicotine         | ng/stick   | 263 ± 12      | 24.7 ± 2.5      | 90.6     |
| N-Nitrososanatabine        | ng/stick   | 268 ± 20      | 37.7 ± 3.4      | 85.9     |
| N-Nitrososanabasine        | ng/stick   | 24.1 ± 1.1    | 4.70 ± 0.39     | 80.4     |
| 4-(m ethynitrosamin o)-1-(3- pyridyl)-1- butanone | ng/stick | 281±16 | 6.61±0.86 | 97.7 |
| Acetamide                  | µg/stick   | 11.9 ± 1.0    | 1.34 ± 0.05     | 88.7     |
| Acrylamide                 | µg/stick   | 3.99 ± 0.39   | 1.04 ± 0.04     | 73.9     |
| Caffeine acid              | µg/stick   | BDL (1.19)    | BDL (0.478)     | NC       |
| Ethyl carbamate            | ng/stick   | BDL (6.43)    | BDL (1.93)      | NC       |
| IQ                         | ng/stick   | 7.75 ± 1.07   | BDL (0.164)     | 98.9     |
| Glu-P-2                    | ng/stick   | BDL (0.301)   | BDL (0.120)     | NC       |
| Glu-P-1                    | ng/stick   | BDL (0.239)   | BDL (0.095)     | NC       |
| PhIP                       | ng/stick   | BDL (0.365)   | BDL (0.1460)    | NC       |
| Trp-P-2                    | ng/stick   | 6.46 ± 1.0    | BDL (0.113)     | 99.1     |
| AaC                        | ng/stick   | 176 ± 16      | NQ (0.443)      | 99.9     |
| Trp-P-1                    | ng/stick   | 4.29 ± 0.52   | BDL (0.098)     | 98.9     |
| MeAaC                      | ng/stick   | 15.3 ± 2.1    | BDL (0.115)     | 99.6     |
| Hydrazine                  | ng/stick   | NQ (12.2)     | BDL (2.04)      | NC       |
| NDMA                       | ng/stick   | 14.2 ± 1.3    | BDL (0.178)     | NC       |
| NEMA                       | ng/stick   | BDL (0.509)   | BDL (0.254)     | NC       |
| NDEA                       | ng/stick   | BDL (0.617)   | BDL (0.308)     | NC       |
| NDiPA                      | ng/stick   | BDL (0.540)   | BDL (0.273)     | NC       |
As shown in table 4, all parameters in HTP have lower levels than conventional cigarettes, albeit with varying degrees. A small decrease is observed in TPM, water and tar (NFDPM). Meanwhile, other parameters are 70-99% lower for HTP.

A number of studies examining 9 TobReg priority constituents in conventional cigarettes and HTP showed that HPHC levels of HTP were largely lower than conventional cigarettes\textsuperscript{13,30,12}. The decreases are shown in table 5.

### Table 5: Content of 9 HPHCs Recommended in Mainstream Aerosols per Stick

| Parameter          | Unit | Cigarette | THP          | % reduction |
|--------------------|------|-----------|--------------|-------------|
| 1,3-Butadiene      | µg   | 108       | BDL (0.029)  | >99.9       |
| Acetaldehyde       | µg   | 2200      | 111          | 95.0        |
| Acrolein           | µg   | 157       | 2.22         | 98.6        |
| Benzene            | µg   | 78.6      | NQ (0.056)   | >99.9       |
| Benzo[a]pyrene     | Ng   | 12.9      | NQ (0.354)   | 97.7        |
| CO                 | Mg   | 32        | NQ (0.233)   | 99.8        |
| Formaldehyde       | µg   | 54.1      | 3.29         | 93.9        |
| NNK                | Ng   | 281       | 6.61         | 97.7        |
| NNN                | Ng   | 263       | 24.7         | 90.6        |

Source: Foster et al., 2018\textsuperscript{13}
As shown in Table 5, all 9 HPHC compounds recommended for reduction (TobReg priority constituents) were shown to have 90% lower levels in HTP. The study by Poynton et al., 2017 on the 9 HPHC compounds and other toxic compounds also showed similar results, as presented in Table 6.

### Table 6: Levels of Several Compounds in HTP Aerosols Compared to Conventional Cigarettes (3R4F)

| Toxicant                      | HTP Mean | HTP Standard deviation | Conventional Cigarettes (3R4F) Mean | Conventional Cigarettes (3R4F) Standard deviation |
|-------------------------------|----------|------------------------|-------------------------------------|-----------------------------------------------|
| **Carbonyl compounds:**       |          |                        |                                     |                                               |
| Formaldehyde, µg              | 11.5     | 3.5                    | 94.9                                | 6.2                                           |
| Acetaldehyde, µg              | 8.22     | 1.44                   | 1732                                | 43                                            |
| Acetone, µg                   | 7.09     | 2.48                   | 726                                 | 16                                            |
| Acrolein, µg                  | NQ       | NQ                     | 172                                 | 3                                             |
| Methyl-ethyl-ketone, µg       | NQ       | NQ                     | 202                                 | 7                                             |
| **Metal:**                    |          |                        |                                     |                                               |
| Copper, ng                    | 88.2     | 33.6                   | 24.7                                | 3.1                                           |
| Zinc, ng                      | 877      | 181                    | 257                                 | 37                                            |
| Iron, ng                      | 260      | 48                     | 34.5                                | 13.9                                          |
| **Semi-volatile:**            |          |                        |                                     |                                               |
| Styrene, µg                   | 0.50     | 0.34                   | 17.4                                | 1.7                                           |
| **PAH:**                      |          |                        |                                     |                                               |
| Naphthalene, ng               | 8.54     | 2.21                   | 1005                                | 125                                           |
| Chrysene, ng                  | 1.86     | 0.82                   | 36.8                                | 3.6                                           |
| **TSNA:**                     |          |                        |                                     |                                               |
| NNN, ng                       | NQ       | NQ                     | 265                                 | 22                                            |
| **Gases and volatile:**       |          |                        |                                     |                                               |
| CO, mg                        | 4.74     | 0.00                   | 29.6                                | 1.5                                           |
| Toluene, µg                   | NQ       | NQ                     | 116                                 | 9                                             |
| **Aromatic amine:**           |          |                        |                                     |                                               |
| 2-amminaphtalene, ng          | 0.4      | 0.19                   | 12.5                                | 0.5                                           |
| 3-aminobiphenyl, ng           | 0.07     | 0.04                   | 2.91                                | 0.76                                          |
| 4-aminothiophenol             | 0.06     | 0.04                   | 2.14                                | 0.50                                          |
| o-toluidine                   | 1.52     | 0.80                   | 115                                 | 5                                             |
| **Volatile nitrosamine:**     |          |                        |                                     |                                               |
| NDMA, ng                      | 15.7     | 2.7                    | 6.95                                | 1.4                                           |
| NDEA, ng                      | 13.4     | 4.6                    | BDL                                 | BDL                                           |
| NPYR, ng                      | 15.1     | 1.3                    | BDL                                 | BDL                                           |
| NDELA, ng                     | 7.67     | 1.82                   | 4.79                                | 3.19                                          |
| **Nicotine and nicotine impurity:** |     |                        |                                     |                                               |
| Nicotine, mg                  | 2.56     | 1.33                   | 1.84                                | 0.08                                          |
| Myosmine, ng                  | 5116     | 948                    | 9809                                | 701                                           |
| Cotinin, ng                   | 4824     | 916                    | 50861                               | 1912                                          |
| β-nicotyrine, ng              | 926      | 410                    | 9790                                | 149                                           |

Source: Poynton et al., 2017

### 4. CONCLUSION

The results showed that all 9 HPHCs (nine TobReg priority constituent) were shown to be lower in HTP compared to conventional cigarettes.

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