



**Cooperation Centre for Scientific Research
Relative to Tobacco**

E-Vapour Sub-Group

**CORESTA Recommended Method
No. 98**

**DETERMINATION OF SELECT
METALS IN E-LIQUID BY ICP-MS**

October 2022



CORESTA RECOMMENDED METHOD N° 98

Title:

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Status: Valid

Note: This document will be periodically reviewed by CORESTA

Document history:

Date of review	Information
October 2022	Version 1

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0. INTRODUCTION

In 2019 the CORESTA E-Vapour Sub-Group reported the results of a proficiency study for the determination of metals in e-liquid samples using laboratories' in-house methods, either microwave digestion or dilution method. In 2021, the Sub-Group initiated a collaborative study following a proposed recommended method based on the dilution approach.

1. FIELD OF APPLICATION

This Recommended Method is applicable to the determination of select metals in e-liquids. The metals determined with this method are: chromium, iron, nickel, copper, zinc, arsenic, cadmium, tin, silver and lead.

2. NORMATIVE REFERENCES

- 2.1 CORESTA Guide N° 18 – *Sample Handling and Sample Collection of E-Cigarettes and E-Vapour Generating Products*
- 2.2 CORESTA Guide N° 28 – *Setting Method LOD and LOQ Values for the Determination of Metals in E-Liquid and E-Vapour Aerosol by ICP-MS*

3. PRINCIPLE

Dilution of e-liquid is carried out by 5 % nitric acid (v/v) at room temperature. The aqueous nitric acid solution is analysed by Inductively Coupled Plasma Mass Spectrometer (ICP-MS) equipped with collision cell and / or reaction cell technology. Collision cell technology is required to remove polyatomic interferences caused by the combination of two or more isotopes from different elements with the same mass/charge ratio as the metal of interest. Reaction cells are used to remove isobaric interferences caused by elements with overlapping isotope masses. The results are reported in units of total element mass on a per sample (ng/sample), per weight (ng/g) or per volume (ng/mL) of sample basis.

4. EQUIPMENT AND APPARATUS

Normal laboratory apparatus and equipment including the following items:

- 4.1 Inductively Coupled Plasma Mass Spectrometer (ICP-MS) with collision cell and / or reaction cell technology
- 4.2 Analytical balance (0,0001 g resolution)
- 4.3 Vortex mixer or similar
- 4.4 Pipettes (10-100 µL, 100-1000 µL, 0,5-5 mL, 1-10 mL)

- 4.5 Polypropylene (PP) flask (1 L)
- 4.6 Polypropylene tubes (graduated 50 mL)
- 4.7 Polypropylene autosampler tubes (15 mL)

5. REAGENTS

- 5.1 Water, resistivity at 25 °C $\geq 18,2 \text{ M}\Omega\cdot\text{cm}$ (Type 1)
- 5.2 Concentrated nitric acid, High purity grade (60-62 % w/w, 1,38 g/mL)
- 5.3 Methanol, Semiconductor grade
- 5.4 ICP-MS Stock Tuning Solution containing Li, Y, Ce, Tl and Co in dilute nitric acid
- 5.5 Nitric acid for PP tube wash, Analytical grade
- 5.6 Certified solution(s) (preferably ISO 17034:2016 certified) containing the following elements at a target value of 100 $\mu\text{g/mL}$: Cr, Fe, Ni, Cu, Zn, As, Ag, Cd, Sn, Pb
- 5.7 Individual solutions of Sc, Te, Y, and Tl at approximately 1000 $\mu\text{g/mL}$ in dilute nitric acid for use as internal standards. Other internal standards may be used following validation by the laboratory.
- 5.8 Collision gases, as per instrument manufacturer recommendation.

6. PREPARATION OF SOLUTIONS

All standards should be prepared in metal-free polypropylene tubes or tubes washed with 20 % (v/v) nitric acid and stored at room temperature. Produce a series of enough calibration standards to cover the range of expected results to be found in the test portions, as in the example given below. Alternative volumes of each solution can be produced as necessary by appropriate modification of the required quantities.

6.1 Extraction Solution

To prepare one litre of extraction solution, add approximately 500 mL of Type 1 water followed by 50 mL of concentrated nitric acid (high purity grade) and 100 mL of methanol to a polypropylene volumetric flask. Bring to volume with Type 1 water to produce a final concentration of 5 % (v/v) solution. Store at room temperature. **Note:** It is recommended to add the methanol to the extraction solution, alternatively, it can be added to individual standards and samples.

6.2 ICP-MS Probe Rinse Solution

To prepare one litre of probe rinsing solution, add approximately 500 mL of Type 1 water followed by 50 mL of concentrated nitric acid to a polypropylene volumetric flask. Bring to volume with Type 1 water to combine sufficient volumes of concentrated nitric acid and Type I water to produce a final concentration of 5 % (v/v) solution. Store at room temperature.

6.3 ICP-MS Stock Tuning Solution

ICP-MS Stock Tuning Solution (Li, Y, Ce, Tl and Co 10 ng/mL in 2 % nitric acid) is commercially available. **Note:** Alternative solutions with higher concentrations of the metals can be diluted with a 2 % (v/v) nitric acid solution to produce the desired final concentration of 10 ng/mL.

6.4 Internal Standard Stock Solution

Add 25 mL of extraction solution to a 50 mL polypropylene tube followed by 0,25 mL of each of Sc, Y and Tl 1000 µg/mL standard solutions and 0,75 mL of Te 1000 µg/mL standard solution. Bring to volume with extraction solution for final concentrations of 5 µg/mL of Sc, Y and Tl and 15 µg/mL of Te. **Note:** Other internal standards may be used following validation by the laboratory.

6.5 Primary Calibration Stock Solution (1° CSS)

Transfer 0,5 mL of the certified multi-element standard stock solution to a 50 mL PP tube and make to volume with extraction solution to produce a final concentration of 1 µg/mL.

6.6 Secondary Calibration Stock Solution (2° CSS)

Transfer 5 mL of 1° CSS to a 50 mL PP tube and make to volume with extraction solution to produce a final concentration of 100 ng/mL.

6.7 Working Calibration Standards (WCS)

Prepare working calibration standards by adding the appropriate amount of 1° CSS or 2° CSS, ISSS and extraction solution to produce final concentrations shown below in Table 1.

Table 1. Working Calibration Standard Preparation

WCS Level	Expected Conc. (ng/mL)	CSS Used to Prepare Standard	CSS Volume (mL)	ISSS* Volume (µL)	MeOH** Volume (mL)	Final Volume (mL)
0	0	N/A	0	100	5	50
1	1,0	2° CSS	0,5	100	5	50
2	5,0	2° CSS	2,5	100	5	50
3	10,0	1° CSS	0,5	100	5	50
4	30,0	1° CSS	1,5	100	5	50
5	60,0	1° CSS	3,0	100	5	50

* Alternatively, internal standards may be added online during sample introduction, instead of adding to standards and samples.

** Addition of MeOH only required if not added to the extraction solution (6.1).

7. PROCEDURES

7.1 Sampling

Sampling is conducted such that the laboratory test sample is representative of the population to be tested.

7.2 Sample preparation

7.2.1 Samples should be mixed prior to weighing to ensure sample homogeneity.

7.2.2 The test samples shall be stored protected from light.

7.3 Sample extraction

- 7.2.1** Using an analytical balance, weigh a known amount (approximately 0,5 g) of the e-liquid sample directly into a 50 mL PP tube.
- 7.2.2** If needed, weigh an additional matrix blank sample at the same amount as above, and spike with 1,0 mL of 1° CSS which will serve as a matrix spike recovery.
- 7.2.3** Add approximately 25 mL of extraction solution to the 50 mL PP tube containing the pre-weighed e-liquid sample.
- 7.2.4** Add 100 µL of ISSS to each sample and recovery. **Note:** Alternatively, internal standards may be added online during sample introduction, instead of adding to standards and samples.
- 7.2.5** If MeOH was not added to the extraction solution (6.1), add 5 mL of MeOH to each sample and recovery.
- 7.2.6** Prepare three reagent blanks by adding 100 µL of ISSS. If MeOH was not added to the extraction solution (6.1) add 5 mL of MeOH to the 50 mL PP tube.
- 7.2.7** Bring samples and reagent blanks to a final volume of 50 mL with extraction solution. Cap, invert and mix samples thoroughly.
- 7.2.8** Pour samples into 15 mL autosampler tubes.
- 7.2.9** Samples are now ready for analysis via ICP-MS.

8. DETERMINATION

Set up and operate the ICP-MS system in accordance with the manufacturer's instructions. Equilibrate and tune the system prior to use.

Where appropriate each laboratory should ensure the ICP-MS instrument is tuned for Pulse and Analog detection modes according to manufacturer's instructions.

8.1 Suggested ICP-MS Injection Parameters

The following are recommended conditions for an Agilent ICP system and may be modified to achieve acceptable performance on other systems.

Table 2. ICP-MS Injection Parameters

Parameter	Value
RF Power	1500 W
RF Matching (Typical Range – Auto)	1,80 V
Plasma gas flow rate	15 L/min
Nebulizer gas flow rate	Ar 0,75 L/min
Dilution gas flow rate	Ar 0,25 L/min
Option gas*	0,1 L/min
Peristaltic pump speed	0,1 rpm
Peristaltic pump tubing	1,02 mm inner diameter
Sampling Depth	12,0 mm

Parameter	Value
Cell Gas Flow-Rate	He 5,0 mL/min H ₂ 4,0 mL/min
Data point	3 points per peak
Repetition	3 times

* Option gas (20 % O₂ / Ar balance) is injected with dilution gas to aid analysis of high organic content samples.

8.2 Suggested Element Specific Analysis Parameters

Table 3. Element Specific Analysis Parameters

Element		Mass	Gas Mode*	Internal standard (mass-element)**
Chromium	Cr	52	He	45-Sc
Iron	Fe	56	H ₂	45-Sc
Nickel	Ni	60	He	45-Sc
Copper	Cu	63	He	45-Sc
Zinc	Zn	66	He	45-Sc
Arsenic	As	75	He	126-Te
Silver	Ag	107	H ₂	89-Y
Cadmium	Cd	111	He	89-Y
Tin	Sn	118	H ₂	89-Y
Lead	Pb	206+207+208	He	205-Tl

* Refer to instrument supplier recommendations.

** **Note:** Other internal standards may be used following validation by the laboratory.

8.3 Calibration Standard Acceptance Criteria

Calibration standards below an element's instrument LOQ should not be included in the calibration curve. A minimum of 5 non-zero calibration points are used to generate the calibration curve.

Regression should be linear with the origin excluded and a weighting of 1/x.

The calibration curve for each element must have a coefficient of determination of 0,9950 or better.

All Calibration Standards, should be within $\pm 20\%$ relative error of the theoretical calculated concentration.

8.4 Reduction of Raw Data from ICP-MS

The element concentration is determined from the regression equation derived from the calibration curve and corrected through the use of internal standardization. Calculation of the element concentration is obtained by using the calculation capabilities of the mass spectrometer software.

8.5 Calculations

Data are obtained from the instrument in units of ng/mL. A number of factors may be applied in order to supply the client with the requested units. For all samples, actual weights and volumes should be substituted for the nominal values below.

Typically, e-liquid results are reported in ng/g of e-liquid. The calculation is as follows:

$$\frac{\text{Conc.} \left(\frac{\text{ng}}{\text{mL}} \right) \times \text{Extraction Volume (50 mL)}}{e - \text{Liquid mass (0,5 g)}} = \text{Final Result (ng/g)}$$

8.6 Quality Control

Each laboratory should perform quality control procedures per their quality system requirements.

9. REPEATABILITY AND REPRODUCIBILITY

In 2021, an international collaborative study involving 13 laboratories was conducted for the determination of metals in e-liquids following a proposed recommended method. The study included four flavour profile e-liquids, with each e-liquid fortified with a different concentration of the ten target metals. For each flavour profile e-liquid, corresponding non-fortified samples were also provided for analysis. Data were reported in units of ng/g. The majority of results for the non-fortified e-liquids were reported as either being below the limit of detection (LOD) or limit of quantification (LOQ) and therefore repeatability and reproducibility estimates were not calculated. Data from the fortified e-liquid samples were analysed in basic conformance with ISO 5725-5:1998. The values for repeatability and reproducibility are provided in Tables 4 to 13.

Table 4: Repeatability (r) and Reproducibility (R) Limits for Arsenic (ng/g)

Sample ID	Nominal Conc. (ng/g)	N° of Labs	Average (ng/g)	Repeatability		Reproducibility	
				r	r %	R	R %
3128701-Unflavoured	500	12	455	24,3	5,3	137,7	30
3128702-Tobacco	1500	12	1380	78,4	5,7	365,3	26
3128704-Menthol	3000	12	2816	224,2	8,0	773,2	27
3128703-Sweet	5000	12	4646	309,7	6,7	1047,3	23

Table 5: Repeatability (r) and Reproducibility (R) Limits for Cadmium (ng/g)

Sample ID	Nominal Conc. (ng/g)	N° of Labs	Average (ng/g)	Repeatability		Reproducibility	
				r	r %	R	R %
3128701-Unflavoured	500	13	463	35,2	7,6	86,5	19
3128702-Tobacco	1500	13	1405	70,4	5,0	237,0	17
3128704-Menthol	3000	13	2852	140,8	4,9	439,3	15
3128703-Sweet	5000	13	4766	203,6	4,3	603,0	13

Table 6: Repeatability (r) and Reproducibility (R) Limits for Chromium (ng/g)

Sample ID	Nominal Conc. (ng/g)	N° of Labs	Average (ng/g)	Repeatability		Reproducibility	
				r	r %	R	R %
3128701-Unflavoured	500	13	466	30,5	6,5	118,4	25
3128702-Tobacco	1500	13	1406	76,9	5,5	295,1	21
3128704-Menthol	3000	13	2887	139,7	4,8	534,7	19
3128703-Sweet	5000	13	4792	258,5	5,4	801,1	17

Table 7: Repeatability (r) and Reproducibility (R) Limits for Copper (ng/g)

Sample ID	Nominal Conc. (ng/g)	N° of Labs	Average (ng/g)	Repeatability		Reproducibility	
				r	r %	R	R %
3128701-Unflavoured	500	13	486	35,3	7,3	129,5	27
3128702-Tobacco	1500	13	1463	83,5	5,7	240,2	16
3128704-Menthol	3000	13	2957	160,1	5,4	569,9	19
3128703-Sweet	5000	13	4904	224,9	4,6	971,0	20

Table 8: Repeatability (r) and Reproducibility (R) Limits for Iron (ng/g)

Sample ID	Nominal Conc. (ng/g)	N° of Labs	Average (ng/g)	Repeatability		Reproducibility	
				r	r %	R	R %
3128701-Unflavoured	500	12	500	62,3	12,4	330,2	66
3128702-Tobacco	1500	12	1417	120,4	8,5	368,2	26
3128704-Menthol	3000	12	2908	191,6	6,6	632,3	22
3128703-Sweet	5000	12	4825	288,8	6,0	1094,5	23

Table 9: Repeatability (r) and Reproducibility (R) Limits for Lead (ng/g)

Sample ID	Nominal Conc. (ng/g)	N° of Labs	Average (ng/g)	Repeatability		Reproducibility	
				r	r %	R	R %
3128701-Unflavoured	500	13	455	17,8	3,9	106,0	23
3128702-Tobacco	1500	13	1376	41,8	3,0	295,1	21
3128704-Menthol	3000	13	2841	85,9	3,0	401,0	14
3128703-Sweet	5000	13	4740	106,7	2,3	784,3	17

Table 10: Repeatability (r) and Reproducibility (R) Limits for Nickel (ng/g)

Sample ID	Nominal Conc. (ng/g)	N° of Labs	Average (ng/g)	Repeatability		Reproducibility	
				r	r %	R	R %
3128701-Unflavoured	500	13	460	37,2	8,1	84,7	18
3128702-Tobacco	1500	13	1394	65,1	4,7	263,6	19
3128704-Menthol	3000	13	2836	137,3	4,8	482,4	17
3128703-Sweet	5000	13	4689	298,4	6,4	793,4	17

Table 11: Repeatability (r) and Reproducibility (R) Limits for Silver (ng/g)

Sample ID	Nominal Conc. (ng/g)	N° of Labs	Average (ng/g)	Repeatability		Reproducibility	
				r	r %	R	R %
3128701-Unflavoured	500	12	457	22,3	4,9	151,3	33
3128702-Tobacco	1500	12	1385	56,5	4,1	407,5	29
3128704-Menthol	3000	12	2659	67,6	2,5	992,6	37
3128703-Sweet	5000	12	4489	143,0	3,2	1499,3	33

Table 12: Repeatability (r) and Reproducibility (R) Limits for Tin (ng/g)

Sample ID	Nominal Conc. (ng/g)	N° of Labs	Average (ng/g)	Repeatability		Reproducibility	
				r	r %	R	R %
3128701-Unflavoured	500	11	465	26,1	5,6	80,0	17
3128702-Tobacco	1500	11	1389	41,1	3,0	214,4	15
3128704-Menthol	3000	11	2811	138,8	4,9	456,0	16
3128703-Sweet	5000	11	4687	125,2	2,7	699,3	15

Table 13: Repeatability (r) and Reproducibility (R) Limits for Zinc (ng/g)

Sample ID	Nominal Conc. (ng/g)	N° of Labs	Average (ng/g)	Repeatability		Reproducibility	
				r	r %	R	R %
3128701-Unflavoured	500	11*	497	43,6	8,8	121,1	24
3128702-Tobacco	1500	12	1401	86,9	6,2	286,3	20
3128704-Menthol	3000	12	2920	162,3	5,6	398,6	14
3128703-Sweet	5000	12	4931	328,4	6,7	525,3	11

* Data from one laboratory reported as below the limit of detection and therefore excluded from the statistical analysis.

10. REFERENCES

- [1] CORESTA E-Vapour Sub-Group Technical Report, Metals Analysis Method for E-Liquids, (EVAP-184-CTR), May 2020, available at <https://www.coresta.org/metals-analysis-method-e-liquids-33731.html>
- [2] CORESTA E-Vapour Sub-Group Technical Report, 2021 Collaborative Study for the Determination of Metals in E-Liquids (EVAP-312-1-CTR), October 2022, available at <https://www.coresta.org/2021-collaborative-study-determination-metals-e-liquids-36718.html>