Implementation and validation of an analytical platform to assess the impact of tobacco products on indoor air quality

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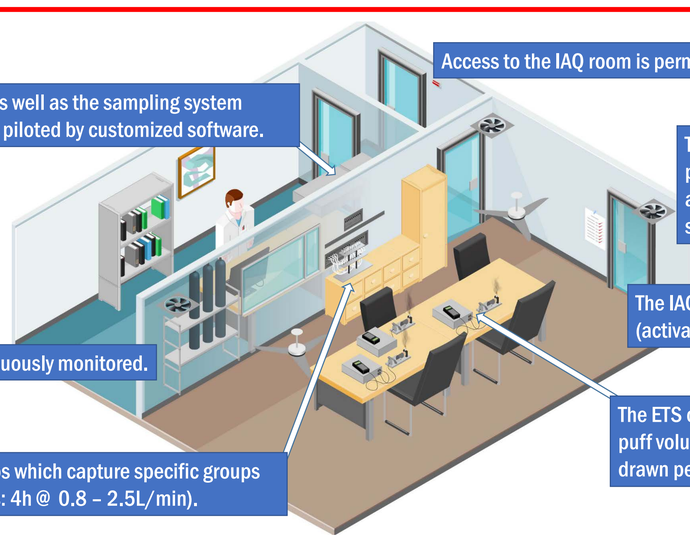
Introduction and Objectives

Health agencies worldwide have concluded that exposure to environmental tobacco smoke (ETS), causes diseases including lung cancer and heart disease in adult non-smokers [1]. Around 8,000 chemical compounds have been identified in tobacco smoke [2]. ETS is defined as a diluted mixture of exhaled mainstream smoke and sidestream smoke of cigarettes.

Studies in environmental controlled rooms have been used over past years to assess the impact of ETS on indoor air quality (IAQ). As new smoking products (MRTPs) are developed, it is important to determine their impact on air quality when used indoors. Before such an assessment can take place it is essential that the analytical methods used to evaluate indoor air quality are validated and shown to be fit for their intended purpose. For this assessment, a purpose-built environmentally controlled room (IAQ room) was used and selected analytical methods, representing eighteen analytes, were validated.

Taking into account that the validated methods will be used for the comparative assessment of the environmental aerosol (EA) of THS 2.2 (a new heat-not-burn tobacco product), ETS of Marlboro Gold cigarettes and background ambient air (BKG), these three different matrices were considered for validation. This approach was particularly relevant since the impact of the EA produced by use of the THS 2.2 on the methods' performances was not known. Validation of the offline methods (carbonyls, VOCs, nicotine and 3-ethenylpyridine, solanesol, UVPM and FPM) was performed using accuracy profiles. This validation procedure [3] is a suitable tool to evaluate the capability of a method to quantify samples with a known accuracy and a fixed risk. It allows a visual representation of the methods' performances and, as such, serves as a reliable mean of comparison between matrices.
The aim of this study is to describe the validation results obtained with the objective of demonstrating that the performances of the methods are fit for their intended purpose, i.e. the comparative assessment of the EA of THS 2.2 and the ETS of cigarettes when used by adult smokers [5].

Facility & Analytical Methods



The technical room houses the online monitoring instrumentation (CO & NO/NO_x sensors) as well as the sampling system which is composed of 26 membrane pumps regulated with individual mass flow controllers piloted by customized software.

Access to the IAQ room is permitted via an airlock under positive pressure, which limits contaminations from other parts of the building.

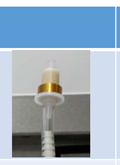
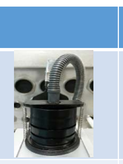
The ventilation rate can be regulated between 87 and 879 m^3/h, corresponding to 1.2 and 12.2 air changes per hour. The effective applied ventilation rate is determined by the injection of a marker (CO_2) in the IAQ room and its concentration decay is measured with a specific online sensor (X-Stream non-dispersive infrared sensor, Emerson).

The IAQ room is equipped with standard office furniture, an airtight ceiling and an air filtration system (activated charcoal & fine dust filter F_7 CH / fine dust filter F_9 /micro-particles filter E_{11}).

The temperature & pressure in the IAQ room can be controlled and the humidity is continuously monitored.

The ETS or EA samples were generated under the Health Canada machine-smoking regime (55 mL puff volume and a 2 s puff duration every 30 s) using 3 smoking machines. 10 and 12 puffs were drawn per cigarette and THS 2.2 tobacco stick, respectively.

The air from the IAQ room is drawn through different types of traps which capture specific groups of analytes that need to be measured (sampling duration & flows: 4h @ 0.8 – 2.5L/min).

	Carbonyls	VOCs	Nicotine & 3-ethenylpyridine	Respirable suspended particles	Online mesurements
Analytes (ISTD)	Formaldehyde (acetone-d_6) Acetaldehyde (acetone-d_6) Acrolein (acetone-d_6) Crotonaldehyde (acetone-d_6) 	1,3-Butadiene (1,3-butadiene-d_6) Isoprene (toluene-d_8) Benzene (benzene-d_6) Acrylonitrile (acrylonitrile-d_3) Toluene (toluene-d_8) 	Nicotine (quinoline) 3-Ethenylpyridine (quinoline) 	UVPM FPM Solanesol RSP gravimetry 	NO NO_x CO  -a-  -b-
Sampling	DNPH-coated silica short-body cartridges (Waters).	Coconut charcoal tube (Anasorb CSC, SKC).	XAD-4 resin (SKC).	PTFE filter of 1 µm pore size and 37 mm diameter (SKC) after filtration through Cyclon (SKC) to collect particles <4µm.	NO/NO_x: internal pump CO: external pump.
Sample preparation	Elution of cartridge with acetonitrile.	30 min extraction of combined sorbent sections on orbital shaker with dichloromethane containing ISTD mix.	15 min extraction of combined sorbent sections in ultrasonic bath with ethyl acetate containing 0.01% triethylamine and ISTD.	After weighting, 60 min extraction of pad on orbital shaker with methanol.	Online measurement, acquisition frequency: 1 data point/5 sec
Analytical method	2 µL injection in HPLC-ESI-MS/MS (Prominence, Shimadzu - 5500 QQQ, ABSciex). Halo RP-C18 Fused-Core 100 x 3.0 mm, 2.7 µm (Advanced Materials Technology). Isocratic separation using 90% acetonitrile/water/tetrahydrofuran/isopropanol (30:59:10:1 v/v/v/v) and 10% acetonitrile at 0.65 mL/min.	1 µL split injection (1:20) in GC-EI-MS (QP 2010 ultra, Shimadzu). Constant velocity mode (36.1 cm/s). 60m x 0.25mm x 0.50µm DB-WAXETR (Agilent). 40°C (2.5min) - 30°C/min-240°C (13 min).	1 µL splitless injection in GC-EI-MS (QP 2010 ultra, Shimadzu). Constant velocity mode (51.3 cm/s). 30 m x 0.25 mm x 1.0 µm ZB-5MS (Phenomenex). 50°C (1min) - 5°C/min-120°C (0 min)-10°C/min-190°C (0 min)-60°C/min-290°C (2.4 min).	RSP : weight determined gravimetrically using micro-balance (XP2U, Mettler Toledo). FPM/UVPM/solanesol : 40/100/100µL injection in HPLC-UV-Fluo (Acquity, Waters). Stainless steel capillary (100 cm x 0.5 mm ID) for FPM/UVPM and Acquity BEH C18 (100 x 3 mm ID mm, 1.7 µm particle size) for solanesol. Isocratic separation: 100% methanol at 0.4/0.4/0.6 mL/min.	NO and NO_x : chemiluminescence detector (APNA 370, Horiba, -a-). CO : non-dispersive infrared sensor (X-Stream, Emerson, -b-) at 2174-2083 cm^{-1} for CO. Results expression: Evolution graph & average value over a period of 4h.
Method adapted from	ISO 16000-3:2011	NIOSH methods 1024 and 1051	ISO 18145:2003	ISO 15593:2001 & 18144:2003	
Adaptations from reference method and remarks	• Detection by MS/MS instead of UV • Chromatographic conditions	• Combination of analytes from different methods and addition of isoprene and acrylonitrile • Extraction solvent • Chromatographic conditions	• MS detection instead of FID • Chromatographic conditions	• Chromatographic conditions	• Water interferences with CO detection minimized using 2 impingers containing activated silica gel.

Results

		Working range		Quantification results					
Chemical Class	Analyte	LWRL	UWRL	BKG		EA of THS 2.2		ETS of Marlboro Gold	
		[µg/m^3]	[µg/m^3]	Average [µg/m^3]	CV per series [%]	Average [µg/m^3]	CV per series [%]	Average [µg/m^3]	CV per series [%]
Carbonyls	Formaldehyde	4.54	138	7.36-9.44	2.5-9.4	7.51-9.38	2.8-11.4	33.1-49.6	1.8-6.7
	Acetaldehyde	1.86	189	2.08-2.97	1.4-12.1	8.71-9-96	1.3-8.1	50.1-68.6	2.3-4.7
	Acrolein	0.15	24.1	<0.15-0.202	32.8	<0.15-0.171	3.5-16.9	6.13-7.89	1.0-3.0
	Crotonaldehyde	0.18	28.6	<0.18-0.291	4.0-20.5	<0.18	-	2.09-2.14	1.0-3.8
VOC	1,3-Butadiene	1.13	675	<1.13	-	<1.13	-	9.39-11.1	4.0-7.0
	Isoprene	0.475	221	<0.475-0.650	5.6	<0.475-0.517	5.7	61.6-69.5	1.9-7.6
	Benzene	0.175	19.3	0.375-0.888	5.9-14.7	0.658-1.16	5.6-7.4	5.88-7.04	2.4-9.1
	Acrylonitrile	0.267	160	<0.267	-	<0.267	-	2.12-2.33	1.2-4.1
	Toluene	0.775	78.2	1.14-1.67	5.6-14.5	2.04-2.50	5.6-7.7	13.4-15.0	4.1-19.7
Nicotine & 3EP	Nicotine	0.126	49.6	0.183-0.187	7.4-11.7	4.76-6.85	0.4-4.4	45.9-54.4	2.2-4.8
	3-Ethenylpyridine	0.242	19.1	<0.242	-	<0.242	-	8.13-10.1	2.2-4.3
RSP	UVPM	0.795	63.7	<0.795	-	<0.795	-	23.9-24.7	1.8-4..5
	FPM	0.064	34.8	<0.064	-	<0.064	-	5.83-6.05	1.6-3.2
	Solanesol	0.469	29.1	<0.469	-	<0.469 -0.477	7.27-26.7	4.23-4.95	1.1-2.6
	RSP gravimetry	14.5	3330	<14.5	-	<14.5	-	136-168	4.2-14.7
Gases	NO [PPM]	0.00241	1	0.0130	64	0.0071	73	0.0424	8
	NO_x [PPM]	0.00235	1	0.0195	44	0.0121	54	0.0513	8
	CO [PPM]	0.915	10	<0.915	-	<0.915	-	1.25	3

Table 1: Working ranges for analytical methods and quantification results obtained using smoking machines

The accuracy profiles for the offline methods were built the following way :

- generation of air samples under Residential I environmental conditions (121 m^3/h ventilation rate and 3 cig/h [4])
- liquid extraction of individual traps
- homogenization of extracts
- spiking of aliquots with analytes solutions of known concentrations
- calculation of trueness (%-recovery, continuous red line) and precision (80% β-expectation tolerance interval, continuous blue line) for each spiking concentration level
- computation of accuracy profiles for each matrix type (see Fig. 1-3 for examples)
- calculation of working ranges at ±25% acceptance limits (see Table 1), defined between Lower Working Range Limit (LWRL, β-expectation tolerance interval crosses acceptance limits) and Upper Working Range Limit (UWRL, highest tested concentration included in acceptance limits).

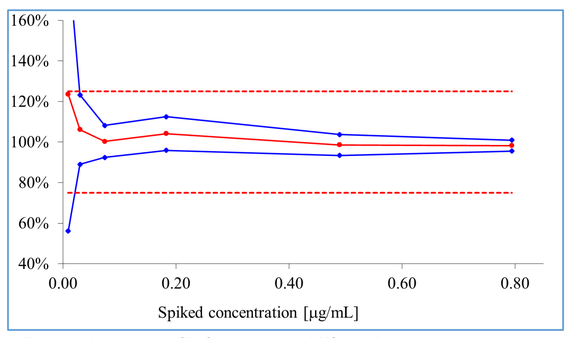


Figure 1: Accuracy profile for benzene in BKG matrix

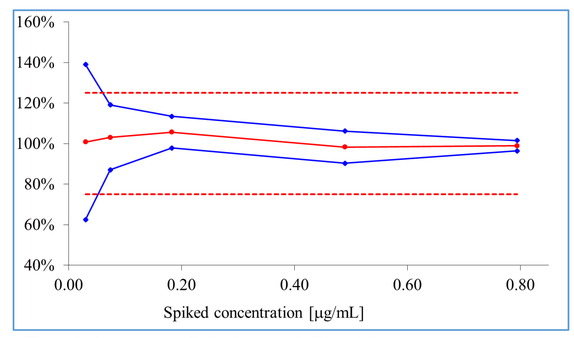


Figure 2: Accuracy profile for benzene in EA matrix

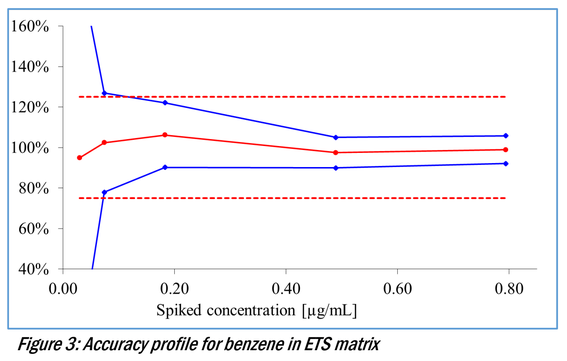


Figure 3: Accuracy profile for benzene in ETS matrix

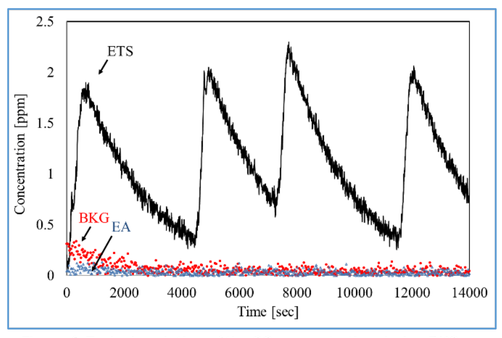


Figure 4: Typical evolution of the CO concentration during BKG, EA and ETS sampling sessions

Considering the low endogenous content of the different types of air samples to be analyzed, the accuracy profiles were expected to show a corresponding degree of similarity (limited matrix effects), and the validation results demonstrated this was the case. Additional validation parameters are described in [4] together with the validation strategy for the online (NO, NO_x and CO) and RSP gravimetry methods. A summary of the concentration ranges obtained in µg/m^3 for each matrix is shown in Table 1. The CV columns gives the lowest and highest coefficients of variation that were calculated for each series considered (when quantified above LWRL).

Conclusion

An IAQ room was built and selected methods required for the assessment of the environmental aerosol impact of a new heated tobacco product (THS 2.2) on indoor air quality were established and validated using the accuracy profile procedure. The validation results, obtained with smoking machines, demonstrated that the methods were fit-for-purpose with regard to their intended use and for the three matrices investigated. Indeed, the established methods' working ranges allowed to either quantify the analytes (±25% accuracy except for crotonaldehyde with ±40% accuracy) in the matrices of interest or, when the levels in EA were below the methods' working ranges, to measure reduction ranging from 76 to 99% when comparing the reporting limit to the analytes' concentrations in ETS. In addition, the environmental aerosol generated by THS 2.2 did not have any appreciable impact on the performances of the methods and the accuracy profiles obtained were generally similar to those of the other air samples at similar concentration ranges.

Abbreviations :
FPM: Particulate Matter detectable by Fluorescence
MRTPs: Modified Risk Tobacco Products
RSP: Respirable Suspended Particles
UVPM: Particulate Matter detectable by UV

Refererences :
[1] R.A. Jenkins, M.R. Guerin, B.A. Tomkins, The chemistry of environmental tobacco smoke: Composition and measurement, 2nd ed., Lewis (2000).
[2] A. Rodgman, T.A. Perfetti, The chemical components of tobacco and tobacco smoke, Second Ed. ed., CRC Press (2013).
[3] M. Feinberg, Validation of analytical methods based on accuracy profiles, Journal of Chromatography A 1158(1-2) (2007) 174-183.
[4] N. Mottier, M. Tharin, M.I. Mitova, E.G. Rouget & al., Validation of selected analytical methods using accuracy profiles to assess the impact of a Tobacco Heating System on indoor air quality, Talanta, in press.
[5] M.I. Mitova , A. Tricker, N. Mottier, E.G. Rouget, M. Tharin & al., Comparison of the impact of the Tobacco Heating System 2.2 and a cigarette on indoor air quality, Regulatory Toxicology and Pharmacology, in press.

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Competing Financial Interest

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