APPENDIX A3.2.1-23

VALIDATION SUMMARY – QUANTIFICATION OF 20 METALS IN AEROSOL BY ICP-MS

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1. OBJECTIVE

The purpose of this validation report is to describe the steps that have been undertaken and to present the results thereafter for the validation of the improved method for the quantification of 20 elements in aerosol by ICP-MS, on the instrument ICP-MS Agilent 7700 PMI ID 9817.

2. RESULTS SUMMARY

The aerosol collection and analytical methods were validated for the analysis of 20 elements (Aluminum (Al), Arsenic (As), Beryllium (Be), Cadmium (Cd), Calcium (Ca), Chromium (Cr), Cobalt (Co), Copper (Cu), Iron (Fe), Lead (Pb), Magnesium (Mg), Manganese (Mn), Molybdenum (Mo), Nickel (Ni), Selenium (Se), Strontium (Sr), Tin (Sn), Titanium (Ti), Tungsten (W), Zinc (Zn)) on a ICP-MS Agilent 7700 equipment (ID9817) using MassHunter software (version B.01.01) on 3R4F and P1 collected under Health Canada (HC) and ISO smoking regimes. The metals which are part of the PMI58 are Arsenic, Cadmium, Chromium, Lead, Nickel and Selenium. The scope of the method has been extended to 20 metals in order to cope with other needs related to product development.

Summarized results are depicted in Chapter 3, Table 2 to Table 23 . The method was shown to be selective, precise, linear and accurate over the range of concentration presented Table **1** and Table 4 to Table 23.

Selectivity was demonstrated for the 20 elements and internal standard in 3R4F and P1 matrices and in blank.

Linearity of the response function was demonstrated for the range of concentration tested using a linear regression with a weighing factor of 1/x applied for all elements under repeatability conditions and under intermediate precision conditions.

Instrumental limit of detection (LOD) and lower limit of quantification (LLOQ) were calculated based on the standard deviation of the lowest working standard solution (STD1) under intermediate precision conditions. LLOQ was found to be lower than the concentration of lowest calibration standard in the calibration curve for all elements. In addition, due to potential environmental contamination coming from the overall process

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(especially aerosol collection) for some elements, a limit of quantification for reporting is investigated. It is calculated statistically (removing outliers) from aerosol collection blanks obtained during the validation and corresponding to $LOQ_{reporting.}$

Instrumental repeatability was found to be good for all matrices. Due to some unquantifiable elements in matrices, the instrumental repeatability was assessed by injecting ten times the same homogenized aerosol treated spiked solution (same lowest spiking level as used for stability assessment). Coefficient of variation for instrumental repeatability for 3R4F varied between 0.8% and 3.7% for all elements except for beryllium (10.2%) and titanium (17.4%), and for P1 between 0.4% and 8.9% for all elements except for titanium (24%). These results are below the acceptance threshold and demonstrate that single analytical injection per smoking replicate is sufficient.

Repeatability limit for the analytical method was evaluated on homogenized aerosol treated spiked solution (due to some unquantifiable elements in matrices, three spiking levels were applied). To exclude aerosol collection variability, the same homogenized aerosol treated spiked solutions stored in fridge for stability assessment were diluted (dilution A and B for 3R4F and dilution B for P1) and analyzed at 4 different testing points (with a different standard preparation for each analysis). The coefficients of variation for the repeatability of the analytical method range between 0.53% and 11.97% for the lowest spiking level and between 0.41% and 4.84% for the other spiking levels for 3R4F matrix, and between 1.87% and 20.98% for the lowest spiking level and between 0.40% and 7.90% for the other spiking levels for P1 matrix. These results are below the acceptance threshold for all matrices.

Intermediate precision limit for the analytical method was evaluated on homogenized sample at three different spiking levels for each matrix (3R4F and P1) as described in the previous paragraph. The coefficients of variation for intermediate precision of the analytical method range between 1.19% and 15.67% for the lowest spiking level and between 0.87% and 6.44% for the other spiking levels for 3R4F matrix, and between 1.87% and 20.98% for the lowest spiking level and between 1.12% and 12.37% for the other spiking levels for P1 matrix. These results are below the acceptance threshold for all matrices.

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Repeatability limit for whole process at nominal content was assessed for 3R4F and P1 matrices under Health Canada and ISO smoking regimes according to study design. These validation parameter results include all process variability (aerosol collection variability, sample preparation and ICP-MS analysis). For 3R4F matrix collected under Health Canada and ISO smoking regimes, only 6 elements (Cu, Zn, As, Se, Cd and Pb) were quantified in all replicates and the maximum coefficient of variation for repeatability is 7.73% for Health Canada smoking regime and 20.66% for ISO smoking regime. For P1 matrix collected under Health Canada and ISO smoking regimes, only selenium was quantified in almost all replicates and the coefficient of variation for repeatability is 14.25% for Health Canada smoking regime and in eleven of the twelve replicates 18.43% for ISO smoking regime.

Intermediate precision limit for whole process at nominal content was assessed 3R4F and P1 under Health Canada and ISO smoking regimes, as described in previous paragraph. For 3R4F matrix collected under Health Canada and ISO smoking regimes, only 6 elements (Cu, Zn, As, Se, Cd and Pb) were quantified in all replicates and the maximum coefficient of variation for intermediate precision is 11.09% for Health Canada smoking regime and 22.93% for ISO smoking regime. For P1 matrix collected under Health Canada and ISO smoking regimes, only selenium was quantified in almost all replicates and the coefficient of variation for intermediate precision is 18.53% for Health Canada smoking regime and 18.43% for ISO smoking regime.

The nominal content measured during the validation for 3R4F under Health Canada smoking regime for quantifiable elements (Cu, Zn, As, Se, Cd, Pb) was compared to data generated during the same period as the validation but using the previous version of the method used. The quantification from the validation was found to be in line for cadmium and lead. A slight increase of concentration was observed for copper and zinc. An important increase of concentration was demonstrated for arsenic and selenium because the trapping efficiency of the previous aerosol collection method was incomplete and was corrected in the new method by the addition of a micro impinger containing 5mL of nitric acid 65% after the EP tube for the aerosol collection.

Results of the validation obtained for 3R4F were compared to data available in the document Analysis of Reference Cigarette Smoke Yield Data from 21 Laboratories for 28 Selected Analytes as a Guide to Selection of New CORESTA Recommended Methods. The

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nominal content for 3R4F obtained during the validation under Health Canada smoking regime was in line with the averages from the inter-laboratory's results.

Results of the validation obtained for 3R4F and P1 under Health Canada were compared to data from Labstat reported in the document Analysis of Philip Morris International THS 2.2 Aerosol from PMI science website. Six elements was analysed by Labstat (chromium, nickel, arsenic, selenium, cadmium and lead) For 3R4F, the validation results were in line with Labstat results except for cadmium (+30.0%) and Selenium (+27.2%). For P1, 5 elements out of 6 provided non quantifiable results. Quantifiable results were obtained for selenium, with an average value obtained during the validation presenting a %difference of -16.7% compared to Labstat.

Bias of the analytical method was evaluated for all matrices (3R4F and P1) spiked at 7 different concentration levels. Spikes were applied on homogenized aerosol diluted solution (dilution A and B). Percentage recoveries were calculated for each level. Working range limit was determined as the lowest and the uppermost level demonstrating satisfactory performance (recovery of analytical method being within acceptance limit). The lowest level being within acceptance limit corresponds to spiking level 1 or 2 and the uppermost level correspond to spiking level 7 for all elements in all matrices (3R4F and P1) except for tungsten. For tungsten the recoveries were out of range for all spiking level for dilution A and are within the acceptance limits from spiking level 4 (3R4F and P1) to spiking level 7 for dilution B.

The robustness evaluation for contamination of quartz EP tube and micro impinger by external environment demonstrated that quartz EP tube and micro impinger containing 5mL of nitric acid 65% can be stored up to 6 days in aerosol collection laboratory before the aerosol collection. The robustness evaluation for mineralization step demonstrated that in case of interruption of mineralization program, the mineralization can be restarted without impact on quantification.

As the accuracy and precision of results cannot be fully guaranteed for tungsten determination, it is recommended to report the tungsten as a semi-quantitative result. The method allows to provide information regarding the detection of the presence of tungsten in aerosol but does not allow to provide accurate results for this element.

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Internal standard stock solution and elements stock solution B were found to be stable up to 43 days in the fridge (T = 5 ± 3°C). The stability of elements stock solution A was not assessed during this validation and for this reason the solution shall not be kept after its preparation. Working calibration solutions were found to be stable up to 3 days in the fridge.

Sample aerosol treated solution (for 3R4F and P1) can be used for analysis for the determination of 20 elements after a storage duration up to 4 days in the fridge (semi quantitative determination for tungsten). Sample aerosol treated solutions can be used for analysis for the determination of 19 elements (except Mo and semi-quantitative determination for tungsten) after a storage duration up to 21 days in the fridge. Sample aerosol treated solutions can be used for analysis for the determination of molybdenum provided that the measured value of Mo is either below $LOQ_{reporting}$ or higher than 0.86ng/item after a storage duration between 4 and 21 days in the fridge.

Measurement solutions in ICP-vial on autosampler at room temperature were found to be stable for 24h for 3R4F and P1 matrices and for standard solutions for all elements except tungsten which allows a maximum batch length of 24 h or possible sample re-injection performed within 24 h (semi quantitative determination for tungsten).

3. CONCLUSION

The aerosol collection and analytical methods have been validated for the analysis of 20 elements (Aluminum (Al), Arsenic (As), Beryllium (Be), Cadmium (Cd), Calcium (Ca), Chromium (Cr), Cobalt (Co), Copper (Cu), Iron (Fe), Lead (Pb), Magnesium (Mg), Manganese (Mn), Molybdenum (Mo), Nickel (Ni), Selenium (Se), Strontium (Sr), Tin (Sn), Titanium (Ti), Tungsten (W), Zinc (Zn)) on a ICP-MS Agilent 7700 equipment (ID9817) using MassHunter software (version B.01.01) on 3R4F and P1 collected under Health Canada and ISO smoking regimes and P4 collecting under CORESTA smoking regime.

As the accuracy and precision of results cannot be fully guaranteed for tungsten determination, it is recommended to report the tungsten as a semi-quantitative result. The method allows to provide information regarding the detection of the presence of tungsten in aerosol but does not allow to provide accurate results for this element.

The method was shown to be selective, precise, linear and accurate over the ranges of concentration presented in Table 1 using a linear regression model and weighting factor 1/x (except for tungsten).

The analytical method was shown to be robust for the analyses of elements and none of the tested parameters was found to be critical.

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Recoveries, coefficient of variations of the repeatability and intermediate precision of the analytical method for the homogenized aerosol extracts were found within the defined limits for 3R4F and P1 matrices for all elements except for tungsten.

Nominal content of validation for 3R4F under Health Canada smoking regime for quantifiable elements (Cu, Zn, As, Se, Cd and Pb) was compared to data generated during the same period as the validation using the previous version of the method used. The quantification from the validation was found to be in line for cadmium and lead. A slight increase of concentration was observed for copper and zinc. An important increase of concentration was demonstrated for arsenic and selenium due to the addition of a micro impinger containing 5mL of nitric acid 65% after the EP tube for the aerosol collection.

Results of the validation obtained for 3R4F were compared to data available in the document Analysis of Reference Cigarette Smoke Yield Data from 21 Laboratories for 28 Selected Analytes as a Guide to Selection of New CORESTA Recommended Methods. The nominal content for 3R4F obtained during the validation under Health Canada smoking regime was in line with the averages from the inter-laboratory's results.

Results of the validation obtained for 3R4F and P1 under Health Canada were compared to data from Labstat reported in the document Analysis of Philip Morris International THS 2.2 Aerosol from PMI science website. Six elements was analysed by Labstat (chromium, nickel, arsenic, selenium, cadmium and lead). For 3R4F, the validation results were in line with Labstat results except for cadmium (+30.0%) and Selenium (+27.2%). For P1, 5 elements out of 6 provided non quantifiable results. Quantifiable results were obtained for selenium, with an average value obtained during the validation presenting a %difference of -16.7% compared to Labstat.

The stability evaluation in fridge at 4°C demonstrate that the internal standard stock solution and the elements stock solution B are stable up to 43 days, the working standard solution are stable up to 3 days.

Sample aerosol treated solution (for 3R4F and P1 matrices) can be used for analysis for the determination of 20 elements after a storage duration up to 4 days in the fridge (semi quantitative determination for tungsten). Sample aerosol treated solutions can be used for analysis for the determination of 19 elements (except Mo and semi-quantitative analysis of tungsten) after a storage duration up to 21 days in the fridge. Sample aerosol treated solutions can be used for analysis for the determination of molybdenum provided that the measured value of Mo is either below LOQreporting or higher than 0.86 ng/item after a storage duration between 4 and 21 days in the fridge.

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Measurement solutions in ICP-vial on autosampler at room temperature were found to be stable for 24h for 3R4F and P1 matrices and for standard solutions for all elements except tungsten which allows a maximum batch length of 24 h or possible sample re-injection performed within 24 h (semi quantitative determination for tungsten)

The stability limits and stability conditions are reported in Table 3.

In Table 2 and in Table 4 to Table 23 is presented the summary of conclusion and results of the validation parameters evaluated during this validation

Table 1 - Range of concentration for working standards in routine and regression model

Elements / Standard	STD1 [pg/mL]	STD2 [pg/mL]	STD3 [pg/mL]	STD4 [pg/mL]	STD5 [pg/mL]	STD6 [pg/mL]	STD7 [pg/mL]	Regression model, weighing system
Be, Mo	10	40	75	125	250	375	500	Linear, 1/x
Co, Cd, Cr, Ni, Sn	30	120	225	375	750	1125	1500	Linear, 1/x
As, Se, Sr,W	50	200	375	625	1250	1875	2500	Linear, 1/x
Cu, Pb, Mn, Ti	300	1200	2250	3750	7500	11250	15000	Linear, 1/x
Al, Fe, Mg, Zn	1000	4000	7500	12500	25000	37500	50000	Linear, 1/x
Ca	10000	40000	75000	125000	250000	375000	500000	Linear, 1/x

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Table 2 - Summarized Conclusions of the Validation Parameters with Pre-Defined Acceptance Criteria

Validation parameter	Conclusion	Comments / Recommendations
Selectivity, #1, #2	Pass	Tested for target elements and ISTD in all matrices and in blanks
Bias of the analytical method #4	Pass, except for tungsten	Tested for spiked matrices
Repeatability of the analytical method #5	Pass	Tested for spiked matrices, under stability condition
Intermediate precision of the analytical method #6	Pass	Tested for spiked matrices, under stability condition
Instrumental repeatability #7	Pass	Tested for all matrices
Linearity, #10	Pass	Regression model: Linear with 1/x for all elements
LLOQ #12, ULOQ #13	Pass	Tested under intermediate precision conditions
Stability #16, #17, #18	Pass, except for tungsten	Detailed information provided in Table 3
Robustness #14, #15	Pass	Tested for EP tube contamination by an external environment and mineralization step
No acceptance criteria was set for: LWRL and UWRL, #3; repeatability and intermediate precision for whole process, #8 and #9; LOD, #11		

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Table 3 - Summary of Results for Stability Testing

Stability	Conclusion	Comments / Recommendations
Stability of elements stock solution B and Internal standard stock solution in fridge at 4°C	Up to 43 days	Stability testing can be extended
Stability of working standard solutions in fridge at 4°C	Up to 3 days	NA
Stability of aerosol treated solution in fridge at 4°C	-Up to 4 days for all elements (except tungsten) and all matrices -Up to 21 days for all elements (except tungsten and molybdenum) and all matrices -Between 4 and 21 days, the measured value of Mo is either below LOQreporting or higher than 0.86ng/item	Semi quantitative determination for tungsten
Stability of standards and samples in auto-sampler at room temperature	Up to 24 hours, except for tungsten	Semi quantitative determination for tungsten

NA = Not Applicable

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Table 4 - Summary of Results of Validation Parameters for Beryllium

Beryllium	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1[ng/item]
Usual dilution	dil B	dil B	dil B	dil B
LOD	0.037	0.037	0.019	0.037
LLOQ	0.125	0.125	0.062	0.125
STD 1	0.15	0.15	0.07	0.15
$LOQ_{reporting}$	0.15	0.15	0.07	0.15
ULOQ	7.31	7.31	3.66	7.31
LWRL	0.24	0.24	0.12	0.24
UWRL	6.09	6.09	3.05	6.09
Nominal content	<LOQ(0.15)	<LOQ(0.15)	<LOQ(0.07)	<LOQ(0.15)
r	NA	NA	NA	NA
IP	NA	NA	NA	NA
CD (95%, n=4)	NA	NA	NA	NA

Table 5 - Summary of Results of Validation Parameters for Magnesium

Magnesium	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
Usual dilution	dil B	dil B	dil B	dil B
LOD	1.08	1.08	0.54	1.08
LLOQ	3.59	3.59	1.80	3.59
STD 1	14.63	14.63	7.31	14.63
$LOQ_{reporting}$	14.63	14.63	7.31	14.63
ULOQ	731.25	731.25	365.63	731.25

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Magnesium	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
LWRL	24.30	24.30	12.15	24.30
UWRL	607.55	607.55	303.77	607.55
Nominal content	18.68	<LOQ(14.63)	<LOQ(7.31)	<LOQ(14.63)
r	3.797	NA	NA	NA
IP	3.797	NA	NA	NA
CD (95%, n=4)	1.003	NA	NA	NA

Table 6 - Summary of Results of Validation Parameters for Aluminium

Aluminium	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
Usual dilution	dil B	dil B	dil B	dil B
LOD	1.68	1.68	0.84	1.68
LLOQ	5.59	5.59	2.80	5.59
STD 1	14.63	14.63	7.31	14.63
$LOQ_{reporting}$	87.32	87.32	43.66	87.32
ULOQ	731.25	731.25	365.63	731.25
LWRL	24.38	24.38	12.19	24.38
UWRL	609.38	609.38	304.69	609.38
Nominal content	<LOQ(87.32)	<LOQ(87.32)	<LOQ(43.66)	<LOQ(87.32)
r	NA	NA	NA	NA
IP	NA	NA	NA	NA
CD (95%, n=4)	NA	NA	NA	NA

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Table 7 - Summary of Results of Validation Parameters for Calcium

Calcium	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
Usual dilution	dil B	dil B	dil B	dil B
LOD	14.69	14.69	7.34	14.69
LLOQ	48.96	48.96	24.48	48.96
STD 1	146.25	146.25	73.13	146.25
$LOQ_{reporting}$	258.07	258.07	129.03	258.07
ULOQ	7312.50	7312.50	3656.25	7312.50
LWRL	244.24	244.24	122.12	244.24
UWRL	6105.94	6105.94	3052.97	6105.94
Nominal content	<LOQ (258.07)	<LOQ (258.07)	<LOQ (129.03)	<LOQ (258.07)
r	NA	NA	NA	NA
IP	NA	NA	NA	NA
CD (95%, n=4)	NA	NA	NA	NA

Table 8 - Summary of Results of Validation Parameters for Titanium

Titanium	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
Usual dilution	dil B	dil B	dil B	dil B
LOD	0.51	0.51	0.26	0.51
LLOQ	1.72	1.72	0.86	1.72
STD 1	4.39	4.39	2.19	4.39
$LOQ_{reporting}$	21.10	21.10	10.55	21.10
ULOQ	219.38	219.38	109.69	219.38

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Titanium	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
LWRL	7.35	7.35	3.67	7.35
UWRL	183.73	183.73	91.86	183.73
Nominal content	<LOQ(21.10)	<LOQ(21.10)	<LOQ(10.55)	<LOQ(21.10)
r	NA	NA	NA	NA
IP	NA	NA	NA	NA
CD (95%, n=4)	NA	NA	NA	NA

Table 9 - Summary of Results of Validation Parameters for Chromium

Chromium	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
Usual dilution	dil B	dil B	dil B	dil B
LOD	0.10	0.10	0.05	0.10
LLOQ	0.33	0.33	0.16	0.33
STD 1	0.44	0.44	0.22	0.44
$LOQ_{reporting}$	2.99	2.99	1.49	2.99
ULOQ	21.94	21.94	10.97	21.94
LWRL	0.73	0.73	0.37	0.73
UWRL	18.26	18.26	9.13	18.26
Nominal content	<LOQ(2.99)	<LOQ(2.99)	<LOQ(1.49)	<LOQ(2.99)
r	NA	NA	NA	NA
IP	NA	NA	NA	NA
CD (95%, n=4)	NA	NA	NA	NA

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Table 10 - Summary of Results of Validation Parameters for Manganese

Manganese	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
Usual dilution	dil B	dil B	dil B	dil B
LOD	0.26	0.26	0.13	0.26
LLOQ	0.87	0.87	0.44	0.87
STD 1	4.39	4.39	2.19	4.39
$LOQ_{reporting}$	4.39	4.39	2.19	4.39
ULOQ	219.38	219.38	109.69	219.38
LWRL	7.32	7.32	3.66	7.32
UWRL	183.00	183.00	91.50	183.00
Nominal content	<LOQ(4.39)	<LOQ(4.39)	<LOQ(2.19)	<LOQ(4.39)
r	NA	NA	NA	NA
IP	NA	NA	NA	NA
CD (95%, n=4)	NA	NA	NA	NA

Table 11 - Summary of Results of Validation Parameters for Iron

Iron	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
Usual dilution	dil B	dil B	dil B	dil B
LOD	0.97	0.97	0.49	0.97
LLOQ	3.24	3.24	1.62	3.24
STD 1	14.63	14.63	7.31	14.63
$LOQ_{reporting}$	17.10	17.10	8.55	17.10
ULOQ	731.25	731.25	365.63	731.25
LWRL	24.40	24.40	12.20	24.40

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Iron	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
UWRL	609.98	609.98	304.99	609.98
Nominal content	<LOQ(17.1)	<LOQ(17.1)	<LOQ(8.55)	<LOQ(17.10)
r	NA	NA	NA	NA
IP	NA	NA	NA	NA
CD (95%, n=4)	NA	NA	NA	NA

Table 12 - Summary of Results of Validation Parameters for Cobalt

Cobalt	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
Usual dilution	dil B	dil B	dil B	dil B
LOD	0.04	0.04	0.02	0.04
LLOQ	0.14	0.14	0.07	0.14
STD 1	0.44	0.44	0.22	0.44
$LOQ_{reporting}$	0.44	0.44	0.22	0.44
ULOQ	21.94	21.94	10.97	21.94
LWRL	0.73	0.73	0.36	0.73
UWRL	183.00	183.00	91.50	183.00
Nominal content	<LOQ(0.44)	<LOQ(0.44)	<LOQ(0.22)	<LOQ(0.44)
r	NA	NA	NA	NA
IP	NA	NA	NA	NA
CD (95%, n=4)	NA	NA	NA	NA

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Table 13 - Summary of Results of Validation Parameters for Nickel

Nickel	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
Usual dilution	dil B	dil B	dil B	dil B
LOD	0.07	0.07	0.03	0.07
LLOQ	0.23	0.23	0.11	0.23
STD 1	0.44	0.44	0.22	0.44
$LOQ_{reporting}$	7.28	7.28	3.64	7.28
ULOQ	21.94	21.94	10.97	21.94
LWRL	0.73	0.73	0.37	0.73
UWRL	18.28	18.28	9.14	18.28
Nominal content	<LOQ(7.28)	<LOQ(7.28)	<LOQ(3.64)	<LOQ(7.28)
r	NA	NA	NA	NA
IP	NA	NA	NA	NA
CD (95%, n=4)	NA	NA	NA	NA

Table 14 - Summary of Results of Validation Parameters for Copper

Copper	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
Usual dilution	dil B	dil B	dil B	dil B
LOD	0.36	0.36	0.18	0.36
LLOQ	1.19	1.19	0.59	1.19
STD 1	4.39	4.39	2.19	4.39
$LOQ_{reporting}$	4.39	4.39	2.19	4.39
ULOQ	219.38	219.38	109.69	219.38
LWRL	7.32	7.32	3.66	7.32

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Copper	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
UWRL	183.00	183.00	91.50	183.00
Nominal content	19.34	<LOQ(4.39)	5.29	<LOQ(4.39)
r	3.418	NA	1.529	NA
IP	4.899	NA	1.529	NA
CD (95%, n=4)	3.904	NA	0.599	NA

Table 15 - Summary of Results of Validation Parameters for Zinc

Zinc	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
Usual dilution	dil B	dil B	dil B	dil B
LOD	1.07	1.07	0.53	1.07
LLOQ	3.55	3.55	1.78	3.55
STD 1	14.63	14.63	7.31	14.63
$LOQ_{reporting}$	42.79	42.79	21.40	42.79
ULOQ	731.25	731.25	365.63	731.25
LWRL	24.38	24.38	12.19	24.38
UWRL	609.38	609.38	304.69	609.38
Nominal content	238.92	86.79	45.67	<LOQ(42.79)
r	52.240	NA	26.684	NA
IP	74.947	NA	29.622	NA
CD (95%, n=4)	59.751	NA	18.532	NA

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Table 16 - Summary of Results of Validation Parameters for Arsenic

Arsenic	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
Usual dilution	dil B	dil B	dil B	dil B
LOD	0.07	0.07	0.04	0.07
LLOQ	0.24	0.24	0.12	0.24
STD 1	0.73	0.73	0.37	0.73
$LOQ_{reporting}$	0.73	0.73	0.37	0.73
ULOQ	36.56	36.56	18.28	36.56
LWRL	1.22	1.22	0.61	1.22
UWRL	30.50	30.50	15.25	30.50
Nominal content	8.51	0.79	2.66	<LOQ(0.73)
r	0.738	NA	0.405	NA
IP	1.969	NA	0.468	NA
CD (95%, n=4)	1.863	NA	0.311	NA

Table 17 - Summary of Results of Validation Parameters for Selenium

Selenium	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
Usual dilution	dil B	dil B	dil B	dil B
LOD	0.18	0.18	0.09	0.18
LLOQ	0.60	0.60	0.30	0.60
STD 1	0.73	0.73	0.37	0.73
$LOQ_{reporting}$	0.73	0.73	0.37	0.73
ULOQ	36.56	36.56	18.28	36.56
LWRL	1.22	1.22	0.61	1.22

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Selenium	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
UWRL	30.53	30.53	15.26	30.53
Nominal content	2.48	1.31	0.75	0.92
r	0.461	0.527	0.227	0.479
IP	0.688	0.685	0.259	0.479
CD (95%, n=4)	0.560	0.511	0.169	0.096

Table 18 - Summary of Results of Validation Parameters for Strontium

Strontium	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
Usual dilution	dil B	dil B	dil B	dil B
LOD	0.16	0.16	0.08	0.16
LLOQ	0.53	0.53	0.27	0.53
STD 1	0.73	0.73	0.37	0.73
$LOQ_{reporting}$	0.73	0.73	0.37	0.73
ULOQ	36.56	36.56	18.28	36.56
LWRL	2.44	1.22	1.22	1.22
UWRL	30.50	30.50	15.25	30.50
Nominal content	<LOQ(0.73)	<LOQ(0.73)	<LOQ(0.37)	<LOQ(0.73)
r	NA	NA	NA	NA
IP	NA	NA	NA	NA
CD (95%, n=4)	NA	NA	NA	NA

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Table 19 - Summary of Results of Validation Parameters for Molybdenum

Molybdenum	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
Usual dilution	dil B	dil B	dil B	dil B
LOD	0.02	0.02	0.01	0.02
LLOQ	0.08	0.08	0.04	0.08
STD 1	0.15	0.15	0.07	0.15
$LOQ_{reporting}$	0.26	0.26	0.13	0.26
ULOQ	7.31	7.31	3.66	7.31
LWRL	0.24	0.24	0.12	0.24
UWRL	6.11	6.11	3.05	6.11
Nominal content	<LOQ(0.26)	<LOQ(0.26)	<LOQ(0.13)	<LOQ(0.26)
r	NA	NA	NA	NA
IP	NA	NA	NA	NA
CD (95%, n=4)	NA	NA	NA	NA

Table 20 - Summary of Results of Validation Parameters for Cadmium

Cadmium	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
Usual dilution	dil A	dil B	dil A	dil B
LOD	0.89	0.04	0.45	0.04
LLOQ	2.98	0.15	1.49	0.15
STD 1	8.78	0.44	4.39	0.44
$LOQ_{reporting}$	8.78	0.44	4.39	0.44
ULOQ	438.75	21.94	219.38	21.94
LWRL	14.67	0.73	7.33	0.73

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Cadmium	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
UWRL	366.72	18.34	183.36	18.34
Nominal content	120.74	<LOQ(0.44)	35.08	<LOQ(0.44)
r	15.832	NA	9.900	NA
IP	30.865	NA	10.559	NA
CD (95%, n=4)	27.652	NA	6.163	NA

Table 21 - Summary of Results of Validation Parameters for Tin

Tin	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
Usual dilution	dil B	dil B	dil B	dil B
LOD	0.05	0.05	0.02	0.05
LLOQ	0.15	0.15	0.08	0.15
STD 1	0.44	0.44	0.22	0.44
$LOQ_{reporting}$	0.44	0.44	0.22	0.44
ULOQ	21.94	21.94	10.97	21.94
LWRL	0.73	0.73	0.36	0.73
UWRL	18.23	18.23	9.11	18.23
Nominal content	<LOQ(0.44)	1.22	<LOQ(0.22)	<LOQ(0.44)
r	NA	NA	NA	NA
IP	NA	NA	NA	NA
CD (95%, n=4)	NA	NA	NA	NA

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Table 22 - Summary of Results of Validation Parameters for Tungsten

Tungsten / semi quantitative determination	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
Usual dilution	dil B	dil B	dil B	dil B
LOD	0.14	0.14	0.07	0.14
LLOQ	0.47	0.47	0.24	0.47
STD 1	0.73	0.73	0.37	0.73
$LOQ_{reporting}$	0.81	0.81	0.41	0.81
ULOQ	36.56	36.56	18.28	36.56
LWRL	9.81	9.81	4.90	9.81
UWRL	30.65	30.65	15.33	30.65
Nominal content	<LOQ(0.81)	<LOQ(0.81)	<LOQ(0.41)	<LOQ(0.81)
r	NA	NA	NA	NA
IP	NA	NA	NA	NA
CD (95%, n=4)	NA	NA	NA	NA

Table 23 - Summary of Results of Validation Parameters for Lead

Lead	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
Usual dilution	dil B	dil B	dil B	dil B
LOD	0.30	0.30	0.15	0.30
LLOQ	0.99	0.99	0.50	0.99
STD 1	4.39	4.39	2.19	4.39
$LOQ_{reporting}$	4.39	4.39	2.19	4.39
ULOQ	219.38	219.38	109.69	219.38

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Lead	Health Canada		ISO	
	3R4F [ng/cig]	P1 [ng/item]	3R4F [ng/cig]	P1 [ng/item]
LWRL	7.31	7.31	3.66	7.31
UWRL	182.81	182.81	91.41	182.81
Nominal content	31.37	<LOQ(4.39)	9.25	<LOQ(4.39)
r	4.264	NA	2.230	NA
IP	6.969	NA	2.230	NA
CD (95%, n=4)	5.911	NA	0.895	NA

4. APPROVALS

	Name	Role	Signature	Date
Author	Eva Garcia	Manager Central Analytical Laboratories		14-JUL-2016
Owner	Serge Maeder	Director PMI Testing Laboratories Governance		14. Jul 2016
QA Review	Florence Kapp	QA Officer Audit		14 JUL 2016

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