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Assessment of novel tobacco heating product THP1.0. Part 3: Comprehensive chemical characterisation of harmful and potentially harmful aerosol emissions

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ABSTRACT

For a tobacco heating product (THP), which heats rather than burns tobacco, the emissions of toxicants in the aerosol were compared with those in cigarette smoke under a machine-puffing regimen of puff volume 55 ml, puff duration 2 s and puff interval 30 s. The list of toxicants included those proposed by Health Canada, the World Health Organization Study Group on Tobacco Product Regulation (TobReg), the US Food and Drug Administration and possible thermal breakdown products. In comparison to the University of Kentucky 3R4F reference cigarette the toxicant levels in the THP1.0 emissions were significantly reduced across all chemical classes. For the nine toxicants proposed by TobReg for mandated reduction in cigarette emissions, the mean reductions in THP1.0 aerosol were 90.6–99.9% per consumable with an overall average reduction of 97.1%. For the abbreviated list of harmful and potentially harmful constituents of smoke specified by the US Food and Drug Administration Tobacco Products Scientific Advisory Committee for reporting in cigarette smoke (excluding nicotine), reductions in the aerosol of THP1.0 were 84.6–99.9% per consumable with an overall average reduction of 97.5%.

1. Introduction

Cigarette smoking is one of the leading preventable causes of human morbidity and mortality, causing diseases such as cardiovascular disorders, chronic obstructive pulmonary disease and lung cancer (US DHHS, 2014). For more than 50 years, scientists have worked to establish smoking-related disease mechanisms and their sources in cigarette smoke, with efforts focusing on a number of toxic chemicals in cigarette smoke (Baker, 2006; Hoffmann and Hoffmann 1998; Liu et al., 2011). Most smoking-related diseases are not caused by nicotine (Benowitz, 2010) but by toxicants present in the inhaled smoke (Farsalinos and Le Houezec, 2015). When a cigarette is lit, the tobacco burns to form smoke containing more than 6500 compounds (Rodgman and Perfetti, 2013), of which about 150 are established toxicants (Fowles and Dybing, 2003). Notably, the US Surgeon General has stated that "burden of death and disease from tobacco use in the United States is overwhelmingly caused by cigarettes and other combusted tobacco products" (US DHHS, 2014).

In 1998, Hoffmann and Hoffmann (1998) published a list of compounds present in tobacco smoke that were known to have biological activity. This list of "Hoffmann analytes", which was based on a substantial body of work in the 1970s and 1980s, provided the first benchmark of toxicants that should be monitored in tobacco and tobacco smoke. Since then, various scientific bodies have acknowledged the presence of more than 100 harmful and potentially harmful constituents (HPHCs), including Group 1 and 2A carcinogens, in tobacco and cigarette smoke (Burns et al., 2008; FDA, 2012a; IARC, 2004; WHO, 2007) and regulatory authorities have begun to mandate the reporting of specific toxicants in smoke emissions from cigarettes (ANVISA, 2007; FDA, 2012b; Health Canada, 1999a,b; Taiwan DOH, 2012). Furthermore, the World Health Organization (WHO) Study Group on Tobacco Product Regulation has proposed mandatory lowering of the emission levels from cigarettes of nine specific toxicants: CO, formaldehyde, acetaldehyde, acrolein, 1,3-butadiene, benzene, benzo[a]pyrene, *N*-nitrosonornicotine (NNN), and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) (Burns et al., 2008).

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Over recent years, an increasing array of tobacco or nicotine next-generation products (NGPs) has become available. They include tobacco heating products (THPs), which heat but do not burn tobacco, and vapour products (e.g., electronic cigarettes [e-cigarettes]), which are likely to present reduced risk in comparison to conventional cigarettes (McNeill et al., 2015; RCP, 2016). Evidence to support this view includes the relatively simple composition of aerosols produced (Marco and Grimalt, 2015) compared with that of cigarette smoke (Rodgman and Perfetti, 2013).

While the use of NGPs, particularly vapour products, has been gradually increasing (European Commission, 2015; Schoenborn and Grindi, 2015; West et al., 2015), their regulation has been slow to develop. In the European Union, e-cigarettes were brought under the revised EU Tobacco Products Directive only in May 2016 (European Commission, 2016); similarly, they have been subject to tobacco laws in the USA since 2016 (FDA, 2016a), with draft regulations proposed for new Premarket Tobacco Product Applications, including the recommended analysis of 29 toxicants specific to these products (FDA, 2016b).

Initial studies to document the classes and levels of toxicants in e-cigarettes (Flora et al., 2016; Lauterbach et al., 2012; Lauterbach and Laugesen, 2012; Margham et al., 2016; Sleiman et al., 2016; Tayyarah and Long, 2014) showed that nearly all toxicants measured were present at much lower levels on a per-puff basis in e-cigarette aerosols than in smoke from a reference cigarette. However, there is no agreed list of toxicants and/or standard methods for analytical testing of constituents in the aerosols generated by NGPs, making cross-product and inter-study comparisons difficult. We previously addressed this issue by conducting a comprehensive analysis of the chemical composition of a commercial vapour product to compare the emissions of all known vapour product and tobacco cigarette priority compounds with those from a conventional cigarette by accredited analytical techniques (Margham et al., 2016). The resulting data set addressed an important gap by reporting the emission levels of 142 chemicals and eight collated measures, covering the widest practicable range of HPHCs in cigarette smoke and constituents of concern in vapour products (Margham et al., 2016).

In this series of publications, a comprehensive assessment approach is applied to evaluate the toxicant reduction potential of the THP1.0 product. As described in the first paper of this series (Eaton et al., 2017), a tobacco consumable rod is heated to temperatures that are sufficient to vaporise volatile compounds, including nicotine, into an inhalable aerosol but not high enough to burn the tobacco. This approach results in levels of combustion-related toxicants that are significantly lower in the generated aerosol than in cigarette smoke (Forster et al., 2015; Gonzalez-Suarez et al., 2016; Schorp et al., 2012; Smith et al., 2016; Zenzen et al., 2012).

Several ways to deliver an aerosol by heating tobacco have been described in patents and in the peer-reviewed literature. Studies of first-generation electrically heated cigarettes (EHCs) indicated that approximately two-thirds of priority compounds were reduced by at least 50% and many were reduced by more than 90%, compared with conventional cigarette smoke; however, formaldehyde yields were increased (Stabbert et al., 2003). Second-generation EHCs included ammonium magnesium phosphate in the cigarette paper to reduce the yield of formaldehyde (Moennikes et al., 2008).

Later characterisation of an EHC smoking system (EHCSS) demonstrated that the mainstream aerosol was distinctly different from that of mainstream smoke (MSS) from a conventional cigarette (Zenzen et al., 2012; Schorp et al., 2012). With very few exceptions, a substantial reduction was observed in the toxicological activity of the EHCSS aerosol relative to that of conventional cigarette smoke when smoked with comparable puffing intensities or at comparable nicotine yields. Recent studies of an updated version of the EHCSS, known as a tobacco heating system (THS), have also shown that the formation of HPHCs is greatly reduced compared with formation during cigarette smoking (Smith et al., 2016; Schaller et al., 2016).

Such studies have led to the commercial launch of THPs in some countries, including Eclipse (R. J. Reynolds, Winston Salem, NC, USA), Ploom TECH (Ploom™, San Francisco, CA, USA), iQOS™ (Philip Morris International, Neuchâtel, Switzerland) and glo™ (THP1.0, British American Tobacco, London, UK). Each of these THPs uses a different heating method characterised by the configuration of the heater relative to whether it is inside or outside the tobacco bed or rod, the temperature profile of the heater (heating rate, maximum temperature and duration) and the physical form and chemical composition of the tobacco material. Thus, it is necessary to understand how the tobacco material influences the aerosol chemistry under different heating conditions. For THP1.0, a multi-step thermophysical and thermochemical characterisation was conducted which confirmed that the aerosol is produced by evaporation and distillation and not by combustion (Eaton et al., 2017).

Cigarette smoke is mainly produced by distillation, pyrolysis and combustion reactions when the tobacco is burnt (Baker, 1987). In a previous study, a model system was used to investigate aerosol emissions from tobacco at different temperatures (Forster et al., 2015). The heating chamber heated samples of blended tobacco to between 100 °C and 200 °C, enabling a systematic investigation of the effect of temperature on selected vapour-phase compounds using the International Organization for Standardization (ISO) machine-smoking protocol. NNN and NNK were quantifiable when the tobacco was heated above 140 °C and 160 °C, respectively, whereas crotonaldehyde and formaldehyde were quantifiable at 180 °C and 200 °C, respectively. The concentrations of seven priority compounds in the aerosol (nicotine, CO, acetaldehyde, crotonaldehyde, formaldehyde, NNN and NNK) showed an increasing trend with temperature. The results demonstrated the practical utility of the model system to study low-temperature toxicant formation and emission from heated tobacco, and showed that, between 100 °C and 200 °C, nicotine and some priority compounds are released from the tobacco as a result of evaporative transfer or initial thermal decomposition (Forster et al., 2015).

To apply this understanding to a commercial product that is designed to heat tobacco with a controlled temperature profile and to provide acceptable sensory performance to the consumer, a comprehensive list of substances was measured in the aerosol emissions from THP1.0. Complemented by the other studies in this series, which include *in vitro* biological assessment of the aerosol emissions (Jaunky et al., 2017; Taylor et al., 2017; Thorne et al., 2017), we intend to provide a comprehensive baseline data package for THP1.0.

2. Experimental

2.1. Test products

The THP1.0 design and its main thermophysical functions have been described in detail (Proctor, 2017; Eaton et al., 2017). The emissions from THP1.0 were compared with those from the University of Kentucky 3R4F Reference Cigarette (University of Kentucky Center for Tobacco Reference Products, Lexington, KY, USA). Additional data were generated from the analysis of the more recently produced University of Kentucky 1R6F reference cigarette and a commercially available THS for quality assurance purposes. For the present study, non-mentholated and mentholated THP1.0 variants were used: THP1.0(T), comprising glo™ heating devices

and Bright Tobacco Kent Neostiks™, and THP1.0(M), comprising glo™ heating devices and Intensely Fresh Kent Neostiks™, sourced from Japan. The THS comprised the iQOS heating device with Essence Tobacco Heatstick™, also sourced from Japan. Each THP1.0 device used in the study was assigned an individual identification code that was etched on the device and recorded in all tests and replicates. Each device was cleaned before use and after a maximum of 20 heating cycles, following a defined cleaning procedure. All devices were fully charged and checked prior to the emission tests. For THP1.0, the consumable tobacco rods used a blend of Virginia tobacco that is formed by a paper reconstitution process and which comprises glycerol 15% dry weight basis (dwb), tobacco 77% dwb and cellulose fibre 8% dwb, with an average nicotine content of 0.65% dwb.

The heating device contains a rechargeable Li-ion battery (USB rechargeable, 3000 mAh capacity) that provides up to eight puffs under the puffing regime used in this study and up to 30 repeated usages from a single charge. The heating chamber consists of two heaters, each controlled separately by a microprocessor. The tobacco rod is heated mainly by conduction from its periphery (Fig. 1a). The tobacco consumable has a diameter of ca. 5.0 mm, with an overall length of 82 mm and a 42 mm tobacco section (Fig. 1b). Further details of THP1.0 and its operation are provided in Eaton et al., (2017). For THP1.0 the consumable tobacco rods were conditioned in and tested directly from the pack. For conditioning, the overwrap was removed and the pack was stored closed at 22 °C and 60% relative humidity (consistent with ISO 3402:1999 (ISO, 1999)) for a minimum of 48 h and a maximum of 120 h. In every test, the consumable rod was weighed and the mass recorded immediately before analysis.

To operate THP1.0 for emission generation, the heater door was opened and the consumable rod inserted into the heating chamber fully, such that the line of the air expansion and cooling channels in the mouthpiece was positioned just outside the opening of the device. A custom-made holder was used to support the device to allow the use of a standard puffing machine. After connection of the mouthpiece of the product to the puffing machine, the heating cycle was started by pressing the activation button on the device for 3 s. The first puff was taken at 40 s, by which time the device had reached operating temperature (as indicated by steady illumination of the LED and vibration of the device). After the eighth puff, the THP1.0 was removed from the puffing machine and the consumable was removed from the device. The process was repeated until the appropriate number of tobacco rods had been consumed in accordance with the analytical method.

The 3R4F reference cigarette is a US-blended king size cigarette with a cellulose acetate filter and ISO tar yield of ca. 9.4 mg per cigarette in 9.0 puffs. The blend composition, physical construction, and MSS toxicant yields have been previously characterised (Roemer et al., 2012; University of Kentucky (2008)). The 1R6F Reference Cigarette is similar to 3R4F and a certificate of analysis has been issued (University of Kentucky (2016)) indicating an ISO tar yield of 8.6 mg in 7.5 puffs. The cigarettes used in this study were prepared in accordance with the Health Canada requirements for intense smoking of cigarettes (Health Canada 1999a,b) and conditioned in accordance with IS0 3402:1999 prior to machine smoking.

2.2. Aerosol emission generation

Analyses were conducted by a single laboratory, Labstat International ULC (Kitchener, ON, Canada). Unless stated otherwise, all aerosol collections were carried out on a linear smoking machine. Where a Cambridge filter pad (CFP) holder was used, the neoprene washer was removed for all samples. Emissions were generated with a 55 ml puff volume, 2 s puff duration, 30 s puff interval and a bell-shaped puff profile. Ventilation blocking was not applied because the air inlet zone of THP1.0 is must operate to achieve the intended aerosol temperature and because data from a study of product use demonstrate that the air inlet zone is not occluded during use of by consumers (Gee et al., 2017). Eight puffs were taken per THP1.0 consumable; the number of consumables per sample varied according to the requirements of the analytical method but was commonly three, and five replicates were conducted per analysis.

The standard Health Canada intense smoking regime (Health Canada, 1999a,b) (55 ml puff volume, 2 s puff duration, 30 s puff interval, bell-shaped puff profile and 100% ventilation blocking) was used to generate 3R4F cigarette smoke emissions. Cigarettes were smoked until the designated butt mark was reached. The number of cigarettes varied with the analytical method but was commonly three per replicate, and five replicates were conducted for each analysis.

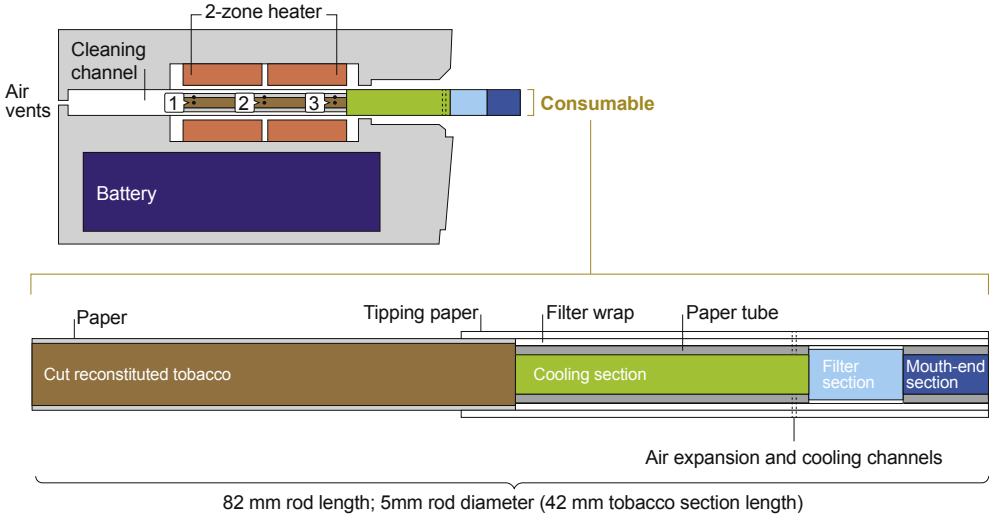

Fig. 1. Schematic drawing of THP1.0. (a) Heating device with a tobacco consumable inserted. (b) Physical construction of the consumable tobacco rod.

2.3. Physical analysis of aerosol and smoke

The aerosol generated from THP1.0(T) and the 3R4F MSS were physically characterised using a DMS500 electrical mobility analyser (Cambustion, Cambridge, UK) to measure particle diameter and particle number and to estimate mass, and a Spraytec laser diffraction system (Malvern Instruments, Malvern, UK) to measure particle diameter (Table 1). Each instrument operates optimally over different size ranges due to the different physical modes of measurement: 5–1000 nm for electrical mobility and 300–10 000 nm and beyond for laser diffraction. Thus, a combination of one or both techniques covers the size ranges expected from fresh condensation aerosols. In general, the particle size distribution and particle number density were similar for cigarette MSS and the aerosol emitted by THP1.0(T), both being respirable, but the size range for cigarette smoke was below the measurable range of Spraytec. The similarities noted above also indicate that the THP1.0 aerosol can be sampled effectively using the same techniques as for MSS.

2.4. Chemical analysis of aerosol emissions

The analytes measured in this study comprise the lists of priority compounds proposed for tobacco product regulation (Burns et al., 2008; FDA, 2012a, 2016b; Hoffmann and Hoffmann, 1998; IARC, 2004), additional substances based on knowledge from previous analysis of vapour product aerosols and the likely thermal decomposition products of glycerol (Margham et al., 2016). Polychlorinated dibenzo-p-dioxins, polychlorinated dibenzofurans and radioactive isotopes were not analysed because in previous studies (Margham et al., 2016) results for vapour products and the 3R4F reference cigarette were below the limits of detection. At present, standardised methods have not been developed for the measurement of some of the priority compounds, namely, *N*-nitrososarcosine, coumarin and aflatoxin B1 in cigarette smoke or NGP aerosols. The three compounds may be present in tobacco but have not been detected in tobacco smoke and, consequently, they were not measured in this study. The analytical methods used by the testing laboratory are based on the Health Canada methods for cigarette smoke analysis and are accredited to ISO/IEC 17025:2005 (ISO, 2005) for all reported constituents of cigarette MSS and vapour product mainstream aerosols (Table 2). The methods are not accredited for THP emissions but additional validation was undertaken by the testing laboratory to assure compatibility with the THP aerosol matrix. Minor modifications were made to specific methods for analysis of the THP1.0 aerosol, including the collection of aerosol condensate using acid-washed quartz fibre discs rather than Cambridge filter pads for the determination of trace metals and checks of matrix effects on calibration and instrumental interference. Overall, 22 different analytical methods were used to quantify the emissions of 126 analytes (plus the calculation of nicotine-free dry particulate matter [NFDPM] by difference) in the aerosol from THP1.0(T), THP1.0(M), THS (quality control), the MSS of 3R4F and 1R6F cigarettes and air/method blanks (Table 2).

Table 1
Mean ± standard deviation particle size distributions and numbers for 3R4F cigarette and THP1.0(T).

DMS electrical mobility analyser		
Product	**3R4F**	**THP1.0**
MMD (nm)	272 ± 19	329 ± 50
CMD (nm)	186 ± 12	39 ± 9
GSD	1.42 ± 0.03	1.80 ± 0.06
N/puff	3.6E+11 ± 5.9E+10	5.26E+10 ± 1.77E+10
Spraytec laser diffraction		
DV10 (nm)	–	253 ± 123
DV50 (nm)	–	575 ± 94
DV90 (nm)	–	1301 ± 234
D4,3 (nm)	–	723 ± 212
GSD	–	1.84 ± 0.21

Abbreviations: THP = tobacco heating product; (T) = non-mentholated consumable variant. MMD = mass median diameter; CMD = count median diameter; GSD = geometric standard deviation; N = total particle number; DV10 = particle size below which 10% of the aerosol lies; DV50 = particle size below which 50% of the aerosol lies; DV90 = particle size below which 90% of the aerosol lies; DV4,3 = volume mean diameter.

2.5. Air/method blank measurements

Since the concentrations of priority compounds in THP1.0 emissions are very much lower than in cigarette smoke, the aerosol and cigarette smoke samples were generated in separate laboratories with segregated air handling systems to prevent potential cross-contamination. In addition, blank control samples were prepared for THP emissions and 3R4F smoke by puffing empty ports on the same linear machines during collection of the aerosol or smoke: the blank controls were analysed with the test samples.

2.6. Data treatment and inclusion of limits of quantification and detection

For some of the constituents tested the emissions were below the limit of detection (LOD) and/or limit of quantification (LOQ) of the analytical method. To enable the percentage difference between THP(1.0) and 3R4F or 1R6F to be calculated for as many constituents from each toxicant subset as possible, <LOD and <LOQ values were imputed as follows. For results < LOD, the value was calculated as one-half of the LOD:

calculated value = LOD/2.

For results <LOQ but >LOD, the value was calculated as the midpoint between the reported LOD and LOQ:

calculated value = LOD + [(LOQ − LOD)/2].

In cases where the THP1.0 and 3R4F or 1R6F reference cigarette emissions were both < LOD or < LOQ, the measurand was omitted from the percentage difference calculation.

3. Results

3.1. Summary of results

Results for the 126 measurands and NFDPM in 3R4F MSS and THP1.0 emissions are presented in Table 3. Table 4 presents the air/method blank measurements for the MSS and THP1.0 emissions. Table 5 presents results of analysis of (a) contemporaneous air/method blanks (in addition to the blanks analysed with THP1.0) (b) a commercial tobacco heating product, THS, included in this study for quality control purposes and (c) data for a very similar commercial product previously reported by Schaller et al., (2016). Tables 6 and 7 summarise the observed reductions in emissions of priority substances per consumable for the TobReg and abbreviated FDA lists, respectively. Tables 8 and 9 summarise the observed reductions in emissions of priority substances in the TobReg and abbreviated FDA lists respectively, calculated on a per-puff basis. Data per puff were calculated by determining the concentration of each constituent in the collected sample, which for THP1.0 was normally five consumables and for 3R4F and 1R6F was normally three cigarettes, and dividing this value by the number of puffs taken during smoke or emission sampling. In general, this recalculation did not have a significant effect on the calculated reductions. As an example, for formaldehyde the calculated

Table 2
Chemical constituents analysed and summary of methods applied to test products, reference products and controls.

Analyte	Method code[a]	Brief description
Ammonia	HC T-101	CFPs are extracted with impinger solution containing 0.1 M H_2SO_4; detection by HPLC/conductivity detector
Mercury	HC T-108	After collection, the impinger solution (acidified potassium permanganate solution) is subjected to microwave digestion. Excess potassium permanganate is reduced with hydroxylamine; detection by cold vapour AAS
Carbonyls: formaldehyde, acetaldehyde, acetone, acrolein, propionaldehyde, crotonaldehyde, methyl ethyl ketone, *n*-butyraldehyde, isobutyraldehyde, glyoxal, methylglyoxal, acetyl-propionyl, diacetyl, acetoin, allyl alcohol	TMS-00155	CFPs are extracted with impinger solution. An aliquot of the extract is derivatized with PFBHA, followed by extraction in toluene. Detection by GC-MS SIM (selected ion monitoring)
Nicotine, carbon monoxide, carbon dioxide, water, glycerol, propylene glycol, diethylene glycol, ethylene glycol, glycidol	HC T-115 & TMS-00115a	CFPs are extracted with IPA. Detection by GC-FID (for nicotine) GC-TCD (for water), NDIR for CO. For ethylene glycol and glycidol a liquid impinger is used.
TSNAs: NAB, NAT, NNK, NNN	TMS-00135	CFPs are extracted with 100 mM ammonium acetate solution. Detection by HPLC-MS/MS
Volatiles: 1,3-butadiene, isoprene, acrylonitrile, benzene, toluene, vinyl chloride, ethylene oxide, propylene oxide, furan, vinyl acetate, nitromethane, ethylbenzene	TMS-00124	CFPs are extracted with methanol impinger solution. Detection by GC-MS SIM
Nitrogen oxides: NO, NOx	HC T-110	Two channel system using ozone reaction (NO) and chemical reduction plus ozone (NOx). Detection by chemiluminescence.
Hydrogen cyanide	HC T-107	CFPs are extracted with 0.1 M NaOH solution. 0.1 M NaOH impinger solution is analysed separately. Detection is by continuous flow analyser
Trace metals: cadmium, lead, chromium, nickel, arsenic, selenium, copper, cobalt, beryllium, zinc, iron, tin	TMS-00109	TPM collected by electrostatic precipitation is extracted with methanol. Gaseous-phase metals are trapped in an impinger with nitric acid solution. The impinger solution is combined with the EP tube extract and subjected to microwave digestion. Detection by ICP-MS
Semi-volatiles: acetamide, acrylamide, pyridine, quinoline, styrene, nitrobenzene, benzo(b)furan	TMS-00112 Appendix G	CFPs are extracted with methanol impinger solution. Detection by GC-MS SIM
Phenolics: Hydroquinone, resorcinol, catechol, phenol, *p*-cresol, *m*-cresol, *o*-cresol	TMS-00139	CFPs are extracted with 1% acetic acid impinger solution and an equal volume of fresh 1% acetic acid. Detection by reversed-phase HPLC with selective fluorescence detection.
PAHs: naphthalene, benzo[*a*]anthracene, chrysene, benzo[*a*]pyrene, indeno[1,2,3-*cd*]pyrene, benzo[*c*]phenanthrene, cyclopenta[*c,d*]pyrene, benz[*j*]aceanthrylene, pyrene	TMS-00120	CFPs are extracted using methanol. The extract is cleaned by passage through a C18 cartridge; the PAHs are eluted using cyclohexane. Detection by GC-MS SIM
PAHs and aza-arenes: 5-methylchrysene, benzo[*b*]fluoranthene, benzo[*k*]fluoranthene, dibenz[*a,h*]anthracene, dibenz[*a,l*]pyrene, dibenz[*a,e*]pyrene, dibenz[*a,i*]pyrene, dibenz[*a,h*]pyrene	TMS-00127	CFPs are extracted using methanol. The extract is cleaned by passage through a C18 cartridge; the PAHs are eluted using cyclohexane. Detection by GC-MS SIM
2-Nitropropane	TMS-00126	The aerosol is collected on a silica cartridge, which is eluted with 30% (v/v) diethyl ether in n-pentane. Detection by GC-TEA
Hydrazine	TMS-00147	CFPs are extracted with impinger solution (aqueous citrate-phosphate buffer:methanol (55:45, v/v) containing 2-nitrobenzaldehyde). Detection by HPLC-MS-MS.
Ethyl Carbamate	TMS-00145	CFPs are extracted with aqueous sulfamate impinger solution. The extract is cleaned by passage through a Chemelut tube. Ethyl carbamate is eluted using dichloromethane. Detection by GC-MS SIM
Nicotine-related impurities Nornicotine, Anatabine, Anabasine, Myosmine, Nicotine-*N*-Oxide, Cotinine, β-Nicotyrine	TMS-00153	CFPs are extracted with 100 mM aqueous ammonium acetate solution. Detection by HPLC-MS/MS
Heterocyclic aromatic amines: IQ, Glu-P-2, Glu-P-1, PhIP, Trp-P-2, A-α-C, Trp-P-1, MeA-α-C	TMS-00146	CFPs are extracted with 0.1 M hydrochloric acid. The extract is cleaned by passage through a mixed mode SPE cartridge; HAAs are eluted using a 5% ammonia in methanol solution. Detection by UPLC-MS/MS
Aromatic amines: 1-Aminonaphthalene, 2-Aminonaphthalene, 3-Aminobiphenyl, 4-Aminobiphenyl, *o*-Toluidine, *o*-Anisidine, 2,6-Dimethylaniline, Benzidine	TMS-00128 Appendix G	CFPs are extracted with 5% HCl solution. After DCM back extraction the aqueous solution is basified and the amines are extracted with hexane. The extracts are dried, derivatized with pentafluoropropionic acid anhydride and trimethylamine, passed through a florisil column. Detection by NCI GC-MS (SIM)
Caffeic Acid	TMS-00143	CFPs are extracted with Type I water. Detection by HPLC-UV
Volatile nitrosamines: NDMA, NEMA, NDEA, NDiPA, NDPA, NDBA, NPIP, NPYR, NMOR, NDELA	TMS-00148	CFPs are extracted with the 20:80 (w/w) Ammonium sulfamate/Sulfuric acid buffer impinger solution. A portion of the extract is acidified, treated with ammonium sulphate and ChemElut® cartridge clean-up using ethyl formate:ethanol (98:2, v/v) as eluent. The extract is reconstituted in 1 ml of 0.01% formic acid solution. Detection by HPLC-MS/MS.

Abbreviations: CFP=Cambridge filter pad; HPLC = high-performance liquid chromatography; AAS = atomic absorption spectroscopy; PFBHA = pentafluorobenzyl hydroxylamine; GC = gas chromatography; MS = mass spectrometry; SIM = selected ion monitoring; FID = flame ionisation detection; TCD = thermal conductivity detection; NDIR = non-dispersive infra-red detection; NAB=N-nitroosanabasine; NAT=N-nitrosoanatabine; NNK = 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone; NNN=*N*-nitrosonornicotine; PAH = polycyclic aromatic hydrocarbon; SPE = solid phase extraction; UPLC = ultra-performance liquid chromatography; UV = ultraviolet; NDMA=*N*-nitrosodimethylamine; NEMA=*N*-nitrosomethylethylamine; NDEA=*N*-nitrosodiethylamine; NDiPA = *N*-nitrosodiisopropylamine; NDPA=*N*-nitrosodipropylamine; NDBA=*N*-nitrosodibutylamine; NPIP=*N*-nitrosopiperidine; NPYR=*N*-nitrosopyrrolidine; NMOR=*N*-nitrosomorpholine; NDELA=*N*-nitrosodiethanolamine.

[a] Methods prefixed HCT are based upon methods published by Health Canada. Methods prefixed TMS were developed internally by Labstat.

Table 3
3R4F reference cigarette mainstream smoke and THP1.0 emission yields for 126 measurands, with calculated reductions for mean THP1.0 emission yields compared with 3R4F yields, on a per-consumable basis.

Parameter	Unit	3R4F		THP1.0(T)			THP1.0(M)		
		Mean ± SD	N	Mean ± SD	N	%Red[n] vs. 3R4F	Mean ± SD	N	%Red[n] vs. 3R4F
Puff count	/consumable	10.9 ± 0.3	5	8 ± 0	5	26.6	8 ± 0	5	26.6
TPM	mg/consumable	46.9 ± 2.8	5	26.1 ± 1.1	5	44.3	25.3 ± 1.4	5	46.1
Water	mg/consumable	15.1 ± 1.4	5	12.1 ± 1.1	5	20.1	10.7 ± 0.9	5	29.2
Nicotine	mg/consumable	2.02 ± 0.08	5	0.462 ± 0.037	5	77.1	0.365 ± 0.021	5	81.9
NFDPM	mg/consumable	29.8 ± 1.4	5	13.6 ± 1.2	5	54.4	14.2 ± 1.3	5	52.3
CO	mg/consumable	32.0 ± 1.0	5	NQ (0.223)	5	99.8	NQ (0.223)	5	99.6
CO_2	mg/consumable	85.1 ± 4.0	5	2.05 ± 0.10	5	97.6	1.99 ± 0.08	5	97.7
Ammonia	µg/consumable	32.5 ± 3.5	5	4.01 ± 0.99	5	87.7	5.02 ± 0.49	5	84.6
Hydrogen cyanide	µg/consumable	343 ± 62	5	BDL (0.525)	5	99.9	NQ (1.75)	5	99.8
Mercury	ng/consumable	4.26 ± 0.50	5	1.28 ± 0.13	5	69.8	1.31 ± 0.12	5	69.2
Cadmium	ng/consumable	105 ± 5	5	BDL (0.162)	5	99.9	BDL (0.162)	5	99.9
Lead	ng/consumable	28.7 ± 0.8	5	11.6 ± 8.7	5	59.5	9.74 ± 6.14	5	66.1
Chromium	ng/consumable	NQ (4.51)	5	4.34 ± 1.14	5	−22.7	4.06 ± 0.15	5	−14.8
Nickel	ng/consumable	NQ (9.49)	5	NQ (0.878)	5	NC	NQ (0.878)	5	NC
Arsenic	ng/consumable	8.01 ± 0.56	5	NQ (0.576)	5	94.6	NQ (0.576)	5	95.3
Selenium	ng/consumable	NQ (2.63)	5	NQ (0.731)	5	NC	NQ (0.731)	5	NC
Copper	ng/consumable	24.8 ± 2.1	5	NQ (2.19)	5	91.5	4.43 ± 3.18	5	82.1
Cobalt	ng/consumable	BDL (0.893)	5	NQ (0.878)	5	NC	NQ (0.878)	5	NC
Beryllium	ng/consumable	BDL (0.936)	5	BDL (0.024)	5	NC	BDL (0.024)	5	NC
Iron	ng/consumable	38.1 ± 10.0	5	19.3 ± 5.4	5	49.3	22.1 ± 6.1	5	41.9
Zinc	ng/consumable	273 ± 17	5	21.5 ± 15.7	5	92.1	20.1 ± 7.8	5	92.6
Tin	ng/consumable	BDL (6.04)	5	NQ (0.876)	5	NC	NQ (0.876)	5	NC
NO	µg/consumable	495 ± 16	5	9.60 ± 0.79	5	98.1	8.61 ± 0.86	5	98.3
NO_x	µg/consumable	555 ± 19	5	12.9 ± 0.8	5	97.7	11.4 ± 0.8	5	97.9
Pyridine	µg/consumable	28.6 ± 2.8	5	2.21 ± 0.29	5	92.3	1.55 ± 0.25	5	94.6
Quinoline	µg/consumable	0.389 ± 0.028	5	NQ (0.011)	5	98.5	BDL (0.003)	5	99.6
Styrene	µg/consumable	16.1 ± 2.0	5	NQ (0.039)	5	99.8	NQ (0.039)	5	99.8
Nitrobenzene	µg/consumable	BDL (0.038)	5	BDL (0.011)	5	NC	BDL (0.011)	5	NC
Benzo(b)furan	µg/consumable	0.627 ± 0.067	5	NQ (0.016)	5	98.3	NQ (0.016)	5	98.3
Hydroquinone	µg/consumable	84.2 ± 1.8	5	0.347 ± 0.035	5	99.6	0.403 ± 0.033	5	99.5
Resorcinol	µg/consumable	1.57 ± 0.22	5	BDL (0.016)	5	99.5	BDL (0.016)	5	99.5
Catechol	µg/consumable	87.4 ± 3.4	5	3.11 ± 0.49	5	96.4	3.37 ± 0.17	5	96.2
Phenol	µg/consumable	13.5 ± 0.8	5	0.174 ± 0.022	5	98.7	0.116 ± 0.017	5	99.1
p-Cresol	µg/consumable	8.72 ± 0.38	5	BDL (0.010)	5	99.9	BDL (0.010)	5	99.9
m-Cresol	µg/consumable	3.48 ± 0.18	5	NQ (0.019)	5	99.6	NQ (0.019)	5	99.6
o-Cresol	µg/consumable	3.94 ± 0.16	5	NQ (0.026)	5	99.6	NQ (0.026)	5	99.7
Propylene glycol	mg/consumable	0.021 ± 0.005	5	0.390 ± 0.023	5	−1724	0.206 ± 0.014	5	−861
Ethylene glycol	mg/consumable	0.035 ± 0.001	5	0.011 ± 0.000	5	69.3	0.008 ± 0.001	5	77.8
Diethylene glycol	mg/consumable	BDL (0.004)	5	BDL (0.002)	5	NC	BDL (0.002)	5	NC
Glycidol	mg/consumable	NQ (0.006)	5	0.044 ± 0.003	5	−883	0.040 ± 0.004	5	−806
Glycerol	mg/consumable	2.35 ± 0.05	5	3.02 ± 0.26	5	−28.4	2.38 ± 0.21	5	−1.02
Naphthalene	ng/consumable	994 ± 94	5	2.2 ± 0.42	5	99.8	2.90 ± 0.34	5	99.7
Pyrene	ng/consumable	79.4 ± 7.5	5	8.97 ± 0.82	5	88.7	10.3 ± 0.7	5	87.1
Benzo[*a*]anthracene	ng/consumable	24.2 ± 2.4	5	1.54 ± 0.11	5	93.7	1.58 ± 0.09	5	93.5
Chrysene	ng/consumable	34.7 ± 3.2	5	2.61 ± 0.27	5	92.5	2.64 ± 0.20	5	92.4
Benzo[*a*]pyrene	ng/consumable	12.9 ± 1.3	5	NQ (0.354)	5	97.7	0.356 ± 0.079	5	97.2
Indeno(1,2,3-*cd*)pyrene	ng/consumable	4.19 ± 0.37	5	NQ (0.337)	5	97.2	NQ (0.337)	5	96.4
Benzo[*c*]phenanthrene	ng/consumable	8.32 ± 0.81	5	0.874 ± 0.171	5	89.5	0.710 ± 0.055	5	91.5
Cyclopenta[*c,d*]pyrene	ng/consumable	7.82 ± 1.12	5	0.515 ± 0.036	5	93.4	0.534 ± 0.049	5	93.2
Benzo[*j*]aceanthrylene	ng/consumable	2.24 ± 0.43	5	BDL (0.104)	5	97.7	BDL (0.104)	5	97.7
1,3-Butadiene	µg/consumable	108 ± 4	5	BDL (0.029)	5	>99.9	BDL (0.029)	5	>99.9
Isoprene	µg/consumable	887 ± 49	5	NQ (0.135)	5	>99.9	NQ (0.135)	5	>99.9
Acrylonitrile	µg/consumable	19.5 ± 1.6	5	BDL (0.032)	5	99.9	BDL (0.032)	5	99.9
Benzene	µg/consumable	78.6 ± 4.6	5	NQ (0.056)	5	>99.9	NQ (0.056)	5	>99.9
Toluene	µg/consumable	131 ± 5	5	NQ (0.204)	5	99.9	NQ (0.204)	5	99.9
Ethylbenzene	µg/consumable	13.4 ± 0.9	5	NQ (0.048)	5	99.8	NQ (0.048)	5	99.8
Ethylene oxide	µg/consumable	19.3 ± 2.0	5	BDL (0.036)	5	99.9	BDL (0.036)	5	99.9
Vinyl chloride	ng/consumable	95.6 ± 9.2	5	BDL (0.657)	5	99.7	BDL (0.657)	5	99.7
Propylene oxide	ng/consumable	903 ± 308	5	BDL (15.6)	5	99.1	BDL (15.6)	5	99.1
Furan	µg/consumable	61.9 ± 3.5	5	1.16 ± 0.01	5	98.1	1.17 ± 0.06	5	98.1
Vinyl acetate	ng/consumable	617 ± 20	5	BDL (11.0)	5	99.1	BDL (11.0)	5	99.1
Nitromethane	ng/consumable	690 ± 58	5	42.4 ± 1.5	5	93.9	38.1 ± 1.1	5	94.5
2-Nitropropane	ng/consumable	58.7 ± 6.1	5	BDL (1.45)	5	98.8	BDL (1.45)	5	98.8
5-Methylchrysene	ng/consumable	0.744 ± 0.205	5	BDL (0.028)	5	98.1	BDL (0.028)	5	98.1
Benzo[*b*]fluoranthene	ng/consumable	12.3 ± 1.5	5	0.548 ± 0.091	5	95.5	0.606 ± 0.091	5	95.0

(*continued on next page*)

Table 3 (*continued*)

Parameter	Unit	3R4F		THP1.0(T)			THP1.0(M)		
		Mean ± SD	N	Mean ± SD	N	%Red^n vs. 3R4F	Mean ± SD	N	%Red^n vs. 3R4F
Benzo[*k*]fluoranthene	ng/consumable	3.70 ± 0.49	5	0.255 ± 0.046	5	93.1	0.290 ± 0.060	5	92.2
Dibenz[*a,h*]anthracene	ng/consumable	0.915 ± 0.124	5	BDL (0.046)	5	95.8	NQ (0.154)	5	94.1
Dibenz[*a,l*]pyrene	ng/consumable	BDL (0.423)	5	BDL (0.254)	5	NC	BDL (0.254)	5	NC
Dibenz[*a,e*]pyrene	ng/consumable	NQ (0.696)	5	BDL (0.125)	5	NC	BDL (0.125)	5	NC
Dibenz[*a,i*]pyrene	ng/consumable	1.66 ± 0.41	5	BDL (0.132)	5	96.0	BDL (0.132)	5	96.0
Dibenz[*a,h*]pyrene	ng/consumable	BDL (0.236)	5	BDL (0.141)	5	NC	BDL (0.141)	5	NC
1-Aminonaphthalene	ng/consumable	17.6 ± 0.6	5	NQ (0.027)	5	99.8	NQ (0.027)	5	99.9
2-Aminonaphthalene	ng/consumable	13.2 ± 0.8	5	NQ (0.012)	5	>99.9	BDL (0.004)	5	>99.9
3-Aminobiphenyl	ng/consumable	3.49 ± 0.27	5	NQ (0.004)	5	>99.9	BDL (0.001)	5	>99.9
4-Aminobiphenyl	ng/consumable	2.29 ± 0.12	5	NQ (0.005)	5	99.8	NQ (0.005)	5	99.9
2,6-Dimethlyaniline	ng/consumable	6.11 ± 0.65	5	0.040 ± 0.004	5	99.4	0.029 ± 0.008	5	99.5
Benzidine	ng/consumable	BDL (0.010)	5	BDL (0.003)	5	NC	BDL (0.003)	5	NC
o-Anisidine	ng/consumable	4.18 ± 0.23	5	0.244 ± 0.031	5	94.2	0.153 ± 0.023	5	96.4
o-Toluidine	ng/consumable	83.3 ± 2.1	5	0.371 ± 0.045	5	99.6	0.310 ± 0.020	5	99.6
N-Nitrosonornicotine	ng/consumable	263 ± 12	5	24.7 ± 2.5	5	90.6	19.1 ± 2.2	5	92.8
N-Nitrosoanatabine	ng/consumable	268 ± 20	5	37.7 ± 3.4	5	85.9	32.8 ± 3.2	5	87.7
N-Nitrosoanabasine	ng/consumable	24.1 ± 1.1	5	4.70 ± 0.39	5	80.4	4.05 ± 0.39	5	83.2
4-(methylnitrosamino)-1-(3-pyridyle)-1-butanone	ng/consumable	281 ± 16	5	6.61 ± 0.86	5	97.7	5.32 ± 0.89	5	98.1
Acetamide	µg/consumable	11.9 ± 1.0	5	1.34 ± 0.05	5	88.7	1.15 ± 0.05	5	90.3
Acrylamide	µg/consumable	3.99 ± 0.39	5	1.04 ± 0.04	5	73.9	0.829 ± 0.039	5	79.2
Caffeic acid	µg/consumable	BDL (1.19)	5	BDL (0.478)	5	NC	BDL (0.478)	5	NC
Ethyl carbamate	ng/consumable	BDL (6.43)	5	BDL (1.93)	5	NC	BDL (1.93)	5	NC
IQ	ng/consumable	7.75 ± 1.07	5	BDL (0.164)	5	98.9	BDL (0.164)	5	98.2
Glu-P-2	ng/consumable	BDL (0.301)	5	BDL (0.120)	5	NC	BDL (0.120)	5	NC
Glu-P-1	ng/consumable	BDL (0.239)	5	BDL (0.095)	5	NC	BDL (0.095)	5	NC
PhIP	ng/consumable	BDL (0.365)	5	BDL (0.146)	5	NC	BDL (0.146)	5	NC
Trp-P-2	ng/consumable	6.46 ± 1.00	5	BDL (0.113)	5	99.1	BDL (0.113)	5	99.1
AαC	ng/consumable	176 ± 16	5	NQ (0.443)	5	99.9	NQ (0.443)	5	99.9
Trp-P-1	ng/consumable	4.29 ± 0.52	5	BDL (0.098)	5	98.9	BDL (0.098)	5	98.9
MeAαC	ng/consumable	15.3 ± 2.1	5	BDL (0.115)	5	99.6	BDL (0.115)	5	99.6
Hydrazine	ng/consumable	NQ (12.2)	5	BDL (2.04)	5	NC	BDL (2.04)	5	NC
NDMA	ng/consumable	14.2 ± 1.3	5	BDL (0.178)	5	99.4	BDL (0.178)	5	99.4
NEMA	ng/consumable	BDL (0.509)	5	BDL (0.254)	5	NC	BDL (0.254)	5	NC
NDEA	ng/consumable	BDL (0.617)	5	BDL (0.308)	5	NC	BDL (0.308)	5	NC
NDiPA	ng/consumable	BDL (0.546)	5	BDL (0.273)	5	NC	BDL (0.273)	5	NC
NDPA	ng/consumable	BDL (0.150)	5	BDL (0.075)	5	NC	BDL (0.075)	5	NC
NDBA	ng/consumable	NQ (1.11)	5	NQ (0.553)	5	NC	BDL (0.166)	5	NC
NPIP	ng/consumable	BDL (0.172)	5	BDL (0.086)	5	NC	BDL (0.086)	5	NC
NPYR	ng/consumable	17.6 ± 1.0	5	BDL (0.198)	5	99.4	BDL (0.198)	5	99.4
NMOR	ng/consumable	BDL (0.550)	5	BDL (0.275)	5	NC	BDL (0.275)	5	NC
NDELA	ng/consumable	NQ (0.283)	5	0.576 ± 0.244	5	−163	0.585 ± 0.234	5	−167
Nornicotine	ng/consumable	22117 ± 1351	5	NQ (47.6)	5	99.5	NQ (47.6)	5	99.4
Anatabine	ng/consumable	6218 ± 343	5	1157 ± 123	5	81.4	1266 ± 44	5	79.6
Anabasine	ng/consumable	1030 ± 120	5	408 ± 50	5	60.4	408 ± 53	5	60.4
Myosmine	ng/consumable	13226 ± 592	5	459 ± 36	5	96.5	500 ± 71	5	96.2
Nicotine-*N*-oxide	ng/consumable	NQ (291)	5	BDL (174)	5	NC	BDL (174)	5	NC
Cotinine	ng/consumable	14320 ± 755	5	298 ± 43	5	97.9	313 ± 15	5	97.8
β-Nicotyrine	ng/consumable	7071 ± 125	5	NQ (127)	5	98.8	NQ (127)	5	98.8
Formaldehyde	µg/consumable	54.1 ± 6.0	5	3.29 ± 0.30	5	93.9	3.51 ± 0.54	5	93.5
Acetaldehyde	µg/consumable	2200 ± 103	5	111 ± 8	5	95.0	115 ± 11	5	94.8
Acetone	µg/consumable	660 ± 24	5	5.97 ± 0.66	5	99.1	6.62 ± 0.51	5	99.0
Propionaldehyde	µg/consumable	132 ± 3	5	5.31 ± 0.15	5	96.0	5.66 ± 0.57	5	95.7
Acrolein	µg/consumable	157 ± 9	5	2.22 ± 0.52	5	98.6	2.50 ± 0.11	5	98.4
Isobutyraldehyde	µg/consumable	45.7 ± 3.6	5	9.78 ± 0.46	5	78.6	9.53 ± 1.11	5	79.1
Methyl Ethyl Ketone	µg/consumable	192 ± 8	5	1.53 ± 0.20	5	99.2	1.77 ± 0.37	5	99.1
n-Butyraldehyde	µg/consumable	15.2 ± 1.5	5	BDL (0.088)	5	99.7	BDL (0.088)	5	99.7
Crotonaldehyde	µg/consumable	42.0 ± 6.2	5	0.567 ± 0.232	5	98.7	0.768 ± 0.321	5	98.2
Acetoin	µg/consumable	NQ (5.61)	5	5.78 ± 1.33	5	−14.0	5.94 ± 1.12	5	−17.2
Glyoxal	µg/consumable	9.56 ± 1.68	5	BDL (0.063)	5	99.7	BDL (0.063)	5	99.7
Methylglyoxal	µg/consumable	26.2 ± 3.4	5	26.4 ± 2.4	5	−0.46	27.7 ± 2.7	5	−5.56
2,3-Butanedione	µg/consumable	260 ± 11	5	38.0 ± 4.4	5	85.4	40.5 ± 3.3	5	84.4
2,3-Pentanedione	µg/consumable	35.0 ± 2.3	5	7.38 ± 1.07	5	78.9	7.94 ± 1.15	5	77.3
Allyl Alcohol	µg/consumable	13.8 ± 2.3	5	1.24 ± 0.12	5	91.0	1.40 ± 0.11	5	89.9

Abbreviations: THP = tobacco heating product; SD = standard deviation; %Red^n = reduction in concentration as a percentage of the level in 3R4F MSS. N = number of replicates tested; TPM = total particulate matter; NFDPM = nicotine-free dry particulate matter; BDL = below detection limit; NQ = not quantified; NC = not calculated; NNN=*N*-nitrosonornicotine; NAT=*N*-nitrosoanatabine; NAB=*N*-nitrosoanabasine; NNK = 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone; NDMA=*N*-nitrosodimethylamine; NEMA=*N*-nitrosomethylethylamine; NDEA=*N*-nitrosodiethylamine; NDiPA = *N*-nitrosodiisopropylamine; NDPA=*N*-nitrosodipropylamine; NDBA=*N*-nitrosodibutylamine; NPIP=*N*-nitrosopiperidine; NPYR=*N*-nitrosopyrrolidine; NMOR=*N*-nitrosomorpholine; NDELA=*N*-nitrosodiethanolamine. IQ = 2-Amino-3-methylimidazo[4,5-f]quinoline; Glu-P-2 = 2-Aminodipyrido[1,2-a:3′,2′-d]imidazole; Glu-P-1 = 2-Amino-6-methyldipyrido[1,2-a:3′,2′-d]imidazole; PhIP = 2-Amino-1-methyl-6-phenylimidazo[4,5-b]pyridine; Trp-P-2 = 1-Methyl-3-amino-5H-pyrido[4,3-b]indole; A-α-C = 2-Amino-9H-pyrido[2,3-b]indole; Trp-P-1 = 3-Amino-1,4-dimethyl-5H-pyrido[4,3-b]indole; MeA-α-C = 2-Amino-3-methyl)-9H-pyrido[2,3-b]indole.

reductions of 93.9% and 93.5% per stick in THP1.0(T) and THP1.0(T), respectively, became 92.0% and 91.4% per puff. Table 10 provides a comparison of emissions in THP1.0 emissions and 1R6F reference cigarette MSS, as this will replace 3R4F when it is no longer available. The results are discussed by compound class below.

The supplementary information includes summary tables of emissions on a nicotine basis (Supplementary Table 1. THP, 3R4F and 1R6F Toxicant yields per mg nicotine) and on a particulate matter basis (Supplementary Table 2. THP, 3R4F and 1R6F Toxicant yields per mg TPM). These tables are provided as supplementary information but are not discussed further in this paper.

3.2. TPM, nicotine, water and NFDPM

TPM, nicotine, water and NFDPM were reduced in THP1.0 emissions compared with 3R4F smoke. The water measurement and NFDPM calculations, however, must be viewed with caution, because, as described by Ghosh and Jeannet (2014), Health Canada method T-115 may not account for all the water released from the THP1.0 consumable during heating. This is subject to separate investigation which will be reported in due course.

3.3. Oxygen-containing substances

CO was below detection limits in the blank and was detected but not quantifiable in THP1.0 emissions, representing >99% reduction compared with levels in MSS. CO_2 was quantified at low levels above the background, having >97% lower than in MSS. NO and NO_x were also detected in THP1.0 emissions, but were >97% lower than levels in MSS.

Ethylene oxide and propylene oxide were both below detection limits in the blank measurements and in the THP1.0 emissions, resulting in reductions compared with MSS of >99%. Furan was not quantified in the blank, but was in the THP1.0 emissions and MSS, with a 98% reduction in the THP emission.

3.4. Nitrogenous species

Ammonia was detected in THP1.0 emissions at levels higher than the blank but substantially lower than in 3R4F MSS, resulting in calculated reductions of 88% and 85% in THP1.0(T) and THP1.0(M), respectively. Hydrogen cyanide was measured in 3R4F MSS but was not detected in blanks and was not detected or not quantified in the THP1.0 emissions, resulting in a 99% reduction. Hydrazine was below the detection limit in the blanks and THP1.0 emissions and not quantified in 3R4F MSS; acrylonitrile was not detected in blanks or THP1.0 emissions, but was measured in 3R4F MSS, thus a greater than 99% reduction was calculated.

Ethyl carbamate was not detected in the blanks, THP1.0 emissions or 3R4F MSS and so reductions were not calculated. Quinoline was not detected or not quantified in THP1.0 emissions or blanks, but was present in the MSS of 3R4F; acetamide and acrylamide were not detected or not quantified in the blanks but were measured at low levels in the THP1.0 emissions and at higher levels in 3R4F MSS; pyridine was detected in all measurements including blanks. The reductions in the THP1.0 emissions were in the range 74–99%.

Of the aliphatic and aromatic amines, only *o*-toluidine was detected in all samples. For THP1.0, the measured concentration was greater than in the blank but significantly lower than in 3R4F smoke. 2,6-Dimethylaniline and *o*-anisidine were not detected in the blanks but were detected in THP1.0 emissions at levels lower than in 3R4F MSS, giving >99% and >94% reductions, respectively. 1- and 2-aminonaphthalene, 3- and 4-aminobiphenyl, IQ (2-amino-3-methylimidazo[4,5-f]quinoline), Trp-P-1 (3-amino-1,4-dimethyl-5H-pyrido[4,3-b]indole) and Trp-P-2 (1-methyl-3-amino-5H-pyrido[4,3-b]indole), and AαC (2-Amino-9H-pyrido[2,3-b]indole) and MeAαC (2-amino-3-methyl)-9H-pyrido[2,3-b]indole) were all below detection limits or could not be quantified in blanks, but were detected in 3R4F smoke. Calculated reductions for these toxicants ranged from 98% to >99%. Benzidine, Glu-P-1 (2-amino-6-methyldipyrido[1,2-a:3′,2′-d]imidazole), Glu-P-2 (2-aminodipyrido [1,2-a:3′,2′-d]imidazole) and PhIP (2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine) were below detection limits in the blanks, THP1.0 emissions and 3R4F MSS and, therefore, reductions were not calculated.

3.5. Metals

Mercury was quantified in THP1.0 emissions at a level below that in 3R4F MSS but was not detected in the blanks, yielding a reduction of 69% relative to 3R4F. Several metals (beryllium, cobalt, nickel, selenium and tin) were either not detected or not quantified in 3R4F and THP1.0 emissions. Chromium was measured in the THP1.0 emissions but not in 3R4F; the limit of quantification for 3R4F was higher than that for THP1.0 and close to the levels quantified in the THP1.0 emissions and blank, suggesting some of the signal was associated with laboratory background. Cadmium was quantified in 3R4F MSS but was below the detection limit for all other samples. Arsenic was detected in 3R4F MSS, was detected but not quantified in THP1.0 emissions and was not detected in the blanks. Copper was quantified in one THP1.0 sample and the THP blank at levels close to the limit of quantification and at a higher level in 3R4F MSS. Iron was measured in the THP1.0 emissions and both blank measurements at similar levels and at about twice that in the 3R4F MSS, suggesting a partial association with laboratory background. Zinc was quantified in THP1.0 emissions at about 10% of the 3R4F smoke yield and was not quantified in the THP blank, but it was quantified at a higher level in the cigarette blank.

3.6. Phenols

All phenols except resorcinol, *p*-cresol and caffeic acid were detected in THP1.0 emissions (although *m*- and *o*-cresol could not be quantified) at levels substantially lower than MSS, resulting in reductions that ranged from 96% to >99%. Caffeic acid was not detected in either THP1.0 emissions or MSS and, therefore, its reduction was not calculated.

3.7. Glycols

Neither ethylene glycol nor propylene glycol were present in the blank measurements, but both were detected in the THP1.0 emissions, with the propylene glycol at higher levels than in 3R4F MSS. Propylene glycol is a constituent of the flavour added to the THP1.0 tobacco consumable. The levels of ethylene glycol in THP1.0(T) and THP1.0(M) emissions were, respectively, 69% and 78% lower than those in 3R4F MSS. Glycidol is a potential thermal breakdown product of glycerol, which is added to the THP1.0 consumable, and was present in THP1.0 emissions but was not quantified in 3R4F MSS, where it is thought to decompose completely. Diethylene glycol was below the detection limit in all samples and blanks. Glycerol was measured in the range 2.35–3.02 mg per consumable and, as it was intentionally added, no comparison of reduction was made.

3.8. Hydrocarbons

The volatile hydrocarbons 1,3-butadiene and isoprene, and the aromatic hydrocarbons benzene, ethyl benzene, styrene and

Table 4
Measured yields in cigarette and THP air/method blanks for 126 measurands.

Parameter	Unit	3R4F blank		THP1.0(T) and THP1.0(M) blank	
		Mean ± SD	N	Mean ± SD	N
Puff count	/consumable	11 ± 0	5	8 ± 0	5
TPM	mg/consumable	0.000 ± 0.000	5	0.000 ± 0.000	5
Water	mg/consumable	BDL (0.064)	5	BDL (0.038)	5
Nicotine	mg/consumable	BDL (0.002)	5	BDL (0.001)	5
NFDPM	mg/consumable	BDL (0.119)	5	BDL (0.071)	5
CO	mg/consumable	BDL (0.159)	5	BDL (0.067)	5
CO_2	mg/consumable	0.922 ± 0.322	5	BDL (0.105)	5
Ammonia	µg/consumable	NQ (4.88)	5	1.72 ± 0.44	5
Hydrogen cyanide	µg/consumable	BDL (1.31)	5	BDL (0.525)	5
Mercury	ng/consumable	BDL (0.857)	5	BDL (0.104)	5
Cadmium	ng/consumable	BDL (1.64)	5	BDL (0.162)	5
Lead	ng/consumable	BDL (4.60)	5	2.39 ± 0.94	5
Chromium	ng/consumable	NQ (4.51)	5	3.83 ± 0.27	5
Nickel	ng/consumable	BDL (2.85)	5	NQ (0.878)	5
Arsenic	ng/consumable	BDL (0.879)	5	BDL (0.173)	5
Selenium	ng/consumable	BDL (0.790)	5	BDL (0.219)	5
Copper	ng/consumable	NQ (8.20)	5	2.87 ± 3.14	5
Cobalt	ng/consumable	BDL (0.893)	5	NQ (0.878)	5
Beryllium	ng/consumable	BDL (0.936)	5	BDL (0.024)	5
Iron	ng/consumable	20.7 ± 9.1	5	15.7 ± 3.8	5
Zinc	ng/consumable	113 ± 44	5	NQ (7.19)	5
Tin	ng/consumable	NQ (20.1)	5	NQ (0.876)	5
NO	µg/consumable	BDL (3.63)	5	NQ (0.569)	5
NO_x	µg/consumable	BDL (7.01)	5	BDL (0.381)	5
Pyridine	µg/consumable	4.73 ± 2.98	5	0.276 ± 0.191	5
Quinoline	µg/consumable	NQ (0.036)	5	BDL (0.003)	5
Styrene	µg/consumable	1.67 ± 1.26	5	NQ (0.039)	5
Nitrobenzene	µg/consumable	BDL (0.038)	5	BDL (0.011)	5
Benzo(b)furan	µg/consumable	0.102 ± 0.023	5	BDL (0.005)	5
Hydroquinone	µg/consumable	BDL (1.35)	5	BDL (0.062)	5
Resorcinol	µg/consumable	BDL (0.395)	5	BDL (0.016)	5
Catechol	µg/consumable	BDL (1.21)	5	BDL (0.026)	5
Phenol	µg/consumable	BDL (1.43)	5	BDL (0.026)	5
p-Cresol	µg/consumable	BDL (0.207)	5	BDL (0.010)	5
m-Cresol	µg/consumable	BDL (0.451)	5	BDL (0.006)	5
o-Cresol	µg/consumable	BDL (0.184)	5	BDL (0.008)	5
Propylene Glycol	mg/consumable	BDL (0.004)	5	BDL (0.002)	5
Ethylene Glycol	mg/consumable	BDL (0.001)	5	BDL (0.001)	5
Diethylene Glycol	mg/consumable	BDL (0.004)	5	BDL (0.002)	5
Glycidol	mg/consumable	BDL (0.002)	5	0.005 ± 0.001	5
Glycerol	mg/consumable	BDL (0.024)	5	BDL (0.014)	5
Naphthalene	ng/consumable	36.1 ± 21.7	5	1.97 ± 1.20	5
Pyrene	ng/consumable	7.87 ± 2.83	5	2.44 ± 0.71	5
Benzo[*a*]anthracene	ng/consumable	1.40 ± 0.79	5	0.329 ± 0.167	5
Chrysene	ng/consumable	2.34 ± 1.20	5	0.720 ± 0.311	5
Benzo[*a*]pyrene	ng/consumable	0.628 ± 0.280	5	BDL (0.106)	5
Indeno(1,2,3-*cd*)pyrene	ng/consumable	NQ (0.562)	5	NQ (0.337)	5
Benzo[*c*]phenanthrene	ng/consumable	0.567 ± 0.447	5	NQ (0.179)	5
Cyclopenta[*c,d*]pyrene	ng/consumable	NQ (0.451)	5	BDL (0.081)	5
Benzo[*j*]aceanthrylene	ng/consumable	NQ (0.576)	5	BDL (0.104)	5
1,3-Butadiene	µg/consumable	BDL (0.190)	5	BDL (0.029)	5
Isoprene	µg/consumable	NQ (0.901)	5	BDL (0.041)	5
Acrylonitrile	µg/consumable	BDL (0.213)	5	BDL (0.032)	5
Benzene	µg/consumable	0.598 ± 0.349	5	BDL (0.017)	5
Toluene	µg/consumable	3.38 ± 1.46	5	BDL (0.061)	5
Ethylbenzene	µg/consumable	0.659 ± 0.289	5	BDL (0.014)	5
Ethylene Oxide	µg/consumable	BDL (0.239)	5	BDL (0.036)	5
Vinyl Chloride	ng/consumable	BDL (4.38)	5	BDL (0.657)	5
Propylene Oxide	ng/consumable	BDL (104)	5	BDL (15.6)	5
Furan	µg/consumable	NQ (0.627)	5	NQ (0.094)	5
Vinyl Acetate	ng/consumable	BDL (73.0)	5	BDL (11.0)	5
Nitromethane	ng/consumable	BDL (56.7)	5	BDL (8.50)	5
2-Nitropropane	ng/consumable	BDL (1.45)	5	BDL (1.45)	5
5-Methylchrysene	ng/consumable	BDL (0.047)	5	BDL (0.028)	5
Benzo[*b*]fluoranthene	ng/consumable	0.573 ± 0.372	5	0.220 ± 0.234	5
Benzo[*k*]fluoranthene	ng/consumable	NQ (0.257)	5	NQ (0.154)	5

Table 4 (*continued*)

Parameter	Unit	3R4F blank		THP1.0(T) and THP1.0(M) blank	
		Mean ± SD	N	Mean ± SD	N
Dibenz[*a*,*h*]anthracene	ng/consumable	NQ (0.257)	5	BDL (0.046)	5
Dibenz[*a*,*l*]pyrene	ng/consumable	BDL (0.423)	5	BDL (0.254)	5
Dibenz[*a*,*e*]pyrene	ng/consumable	BDL (0.209)	5	BDL (0.125)	5
Dibenz[*a*,*i*]pyrene	ng/consumable	BDL (0.219)	5	BDL (0.132)	5
Dibenz[*a*,*h*]pyrene	ng/consumable	BDL (0.236)	5	BDL (0.141)	5
1-Aminonaphthalene	ng/consumable	NQ (0.091)	5	BDL (0.008)	5
2-Aminonaphthalene	ng/consumable	BDL (0.012)	5	BDL (0.004)	5
3-Aminobiphenyl	ng/consumable	BDL (0.004)	5	BDL (0.001)	5
4-Aminobiphenyl	ng/consumable	BDL (0.005)	5	BDL (0.001)	5
2,6-Dimethlyaniline	ng/consumable	BDL (0.021)	5	NQ (0.021)	5
Benzidine	ng/consumable	BDL (0.010)	5	BDL (0.003)	5
o-Anisidine	ng/consumable	BDL (0.077)	5	BDL (0.023)	5
o-Toluidine	ng/consumable	0.436 ± 0.420	5	0.057 ± 0.051	5
NNN	ng/consumable	BDL (0.197)	5	NQ (0.328)	5
NAT	ng/consumable	BDL (0.390)	5	BDL (0.195)	5
NAB	ng/consumable	BDL (0.107)	5	BDL (0.054)	5
NNK	ng/consumable	BDL (0.301)	5	BDL (0.151)	5
Acetamide	µg/consumable	NQ (0.267)	5	NQ (0.080)	5
Acrylamide	µg/consumable	BDL (0.203)	5	BDL (0.061)	5
Caffeic Acid	µg/consumable	BDL (1.19)	5	BDL (0.478)	5
Ethyl Carbamate	ng/consumable	BDL (6.43)	5	BDL (1.93)	5
IQ	ng/consumable	BDL (0.410)	5	BDL (0.164)	5
Glu-P-2	ng/consumable	BDL (0.301)	5	BDL (0.120)	5
Glu-P-1	ng/consumable	BDL (0.239)	5	BDL (0.095)	5
PhIP	ng/consumable	BDL (0.365)	5	BDL (0.146)	5
Trp-P-2	ng/consumable	BDL (0.282)	5	BDL (0.113)	5
AαC	ng/consumable	NQ (1.11)	5	NQ (0.443)	5
Trp-P-1	ng/consumable	BDL (0.245)	5	BDL (0.098)	5
MeAαC	ng/consumable	BDL (0.288)	5	BDL (0.115)	5
Hydrazine	ng/consumable	BDL (4.08)	5	BDL (2.04)	5
NDMA	ng/consumable	BDL (0.356)	5	BDL (0.178)	5
NEMA	ng/consumable	BDL (0.509)	5	BDL (0.254)	5
NDEA	ng/consumable	BDL (0.617)	5	BDL (0.308)	5
NDiPA	ng/consumable	BDL (0.546)	5	BDL (0.273)	5
NDPA	ng/consumable	BDL (0.150)	5	BDL (0.075)	5
NDBA	ng/consumable	NQ (1.11)	5	NQ (0.553)	5
NPIP	ng/consumable	BDL (0.172)	5	BDL (0.086)	5
NPYR	ng/consumable	BDL (0.396)	5	BDL (0.198)	5
NMOR	ng/consumable	BDL (0.550)	5	BDL (0.275)	5
NDELA	ng/consumable	NQ (0.283)	5	0.846 ± 0.152	5
Nornicotine	ng/consumable	BDL (79.4)	5	BDL (47.6)	5
Anatabine	ng/consumable	BDL (79.3)	5	BDL (47.6)	5
Anabasine	ng/consumable	BDL (69)	5	BDL (57.4)	5
Myosmine	ng/consumable	BDL (148)	5	BDL (88.8)	5
Nicotine-*N*-Oxide	ng/consumable	BDL (291)	5	BDL (174)	5
Cotinine	ng/consumable	NQ (104)	5	NQ (62.4)	5
β-Nicotyrine	ng/consumable	BDL (212)	5	BDL (38.1)	5
Formaldehyde	µg/consumable	6.16 ± 0.75	5	1.17 ± 0.20	5
Acetaldehyde	µg/consumable	14.9 ± 2.2	5	2.23 ± 0.50	5
Acetone	µg/consumable	BDL (1.58)	5	NQ (0.526)	5
Propionaldehyde	µg/consumable	NQ (4.03)	5	BDL (0.121)	5
Acrolein	µg/consumable	BDL (2.32)	5	BDL (0.232)	5
Isobutyraldehyde	µg/consumable	BDL (0.413)	5	BDL (0.041)	5
Methyl Ethyl Ketone	µg/consumable	BDL (1.28)	5	BDL (0.128)	5
n-Butyraldehyde	µg/consumable	BDL (0.878)	5	BDL (0.088)	5
Crotonaldehyde	µg/consumable	BDL (1.56)	5	BDL (0.156)	5
Acetoin	µg/consumable	BDL (1.68)	5	0.599 ± 1.152	5
Glyoxal	µg/consumable	BDL (0.630)	5	BDL (0.063)	5
Methylglyoxal	µg/consumable	BDL (0.384)	5	BDL (0.038)	5
2,3-Butanedione	µg/consumable	6.12 ± 2.32	5	0.309 ± 0.643	5
2,3-Pentanedione	µg/consumable	BDL (0.878)	5	BDL (0.088)	5
Allyl Alcohol	µg/consumable	0.544 ± 0.157	5	NQ (0.045)	5

Abbreviations: THP = tobacco heating product; SD = standard deviation; (T) = non-mentholated consumable variant. (M) = mentholated consumable variant; N = number off replicates tested; TPM = total particulate matter; NFDPM = nicotine-free dry particulate matter; BDL = below detection limit; NQ = not quantified; NC = not calculated; NNN=*N*-nitrosonornicotine; NAT=*N*-nitrosoanatabine; NAB=*N*-nitrosoanabasine; NNK = 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone; NDMA=*N*-nitrosodimethylamine; NEMA=*N*-nitrosomethylethylamine; NDEA=*N*-nitrosodiethylamine; NDiPA = *N*-nitrosodiisopropylamine; NDPA=*N*-nitrosodipropylamine; NDBA=*N*-nitrosodibutylamine; NPIP=*N*-nitrosopiperidine; NPYR=*N*-nitrosopyrrolidine; NMOR=*N*-nitrosomorpholine; NDELA=*N*-nitrosodiethanolamine. IQ = 2-Amino-3-methylimidazo[4,5-f]quinoline; Glu-P-2 = 2-Aminodipyrido[1,2-a:3′,2′-d]imidazole; Glu-P-1 = 2-Amino-6-methyldipyrido[1,2-a:3′,2′-d]imidazole; PhIP = 2-Amino-1-methyl-6-phenylimidazo[4,5-b]pyridine; Trp-P-2 = 1-Methyl-3-amino-5H-pyrido[4,3-b]indole; A-α-C = 2-Amino-9H-pyrido[2,3-b]indole; Trp-P-1 = 3-Amino-1,4-dimethyl-5H-pyrido[4,3-b]indole; MeA-α-C = 2-Amino-3-methyl)-9H-pyrido[2,3-b]indole.

toluene were detected in the 3R4F MSS but were not quantified in THP1.0 emissions. Consequently, the reductions in THP1.0 emissions were all greater than 99%.

Of pyrene and the 16 polyaromatic hydrocarbons in the FDA abbreviated list (naphthalene, benzo[c]phenanthrene, benzo[a]anthracene, chrysene, cyclopenta-[c,d]pyrene, 5-methylchrysene, benzo[b]fluoranthene, benzo[k]fluoranthene, benzo[j]aceanthrylene, benzo[a]pyrene, indeno[1,2,3-cd]pyrene, dibenzo[a,h]anthracene, dibenzo[a,l]pyrene, dibenzo[a,e]pyrene, dibenzo[a,i]pyrene and dibenzo[a,h]pyrene) all but 3 (dibenzo[a,l]pyrene, dibenzo[a,e]pyrene and dibenzo[a,h]pyrene) were measured in MSS and all except dibenzo[a,l]pyrene, dibenzo[a,e]pyrene, dibenzo[a,h]pyrene, dibenzo[a,h]anthracene and indeno[1,2,3-cd]pyrene) were measured in THP1.0 emissions. Reduction relative to 3R4F MSS ranged from 87% to >99%.

Naphthalene, pyrene, benzo[a]anthracene, chrysene, benzo[a]pyrene, benzo[c]phenanthrene, cyclopenta-[c,d]pyrene, benzo[b]fluoranthene and benzo[k]fluoranthene were detected in THP1.0 emissions and 3R4F MSS. Naphthalene, pyrene, benzo[a]anthracene, chrysene and benzo[b]fluoranthene were detected in the blanks, and of these, the levels of naphthalene in the THP1.0 emissions were similar to the blank, suggesting it may arise from chemical background. The polyaromatic hydrocarbon reductions in THP1.0 emissions ranged from 87% to >99% compared with those in 3R4F MSS.

Of the substituted hydrocarbons, nitrobenzene was not detected in the blanks, THP1.0 emissions or 3R4F MSS. 2-Nitropropane, vinyl acetate and vinyl chloride were detected in 3R4F MSS but not in THP1.0 emissions, resulting in reductions from 98% to above 99%. Nitromethane was present in THP1.0 emissions but at much lower levels than those in 3R4F MSS, resulting in a 94% reduction. All levels were below detection limits in the THP blanks.

3.9. Nitrosamines

The tobacco-specific nitrosamines were all measured in THP1.0 emissions at levels 80% (*N*-nitrosoanabasine) to 98% lower than in 3R4F smoke, but were not detected or could not be quantified in the blanks.

Of the volatile nitrosamines, only *N*-nitrosodiethanolamine was quantifiable in THP1.0 emissions at levels less than the blank but was not quantified in 3R4F MSS, suggesting its presence was due to background contamination. All remaining compounds in this class were not detected or could not be quantified in THP1.0 emissions or in the blanks. *N*-nitrosodimethylamine, *N*-nitrosodibutylamine and *N*-nitrosopyrrolidine were detected in 3R4F smoke, but *N*-nitrosodibutylamine could not be quantified, and *N*-nitrosomethylethylamine, *N*-nitrosodiethylamine, *N*-nitrosodiisopropylamine, *N*-nitrosodipropylamine, *N*-nitrosopiperidine and *N*-nitrosomorpholine were not detected in 3R4F MSS.

3.10. Nicotine-related compounds

Nicotine and related alkaloids were below the LOQ in the blanks. Nicotine-*N*-oxide was detected but could not be quantified in 3R4F MSS and was not detected in THP1.0 emissions. Nicotine and related alkaloids were detected in THP1.0 emissions (but nornicotine and β-nicotyrine could not be quantified) and in 3R4F MSS. This is to be expected based on their presence in the reconstituted tobacco sheet used in THP 1.0. The reductions in the THP emissions ranged from 60% (anabasine) to >99%.

3.11. Carbonyl compounds

Acetoin was present in THP1.0 emissions at levels higher than those in the 3R4F MSS, which was below LOQ and, therefore resulted in a calculated increase relative to MSS. Similarly, methylglyoxal was measured at a slightly greater level in THP10 emissions than in MSS, resulting in a calculated increase. All other carbonyls except *n*-butyraldehyde and glyoxal were measured in THP1.0 emissions but were at higher levels in 3R4F MSS, resulting in calculated reductions of 77%–99%. Formaldehyde, acetaldehyde, acetoin and 2,3-butanedione were measured in blanks. Allyl alcohol was not quantified in the THP blank but was present in the 3R4F blank and was measured in THP1.0 emissions at roughly one-tenth of the level in MSS.

3.12. Comparison of results for THS control sample and published data

For the data presented in Table 5, several determinands were not included in the Schaller et al., (2016) study and others were reported to be below the LOQ. For many of the analytes measured and published results overlapped within 2 standard deviations, but differences were observed for substances including water, NFDPM, CO, Cr, pyrene, acrylonitrile, NNN, NNK, crotonal, pyridine, styrene, hydroquinone and toluene, which were present at low levels and for some metals (mercury, lead and nickel) that were not explained by the blank.

3.13. Comparison of results for 3R4F and 1R6F

The measured values for 1R6F (Table 10) overlapped within 2 standard deviations with the certified values (+/− certified uncertainty) assigned by the University of Kentucky Center for Tobacco Reference Products (UKCTRP, 2016), indicating acceptable accuracy of analytical data for this reference product within the constraints of five-replicate analyses on a single occasion. Published reference data for the 3R4F product are limited to preliminary FTC smoking results (UKCTRP, undated). Measured values were therefore compared with those reported by Roemer and coworkers (Roemer et al., 2012, Appendix, Table A) and were consistent with the tabulated values.

3.14. Emission yields for TobReg and US FDA priority constituents

Tables 6 and 7 summarise the yields of constituents for the TobReg 9 priority constituents and the US FDA abbreviated list of constituents on a per consumable basis. The calculated average reductions were 97.0% (THP1.0T) and 97.1% (THP1.0 M) for the TobReg list and 97.6% (THP1.0T) and 97.4% (THP1.0 M), excluding nicotine, for the FDA abbreviated list.

Tables 8 and 9 summarise the yields of constituents for the TobReg 9 priority constituents and the US FDA abbreviated list of constituents on a per consumable and a per puff basis. The calculated average reductions on a per puff basis were 96.1% (THP1.0T) and 96.2% (THP1.0 M) for the TobReg list and 96.8% (THP1.0T) and 96.6% (THP1.0 M), excluding nicotine, for the FDA abbreviated list.

4. Discussion

This study describes the measurement of 126 substances in the emissions from THP1.0 and the MSS of 3R4F and 1R6F reference cigarettes. These are reported on a per-consumable or per-cigarette basis. The yields are compared and reported as percentage reductions per consumable for all measurands and summarised by considering the World Health Organization (WHO) Study Group on

Table 5
Air/method blanks, emission yields for THS and similar data reported by Schaller et al., (2016).

Parameter	Unit	THS blank		THS this study		THS2.2 FR1 Schaller et al.	
		Mean ± SD	N	Mean ± SD	N	Mean ± SD	N
Puff count	/consumable	12 ± 0	5	12 ± 0	5	12 ± 0	5
TPM	mg/consumable	0.144 ± 0.257	5	48.9 ± 0.7	5	48.2 ± 2.4	5
Water	mg/consumable	0.151 ± 0.112	5	25.4 ± 2.0	5	36.5 ± 3.1	5
Nicotine	mg/consumable	BDL (0.001)	5	1.16 ± 0.03	5	1.32 ± 0.16	5
NFDPM	mg/consumable	NQ (0.237)	5	22.3 ± 2.2	5	10.3 ± 0.9	5
CO	mg/consumable	BDL (0.067)	5	0.305 ± 0.017	5	0.531 ± 0.068	5
CO_2	mg/consumable	BDL (0.105)	5	5.79 ± 0.20	5	n.a	5
Ammonia	µg/consumable	1.53 ± 0.24	5	10.6 ± 0.7	5	14.2 ± 1.1	5
Hydrogen cyanide	µg/consumable	NQ (1.75)	5	3.21 ± 0.98	5	4.81 ± 0.35	5
Mercury	ng/consumable	BDL (0.104)	5	1.99 ± 0.12	5	1.17 ± 0.05	5
Cadmium	ng/consumable	BDL (0.162)	5	BDL (0.162)	5	NQ (0.350)	5
Lead	ng/consumable	1.65 ± 0.90	5	42.9 ± 15.3	5	NQ (3.35)	5
Chromium	ng/consumable	4.50 ± 0.61	5	4.57 ± 0.71	5	NQ (0.55)	5
Nickel	ng/consumable	NQ (0.878)	5	1.22 ± 0.72	5	NQ (0.55)	5
Arsenic	ng/consumable	BDL (0.173)	5	0.822 ± 0.08	5	NQ (1.13)	5
Selenium	ng/consumable	BDL (0.219)	5	BDL (0.219)	5	NQ (0.550)	5
Copper	ng/consumable	2.40 ± 1.24	5	10.6 ± 12.6	5	n.a	5
Cobalt	ng/consumable	NQ (0.878)	5	1.16 ± 0.85	5	n.a	5
Beryllium	ng/consumable	BDL (0.024)	5	BDL (0.024)	5	n.a	5
Iron	ng/consumable	25.0 ± 11.3	5	43.6 ± 8.6	5	n.a	5
Zinc	ng/consumable	NQ (7.19)	5	82.9 ± 34.3	5	n.a	5
Tin	ng/consumable	NQ (0.876)	5	NQ (0.876)	5	n.a	5
NO	µg/consumable	BDL (0.171)	5	13.2 ± 1.1	5	16.8 ± 2.3	5
NO_x	µg/consumable	BDL (0.381)	5	14.9 ± 1.2	5	17.3 ± 2.6	5
Pyridine	µg/consumable	0.279 ± 0.249	5	4.05 ± 0.11	5	7.54 ± 0.26	5
Quinoline	µg/consumable	BDL (0.003)	5	NQ ()	5	NQ (0.012)	5
Styrene	µg/consumable	NQ (0.039)	5	0.356 ± 0.039	5	0.608 ± 0.058	5
Nitrobenzene	µg/consumable	BDL (0.011)	5	BDL (0.011)	5	NQ (0.188)	5
Benzo(b)furan	µg/consumable	NQ (0.016)	5	0.026 ± 0.003	5	n.a	5
Hydroquinone	µg/consumable	BDL (0.062)	5	5.40 ± 0.10	5	8.10 ± 0.48	5
Resorcinol	µg/consumable	BDL (0.016)	5	NQ (0.055)	5	0.041 ± 0.003	5
Catechol	µg/consumable	BDL (0.026)	5	13.0 ± 0.2	5	16.3 ± 1.5	5
Phenol	µg/consumable	BDL (0.026)	5	1.46 ± 0.08	5	1.16 ± 0.12	5
p-Cresol	µg/consumable	BDL (0.010)	5	0.060 ± 0.005	5	0.072 ± 0.008	5
m-Cresol	µg/consumable	BDL (0.006)	5	0.029 ± 0.002	5	0.029 ± 0.004	5
o-Cresol	µg/consumable	BDL (0.008)	5	0.063 ± 0.004	5	0.069 ± 0.008	5
Propylene glycol	mg/consumable	BDL (0.002)	5	0.395 ± 0.010	5	n.a	5
Ethylene glycol	mg/consumable	BDL (0.001)	5	0.008 ± 0.001	5	n.a	5
Diethylene glycol	mg/consumable	BDL (0.002)	5	BDL (0.002)	5	n.a	5
Glycidol	mg/consumable	NQ (0.004)	5	0.038 ± 0.006	5	n.a	5
Glycerol	mg/consumable	BDL (0.014)	5	4.28 ± 0.08	5	4.63 ± 0.83	5
Naphthalene	ng/consumable	1.48 ± 0.51	5	4.01 ± 0.37	5	n.a	5
Pyrene	ng/consumable	1.94 ± 0.38	5	5.88 ± 0.23	5	NQ (5.00)	5
Benzo[*a*]anthracene	ng/consumable	NQ (0.243)	5	1.54 ± 0.04	5	n.a	5
Chrysene	ng/consumable	0.496 ± 0.097	5	2.45 ± 1.0	5	1.45 ± 0.14	5
Benzo[*a*]pyrene	ng/consumable	BDL (0.106)	5	0.582 ± 0.024	5	NQ (1.00)	5
Indeno(1,2,3-*cd*)pyrene	ng/consumable	BDL (0.101)	5	NQ (0.337)	5	n.a	5
Benzo[*c*]phenanthrene	ng/consumable	NQ (0.179)	5	0.643 ± 0.024	5	n.a	5
Cyclopenta[*c,d*]pyrene	ng/consumable	BDL (0.081)	5	0.598 ± 0.018	5	n.a	5
Benzo[*j*]aceanthrylene	ng/consumable	BDL (0.104)	5	BDL (0.104)	5	n.a	5
1,3-Butadiene	µg/consumable	BDL (0.029)	5	0.224 ± 0.016	5	0.294 ± 0.042	5
Isoprene	µg/consumable	BDL (0.041)	5	1.55 ± 0.20	5	2.35 ± 0.39	5
Acrylonitrile	µg/consumable	BDL (0.032)	5	NQ (0.107)	5	0.258 ± 0.041	5
Benzene	µg/consumable	BDL (0.017)	5	0.457 ± 0.029	5	0.649 ± 0.074	5
Toluene	µg/consumable	NQ (0.204)	5	1.33 ± 0.11	5	2.59 ± 0.43	5
Ethylbenzene	µg/consumable	NQ (0.048)	5	0.137 ± 0.017	5	n.a	5
Ethylene oxide	µg/consumable	BDL (0.119)	5	0.142 ± 0.020	5	0.201 ± 0.014	5
Vinyl chloride	ng/consumable	BDL (0.657)	5	BDL (0.658)	5	NQ (3.54)	5
Propylene oxide	ng/consumable	BDL (15.6)	5	134 ± 5	5	148 ± 18	5
Furan	µg/consumable	NQ (0.094)	5	5.38 ± 0.59	5	n.a	5
Vinyl Acetate	ng/consumable	BDL (11.0)	5	66.2 ± 6.9	5	n.a	5
Nitromethane	ng/consumable	BDL (8.50)	5	38.4 ± 2.3	5	n.a	5
2-Nitropropane	ng/consumable	BDL (1.45)	5	6.81 ± 1.14	5	n.a	5
5-Methylchrysene	ng/consumable	BDL (0.028)	5	BDL (0.028)	5	n.a	5
Benzo[*b*]fluoranthene	ng/consumable	NQ (0.191)	5	0.793 ± 0.072	5	n.a	5

(*continued on next page*)

Table 5 (*continued*)

Parameter	Unit	THS blank		THS this study		THS2.2 FR1 Schaller et al.	
		Mean ± SD	N	Mean ± SD	N	Mean ± SD	N
Benzo[*k*]fluoranthene	ng/consumable	NQ (0.154)	5	0.392 ± 0.057	5	n.a	5
Dibenz[*a,h*]anthracene	ng/consumable	NQ (0.154)	5	BDL (0.046)	5	NQ (0.100)	5
Dibenz[*a,l*]pyrene	ng/consumable	BDL (0.254)	5	BDL (0.254)	5	n.a	5
Dibenz[*a,e*]pyrene	ng/consumable	BDL (0.125)	5	BDL (0.125)	5	n.a	5
Dibenz[*a,i*]pyrene	ng/consumable	BDL (0.132)	5	BDL (0.132)	5	n.a	5
Dibenz[*a,h*]pyrene	ng/consumable	BDL (0.141)	5	BDL (0.141)	5	n.a	5
1-Aminonaphthalene	ng/consumable	NQ (0.027)	5	0.030 ± 0.013	5	0.077 ± NR	5
2-Aminonaphthalene	ng/consumable	0.015 ± 0.010	5	0.016 ± 0.008	5	0.046 ± 0.008	5
3-Aminobiphenyl	ng/consumable	0.007 ± 0.003	5	0.005 ± 0.002	5	NQ (0.032)	5
4-Aminobiphenyl	ng/consumable	0.006 ± 0.005	5	NQ (0.005)	5	NQ (0.051)	5
2,6-Dimethlyaniline	ng/consumable	BDL (0.006)	5	0.253 ± 0.067	5	n.a	5
Benzidine	ng/consumable	BDL (0.003)	5	BDL (0.003)	5	n.a	5
o-Anisidine	ng/consumable	BDL (0.023)	5	0.166 ± 0.012	5	n.a	5
o-Toluidine	ng/consumable	0.099 ± 0.049	5	0.938 ± 0.092	5	1.26 ± 0.19	5
NNN	ng/consumable	BDL (0.098)	5	11.5 ± 0.8	5	17.2 ± 1.25	5
NAT	ng/consumable	BDL (0.195)	5	21.0 ± 1.1	5	20.5 ± 0.5	5
NAB	ng/consumable	BDL (0.054)	5	3.14 ± 0.26	5	NQ (3.15)	5
NNK	ng/consumable	BDL (0.151)	5	10.6 ± 0.2	5	6.7 ± 0.6	5
Acetamide	µg/consumable	BDL (0.024)	5	3.07 ± 0.29	5	4.02 ± 0.18	5
Acrylamide	µg/consumable	BDL (0.061)	5	1.35 ± 0.14	5	1.73 ± 0.12	5
Caffeic Acid	µg/consumable	BDL (0.478)	5	BDL (0.478)	5	n.a	5
Ethyl Carbamate	ng/consumable	BDL (1.93)	5	BDL (1.93)	5	n.a	5
IQ	ng/consumable	BDL (0.164)	5	NQ (0.547)	5	n.a	5
Glu-P-2	ng/consumable	BDL (0.120)	5	BDL (0.120)	5	n.a	5
Glu-P-1	ng/consumable	BDL (0.095)	5	BDL (0.095)	5	n.a	5
PhIP	ng/consumable	BDL (0.146)	5	BDL (0.146)	5	n.a	5
Trp-P-2	ng/consumable	BDL (0.113)	5	BDL (0.113)	5	n.a	5
AαC	ng/consumable	NQ (0.443)	5	0.800 ± 0.295	5	n.a	5
Trp-P-1	ng/consumable	BDL (0.098)	5	BDL (0.098)	5	n.a	5
MeAαC	ng/consumable	BDL (0.115)	5	BDL (0.115)	5	n.a	5
Hydrazine	ng/consumable	BDL (2.04)	5	BDL (2.04)	5	n.a	5
NDMA	ng/consumable	BDL (0.178)	5	BDL (0.178)	5	n.a	5
NEMA	ng/consumable	BDL (0.254)	5	BDL (0.254)	5	n.a	5
NDEA	ng/consumable	BDL (0.308)	5	BDL (0.308)	5	n.a	5
NDiPA	ng/consumable	BDL (0.273)	5	BDL (0.273)	5	n.a	5
NDPA	ng/consumable	BDL (0.075)	5	BDL (0.075)	5	n.a	5
NDBA	ng/consumable	BDL (0.166)	5	BDL (0.166)	5	n.a	5
NPIP	ng/consumable	BDL (0.086)	5	BDL (0.086)	5	n.a	5
NPYR	ng/consumable	BDL (0.198)	5	BDL (0.198)	5	n.a	5
NMOR	ng/consumable	BDL (0.275)	5	BDL (0.275)	5	n.a	5
NDELA	ng/consumable	NQ (0.142)	5	NQ (0.142)	5	n.a	5
Nornicotine	ng/consumable	BDL (47.6)	5	320 ± 28	5	n.a	5
Anatabine	ng/consumable	BDL (47.6)	5	2165 ± 110	5	n.a	5
Anabasine	ng/consumable	BDL (57.4)	5	608 ± 43	5	n.a	5
Myosmine	ng/consumable	BDL (88.8)	5	1080 ± 37	5	n.a	5
Nicotine-*N*-oxide	ng/consumable	BDL (174)	5	NQ (581)	5	n.a	5
Cotinine	ng/consumable	77.4 ± 22.5	5	996 ± 55	5	n.a	5
β-Nicotyrine	ng/consumable	BDL (38.1)	5	NQ (127)	5	n.a	5
Formaldehyde	µg/consumable	1.46 ± 0.22	5	5.93 ± 0.87	5	5.53 ± 0.69	5
Acetaldehyde	µg/consumable	2.23 ± 0.55	5	327 ± 20	5	219 ± 31	5
Acetone	µg/consumable	NQ (0.526)	5	30.2 ± 3.0	5	40.7 ± 6.2	5
Propionaldehyde	µg/consumable	NQ (0.403)	5	16.7 ± 1.3	5	14.5 ± 2.4	5
Acrolein	µg/consumable	BDL (0.232)	5	9.98 ± 1.13	5	11.3 ± 2.4	5
Isobutyraldehyde	µg/consumable	BDL (0.041)	5	20.2 ± 1.7	5	26.1 ± 2.3	5
Methyl Ethyl Ketone	µg/consumable	BDL (0.128)	5	6.80 ± 0.75	5	7.18 ± 1.19	5
n-Butyraldehyde	µg/consumable	BDL (0.088)	5	1.20 ± 0.13	5	n.a	5
Crotonaldehyde	µg/consumable	BDL (0.156)	5	2.00 ± 0.40	5	4.14 ± 0.23	5
Acetoin	µg/consumable	1.24 ± 0.55	5	9.97 ± 1.53	5	n.a	5
Glyoxal	µg/consumable	BDL (0.063)	5	BDL (0.063)	5	n.a	5
Methylglyoxal	µg/consumable	BDL (0.038)	5	22.5 ± 1.7	5	n.a	5
2,3-Butanedione	µg/consumable	0.908 ± 0.410	5	66.3 ± 9.5	5	n.a	5
2,3-Pentanedione	µg/consumable	0.522 ± 0.205	5	12.8 ± 1.4	5	n.a	5
Allyl Alcohol	µg/consumable	NQ (0.045)	5	5.13 ± 0.47	5	n.a	5

Abbreviations: THS = tobacco heating system; SD = standard deviation; N = number of replicates tested; BDL = below detection limit; NQ = not quantified; NR = not reported; NNN=*N*-nitrosonornicotine; NAT=*N*-nitrosoanatabine; NAB=*N*-nitrosoanabasine; NNK = 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone; NDMA=*N*-nitrosodimethylamine; NEMA=*N*-nitrosomethylethylamine; NDEA=*N*-nitrosodiethylamine; NDiPA = *N*-nitrosodiisopropylamine; NDPA=*N*-nitrosodipropylamine; NDBA=*N*-nitrosodibutylamine; NPIP=*N*-nitrosopiperidine; NPYR=*N*-nitrosopyrrolidine; NMOR=*N*-nitrosomorpholine; NDELA=*N*-nitrosodiethanolamine. IQ = 2-Amino-3-methylimidazo[4,5-f]quinoline; Glu-P-2 = 2-Aminodipyrido[1,2-a:3′,2′-d]imidazole; Glu-P-1 = 2-Amino-6-methyldipyrido[1,2-a:3′,2′-d]imidazole; PhIP = 2-Amino-1-methyl-6-phenylimidazo[4,5-b]pyridine; Trp-P-2 = 1-Methyl-3-amino-5H-pyrido[4,3-b]indole; A-α-C = 2-Amino-9H-pyrido[2,3-b]indole; Trp-P-1 = 3-Amino-1,4-dimethyl-5H-pyrido[4,3-b]indole; MeA-α-C = 2-Amino-3-methyl)-9H-pyrido[2,3-b]indole.

Table 6
3R4F reference cigarette mainstream smoke yields and THP1.0 emission yields for the nine TobReg priority constituents presented on a consumable basis.

Parameter	Unit	3R4F	THP1.0(T)		THP1.0(M)	
		Mean per consumable	Mean per consumable	%Red[n] per Consumable	Mean per consumable	%Red[n] per consumable
1,3-Butadiene	µg	108	BDL (0.029)	>99.9	BDL (0.029)	>99.9
Acetaldehyde	µg	2200	111	95.0	115	94.8
Acrolein	µg	157	2.22	98.6	2.50	98.4
Benzene	µg	78.6	NQ (0.056)	>99.9	NQ (0.056)	>99.9
Benzo[*a*]pyrene	ng	12.9	NQ (0.354)	97.7	0.356	97.2
CO	mg	32.0	NQ (0.223)	99.8	NQ (0.223)	99.6
Formaldehyde	µg	54.10	3.29	93.9	3.51	93.5
NNK	ng	281	6.61	97.7	5.32	98.1
NNN	ng	263	24.7	90.6	19.1	92.8
			Average	97.0	**Average**	97.1

[a]Values calculated using replicate data per analyte (N = 5) Abbreviations: TobReg = WHO World Health Organization Study Group on Tobacco Product Regulation; THP = tobacco heating product; (T) = non-mentholated consumable variant. (M) = mentholated consumable variant; %Red[n] = reduction in concentration as a percentage of the level in 3R4F MSS. NNK = 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone; NNN=*N*-nitrosonornicotine; BDL = below detection limit; NQ = not quantified.

Table 7
3R4F reference cigarette mainstream smoke yields and THP1.0 emission yields for the 18 priority constituents in the US Food and Drug Administration abbreviated list, presented on a per-consumable basis.

Parameter	Unit	3R4F	THP1.0(T)		THP1.0(M)	
		Mean per Consumable	Mean per Consumable	%Red[n] per Consumable	Mean per Consumable	%Red[n] per Consumable
1,3-Butadiene	µg	108	BDL (0.029)	>99.9	BDL (0.029)	>99.9
1-Aminonaphthalene	ng	17.6	NQ (0.027)	99.9	NQ (0.027)	99.8
2-Aminonaphthalene	ng	13.2	NQ (0.012)	>99.9	BDL (0.004)	>99.9
4-Aminobiphenyl	ng	2.29	NQ (0.005)	99.8	NQ (0.005)	99.9
Acetaldehyde	µg	2200	111	95.0	115	94.8
Acrolein	µg	157	2.22	98.6	2.50	98.2
Acrylonitrile	µg	19.5	BDL (0.032)	99.9	BDL (0.032)	99.9
Ammonia	µg	32.5	4.01	87.7	5.01	84.6
Benzene	µg	78.6	NQ (0.056)	>99.9	NQ (0.056)	>99.9
Benzo[*a*]pyrene	ng	12.9	NQ (0.354)	97.7	0.356	97.2
CO	mg	32.0	NQ (0.223)	99.8	NQ (0.223)	99.6
Crotonaldehyde	µg	42.0	0.567	98.7	0.767	98.2
Formaldehyde	µg	54.10	3.29	93.9	3.51	93.5
Isoprene	µg	887	NQ (0.135)	>99.9	NQ (0.135)	>99.9
Nicotine	mg	2.02	0.462	77.1	0.365	81.9
NNK	ng	281	6.61	97.7	5.32	98.1
NNN	ng	263	24.7	90.6	19.1	92.8
Toluene	µg	131	NQ (0.204)	99.9	NQ (0.204)	99.9
			Average	96.4	**Average**	96.6
			Average excluding nicotine	97.6	**Average excluding nicotine**	97.4

[a]Values calculated using replicate data per analyte (N = 5) Abbreviations: THP = tobacco heating product; (T) = non-mentholated consumable variant. (M) = mentholated consumable variant; %Red[n] = reduction in concentration as a percentage of the level in 3R4F MSS. NNK = 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone; NNN=*N*-nitrosonornicotine; BDL = below detection limit; NQ = not quantified.

Table 8
3R4F reference cigarette mainstream smoke yields and THP1.0 emission yields for the nine TobReg priority constituents, presented on per-consumable and per-puff bases, with calculated reductions per puff.

Parameter	Unit	3R4F		THP1.0(T)			THP1.0 (M)		
		Mean per consumable	Mean per puff[a]	Mean per consumable	Mean per puff [a]	%Red[n] per puff	Mean per consumable	Mean per puff [a]	%Red[n] per puff
1,3-Butadiene	µg	108	11.1	BDL (0.029)	0.002	>99.9	BDL (0.029)	0.002	>99.9
Acetaldehyde	µg	2200	208	111	13.9	93.3	115	14.4	93.1
Acrolein	µg	157	14.9	2.22	0.278	98.1	2.50	0.313	97.9
Benzene	µg	78.6	8.08	NQ (0.056)	0.005	99.9	NQ (0.056)	0.005	99.9
Benzo[*a*]pyrene	ng	12.9	1.26	NQ (0.354)	0.037	97.1	0.356	0.045	96.5
CO	mg	32.0	2.99	NQ (0.223)	0.010	99.7	NQ (0.223)	0.015	99.5
Formaldehyde	µg	54.10	5.11	3.29	0.411	92.0	3.51	0.439	91.4
NNK	ng	281	26.6	6.61	0.826	96.9	5.32	0.665	97.5
NNN	ng	263	24.8	24.7	3.09	87.6	19.1	2.39	90.4
					Average	96.1		**Average**	96.2

[a] Values calculated using replicate data per analyte (N = 5) Abbreviations: TobReg = WHO World Health Organization Study Group on Tobacco Product Regulation; THP = tobacco heating product; (T) = non-mentholated consumable variant. (M) = mentholated consumable variant; %Red[n] = reduction in concentration as a percentage of level in 3R4F MSS. NNK = 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone; NNN=*N*-nitrosonornicotine; BDL = below detection limit; NQ = not quantified.

Table 9
3R4F reference cigarette mainstream smoke yields and THP1.0 emission yields for the 18 priority constituents in the US Food and Drug Administration abbreviated list, presented on per-consumable and per-puff bases, with calculated reductions per puff.

Parameter	Unit	3R4F		THP1.0 (T)			THP1.0 (M)		
		Mean per consumable	Mean per Puff[a]	Mean per consumable	Mean per puff[a]	%Red[n] per puff	Mean per consumable	Mean per puff[a]	%Red[n] per puff
1,3-Butadiene	µg	108	11.1	BDL (0.029)	0.002	>99.9	BDL (0.029)	0.002	>99.9
1-Aminonaphthalene	ng	17.6	1.61	NQ (0.027)	0.003	99.8	NQ (0.027)	0.003	99.8
2-Aminonaphthalene	ng	13.2	1.20	NQ (0.012)	0.001	>99.9	BDL (0.004)	4.00E-04	>99.9
4-Aminobiphenyl	ng	2.29	0.210	NQ (0.005)	0.001	99.7	NQ (0.005)	2.50E-04	99.9
Acetaldehyde	µg	2200	208	111	13.9	93.3	115	14.4	93.1
Acrolein	µg	157	14.9	2.22	0.278	98.1	2.50	0.313	97.9
Acrylonitrile	µg	19.5	2.00	BDL (0.032)	0.002	99.9	BDL (0.032)	0.002	99.9
Ammonia	µg	32.5	2.97	4.01	0.502	83.1	5.01	0.627	78.9
Benzene	µg	78.6	8.08	NQ (0.056)	0.005	99.9	NQ (0.056)	0.005	99.9
Benzo[*a*]pyrene	ng	12.9	1.26	NQ (0.354)	0.037	97.1	0.356	0.045	96.5
CO	mg	32.0	2.99	NQ (0.223)	0.010	99.7	NQ (0.223)	0.015	99.5
Crotonaldehyde	µg	42.0	3.96	0.567	0.071	98.2	0.767	0.096	97.6
Formaldehyde	µg	54.10	5.11	3.29	0.411	92.0	3.51	0.439	91.4
Isoprene	µg	887	91.2	NQ (0.135)	0.008	>99.9	NQ (0.135)	0.009	>99.9
Nicotine	mg	2.02	0.185	0.462	0.058	68.7	0.365	0.046	75.3
NNK	ng	281	26.6	6.61	0.826	96.9	5.32	0.665	97.5
NNN	ng	263	24.8	24.7	3.09	87.6	19.1	2.39	90.4
Toluene	µg	131	13.5	NQ (0.204)	0.022	99.8	NQ (0.204)	0.017	99.9
					Average	95.2		**Average**	95.4
					Average excluding Nicotine	96.8		**Average excluding Nicotine**	96.6

[a] Values calculated using replicate data per analyte (N = 5) Abbreviations: THP = tobacco heating product; (T) = non-mentholated consumable variant. (M) = mentholated consumable variant; %Red[n] = reduction in concentration as a percentage of level in 3R4F MSS. NNK = 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone; NNN=*N*-nitrosonornicotine; BDL = below detection limit; NQ = not quantified.

Tobacco Product Regulation list of nine toxicants prioritised for mandatory reduction in cigarette smoke and the 18 constituents of the US Food and Drug Administration abbreviated HPHC reporting list. For further illustration, Fig. 2 compares the relative abundances of 37 substances previously reported by Schaller et al. (2016) between THP1.0 emissions and 3R4F MSS.

For the 102 THP1.0 determinands for which numerical data were obtained, comparison of their concentrations in emissions of THP1.0 with those in 3R4F MSS per consumable demonstrated an overall average reduction of >95%. Comparisons were made without subtraction of air/method blank values and by using the Health Canada intense 55 ml, 2s, 30 s smoking regime, which generates higher constituent emissions than the ISO regime. The ISO regime is regarded by many as the low end of exposure and the Health Canada intense regime as closer to the maximum (Baker, 2002).

Data for 24 measurands (Table 3) were excluded from the reduction calculations because their concentrations were below the limits of quantification in THP1.0 emissions, 3R4F MSS or both. The concentrations of seven measurands – chromium, propylene glycol, glycidol, glycerol, *N*-nitrosodiethanolamine, acetoin and methylglyoxal – were greater in emissions from THP1.0 than in 3R4F MSS. Of these, three are attributable to intentional chemical modifications of THP1.0 (i.e., the inclusion of propylene glycol and glycerol in the consumable) and the remainder to their presence at levels close to the limit of quantification. Furthermore, for several substances, the results for samples were similar to the blank values.

Table 4 demonstrates the importance of measuring the background levels of the target substances in laboratory air or reagents, as discussed by Margham et al. (2016) for e-cigarette aerosol measurements, in order to place the reported yields in context. For most substances, the values from both THP and cigarette blank measurements were at or below the limit of quantification or detection of the analytical methods (113 of 126 for one or both measurements). Measured values were reported for iron, pyridine, five polyaromatic hydrocarbons, *o*-toluidine, formaldehyde, acetaldehyde and 2,3-butanedione. While the contribution of laboratory air as a source of contamination is reduced for THP measurement because fewer puffs are taken (eight or 12 per consumable, with a total of 50 or 60 per determination) compared with e-cigarettes (200 in Margham et al. (2016)) it demonstrates that the low levels of substances in the emissions from products such as THP1.0 cannot be clearly evaluated without knowledge of their background levels.

For purposes of quality assurance, the concentrations of the same measurands observed in emissions from a commercial tobacco heating product, THS, were assessed and the observed results (Table 5) compared with values previously reported by Schaller et al., (2016). The comparability of results is further illustrated in Fig. 2, which presents data for the same substances as in Fig. 7 of Schaller et al. For the determination of water (and indirectly NFDPM) the present study employed methodology based on Health Canada T-115, whereas the data reported by Schaller et al. originated from the use of a separate method with in-holder extraction (Ghosh and Jeannet, 2014), which is understood to result in higher results for water and, thus, lower results for NFDPM. Otherwise, considering that products were sampled at different times and analysed in different laboratories, agreement between the observed and published values was acceptable and demonstrated the reliability of the measurements.

The aerosol chemistry data demonstrate that this mechanism of tobacco heating produces significantly lower levels of HPHCs than are present in MSS smoke. For some substances, the results were below the LOQ or LOD of the method, illustrating that some of the analytical methods, which were extended from methods for cigarette smoke, may have limited application for this new class of tobacco product, and would require refinement if lower LOQs and LODs were required. The impact of blank results also demonstrates the need to manage chemical background for some analytes when testing products similar to THP1.0.

Table 10
1R6F reference cigarette mainstream smoke yields and THP1.0 emission yields for 126 measurands, with calculated reductions for mean THP1.0 emission yields compared with 1R6F yields, on a per-consumable basis.

Parameter	Unit	1R6F		THP1.0(T)			THP1.0(M)		
		Mean ± SD	N	Mean ± SD	N	%Red[n] vs. 1R6F	Mean ± SD	N	%Red[n] vs. 1R6F
Puff count	/consumable	8.8 ± 0.3	5	8 ± 0	5		8 ± 0	5	
TPM	mg/consumable	45.5 ± 2.2	5	26.1 ± 1.1	5		25.3 ± 1.4	5	
Water	mg/consumable	14.4 ± 1.0	5	12.1 ± 1.1	5		10.7 ± 0.9	5	
Nicotine	mg/consumable	2.00 ± 0.08	5	0.462 ± 0.037	5	76.9	0.365 ± 0.021	5	81.8
NFDPM	mg/consumable	29.2 ± 1.5	5	13.6 ± 1.2	5	53.5	14.2 ± 1.3	5	51.3
CO	mg/consumable	29.4 ± 0.6	5	NQ (0.223)	5	99.7	NQ (0.223)	5	99.6
CO_2	mg/consumable	72.4 ± 1.5	5	2.05 ± 0.10	5	97.2	1.99 ± 0.08	5	97.3
Ammonia	µg/consumable	34.7 ± 2.0	5	4.01 ± 0.99	5	88.4	5.02 ± 0.49	5	85.5
Hydrogen Cyanide	µg/consumable	332 ± 43	5	BDL (0.525)	5	99.9	NQ (1.75)	5	99.8
Mercury	ng/consumable	3.89 ± 0.32	5	1.28 ± 0.13	5	67.0	1.31 ± 0.12	5	66.3
Cadmium	ng/consumable	88.8 ± 1.9	5	BDL (0.162)	5	99.9	BDL (0.162)	5	99.9
Lead	ng/consumable	28.1 ± 0.6	5	11.6 ± 8.7	5	58.6	9.74 ± 6.14	5	65.3
Chromium	ng/consumable	NQ (4.51)	5	4.34 ± 1.14	5	−27.2	4.06 ± 0.15	5	−18.9
Nickel	ng/consumable	NQ (9.49)	5	NQ (0.878)	5	NC	NQ (0.878)	5	NC
Arsenic	ng/consumable	7.57 ± 0.27	5	NQ (0.576)	5	94.3	NQ (0.576)	5	95.1
Selenium	ng/consumable	NQ (2.63)	5	NQ (0.731)	5	NC	NQ (0.731)	5	NC
Copper	ng/consumable	30.6 ± 2.0	5	NQ (2.19)	5	93.1	4.43 ± 3.18	5	85.5
Cobalt	ng/consumable	BDL (0.893)	5	NQ (0.878)	5	NC	NQ (0.878)	5	NC
Beryllium	ng/consumable	BDL (0.936)	5	BDL (0.024)	5	NC	BDL (0.024)	5	NC
Iron	ng/consumable	35.5 ± 4.7	5	19.3 ± 5.4	5	45.7	22.1 ± 6.1	5	37.7
Zinc	ng/consumable	336 ± 8	5	21.5 ± 15.7	5	93.6	20.1 ± 7.8	5	94.0
Tin	ng/consumable	BDL (6.04)	5	NQ (0.876)	5	NC	NQ (0.876)	5	NC
NO	µg/consumable	357 ± 24	5	9.60 ± 0.79	5	97.3	8.61 ± 0.86	5	97.6
NO_x	µg/consumable	405 ± 26	5	12.9 ± 0.8	5	96.8	11.4 ± 0.8	5	97.2
Pyridine	µg/consumable	30.4 ± 2.4	5	2.21 ± 0.29	5	92.7	1.55 ± 0.25	5	94.9
Quinoline	µg/consumable	0.427 ± 0.009	5	NQ (0.011)	5	98.6	BDL (0.003)	5	99.6
Styrene	µg/consumable	14.8 ± 0.9	5	NQ (0.039)	5	99.8	NQ (0.039)	5	99.8
Nitrobenzene	µg/consumable	BDL (0.038)	5	BDL (0.011)	5	NC	BDL (0.011)	5	NC
Benzo(b)furan	µg/consumable	0.705 ± 0.034	5	NQ (0.016)	5	98.5	NQ (0.016)	5	98.5
Hydroquinone	µg/consumable	88.7 ± 6.2	5	0.347 ± 0.035	5	99.6	0.403 ± 0.033	5	99.5
Resorcinol	µg/consumable	1.80 ± 0.15	5	BDL (0.016)	5	99.6	BDL (0.016)	5	99.6
Catechol	µg/consumable	91.8 ± 5.3	5	3.11 ± 0.49	5	96.6	3.37 ± 0.17	5	96.3
Phenol	µg/consumable	12.5 ± 0.6	5	0.174 ± 0.022	5	98.6	0.116 ± 0.017	5	99.1
p-Cresol	µg/consumable	7.77 ± 0.41	5	BDL (0.010)	5	99.9	BDL (0.010)	5	99.9
m-Cresol	µg/consumable	2.98 ± 0.07	5	NQ (0.019)	5	99.6	NQ (0.019)	5	99.6
o-Cresol	µg/consumable	3.12 ± 0.13	5	NQ (0.026)	5	99.5	NQ (0.026)	5	99.6
Propylene Glycol	mg/consumable	0.410 ± 0.039	5	0.390 ± 0.023	5	4.78	0.206 ± 0.014	5	49.9
Ethylene Glycol	mg/consumable	0.038 ± 0.002	5	0.011 ± 0.000	5	71.1	0.008 ± 0.001	5	79.1
Diethylene Glycol	mg/consumable	BDL (0.004)	5	BDL (0.002)	5	NC	BDL (0.002)	5	NC
Glycidol	mg/consumable	NQ (0.006)	5	0.044 ± 0.003	5	−773	0.040 ± 0.004	5	−705
Glycerol	mg/consumable	1.36 ± 0.05	5	3.02 ± 0.26	5	−122	2.38 ± 0.21	5	−74.6
Naphthalene	ng/consumable	1047 ± 76	5	2.2 ± 0.42	5	99.8	2.90 ± 0.34	5	99.7
Pyrene	ng/consumable	68.4 ± 10.3	5	8.97 ± 0.82	5	86.9	10.3 ± 0.7	5	85.0
Benzo[*a*]anthracene	ng/consumable	21.4 ± 3.2	5	1.54 ± 0.11	5	92.8	1.58 ± 0.09	5	92.6
Chrysene	ng/consumable	29.8 ± 5.0	5	2.61 ± 0.27	5	91.2	2.64 ± 0.20	5	91.1
Benzo[*a*]pyrene	ng/consumable	11.4 ± 1.7	5	NQ (0.354)	5	97.4	0.356 ± 0.079	5	96.9
Indeno(1,2,3-*cd*)pyrene	ng/consumable	3.73 ± 0.52	5	NQ (0.337)	5	96.8	NQ (0.337)	5	95.9
Benzo[*c*]phenanthrene	ng/consumable	8.31 ± 1.40	5	0.874 ± 0.171	5	89.5	0.710 ± 0.055	5	91.5
Cyclopenta[*c,d*]pyrene	ng/consumable	6.40 ± 1.09	5	0.515 ± 0.036	5	91.9	0.534 ± 0.049	5	91.6
Benzo[*j*]aceanthrylene	ng/consumable	2.09 ± 0.30	5	BDL (0.104)	5	97.5	BDL (0.104)	5	97.5
1,3-Butadiene	µg/consumable	114 ± 4	5	BDL (0.029)	5	>99.9	BDL (0.029)	5	>99.9
Isoprene	µg/consumable	859 ± 46	5	NQ (0.135)	5	>99.9	NQ (0.135)	5	>99.9
Acrylonitrile	µg/consumable	18.5 ± 1.9	5	BDL (0.032)	5	99.9	BDL (0.032)	5	99.9
Benzene	µg/consumable	76.0 ± 5.8	5	NQ (0.056)	5	>99.9	NQ (0.056)	5	>99.9
Toluene	µg/consumable	116 ± 9	5	NQ (0.204)	5	99.8	NQ (0.204)	5	99.9
Ethylbenzene	µg/consumable	11.9 ± 1.0	5	NQ (0.048)	5	99.8	NQ (0.048)	5	99.8
Ethylene Oxide	µg/consumable	17.2 ± 0.9	5	BDL (0.036)	5	99.9	BDL (0.036)	5	99.9
Vinyl Chloride	ng/consumable	109 ± 19	5	BDL (0.657)	5	99.7	BDL (0.657)	5	99.7
Propylene Oxide	ng/consumable	1692 ± 232	5	BDL (15.6)	5	99.5	BDL (15.6)	5	99.5
Furan	µg/consumable	59.9 ± 5.9	5	1.16 ± 0.01	5	98.1	1.17 ± 0.06	5	98.1
Vinyl Acetate	ng/consumable	614 ± 54	5	BDL (11.0)	5	99.1	BDL (11.0)	5	99.1
Nitromethane	ng/consumable	555 ± 57	5	42.4 ± 1.5	5	92.4	38.1 ± 1.1	5	93.1
2-Nitropropane	ng/consumable	54.0 ± 9.7	5	BDL (1.45)	5	98.7	BDL (1.45)	5	98.7
5-Methylchrysene	ng/consumable	0.601 ± 0.105	5	BDL (0.028)	5	97.7	BDL (0.028)	5	97.7
Benzo[*b*]fluoranthene	ng/consumable	10.6 ± 1.4	5	0.548 ± 0.091	5	94.8	0.606 ± 0.091	5	94.3

(*continued on next page*)

Table 10 (*continued*)

Parameter	Unit	1R6F		THP1.0(T)			THP1.0(M)		
		Mean ± SD	N	Mean ± SD	N	%Red[n] vs. 1R6F	Mean ± SD	N	%Red[n] vs. 1R6F
Benzo[*k*]fluoranthene	ng/consumable	3.10 ± 0.43	5	0.255 ± 0.046	5	91.8	0.290 ± 0.060	5	90.7
Dibenz[*a,h*]anthracene	ng/consumable	0.892 ± 0.086	5	BDL (0.046)	5	95.7	NQ (0.154)	5	94.0
Dibenz[*a,l*]pyrene	ng/consumable	BDL (0.423)	5	BDL (0.254)	5	NC	BDL (0.254)	5	NC
Dibenz[*a,e*]pyrene	ng/consumable	NQ (0.696)	5	BDL (0.125)	5	NC	BDL (0.125)	5	NC
Dibenz[*a,i*]pyrene	ng/consumable	1.47 ± 0.09	5	BDL (0.132)	5	95.5	BDL (0.132)	5	95.5
Dibenz[*a,h*]pyrene	ng/consumable	BDL (0.236)	5	BDL (0.141)	5	NC	BDL (0.141)	5	94.0
1-Aminonaphthalene	ng/consumable	17.2 ± 0.6	5	NQ (0.027)	5	99.8	NQ (0.027)	5	99.9
2-Aminonaphthalene	ng/consumable	11.8 ± 0.9	5	NQ (0.012)	5	>99.9	BDL (0.004)	5	>99.9
3-Aminobiphenyl	ng/consumable	3.07 ± 0.25	5	NQ (0.004)	5	>99.9	BDL (0.001)	5	>99.9
4-Aminobiphenyl	ng/consumable	1.91 ± 0.23	5	NQ (0.005)	5	99.8	NQ (0.005)	5	99.9
2,6-Dimethlyaniline	ng/consumable	7.13 ± 0.58	5	0.040 ± 0.004	5	99.4	0.029 ± 0.008	5	99.6
Benzidine	ng/consumable	BDL (0.010)	5	BDL (0.003)	5	NC	BDL (0.003)	5	NC
o-Anisidine	ng/consumable	4.00 ± 0.14	5	0.244 ± 0.031	5	93.9	0.153 ± 0.023	5	96.2
o-Toluidine	ng/consumable	84.6 ± 2.2	5	0.371 ± 0.045	5	99.6	0.310 ± 0.020	5	99.6
Nitrosonornicotine (NNN)	ng/consumable	191 ± 8	5	24.7 ± 2.5	5	87.0	19.1 ± 2.2	5	90.0
Nitrosoanatabine (NAT)	ng/consumable	246 ± 12	5	37.7 ± 3.4	5	84.7	32.8 ± 3.2	5	86.7
Nitrosoanabasine (NAB)	ng/consumable	21.3 ± 1.6	5	4.70 ± 0.39	5	77.9	4.05 ± 0.39	5	81.0
4-(*N*-Nitrosomethylamino)-1-(3-pyridyle)-1-butanone (NNK)	ng/consumable	208 ± 7	5	6.61 ± 0.86	5	96.8	5.32 ± 0.89	5	97.4
Acetamide	µg/consumable	14.0 ± 1.0	5	1.34 ± 0.05	5	90.4	1.15 ± 0.05	5	91.8
Acrylamide	µg/consumable	4.49 ± 0.34	5	1.04 ± 0.04	5	76.8	0.829 ± 0.039	5	81.5
Caffeic Acid	µg/consumable	BDL (1.19)	5	BDL (0.478)	5	NC	BDL (0.478)	5	NC
Ethyl Carbamate	ng/consumable	BDL (6.43)	5	BDL (1.93)	5	NC	BDL (1.93)	5	NC
IQ	ng/consumable	7.57 ± 1.06	5	BDL (0.164)	5	98.9	BDL (0.164)	5	98.2
Glu-P-2	ng/consumable	BDL (0.301)	5	BDL (0.120)	5	NC	BDL (0.120)	5	NC
Glu-P-1	ng/consumable	BDL (0.239)	5	BDL (0.095)	5	NC	BDL (0.095)	5	NC
PhIP	ng/consumable	BDL (0.365)	5	BDL (0.146)	5	NC	BDL (0.146)	5	NC
Trp-P-2	ng/consumable	8.53 ± 1.01	5	BDL (0.113)	5	99.3	BDL (0.113)	5	99.3
Aαc	ng/consumable	134 ± 14	5	NQ (0.443)	5	99.9	NQ (0.443)	5	99.9
Trp-P-1	ng/consumable	3.71 ± 0.42	5	BDL (0.098)	5	98.7	BDL (0.098)	5	98.7
MeAαC	ng/consumable	11.1 ± 1.6	5	BDL (0.115)	5	99.5	BDL (0.115)	5	99.5
Hydrazine	ng/consumable	NQ (12.2)	5	BDL (2.04)	5	NC	BDL (2.04)	5	NC
NDMA	ng/consumable	16.0 ± 1.5	5	BDL (0.178)	5	99.4	BDL (0.178)	5	99.4
NEMA	ng/consumable	BDL (0.509)	5	BDL (0.254)	5	NC	BDL (0.254)	5	NC
NDEA	ng/consumable	BDL (0.617)	5	BDL (0.308)	5	NC	BDL (0.308)	5	NC
NDiPA	ng/consumable	BDL (0.546)	5	BDL (0.273)	5	NC	BDL (0.273)	5	NC
NDPA	ng/consumable	BDL (0.150)	5	BDL (0.075)	5	NC	BDL (0.075)	5	NC
NDBA	ng/consumable	NQ (1.11)	5	NQ (0.553)	5	NC	BDL (0.166)	5	NC
NPIP	ng/consumable	BDL (0.172)	5	BDL (0.086)	5	NC	BDL (0.086)	5	NC
NPYR	ng/consumable	15.9 ± 1.2	5	BDL (0.198)	5	99.4	BDL (0.198)	5	99.4
NMOR	ng/consumable	BDL (0.550)	5	BDL (0.275)	5	NC	BDL (0.275)	5	NC
NDELA	ng/consumable	NQ (0.283)	5	0.576 ± 0.244	5	−110	0.585 ± 0.234	5	−113
Nornicotine	ng/consumable	21002 ± 1323	5	NQ (47.6)	5	99.5	NQ (47.6)	5	99.4
Anatabine	ng/consumable	5719 ± 298	5	1157 ± 123	5	79.8	1266 ± 44	5	77.9
Anabasine	ng/consumable	978 ± 83	5	408 ± 50	5	58.3	408 ± 53	5	58.2
Myosmine	ng/consumable	13201 ± 562	5	459 ± 36	5	96.5	500 ± 71	5	96.2
Nicotine-*N*-Oxide	ng/consumable	NQ (969)	5	BDL (174)	5	NC	BDL (174)	5	NC
Cotinine	ng/consumable	13456 ± 581	5	298 ± 43	5	97.8	313 ± 15	5	97.7
β-Nicotyrine	ng/consumable	7199 ± 508	5	NQ (127)	5	98.9	NQ (127)	5	98.9
Formaldehyde	µg/consumable	68.4 ± 3.9	5	3.29 ± 0.30	5	95.2	3.51 ± 0.54	5	94.9
Acetaldehyde	µg/consumable	1859 ± 169	5	111 ± 8	5	94.0	115 ± 11	5	93.8
Acetone	µg/consumable	520 ± 42	5	5.97 ± 0.66	5	98.9	6.62 ± 0.51	5	98.7
Propionaldehyde	µg/consumable	116 ± 13	5	5.31 ± 0.15	5	95.4	5.66 ± 0.57	5	95.1
Acrolein	µg/consumable	148 ± 22	5	2.22 ± 0.52	5	98.5	2.50 ± 0.11	5	98.3
Isobutyraldehyde	µg/consumable	38.8 ± 4.8	5	9.78 ± 0.46	5	74.8	9.53 ± 1.11	5	75.4
Methyl Ethyl Ketone	µg/consumable	150 ± 14	5	1.53 ± 0.20	5	99.0	1.77 ± 0.37	5	98.8
n-Butyraldehyde	µg/consumable	12.7 ± 2.5	5	BDL (0.088)	5	99.7	BDL (0.088)	5	99.7
Crotonaldehyde	µg/consumable	39.5 ± 3.2	5	0.567 ± 0.232	5	98.6	0.768 ± 0.321	5	98.1
Acetoin	µg/consumable	6.10 ± 2.49	5	5.78 ± 1.33	5	5.28	5.94 ± 1.12	5	2.59
Glyoxal	µg/consumable	12.1 ± 1.5	5	BDL (0.063)	5	99.7	BDL (0.063)	5	99.7
Methylglyoxal	µg/consumable	33.3 ± 2.5	5	26.4 ± 2.4	5	20.8	27.7 ± 2.7	5	16.8
2,3-Butanedione	µg/consumable	209 ± 17	5	38.0 ± 4.4	5	81.9	40.5 ± 3.3	5	80.7
2,3-Pentanedione	µg/consumable	31.9 ± 4.2	5	7.38 ± 1.07	5	76.9	7.94 ± 1.15	5	75.1
Allyl Alcohol	µg/consumable	11.6 ± 1.3	5	1.24 ± 0.12	5	89.3	1.40 ± 0.11	5	87.9

Abbreviations: THS = tobacco heating system; SD = standard deviation; %Red[n] = reduction in concentration as a percentage of level in 3R4F MSS. N = number of replicates tested; BDL = below detection limit; NQ = not quantified; NC = not calculated; NNN=*N*-nitrosonornicotine; NAT=*N*-nitrosoanatabine; NAB=*N*-nitrosoanabasine; NNK = 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone; NDMA=*N*-nitrosodimethylamine; NEMA=*N*-nitrosomethylethylamine; NDEA=*N*-nitrosodiethylamine; NDiPA = *N*-nitrosodiisopropylamine; NDPA=*N*-nitrosodipropylamine; NDBA=*N*-nitrosodibutylamine; NPIP=*N*-nitrosopiperidine; NPYR=*N*-nitrosopyrrolidine; NMOR=*N*-nitrosomorpholine; NDELA=*N*-nitrosodiethanolamine. IQ = 2-Amino-3-methylimidazo[4,5-f]quinoline; Glu-P-2 = 2-Aminodipyrido[1,2-a:3′,2′-d]imidazole; Glu-P-1 = 2-Amino-6-methyldipyrido[1,2-a:3′,2′-d]imidazole; PhIP = 2-Amino-1-methyl-6-phenylimidazo[4,5-b]pyridine; Trp-P-2 = 1-Methyl-3-amino-5H-pyrido[4,3-b]indole; A-α-C = 2-Amino-9H-pyrido[2,3-b]indole; Trp-P-1 = 3-Amino-1,4-dimethyl-5H-pyrido[4,3-b]indole; MeA-α-C = 2-Amino-3-methyl)-9H-pyrido[2,3-b]indole.

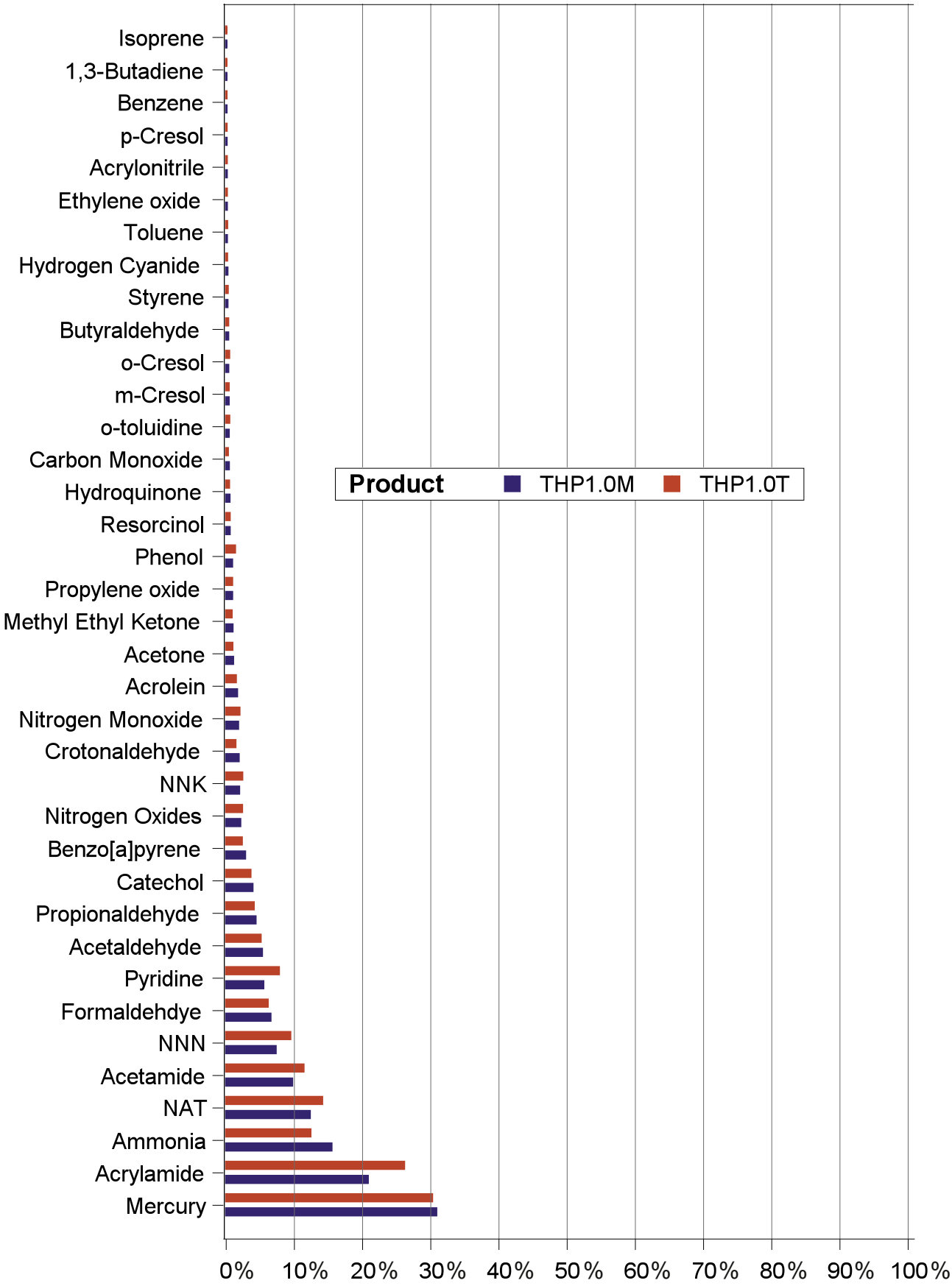

Fig. 2. Relative abundances in THP1.0 and 3R4F per consumable or cigarette.

5. Conclusions

In comparison to the University of Kentucky 3R4F Reference Cigarette (3R4F) the toxicant levels in THP1.0 emissions were significantly reduced across all chemical classes. For the nine toxicants proposed by the World Health Organization Study Group on Tobacco Product Regulation for mandatory reduction in cigarette emissions (Table 6), the mean reductions in THP1.0 aerosol were 90.6–99.9% per consumable, with an overall average reduction of 97.1%. For the abbreviated list of HPHCs of smoke specified by US Food and Drug Administration Tobacco Products Scientific Advisory Committee for reporting in cigarette smoke (excluding nicotine; Table 7), reductions in the aerosol of THP1.0 were 84.6–99.9% per consumable, with an overall average reduction of 97.5%. Generally, the toxicant profile of the THP1.0 aerosol was similar to that of THS, with relatively low levels of the targeted cigarette smoke toxicants.

Author declaration

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.yrtph.2017.10.006.

Transparency document

Transparency document related to this article can be found online at https://doi.org/10.1016/j.yrtph.2017.10.006.

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