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ANALYTICAL METHOD OF ANALYSIS: DETERMINATION OF ICH Q3D ELEMENTAL IMPURITIES BY INDUCTIVELY COUPLED PLASMA MASS SPECTROMETRY (ICP-MS) IN D-GALACTOSE

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1. PURPOSE:

1.1. To provide a procedure for the assessment of Elemental Impurities via the NexION 350X S/N 85VN5093001 ICP-MS. This procedure was assessed as a full quantitative option-3 procedure as per validation report, BSI-RPT-2077 v1.0, and follows the validation parameters for quantitation procedures as outlined in USP <233>.

1.2. This method was previously validated as per validation report BSI-RPT-0739. The protocol was to revalidate the method with a lower aluminum and barium limit of quantitation along with updating internal standard and rinse utilized.

1.3. Elements under USP <232> will be considered and are as follows:

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

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

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

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

1.3.5. Class 4: Al, Fe, Mn, and Zn

2. SCOPE:

2.1. Applies to D-Galactose 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. The Laboratory Technology Manager, or other qualified designated individual, is responsible for the control, implementation, training, and maintenance of this Protocol.

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

3.3. If any abnormalities are determined during routine use of the ICP-MS or during calibration, the QC Managers 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. BSI-PRL-0498, Analytical Validation Protocol Determination of ICH Q3D Elemental Impurities (Class 1, 2A, 2B, 3, & 4) by Inductively Coupled Plasma Mass Spectrometry (ICPMS) in D-Galactose

4.2. BSI-RPT-0739, Analytical Method Validation Report: Elemental Impurities in D-Galactose

4.3. BSI-RPT-2077, Analytical Method Validation Report: Determination of Elemental Impurities in D-Galactose Revalidation

4.4. BSI-SOP-0303, NexION 350X ICP-MS SOP

4.5. BSI-SOP-0304, NexION 350X ICP-MS Care and Maintenance SOP

4.6. BSI-SOP-0436, Analytical Methods Validation Master Plan

4.7. ICH Guideline for Elemental Impurities Q3D Current

4.8. NexION Operation with Syngistix Software Guide

4.9. USP <232> Elemental Impurities- Limits

4.10. USP <233> Elemental Impurities- Procedures

4.11. USP <730> Plasma Spectrochemistry

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

TABLE 1: LIMITS FOR D-GALACTOSE (100 GRAM/DAY PATIENT EXPOSURE)

Element	ICH Class	Parenteral PDE Limits (µg/day)	0.1J LOQ (µg/g) in sample	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	0.015	0.045	0.075	0.15	0.225
Cd	1	2.0	0.002	0.006	0.01	0.02	0.03
Hg	1	3.0	0.003	0.009	0.015	0.03	0.045
Pb	1	5.0	0.005	0.015	0.025	0.05	0.075
Co	2A	5.0	0.005	0.015	0.025	0.05	0.075
Ni	2A	20	0.02	0.06	0.10	0.20	0.30
V	2A	10	0.01	0.03	0.05	0.10	0.15
Tl	2B	8.0	0.008	0.024	0.04	0.08	0.12
Se	2B	[1]50	0.05	0.15	0.25	0.50	0.75
Ag	2B	10	0.01	0.03	0.05	0.10	0.15
Au	2B	100	0.10	0.30	0.50	1.0	1.5
Pd	2B	10	0.01	0.03	0.05	0.10	0.15
Ir	2B	10	0.01	0.03	0.05	0.10	0.15
Os	2B	10	0.01	0.03	0.05	0.10	0.15
Pt	2B	10	0.01	0.03	0.05	0.10	0.15
Rh	2B	10	0.01	0.03	0.05	0.10	0.15
Ru	2B	10	0.01	0.03	0.05	0.10	0.15
Ba	2B	[1]25	0.025	0.075	0.125	0.25	0.375
Sb	3	90	0.09	0.27	0.45	0.90	1.35
Li	3	250	0.25	0.75	1.25	2.5	3.75
Mo	3	[1]50	0.05	0.15	0.25	0.5	0.75
Cu	3	[1]25	0.025	0.075	0.125	0.25	0.375
Sn	3	600	0.60	1.8	3.0	6.0	9.0
Cr	3	[1]50	0.05	0.15	0.25	0.50	0.75
Al	4	[1]25	0.025	0.075	0.125	0.25	0.375
Fe	4	[1]200	0.20	0.60	1.0	2.0	3.0
Mn	4	[1]25	0.025	0.075	0.125	0.25	0.375
Zn	4	[1]200	0.20	0.60	1.0	2.0	3.0

[1]PDE calculated based on customer specification

5. MATERIALS AND EQUIPMENT:

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

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, or equivalent

5.3. Consumable Supplies
- 5.3.1. SCP Digitubes® 15 mL, 50 mL, and 100 mL
- 5.3.2. Pipette Tips of various sizes
- 5.3.3. SiliaPrep MB SPE Cartridges, Silica-Based AMPA

5.4. Personnel
- 5.4.1. All personnel that executed the protocol are trained on ICP-MS analysis or are considered Subject Matter Experts. The test method will be assigned a mark as read training to QC analysts involved with the execution.

TABLE 2: REFERENCE STANDARDS

Identification[1]	Manufacturer	Concentrations / Elements
Pharma-CAL Custom Standard Parenteral STD# 1 IA AQ0-145-201	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 (50 µg/mL), Tl (8 µg/mL), V (10 µg/mL)
USP232/ICH Q3D Parenteral STD#2 IA 140-131-211	SCP Science	Au (100 µg/mL); Ir, Os, Pd, Pt, Rh, & Ru (10 µg/mL)
1,000 µg/mL Barium Standard	SCP Science	Ba (1,000 µg/mL)
1,000 µg/mL Antimony Standard	SCP Science	Sb (1,000 µg/mL)
1,000 µg/mL Lithium Standard	SCP Science	Li (1,000 µg/mL)
1,000 µg/mL Molybdenum Standard	SCP Science	Mo (1,000 µg/mL)
1,000 µg/mL Copper Standard	SCP Science	Cu (1,000 µg/mL)
1,000 µg/mL Tin Standard	SCP Science	Sn (1,000 µg/mL)
1,000 µg/mL Chromium Standard	SCP Science	Cr (1,000 µg/mL)
1,000 µg/mL Aluminum Standard	SCP Science	Al (1,000 µg/mL)
1,000 µg/mL Iron Standard	SCP Science	Fe (1,000 µg/mL)
1,000 µg/mL Manganese Standard	SCP Science	Mn (1,000 µg/mL)
1,000 µg/mL Zinc Standard	SCP Science	Zn (1,000 µg/mL)
Pharma-CAL Custom Standard AQ0-086-125 (Internal Standard)	SCP Science	Be, Sc, Y, Re (10 µg/mL); Te (25 µg/mL); Ge, Tb, Bi (5 µg/mL)

[1]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 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 standards listed in Table 2 will be used to prepare the intermediate standard used in 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)

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 (Prepare same day).

6.4. Internal Standard/Complexing Solution

6.4.1. Weigh approximately 1.0 gram of Thiourea into a 50 mL Digitube®.

6.4.2. Add approximately 20 mL of deionized water and mix to dissolve.

6.4.3. Filter solution through a SiliaPrep Cation Solid Phase Extraction (SPE) cartridge into a separate 50 mL digitube.

6.4.4. Add 2.5 mL of Pharma CAL Custom Standard (Internal standard) Stock followed by 25 mL of hydrochloric acid.

6.4.5. Dilute to a final volume of 50 mL with deionized water and mix well.

6.5. 2% Thiourea Solution

6.5.1. Weigh approximately 1.0 gram of Thiourea into a 50 mL Digitube®.

6.5.2. Add approximately 20 mL of deionized water and mix to dissolve.

6.5.3. Filter solution through a SiliaPrep Cation Solid Phase Extraction (SPE) cartridge into a separate 50 mL digitube.

6.5.4. Dilute to a final volume of 50 mL with deionized water and mix well.

6.6. Intermediate Standard Preparation

6.6.1. Prepare a standard solution containing the elements listed in Table 3, using the standards STD#1 IA, STD#2 IA, and individual stock standards. Prepare by adding intermediate and stocks standards to a 15 mL Digitube®. Add DI Water to approximately 8 mL and add hydrochloric acid (HCl). Dilute to volume using DI Water. Do not allow stock standards to contact concentrated acids while preparing solutions.

TABLE 3: INTERMEDIATE STANDARD PREPARATION

Identification	Element	Stock Identification	Amount Added (mL)	HCl (mL)	Final Volume Deionized Water (mL)	Final Concentration (µg/mL)
Intermediate Standard	As	STD# 1 IA AQ0-145-201	1.0	1.0	10.0	1.5
	Cd					0.20
	Hg					0.30
	Pb					0.50
	Co					0.50
	Ni					2.0
	V					1.0
	Se					5.0
	Ag					1.0
	Tl					0.80
	Au	STD# 2 IA 140-131-211	1.0			10
	Pd					1.0.
	Ir					10
	Os					1.0
	Pt					1.0
	Rh					1.0
	Ru					1.0
	Ba	1,000 µg/mL Ba Std	0.025			2.5
	Sb	1,000 µg/mL Sb Std	0.090			9.0
	Li	1,000 µg/mL Li Std	0.250			25
	Mo	1,000 µg/mL Mo Std	0.050			5.0
	Cu	1,000 µg/mL Cu Std	0.025			2.5
	Sn	1,000 µg/mL Sn Std	0.600			60
	Cr	1,000 µg/mL Cr Std	0.050			5.0
	Al	1,000 µg/mL Al Std	0.025			2.5
	Fe	1,000 µg/mL Fe Std	0.200			20
	Mn	1,000 µg/mL Mn Std	0.025			2.5
	Zn	1,000 µg/mL Zn Std	0.200			20

6.7. 0.5J Calibration Standard Preparation

6.7.1. Prepare a solution containing the elements listed in Table 4 below in 5.0% HNO_3, 2.5% H_2SO_4, 1.0% HCl and 0.04% (400 µg/mL) Thiourea. Add intermediate standard to a separate 50 mL Digitube® followed by addition of approximately 35 mL of DI Water. Add acid mixture and dilute to 45 mL using DI Water. Add internal standard/complexing solution and dilute to volume using DI Water. Do not allow standards to contact concentrated acids while preparing solutions. Standards are stable for 24 hours.

TABLE 4: 0.5J CALIBRATION STANDARD

Identification	Element	Intermediate Standard (mL)	Acid Digestion Mix (mL)	Internal Standard/ Complexing Solution (mL)	Final Volume Deionized Water (mL)	Final Concentration (µg/L)
0.5J Calibration Standard	As	0.050	3.75	1.0	50	1.5
	Cd					0.20
	Hg					0.30
	Pb					0.50
	Co					0.50
	Ni					2.0
	V					1.0
	Se					5.0
	Ag					1.0
	Tl					0.80
	Au					10
	Pd					1.0
	Ir					1.0
	Os					1.0
	Pt					1.0
	Rh					1.0
	Ru					1.0
	Ba					2.5
	Sb					9.0
	Li					25
	Mo					5.0
	Cu					2.5
	Sn					60
	Cr					5.0
	Al					2.5
	Fe					20
	Mn					2.5
	Zn					20

6.8. 1.5J Calibration Standard Preparation

6.8.1. Prepare a solution containing the elements listed in Table 5 below in 5.0% HNO_3, 2.5% H_2SO_4, 1.0% HCl and 0.04% (400 µg/mL) Thiourea. Add intermediate standard to a separate 50 mL Digitube® followed by addition of approximately 35 mL of DI Water. Add acid mixture and dilute to 45 mL using DI Water. Add internal standard/complexing solution and dilute to volume using DI Water. Do not allow standards to contact concentrated acids while preparing solutions. Standards are stable for 24 hours.

TABLE 5: 1.5J CALIBRATION STANDARD

Identification	Element	Intermediate Standard (mL)	Acid Digestion Mix (mL)	Internal Standard/ Complexing Solution (mL)	Final Volume Deionized Water (mL)	Final Concentration (µg/L)
1.5J Calibration Standard	As	0.150	3.75	1.0	50	4.5
	Cd					0.60
	Hg					0.90
	Pb					1.5
	Co					1.5
	Ni					6.0
	V					3.0
	Se					15
	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					7.5
	Sb					27
	Li					75
	Mo					15
	Cu					7.5
	Sn					180
	Cr					15
	Al					7.5
	Fe					60
	Mn					7.5
	Zn					60

6.9. 2.0J Calibration Standard Preparation

6.9.1. Prepare a solution containing the elements listed in Table 6 below in 5.0% HNO_3, 2.5% H_2SO_4, 1.0% HCl and 0.04% (400 µg/mL) Thiourea. Add intermediate standard to a separate 50 mL Digitube® followed by addition of approximately 35 mL of DI Water. Add acid mixture and dilute to 45 mL using DI Water. Add internal standard/complexing solution and dilute to volume using DI Water. Do not allow standards to contact concentrated acids while preparing solutions. Standards are stable for 24 hours.

TABLE 6: 2.0J CALIBRATION STANDARD

Identification	Element	Intermediate Standard (mL)	Acid Digestion Mix (mL)	Internal Standard/ Complexing Solution (mL)	Final Volume Deionized Water (mL)	Final Concentration (µg/L)
2.0J Calibration Standard	As	0.200	3.75	1.0	50	6.0
	Cd					0.80
	Hg					1.2
	Pb					2.0
	Co					2.0
	Ni					8.0
	V					4.0
	Se					20
	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					10
	Sb					36
	Li					100
	Mo					20
	Cu					10
	Sn					240
	Cr					20
	Al					10
	Fe					80
	Mn					10
	Zn					80

6.10. Calibration Blank

6.10.1. Prepare a solution containing 5.0% HNO_3, 2.5% H_2SO_4, 1.0% HCl and 0.04% (400 µg/mL) Thiourea as per Table 7 below. Do not allow Internal Standard/ Complexing Solution to contact concentrated acids. To a separate 50 mL Digitube® add approximately 35 mL of DI Water. Add acid mixture and dilute to 45 mL using DI Water. Add internal standard/complexing solution and dilute to volume using DI Water.

TABLE 7: CALIBRATION BLANK

Description	Internal Standard/ Complexing Solution (mL)	Acid Digestion Mix (mL)	Final Volume Deionized Water (mL)
Cal Blank	1.0	3.75	50

6.11. Method Blank Preparation

6.11.1. Add 30 mL of deionized water and 3.75 mL of Acid Digestion mixture to a 50 mL Digitube®.

6.11.2. Add deionized water to approximately 45 mL and then transfer 1.0 mL of Internal Standard/ Complexing Solution.

6.11.3. Dilute to a final volume of 50 mL with deionized water and mix well.

6.12. Sample Preparation

6.12.1. Weigh approximately 1,000 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/ Complexing Solution.

6.12.5. Dilute to a final volume of 50 mL with deionized water and mix thoroughly.

6.12.6. Samples are to be prepared fresh for each analysis.

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:

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

The correction equations can be derived from the following equation:
$M_c = M_u - [M_{(rm)} \times (A_{(i.e.)}/A_{(rm)})]$

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
$A_{(i.e.)}$ = Percent Abundance of Interfering Element (i.e.) at the analyte mass
$A_{(rm)}$ = Percent Abundance of Interfering Element at the Reference Mass (rm)

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

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 correction 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, BSI-SOP-0303, for Daily Check procedures.

7.2. A calibration curve of no less than two standards 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 standard after the calibration. The calibration check must recover ± 20% of the calculated theoretical concentration for multi-element analysis and ±10% for single element determinations.

7.5. The check standard must be verified after the calibration. A re-analysis of the check standard will be performed a minimum of once every 10 samples and at the end of the analytical run.

7.6. The drift between bracketing standard checks must be NMT 20% for each Target element.

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	Not Applicable
1.5J Check Std 1	QC Check	Not Applicable
Method Blank	Sample	Not Applicable
Sample(s) 10 or less	Sample	Not Applicable
1.5J Check Std 2	QC Check	Not Applicable

7.8. Instrument Setup and Parameters

7.8.1. Instrument settings are only listed 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, aluminum, and selenium are analyzed using hydrogen reaction gas in order toremove poly atomic interferences. A hydrogen DRC (Dynamic Reaction Cell) flow rate of approximately 4 mL/min should be used.

7.8.4. The instrument method is stored under the Approved Test Method Folder labelled as "Galactose_Updated_EI.mth" for elemental impurities testing.

TABLE 9: ICP-MS PARAMETERS

ICP-MS System	Perkin Elmer NexION350X Inductively Coupled Plasma Mass Spectrometry (ICP-MS) with Syngistix Software
Sweeps/Readings	20
Replicates	3
Nebulizer Gas	Argon
Collision Cell Gas	Helium
Reaction Cell 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 with 0.04% Thiourea (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	45Sc	STD	5.0-100	109Ag	125Te	KED	0.20-4.0
27Al	45Sc	H_2 DRC	0.50-10	111Cd	125Te	KED	0.04-0.80
27Al	45Sc	KED	0.50-10	113Cd	125Te	KED	0.04-0.80
51V	45Sc	KED	0.20-4.0	118Sn	125Te	KED	12-240
52Cr	45Sc	KED	1.0-20	119Sn	125Te	KED	12-240
53Cr	45Sc	KED	1.0-20	120Sn	125Te	KED	12-240
55Mn	45Sc	KED	0.50-10	121Sb	125Te	KED	1.8-36
57Fe	45Sc	KED	4.0-80	123Sb	125Te	KED	1.8-36
58Ni	45Sc	KED	0.40-8.0	135Ba	159Tb	KED	0.50-10
59Co	45Sc	KED	0.10-2.0	136Ba	159Tb	KED	0.50-10
60Ni	45Sc	KED	0.40-8.0	137Ba	159Tb	KED	0.50-10
62Ni	45Sc	KED	0.40-8.0	138Ba	159Tb	KED	0.50-10
63Cu	45Sc	KED	0.50-10	188Os	209Bi	KED	0.20-4.0
65Cu	45Sc	KED	0.50-10	189Os	209Bi	KED	0.20-4.0
67Zn	45Sc	KED	4.0-80	190Os	209Bi	KED	0.20-4.0
68Zn	45Sc	KED	4.0-80	191Ir	209Bi	KED	0.20-4.0
75As	72Ge	KED	0.30-6.0	192Os	209Bi	KED	0.20-4.0
75As	89Y	H_2 DRC	0.30-6.0	193Ir	209Bi	KED	0.20-4.0
77Se	89Y	H_2 DRC	1.0-20	194Pt	209Bi	KED	0.20-4.0
78Se	89Y	H_2 DRC	1.0-20	195Pt	209Bi	KED	0.20-4.0
95Mo	89Y	KED	1.0-20	196Pt	209Bi	KED	0.20-4.0
97Mo	89Y	KED	1.0-20	197Au	209Bi	KED	2.0-40
98Mo	89Y	KED	1.0-20	199Hg	209Bi	KED	0.06-1.2
99Ru	89Y	KED	0.20-4.0	200Hg	209Bi	KED	0.06-1.2
101Ru	89Y	KED	0.20-4.0	202Hg	209Bi	KED	0.06-1.2
103Rh	89Y	KED	0.20-4.0	203Tl	209Bi	KED	0.16-3.2
105Pd	89Y	KED	0.20-4.0	205Tl	209Bi	KED	0.16-3.2
106Pd	89Y	KED	0.20-4.0	206Pb	209Bi	KED	0.10-2.0
107Ag	125Te	KED	0.20-4.0	207Pb	209Bi	KED	0.10-2.0
108Pd	89Y	KED	0.20-4.0	208Pb	209Bi	KED	0.10-2.0

8. REPORTING

8.1. For all elements, any result below the 0.1J target concentration will be reported as less than the corresponding LOQ value listed in Table 1. Results above the 0.1J Target Concentration will be reported in µg/g (ppm) according to Table 11 below. If there are multiple isotopes present in the method and the result is above the LOQ target concentration, report the averageresult from the isotopes.

TABLE 11: RESULT REPORTING

Result	Reporting
If < LOQ	Report as < LOQ
If ≥ LOQ and < 1.0 ppm	Report to two (2) decimal places
If ≥ LOQ and ≥ 1.0 ppm	Report to whole number