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BIOSPECTRA

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ANALYTICAL METHOD FOR THE DETERMINATION OF ICH Q3D ELEMENTAL IMPURITIES (CLASS 1, 2A, 2B, 3 & 4) BY INDUCTIVELY COUPLED PLASMA MASS SPECTROMETRY (ICP-MS) IN HEPES

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1. PURPOSE:

1.1. To provide a procedure for the assessment of Elemental Impurities in HEPES products via the NexION 350X S/N 85VN5093001 ICP-MS. This procedure was assessed as a fully quantitative option-3 procedure as per validation report 20-003408 v2.0 and follows the validation parameters for quantitation procedures as outlined in USP <233>.

1.2. Elements under validated for this test method include:

1.2.1. Class 1: Hg, As, Cd, and Pb

1.2.2. Class 2A: Co, V, and Ni

1.2.3. Class 2B: Tl, Au, Pd, Ir, Os, Rh, Ru, Se, Ag, and Pt

1.2.4. Class 3: Li, Sb, Ba, Mo, Cu, Cr, and Sn

1.2.5. Class 4: Fe, Mn, Ca, K, Mg, and Zn

2. SCOPE:

2.1. Applies to all HEPES products manufactured at BioSpectra.

2.2. Applies to the NexION 350X S/N 85VN5093001 ICP-MS located in the Quality Control (QC) Laboratory at the BioSpectra Bangor, PA facility.

3. RESPONSIBILITIES:

3.1. QC Management, or other qualified designated individual, is responsible for the control, implementation, training, and maintenance of this method.

3.2. The QC Staff are responsible for complying with the requirements of this Test Method.

3.3. If any abnormalities are determined during routine use of the ICP-MS or during calibration, the QC Manager shall be promptly notified. If necessary, the ICP-MS will be serviced and recalibrated by Perkin Elmer before being approved for use.

4. REFERENCES:

4.1. DCN 16-001438: Analytical Methods Validation Master Plan

4.2. DCN 16-001923: NexION 350X ICP-MS SOP

4.3. DCN 16-001931: NexION 350X ICP-MS Care and Maintenance SOP

4.4. DCN 20-003408: Analytical Method Validation Protocol

4.5. DCN 20-003555: Analytical Method Validation Report

4.6. ICH Q3D Elemental Impurities Guidance for Industry FDA (September 2015)

4.7. ICH Guideline for Elemental Impurities Q3D Current

4.8. USP <232> Elemental Analysis

4.9. USP <233> Elemental Analysis-Procedures

4.10. USP <730> Plasma Spectrochemistry

4.11. USP <1730> Plasma Spectrochemistry—Theory and Practice

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TABLE 1: LIMITS FOR HEPES (10 GRAM/DAY PATIENT EXPOSURE)

Elements	ICH Class	Parenteral PDE Limits (µg/day)	0.3J LOQ (µg/g) in sample	0.5J Target (µg/g) in sample	1.0J Target (µg/g) in sample	1.5J Target (µg/g) in sample
As	1	15	0.45	0.75	1.5	2.25
Cd	1	2.0	0.06	0.10	0.20	0.30
Hg	1	3.0	0.09	0.15	0.30	0.45
Pb	1	5.0	0.15	0.25	0.50	0.75
Co	2A	5.0	0.15	0.25	0.50	0.75
Ni	2A	20	0.60	1.0	2.0	3.0
V	2A	10	0.30	0.50	1.0	1.5
Tl	2B	8	0.24	0.40	0.80	1.2
Se	2B	80	2.4	4.0	8.0	12.0
Ag	2B	10	0.30	0.50	1.0	1.5
Au	2B	100	3.0	5.0	10	15
Pd	2B	10	0.30	0.50	1.0	1.5
Ir	2B	10	0.30	0.50	1.0	1.5
Os	2B	10	0.30	0.50	1.0	1.5
Pt	2B	10	0.30	0.50	1.0	1.5
Rh	2B	10	0.30	0.50	1.0	1.5
Ru	2B	10	0.30	0.50	1.0	1.5
Ba	3	700	21	35	70	105
Sb	3	90	2.7	4.5	9.0	13.5
Li	3	250	7.5	12.5	25	37.5
Mo	3	150	4.5	7.5	15	22.5
Cu	3	*50	1.5	2.5	5.0	7.5
Sn	3	600	18	30	60	90
Cr	3	*50	1.5	2.5	5.0	7.5
Fe	4	*50	1.5	2.5	5.0	7.5
Mn	4	*50	1.5	2.5	5.0	7.5
Zn	4	*50	1.5	2.5	5.0	7.5
Ca	4	*500	15	25	50	75
K	4	*500	15	25	50	75
Mg	4	*50	1.5	2.5	5.0	7.5

*PDE calculated based on lower customer specification

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5. MATERIALS AND EQUIPMENT:

5.1. Equipment
- 5.1.1. Analytical Balance
- 5.1.2. ICP-MS: NexION 350X S/N 85VN5093001

5.2. Reagents
- 5.2.1. Nitric Acid, Trace metals grade or equivalent
- 5.2.2. Hydrochloric Acid, Trace metals grade or equivalent
- 5.2.3. Sulfuric acid, Trace metals grade or equivalent
- 5.2.4. Deionized water (Type 1 Ultrapure)
- 5.2.5. Thiourea, 99+ % grade
- 5.2.6. NexION Setup Solution
- 5.2.7. NexION KED Setup Solution
- 5.2.8. SiliaPrep MB SPE Cartridges, Silica-Based AMPA, 500 mg, 4 mL, 40-63 µm, 60 Å
- 5.2.9. Solid Phase Extraction Cartridges DigiSEP - Green Label 250 mg/6 ml

5.3. Consumable Supplies
- 5.3.1. SCP Digitubes® 15 mL, 50 mL and 100 mL
- 5.3.2. Pipette Tips of various sizes

TABLE 2: REFERENCE STANDARDS

Identification**	Manufacturer	Concentrations / Elements
Pharma-CAL Custom Standard Parenteral STD# 1 IA 140-131-201*	SCP Science	Ag (10 µg/mL), As (15 µg/mL), Cd (2 µg/mL), Co (5 µg/mL), Hg (3 µg/mL), Ni (20 µg/mL), Pb (5 µg/mL), Se (80 µg/mL), Tl (8 µg/mL), V(10µg/mL)
USP232/ICH Q3D Parenteral STD# 2 IA 140-131-215*	SCP Science	100 µg/mL; Au, 10 µg/mL Ir, Os, Pd, Pt, Rh, Ru
Pharma-CAL Custom Standard Parenteral STD# 3 AQ0-150-191*	SCP Science	Ba (700 µg/mL), Cr (50 µg/mL), Cu (50 µg/mL), Fe (50 µg/mL), Li (250 µg/mL), Mn (50 µg/mL), Mo (150 µg/mL), Sb (90 µg/mL), Ca (500 µg/mL), K (500 µg/mL) Sn (600 µg/mL), Zn (50 µg/mL)
Magnesium Stock Standard N9300179	Perkin Elmer	Mg (1,000 µg/mL)
Pharma-CAL Custom Standard AQ0-086-125* (Internal Standard)	SCP Science	10 µg/mL Be, Sc, Y, Re; 25 µg/mL Te; 5 µg/mL Ge, Tb, Bi

* SCP Science catalog numbers ending in 1 denote 125 mL bottle sizes and catalog numbers ending in 5 denote 500 mL bottle sizes.
** Additional standards/custom standards can be used as long as the concentration remains the same in final preparations.

6. PROCEDURE:

6.1. All standards will be prepared volumetrically from stock solutions purchased from certified vendors. If the vendor supplied stock reference standard is within 2% of the nominal value as per the certificate of analysis, then the nominal value will be used to calculate the concentration of the standard. If the stock standard certificate of analysis value is greater than or less than 2% of the nominal value, then the certificate of analysis value will be used for the stock standard concentration.

6.2. **Stock Standards**

6.2.1. The stock reference standards listed in Table 2 will be used to prepare the intermediate standard for the preparation of the calibration standards and spiked samples.

6.3. **Acid Digestion Mix**

[2:1] Nitric Acid (HNO_3): Sulfuric Acid (H_2SO_4) (Prepare same day)

6.3.1. Caution: Combining nitric acid and sulfuric acid generates excessive heat. Never seal cap tightly before solution has completely cooled.

6.3.2. To prepare, add 50 mL of nitric acid to a 100 mL Digitube® and then slowly add 25 mL of sulfuric acid. Solution can be placed in a cold-water bath to aid cooling.

6.3.3. Scale proportionally as needed for use.

6.4. **2% Thiourea Complexing Solution**

6.4.1. Weigh approximately 1.0 gram of Thiourea into a 50 mL Digitube® and dilute to a 50 mL final volume with deionized water.

6.4.2. Mix solution until the thiourea is completely dissolved.

6.4.3. Filter solution through both Cation Solid Phase Extraction (SPE) cartridges listed in Section 5.2 before using.

6.4.4. Scale proportionally as needed for use.

6.5. **Internal Standard Solution**

6.5.1. Add approximately 20 mL of deionized water into a 50 mL Digitube.®

6.5.2. Add 2.5 mL of Pharma CAL Custom Standard (Internal standard) Stock

6.5.3. Slowly add 25 mL of hydrochloric acid and dilute to 50 mL volume with deionized water.

6.5.4. Scale proportionally as needed for use.

6.6. Intermediate Standard

6.6.1. Prepare an intermediate standard solution containing the elements listed in Table 3.
6.6.2. Add 1.0 mL of each STD#1 IA, STD#2 IA, and STD#3.
6.6.3. Add 0.050 mL of 1,000 µg/mL Mg standard.
6.6.4. Add approximately 5 mL of DI Water. Do not allow stock standards to contact concentrated acids while preparing solutions.
6.6.5. Add 1.0 mL of HCl and dilute to volume using DI Water. Mix well.
6.6.6. Do not allow concentrated acids to contact Stock Standards. Prepare fresh each day.

TABLE 3: INTERMEDIATE STANDARD

Identification	Element	Stock Identification	Amount added (mL)	HCl (mL)	Final Volume (mL)	Final Concentration (µg/mL)
Intermediate Standard	As	STD# 1 IA 140-131-201*	1.0	1.0	10	1.5
	Cd					0.20
	Hg					0.30
	Pb					0.50
	Co					0.50
	Ni					2.0
	V					1.0
	Se					8.0
	Ag					1.0
	Tl					0.80
	Au	STD# 2 IA 140-131-215*	1.0			10
	Pd					1.0
	Ir					1.0
	Os					1.0
	Pt					1.0
	Rh					1.0
	Ru					1.0
	Ba	STD# 3 AQ0-150-191*	1.0			70
	Sb					9.0
	Li					25
	Mo					15
	Cu					5.0
	Sn					60
	Cr					5.0
	Fe					5.0
	Mn					5.0
	Zn					5.0
	Ca					50
	K					50
	Mg	Magnesium 1,000 µg/mL	0.050			5.0

* SCP Science catalog numbers ending in 1 denote 125 mL bottle sizes and catalog numbers ending in 5 denote 500 mL bottle sizes

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6.7. 0.5J Calibration Standard Preparation

6.7.1. Prepare a solution containing the elements listed in Table 4 below in a solution containing 5.0% HNO_3, 2.5% H_2SO_4, 1.0% HCl and 400 µg/mL Thiourea.

6.7.2. Add 0.050 mL of Intermediate Standard to a 50 mL Digitube® and add approximately 35 mL of DI Water.

6.7.3. Add 3.75 mL of Acid Digestion Mix and add DI Water to approximately 45 mL mark.

6.7.4. Add 1.0 mL of 2% Thiourea Solution and 1.0 mL Internal Standard before diluting to 50 mL final volume using DI Water.

6.7.5. Do not allow concentrated acids to contact Intermediate Standard. Prepare fresh each day.

TABLE 4: 0.5J CALIBRATION STANDARD

Identification	Element	Intermediate Standard (mL)	Acid Digestion Mix (mL)	Internal Standard Solution (mL)	2% Thiourea (mL)	Final Volume (mL)	Final Concentration (µg/L)
0.5J Calibration Standard	As	0.050	3.75	1.0	1.0	50	1.5
	Cd						0.20
	Hg						0.30
	Pb						0.50
	Co						0.50
	Ni						2.0
	V						1.0
	Se						8.0
	Ag						1.0
	Tl						0.8
	Au						10
	Pd						1.0
	Ir						1.0
	Os						1.0
	Pt						1.0
	Rh						1.0
	Ru						1.0
	Ba						70
	Sb						9.0
	Li						25
	Mo						15
	Cu						5.0
	Sn						60
	Cr						5.0
	Fe						5.0
	Mn						5.0
	Zn						5.0
	Ca						50
	K						50
	Mg						5.0

6.8. 1.5J Calibration Standard Preparation

6.8.1. Prepare a solution containing the elements listed in Table 5 below in a solution containing 5.0% HNO_3, 2.5% H_2SO_4, 1.0% HCl and 400 µg/mL Thiourea.

6.8.2. Add 0.150 mL of Intermediate Standard to a 50 mL Digitube® and add approximately 35 mL of DI Water.

6.8.3. Add 3.75 mL of Acid Digestion Mix and add DI Water to approximately 45 mL mark.

6.8.4. Add 1.0 mL of 2% Thiourea Solution and 1.0 mL Internal Standard before diluting to 50 mL final volume using DI Water.

6.8.5. Do not allow concentrated acids to contact Intermediate Standard. Prepare fresh each day.

TABLE 5: 1.5J CALIBRATION STANDARD

Identification	Element	Intermediate Standard (mL)	Acid Digestion Mix (mL)	Internal Standard Solution (mL)	2% Thiourea (mL)	Final Volume (mL)	Final Concentration (µg/L)
1.5J Calibration Standard	As	0.150	3.75	1.0	1.0	50	4.5
	Cd						0.60
	Hg						0.90
	Pb						1.5
	Co						1.5
	Ni						6.0
	V						3.0
	Se						24
	Ag						3.0
	Tl						2.4
	Au						30
	Pd						3.0
	Ir						3.0
	Os						3.0
	Pt						3.0
	Rh						3.0
	Ru						3.0
	Ba						210
	Sb						27
	Li						75
	Mo						45
	Cu						15
	Sn						180
	Cr						15
	Fe						15
	Mn						15
	Zn						15
	Ca						150
	K						150
	Mg						15

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6.9. 2.0J Calibration Standard Preparation

6.9.1. Prepare a solution containing the elements listed in Table 6 below in a solution containing 5.0% HNO_3, 2.5% H_2SO_4, 1.0% HCl and 400 µg/mL Thiourea.

6.9.2. Add 0.200 mL of Intermediate Standard to a 50 mL Digitube® and add approximately 35 mL of DI Water.

6.9.3. Add 3.75 mL of Acid Digestion Mix and add DI Water to approximately 45 mL mark.

6.9.4. Add 1.0 mL of 2% Thiourea Solution and 1.0 mL Internal Standard before diluting to 50 mL final volume using DI Water.

6.9.5. Do not allow concentrated acids to contact Intermediate Standard. Prepare fresh each day.

TABLE 6: 2.0J CALIBRATION STANDARD

Identification	Element	Intermediate Standard (mL)	Acid Digestion Mix (mL)	Internal Standard Solution (mL)	2% Thiourea (mL)	Final Volume (mL)	Final Concentration (µg/L)
2.0J Calibration Standard	As	0.200	3.75	1.0	1.0	50	6.0
	Cd						0.80
	Hg						1.2
	Pb						2.0
	Co						2.0
	Ni						8.0
	V						4.0
	Se						32
	Ag						4.0
	Tl						3.2
	Au						40
	Pd						4.0
	Ir						4.0
	Os						4.0
	Pt						4.0
	Rh						4.0
	Ru						4.0
	Ba						280
	Sb						36
	Li						100
	Mo						60
	Cu						20
	Sn						240
	Cr						20
	Fe						20
	Mn						20
	Zn						20
	Ca						200
	K						200
	Mg						20

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6.10. Calibration Blank

6.10.1. Prepare a solution Table 6 containing 5.0% HNO_3, 2.5% H_2SO_4, 1.0% HCl and 400 µg/mL Thiourea as described in Table 7 below.
6.10.2. Add approximately 35 mL of DI Water to a 50 mL Digitube®.
6.10.3. Add 3.75 mL of Acid Digestion Mix and add DI Water to approximately 45 mL mark.
6.10.4. Add 1.0 mL of 2% Thiourea Solution and 1.0 mL Internal Standard before diluting to 50 mL final volume using DI Water.
6.10.5. Prepare fresh each day.

TABLE 7: CALIBRATION BLANK

Description	Acid Digestion Mix (mL)	Internal Standard Solution (mL)	2% Thiourea (mL)	Final Volume (mL)
Cal Blank	3.75	1.0	1.0	50

6.11. Method Blank Preparation

6.11.1. Refer to Calibration Blank

6.12. Sample Preparation

6.12.1. Weigh approximately 100 mg of the sample into a 50 mL Digitube®.
6.12.2. Add 30 mL of deionized water and swirl solution to mix.
6.12.3. Add 3.75 mL of Acid Digestion mixture.
6.12.4. Add deionized water to approximately 45 mL and then transfer 1.0 mL of Internal Standard Solution followed by 1.0 mL of 2% Thiourea.
6.12.5. Dilute to a final volume of 50 mL with deionized water and mix thoroughly.
6.12.6. Samples are stable for 24 hours.

6.13. Isobaric Overlap Corrections

6.13.1. An isobaric interference results from equal mass isotopes of different elements present in the sample solution. Analysis sequences that are processed utilizing multi-element standards will require the use of correction equations to compensate for known isobaric overlaps originating from the elemental standard and sample. The following correction equations should be used:

KED Mode:

$M_c(58) = M_u(58) \times 1 - M_{(rm)}(57) \times 0.13208$
$M_c(98) = M_u(98) \times 1 - M_{(rm)}(99) \times 0.14655$
$M_c(106) = M_u(106) \times 1 - M_{(rm)}(111) \times 0.09766$
$M_c(108) = M_u(108) \times 1 - M_{(rm)}(111) \times 0.06953$
$M_c(120) = M_u(120) \times 1 - M_{(rm)}(125) \times 0.01273$
$M_c(123) = M_u(123) \times 1 - M_{(rm)}(125) \times 0.12588$
$M_c(190) = M_u(190) \times 1 - M_{(rm)}(195) \times 0.00036$
$M_c(192) = M_u(192) \times 1 - M_{(rm)}(195) \times 0.02315$
$M_c(196) = M_u(196) \times 1 - M_{(rm)}(202) \times 0.005023$

H_2 DRC Mode

$M_c(78) = M_u(78) \times 1 - M_{(rm)}(83) \times 0.03043$

The correction equations can be derived from the following equation:

$M_c = M_u - [M_{(rm)} \times (A_{(ie)}/A_{(rm)})]$

Where:

M_c = Corrected Count Rate for the analyte
M_u = Uncorrected count rate for the analyte
$M_{(rm)}$ = Count Rate of Reference Mass (rm) for the Interfering Element
$A_{(ie)}$ = Percent Abundance of Interfering Element at the analyte mass
$A_{(rm)}$ = Percent Abundance of Interfering Element at the Reference Mass (rm)

Example:

$M_c(58) = M_u(58) \times 1 - M_{(rm)}(57) \times (0.28 / 2.12)$

Where $0.28/ 2.12 = 0.13208$

6.13.2. All correction coefficients were calculated based on the Agilent Technologies 2016 Relative Isotopic Abundance Table.

6.13.3. Multiplier used in the correct equation may differ slightly from the multiplier used in the Syngistix instrument method due to rounding.

7. INSTRUMENT PROCEDURE:

7.1. Perform the ICP-MS daily performance check prior to beginning the analytical sequence. Refer to NexION 350X ICP-MS SOP DCN 16-001923 for Daily Check procedures.

7.2. A calibration curve consisting of three standards (0.5J, 1.5J and 2.0J) and a blank must be used. The calibration correlation coefficient (R) must be ≥ 0.99.

7.3. Set up the sequence as per Table 8.

7.4. Confirm the calibration by analyzing the 1.5J check standard after the calibration blank check subsequent to the calibration standards. The calibration check standard must recover ± 20% of the theoretical concentration for multi-element analysis and ±10% for single element determinations.

7.5. The check standard must also be re-analyzed at a minimum of once every 10 samples and as the last injection of the analytical sequence.

7.6. A drift of no more than (NMT) 20% is allowed between bracketing standards.

7.7. The sample concentration is calculated as:

$$\text{Conc. } (\mu g/g) = \frac{\text{Solution Conc. } (\mu g/L) \times \text{Solution vol. (L)} \times \text{Dilution Factor}}{\text{Sample Mass (g)}}$$

TABLE 8: EXAMPLE SAMPLE ANALYSIS SEQUENCE

ID	Type	Level
Cal Blank	Cal Blank	Level 1
0.5J Cal Std	Cal Std	Level 2
1.5J Cal Std	Cal Std	Level 3
2.0J Cal Std	Cal Std	Level 4
Cal Blank Check	QC Check	N/A
1.5J Check Std 1	QC Check	N/A
Method Blank	Sample	N/A
Sample(s) 10 or less	Sample	N/A
1.5J Check Std 2	QC Check	N/A

7.8. Instrument Setup and Parameters

7.8.1. Instrument settings are listed only as guidelines. Settings may be changed in order to accommodate changes in sample matrix or hardware configurations.

7.8.2. The AMS-II makeup gas must be engaged during analysis using a minimum dilution gas ratio of 15%.

7.8.3. The elements arsenic and selenium are analyzed using hydrogen reaction gas in order to remove polyatomic interferences. A hydrogen DRC flow rate of approximately 4-5 mL/min should be used.

7.8.4. The instrument method is stored under the Approved Test Method Folder labelled as "HEPES_Final_EI_Profile.mth" for elemental impurities testing along with "HEPES_TraceMetals.mth" for trace metal or finished good analyses.

TABLE 9: ICP-MS PARAMETERS

ICP-MS System	Perkin Elmer NexION350X Inductively Coupled Plasma Mass Spectrometry (ICP-MS) with Syngistix Software
Sweeps/Reading	20
Replicates	3
Nebulizer Gas	Argon
Collision Gas	Helium
Reaction Gas	Hydrogen
Dilution Gas	Argon
Sample and Skimmer Cone	Platinum
Sample Rinses	Rinse-1: 60 sec at 45 rpm 5.0% HNO_3, 2.5% HCl (or as applicable to mitigate carry over)

TABLE 10: LINEAR RANGE AND CORRESPONDING TUNING MODE

Isotope	Internal Standard	Mode	Linear Range (µg/L)	Isotope	Internal Standard	Mode	Linear Range (µg/L)
7Li	9Be	STD	15-100	108Pd	89Y	KED	0.60-4.0
24Mg	45Sc	KED	3.0-20	109Ag	125Te	KED	0.60-4.0
39K	45Sc	KED	30-200	111Cd	125Te	KED	0.12-0.80
44Ca	45Sc	KED	30-200	118Sn	125Te	KED	36-240
51V	45Sc	KED	0.60-4.0	119Sn	125Te	KED	36-240
52Cr	45Sc	KED	3.0-20	120Sn	125Te	KED	36-240
53Cr	45Sc	KED	3.0-20	121Sb	125Te	KED	5.4-36
55Mn	45Sc	KED	3.0-20	123Sb	125Te	KED	5.4-36
57Fe	45Sc	KED	3.0-20	135Ba	159Tb	KED	42-280
58Ni	45Sc	KED	1.2-8.0	137Ba	159Tb	KED	42-280
59Co	45Sc	KED	0.30-2.0	138Ba	159Tb	KED	42-280
60Ni	45Sc	KED	1.2-8.0	188Os	209Bi	KED	0.60-4.0
62Ni	45Sc	KED	1.2-8.0	189Os	209Bi	KED	0.60-4.0
63Cu	45Sc	KED	3.0-20	190Os	209Bi	KED	0.60-4.0
65Cu	45Sc	KED	3.0-20	191Ir	209Bi	KED	0.60-4.0
67Zn	125Te	KED	3.0-20	192Os	209Bi	KED	0.60-4.0
68Zn	125Te	KED	3.0-20	193Ir	209Bi	KED	0.60-4.0
75As	89Y	H_2 DRC	0.90-6.0	194Pt	209Bi	KED	0.60-4.0
77Se	89Y	H_2 DRC	4.8-32	195Pt	209Bi	KED	0.60-4.0
78Se	89Y	H_2 DRC	4.8-32	196Pt	209Bi	KED	0.60-4.0
95Mo	89Y	KED	9.0-60	197Au	209Bi	KED	6.0-40
97Mo	89Y	KED	9.0-60	199Hg	209Bi	KED	0.18-1.2
98Mo	89Y	KED	9.0-60	200Hg	209Bi	KED	0.18-1.2
99Ru	89Y	KED	0.60-4.0	202Hg	209Bi	KED	0.18-1.2
101Ru	89Y	KED	0.60-4.0	203Tl	209Bi	KED	0.48-3.2
103Rh	89Y	KED	0.60-4.0	205Tl	209Bi	KED	0.48-3.2
105Pd	89Y	KED	0.60-4.0	206Pb	209Bi	KED	0.30-2.0
106Pd	89Y	KED	0.60-4.0	207Pb	209Bi	KED	0.30-2.0
107Ag	125Te	KED	0.60-4.0	208Pb	209Bi	KED	0.30-2.0

8. REPORTING:

8.1. Any result below the 0.3J target concentration will be reported as less than the corresponding LOQ value listed in Table 1. Results above the 0.3J target LOQ concentration will be reported in µg/g to 2 significant figures. The average result will be reported for multiple isotopes of the same element that are above the LOQ concentration.

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