

APPENDIX 5: PMI LIST OF ANALYTES AND CONSTITUENTS

PMI has been measuring constituents in tobacco smoke, as well as heated tobacco product aerosol, for many years. During that time, our list of identified constituents has grown as knowledge of smoke chemistry and toxicology has evolved. In May 2010, we developed a set of criteria for identifying relevant analytes for quantification specifically in the aerosols of heated tobacco products. The current PMI list includes in total 58 analytes and constituents, most of which are identified as harmful and potentially harmful constituents (HPHCs). The selection was performed according to the following criteria:

1. Constituents and analytes with existing International Organization for Standardization (ISO) testing methods;
2. Priority toxicants in tobacco smoke as identified by regulatory bodies, or proposed by cognizant authorities;
3. Constituents with established biomarkers of exposure;
4. Potentially harmful constituents which are predominately formed at temperatures below 400°C and are not included in Criteria 2. These were chosen on the basis of their classification by the International Agency for Research on Cancer (IARC) as Group 1 carcinogens (carcinogenic to humans) and their quantifiable presence in mainstream THS aerosol and cigarette smoke; and
5. Potentially harmful constituents which are predominately formed at temperatures above 400°C and are not included in Criteria 2. These were chosen on the basis of their Group 1 IARC classification and abundance in mainstream cigarette smoke.

Our list of HPHCs includes the following cigarette smoke constituents identified by relevant regulatory and/or public health bodies:

- All priority toxicants identified by Health Canada in its tobacco industry reporting regulations for cigarette smoke (“Health Canada list” below);
- All priority toxicants identified by the World Health Organization Study Group on Tobacco Product Regulation (“WHO TobReg list” below);
- Group 1 Carcinogens currently listed by the International Agency for Research on Cancer which are measurable in cigarette smoke (“IARC Group 1” below); and
- All HPHCs currently listed on the US Food and Drug Administration abbreviated list of “Harmful and Potentially Harmful Constituents in Tobacco Products and Tobacco Smoke” (“FDA Abbreviated list” below).

Criteria four and five are important because the THS is designed to heat tobacco to a temperature of not more than 300°C in order to prevent combustion of the tobacco, which typically occurs at temperatures of 400°C or higher. In addition to being indicators of potential toxicity of the aerosol, these HPHCs can also serve as indicators of combustion. However, it

is important to recognize that thermal degradation occurs across a wide range of temperatures. Therefore, even at temperatures not exceeding 300°C, the EHTP aerosol will contain some HPHCs that are formed predominantly at higher temperatures. Although, due to the lower temperatures, these HPHCs appear in very small amounts in the EHTP aerosol relative to the amounts found in cigarette smoke.

Table 1: PMI List of Analytes and Constituents.

Analyte / Constituent	ISO standard method	Health Canada list	WHO TobReg list	FDA Abbreviated list	IARC Group 1	Biomarker of exposure
Benzo(a)pyrene	✓	✓	✓	✓	✓	3-OHBaP in urine
Carbon monoxide (CO)	✓	✓	✓	✓		COHb in blood CO in exhalate
Nicotine	✓	✓	✓	✓		Nicotine in plasma Cotinine in plasma Nicotine equivalents in urine
Total particulate matter (TPM)	✓	✓				
Nicotine Free Dry Particulate Matter (NFDPM)	✓	✓				
Water	✓	✓				
1-Aminonaphthalene		✓	✓	✓		1-NA in urine
2-Aminonaphthalene (2-NA)		✓	✓	✓	✓	2-NA in urine
3-Aminobiphenyl		✓	✓			
4-Aminobiphenyl (4-ABP)		✓	✓	✓	✓	4-ABP in urine
Acetaldehyde		✓	✓	✓		
Acetone		✓	✓			
Acrylonitrile		✓	✓	✓		CEMA in urine

Analyte / Constituent	ISO standard method	Health Canada list	WHO TobReg list	FDA Abbreviated list	IARC Group 1	Biomarker of exposure
Acrolein		✓	✓	✓		3-HPMA in urine
Ammonia		✓	✓	✓		
1,3-Butadiene		✓	✓	✓	✓	MHBMA in urine
Benzene		✓	✓	✓	✓	S-PMA in urine
Butyraldehyde		✓	✓			
Catechol		✓	✓			
<i>m</i> -Cresol		✓	✓			
<i>p</i> -Cresol		✓	✓			
<i>o</i> -Cresol		✓	✓			
Crotonaldehyde		✓	✓	✓		HMPMA in urine
Formaldehyde		✓	✓	✓	✓	
Hydrogen Cyanide		✓	✓			
Hydroquinone		✓	✓			
Isoprene		✓	✓	✓		
Methyl ethyl ketone		✓				
Propionaldehyde		✓	✓			
Nitric oxide		✓				
N-Nitrosoanabasine (NAB)		✓	✓			
N-Nitrosoanatabine (NAT)		✓	✓			
4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)		✓	✓	✓	✓	Total NNAL in urine
N-Nitrosornicotine (NNN)		✓	✓	✓	✓	Total NNN in urine
Nitrogen oxides		✓	✓			
Phenol		✓	✓			
Pyridine		✓	✓			
Quinoline		✓	✓			
Resorcinol		✓	✓			
Styrene		✓				

This appendix to the Philip Morris Products S.A. Technical & Scientific Dossier For the Electrically Heated Tobacco Product (EHTP) as part of the Tobacco Heating System (THS), Version 2.0, dated 27 May 2016, has been reformatted for publication on pmiscience.com.

Analyte / Constituent	ISO standard method	Health Canada list	WHO TobReg list	FDA Abbreviated list	IARC Group 1	Biomarker of exposure
Toluene		✓	✓	✓		S-BMA in urine
Arsenic		✓	✓		✓	
Cadmium		✓	✓		✓	
Chromium		✓			✓	
Lead		✓	✓			
Mercury		✓	✓			
Nickel		✓			✓	
Selenium		✓				
Pyrene						Total 1-OHP in urine
<i>o</i> -Toluidine (<i>o</i> -TOL)					✓	<i>o</i> -TOL in urine
Acrylamide						
Acetamide						
Propylene oxide						
Ethylene oxide					✓	HEMA in urine
Nitrobenzene						
Vinyl chloride					✓	
Dibenz(a,h)anthracene						
Benz(a)anthracene						

REFERENCES

Health Canada (2008). Tobacco Industry Reporting: Tobacco Reporting Regulations. Schedule 2.

International Agency for Research on Cancer (2015). Agents Classified by the IARC Monographs, Volumes 1–113.

US Food and Drug Administration (2012). Guidance for Industry – Reporting Harmful and Potentially Harmful Constituents in Tobacco Products and Tobacco Smoke Under Section 904(a)(3) of the Federal Food, Drug, and Cosmetic Act.

World Health Organization (2015). Report on the Scientific Basis of Tobacco Product Regulation: Fifth Report of a WHO Study Group. WHO Technical Report Series 989.