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ANALYTICAL METHOD VALIDATION REPORT: DETERMINATION OF ICH Q3D ELEMENTAL IMPURITIES + IRON BY INDUCTIVELY COUPLED PLASMA MASS SPECTROMETRY (ICP-MS) IN SODIUM DECANOATE

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1. PURPOSE:

1.1. The purpose of this validation report is to establish documented evidence that the test protocol for Elemental Impurities in Sodium Decanoate, BSI-PRL-0454 v. 1.0, performs according to USP and BioSpectra requirements.

1.1.1. Elements under USP <232>, <233> will be considered and are as follows:

1.1.1.1. Class 1: Hg, As, Cd, and Pb
1.1.1.2. Class 2A: Co, V, and Ni
1.1.1.3. Class 2B: Tl, Au, Pd, Ir, Os, Rh, Ru, Se, Ag, and Pt
1.1.1.4. Class 3: Li, Sb, Sn, Ba, Mo, Cu, and Cr
1.1.1.5. Class 4: Fe

2. SCOPE:

2.1. Applies to Sodium Decanoate and related 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.
2.3. This report applies to the protocol validation for elemental impurities in Sodium Decanoate, by Inductively Coupled Plasma-Mass Spectrometry (ICP-MS) performed at BioSpectra Inc.

3. REFERENCES:

3.1. BSI-PRL-0454, Analytical Method Validation Protocol: Determination of ICH Q3D Elemental Impurities (Class 1, 2A, 2B, 3 and 4) by Inductively Coupled Plasma Mass Spectrometry (ICP-MS) in Sodium Decanoate
3.2. BSI-SOP-0303, NexION 350X ICP-MS SOP
3.3. BSI-SOP-0304, NexION 350X ICP-MS Care and Maintenance
3.4. BSI-SOP-0426, Operation and Maintenance of CEM Mars 6 Digestion Microwave SOP
3.5. BSI-SOP-0436, Analytical Method Validation Master Plan
3.6. ICH Guideline for Elemental Impurities Q3D
3.7. NexION Operation with Syngistix Software Guide
3.8. USP <232>, <233>
3.9. USP <730> Plasma Spectrochemistry
3.10. USP <1730> Plasma Spectrochemistry—Theory and Practice

4. BACKGROUND:

4.1. This validation was executed using a parenteral PDE daily dose calculation of 10 grams per day and was performed as per ICH Q3D and USP General Chapters <232> and <233>, Elemental Impurities –Procedures, Validation of Quantitative Procedures. (See Table 1)
4.2. The test protocol validation report includes the following parameters:

4.2.1. Specificity
4.2.2. Linearity and Range
4.2.3. Limit of Quantification (LOQ)
4.2.4. Accuracy by "Spiked Recovery"
4.2.5. Precision (Repeatability)
4.2.6. Intermediate Precision (Ruggedness)
4.2.7. Standard and Sample Solution Stability

TABLE 1: LIMITS FOR SODIUM DECANOATE (10 GRAM/DAY EXPOSURE)						
Element	**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	0.24	0.40	0.80	1.2
Se	2B	80	2.4	4.0	8.0	12
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	1500	45	75	150	225
Cu	3	300	9.0	15	30	45
Sn	3	600	18	30	60	90
Cr	3	1100	33	55	110	165
Fe	4	[1]50	1.5	2.5	5.0	7.5

[1]PDE calculated based on customer specification.

5. MATERIALS AND EQUIPMENT:

TABLE 2: EQUIPMENT

Type	Supplier	Model	Serial Number	Cal. Due
Analytical Balance	Sartorius	MSE224S	36707108	04/2022
Mechanical Pipette	Eppendorf	Research Plus (20-200 µL)	Q31264C	02/28/22
Mechanical Pipette	Eppendorf	Research Plus (20-200 µL)	G25447D	01/19/22
Mechanical Pipette	Eppendorf	Research Plus (100-1000 µL)	G26211D	05/31/22
Mechanical Pipette	Eppendorf	Research Plus (100-1000 µL)	R14419C	02/28/22
Mechanical Pipette	Eppendorf	Research Plus (0.5-5 mL)	J18397D	05/31/22
Mechanical Pipette	Eppendorf	Research Plus (1-10 mL)	L31359I	02/28/22
ICP-MS	Perkin Elmer	NexION 350X	85VN5093001	01/2022
Digestion Microwave	CEM	Mars 6	MY2255	09/22/22
Deionized water system	Millipore	IQ-7005/ Element POD	F9SA14284H	06/2022

TABLE 3: REAGENTS

Type	Grade	Supplier	Catalog Number	Lot Number	Expiration
70% Nitric Acid	Trace Metal	VWR	87003-261	1121040	04/15/23
70% Nitric Acid	Trace Metal	VWR	87003-261	1121060	07/12/23
36% Hydrochloric Acid	Trace Metal	VWR	87003-253	4120110	12/23/23
Sulfuric Acid	Trace Metal	Fisher	A510-P212	3119020	05/21/22
Deionized water	Type I Ultrapure	In-House	N/A	N/A	N/A
Thiourea	99+% Pure	ACROS	220052500	A0407315	10/31/23
ICP-MS Setup Solution	N/A	Perkin Elmer	N8145051	37-147GSX1	02/28/23
ICP-MS KED Setup Solution	N/A	Perkin Elmer	N8145052	35-83GST1	12/30/21
SiliaPrep SPE Filter	Silica-Based AMPA	Silicycle	R85130B	172546	N/A

5.1. Consumable Supplies

5.1.1. SCP Digitubes® 15 mL, 50 mL and 100 mL

5.1.2. Pipette Tips of various sizes

TABLE 4: REFERENCE STANDARDS				
Identification	**Manufacturer**	**Lot Number**	**Expiration**	**Concentrations / Elements**
Pharma-CAL Standard Parenteral STD# 1 IA 140-131-201	SCP Science	S210429002	05/2022	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 (10 µg/mL)
USP232/ICH Q3D Parenteral STD# 2 IA 140-131-215	SCP Science	S210811029	11/2022	Au (100 µg/mL); Ir, Os, Pd, Pt, Rh, & Ru (10 µg/mL)
Pharma-CAL Standard Parenteral STD# 3 IA 140-131-221	SCP Science	S210331019	07/2022	Ba (700 µg/mL), Cr (1,100 µg/mL), Cu (300 µg/mL), Li (250 µg/mL), Mo (1,500 µg/mL), Sb (90 µg/mL), Sn (600 µg/mL)
Iron Stock Standard N9303771	Perkin Elmer	25-59FEY1	08/30/22	Fe (1,000 µg/mL)
Pharma-CAL Custom Standard AQ0-086-125 (Internal Standard)	SCP Science	S210104029	01/2022	Be, Sc, Y, Re (10 µg/mL); Te (25 µg/mL);Ge, Tb, Bi (5 µg/mL)

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. Acid Digestion Mix

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

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

6.5.2. 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.

6.5.3. Scale as necessary for use (Prepare same day).

6.3. Internal Standard/Complexing Solution

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

6.5.2. Added approximately 20 mL of deionized water and mixed to dissolve.

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

6.5.4. Added 2.5 mL of Internal Standard Intermediate followed by 25 mL of hydrochloric acid.

6.5.5. Diluted to a final volume of 50 mL with deionized water and mix well.

6.5.6. Scaled proportionally as needed for use.

6.4. 2% Thiourea Solution

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

6.4.2. Added approximately 20 mL of deionized water and mixed to dissolve.

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

6.4.4. Diluted to a final volume of 50 mL with deionized water and mix well.

6.4.5. Scaled proportionally as needed for use.

6.5. Intermediate Standard Preparation

6.5.1. Prepared a standard solution containing the elements listed in Table 5 using the standards STD#1 IA, STD#2 IA, STD#3 IA, and individual single source Iron 1,000 µg/mL standard. Prepared by adding stock standards to a 15 mL Digitube®. Added DI water to approximately 8 mL then added hydrochloric acid (HCl). Diluted to volume using DI Water.

TABLE 5: 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
	Tl					0.80
	Se					8.0
	Ag					1.0
	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 IA 140-131-221	1.0			70
	Sb					9.0
	Li					25
	Mo					150
	Cu					30
	Sn					60
	Cr					110
	Fe	1,000 µg/mL Fe Std	0.050			5.0

6.6. 0.5J Calibration Standard Preparation

6.6.1. Prepared a solution containing the elements listed in Table 6 below in 5.33% HNO_3, 2.67% H_2SO_4, 1.0% HCl, and 0.04% (400 µg/mL) Thiourea. Added intermediate standard to a separate 50 mL Digitube® followed by addition of approximately 35 mL of DI Water. Added acid mixture then diluted to 45 mL using DI Water. Added internal standard/complexing solution and diluted to volume using DI Water. Intermediate standards were not allowed to contact concentrated acids while preparing solutions.

TABLE 6: 0.5J CALIBRATION STANDARD

Identification	Element	Intermediate Standard (mL)	Acid Mix (mL)	Internal Standard/ Complexing Solution (mL)	Final Volume (mL)	Final Concentration (µg/L)
0.5J Calibration Standard	As	0.050	4.0	1.0	50	1.5
	Cd					0.20
	Hg					0.30
	Pb					0.50
	Co					0.50
	Ni					2.0
	V					1.0
	Tl					0.80
	Se					8.0
	Ag					1.0
	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					150
	Cu					30
	Sn					60
	Cr					110
	Fe					5.0

6.7. 1.5J Calibration Standard Preparation

6.7.1. Prepared a solution containing the elements listed in Table 7 below in 5.33% HNO_3, 2.67% H_2SO_4, 1.0% HCl, and 0.04% (400 µg/mL) Thiourea. Added intermediate standard to a separate 50 mL Digitube® followed by addition of approximately 35 mL of DI Water. Added acid mixture then diluted to 45 mL using DI Water. Added internal standard/complexing solution and diluted to volume using DI Water. Intermediate standards were not allowed to contact concentrated acids while preparing solutions.

TABLE 7: 1.5J CALIBRATION STANDARD

Identification	Element	Intermediate Standard (mL)	Acid Mix (mL)	Internal Standard/ Complexing Solution (mL)	Final Volume (mL)	Final Concentration (µg/L)
1.5J Calibration Standard	As	0.150	4.0	1.0	50	4.5
	Cd					0.60
	Hg					0.90
	Pb					1.5
	Co					1.5
	Ni					6.0
	V					3.0
	Tl					2.4
	Se					24
	Ag					3.0
	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					450
	Cu					90
	Sn					180
	Cr					330
	Fe					15

6.8. 2.0J Calibration Standard Preparation

6.8.1. Prepared a solution containing the elements listed in Table 8 below in 5.33% HNO_3, 2.67% H_2SO_4, 1.0% HCl, and 0.04% (400 µg/mL) Thiourea. Added intermediate standard to a separate 50 mL Digitube® followed by addition of approximately 35 mL of DI Water. Added acid mixture then diluted to 45 mL using DI Water. Added internal standard/complexing solution and diluted to volume using DI Water. Intermediate standards were not allowed to contact concentrated acids while preparing solutions.

TABLE 8: 2.0J CALIBRATION STANDARD

Identification	Element	Intermediate Standard (mL)	Acid Mix (mL)	Internal Standard/ Complexing Solution (mL)	Final Volume (mL)	Final Concentration (µg/L)
2.0J Calibration Standard	As	0.200	4.0	1.0	50	6.0
	Cd					0.80
	Hg					1.2
	Pb					2.0
	Co					2.0
	Ni					8.0
	V					4.0
	Tl					3.2
	Se					32
	Ag					4.0
	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					600
	Cu					120
	Sn					240
	Cr					440
	Fe					20

6.9. Calibration Blank

6.9.1. Prepared a solution containing 5.33% HNO_3, 2.67% H_2SO_4, 1.0% HCl and 0.04% (400 µg/mL) Thiourea as per Table 9 below. Internal Standard Solution was not allowed to contact concentrated acids. To a separate 50 mL Digitube®, added approximately 35 mL of DI Water. Added acid mixture then diluted to 45 mL using DI Water. Added Internal Standard/Complexing Solution anddiluted to volume using DI Water.

TABLE 9: CALIBRATION BLANK

Description	Acid Mix (mL)	Internal Standard/ Complexing Solution (mL)	Final Volume (mL)
Cal Blank	4.0	1.0	50

6.10. Method Blank Preparation

6.10.1. Added 4.0 mL of Acid Digestion Mixture into a clean 20 mL digestion vessel, placed a plug on the vessel, and properly torqued the vessel cap. Placed vessel in the microwave carousel then digested and completed preparation according to Section 6.12 below.

6.11. Sample Preparation

6.11.1. Weighed approximately 100 mg of the sample into a clean 20 mL digestion vessel and added 4.0 mL of Acid Digestion Mixture.

6.11.2. Properly torqued vessel cap and placed in microwave carousel. Digested and completed preparation according to Section 6.12 below.

6.12. Microwave Digestion Procedure

6.12.1. Refer to BSI-SOP-0426 for general usage guidelines of the Mars 6 Microwave Digestion System.

6.12.2. Prepared at least one method blank per digestion run. Method blank was prepared in the same manner as the sample without the addition of the sample (see above).

6.12.3. Digested the sample using the program listed in Table 10.

TABLE 10: TEMPERATURE CONTROLLED MICROWAVE DIGESTION PROGRAM

Power (Watts)	Percent Power	Ramp (Minutes)	Temperature (°C)	Hold (Minutes)
1800	100	15:00	150	10:00
1800	100	6:00	175	5:00

6.12.4. After digestion, placed the vessels into an ice bath and allowed the vessels to cool for approximately 40 minutes. Before opening, the vessels were turned sideways and slowly rotated in order to collect the condensation on the inside of the vessel walls.

6.12.5. Quantitatively transferred the vessel contents into a 50 mL Digitube® containing approximately 5 mL of deionized water and 1.0 mL of Internal Standard/Complexing Solution. Rinsed the bottom of the plug into the 50 mL Digitube® using deionized water.

6.12.6. Extracted any remaining volatile elements by adding 15 mL of a pre-mixed solution of 0.500 mL of 2% Thiourea diluted to 15 mL using deionized water to the digestion vessel. Added this directly to the 50 mL Digitube®.

6.12.7. Rinsed the vessel an additional two times using deionized water and transferred each rinse to the 50 mL Digitube®. Diluted to a final volume of 50 mL using deionized water and mixed well.

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

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 (ie) 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. Performed 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 was used. The calibration correlation coefficient (R) was ≥ 0.99.

7.3. Set up the sequence as per Table 11.

7.4. Confirmed 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 was verified after each calibration. A re-analysis of the check standard was to be performed a minimum of once every 10 samples and at the end of the analytical run.

7.6. The drift between the 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 11: 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 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 was engaged during analysis using a minimum dilution gas ratio of 15%.

7.8.3. The elements arsenic, iron, and selenium were analyzed using hydrogen reaction gas in order to remove poly atomic interferences. A hydrogen DRC (Dynamic Reaction Cell) flow rate of approximately 4 mL/min was used.

TABLE 12: ICP-MS PARAMETERS

ICP-MS System	Perkin Elmer NexION 350X Inductively Coupled Plasma Mass Spectrometry (ICP-MS) with Syngistix Software Version2.4
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 13: LINEAR RANGE AND CORRESPONDING TUNE MODE							
Isotope	**Internal Standard**	**Mode**	**Linear Range (µg/L)**	**Isotope**	**Internal Standard**	**Mode**	**Linear Range (µg/L)**
7Li	9Be	STD	15-100	113Cd	125Te	KED	0.12-0.80
51V	45Sc	KED	0.60-4.0	118Sn	125Te	KED	36-240
52Cr	45Sc	KED	66-440	119Sn	125Te	KED	36-240
53Cr	45Sc	KED	66-440	120Sn	125Te	KED	36-240
56Fe	72Ge	H_2 DRC	3.0-20	121Sb	125Te	KED	5.4-36
57Fe	72Ge	KED	3.0-20	123Sb	125Te	KED	5.4-36
58Ni	72Ge	KED	1.2-8.0	135Ba	159Tb	KED	42-280
59Co	72Ge	KED	0.30-2.0	137Ba	159Tb	KED	42-280
60Ni	72Ge	KED	1.2-8.0	138Ba	159Tb	KED	42-280
62Ni	72Ge	KED	1.2-8.0	188Os	209Bi	KED	0.60-4.0
63Cu	72Ge	KED	18-120	189Os	209Bi	KED	0.60-4.0
65Cu	72Ge	KED	18-120	190Os	209Bi	KED	0.60-4.0
75As	72Ge	H_2 DRC	0.90-6.0	191Ir	209Bi	KED	0.60-4.0
75As	72Ge	KED	0.90-6.0	192Os	209Bi	KED	0.60-4.0
77Se	89Y	H_2 DRC	4.8-32	193Ir	209Bi	KED	0.60-4.0
78Se	89Y	H_2 DRC	4.8-32	194Pt	185Re	KED	0.60-4.0
95Mo	89Y	KED	90-600	195Pt	185Re	KED	0.60-4.0
97Mo	89Y	KED	90-600	196Pt	185Re	KED	0.60-4.0
98Mo	89Y	KED	90-600	197Au	209Bi	KED	6.0-40
99Ru	125Te	KED	0.60-4.0	199Hg	185Re	KED	0.18-1.2
101Ru	125Te	KED	0.60-4.0	200Hg	185Re	KED	0.18-1.2
103Rh	125Te	KED	0.60-4.0	202Hg	185Re	KED	0.18-1.2
105Pd	125Te	KED	0.60-4.0	203Tl	209Bi	KED	0.48-3.2
106Pd	125Te	KED	0.60-4.0	205Tl	209Bi	KED	0.48-3.2
107Ag	125Te	KED	0.60-4.0	206Pb	209Bi	KED	0.30-2.0
108Pd	125Te	KED	0.60-4.0	207Pb	209Bi	KED	0.30-2.0
109Ag	125Te	KED	0.60-4.0	208Pb	209Bi	KED	0.30-2.0
111Cd	125Te	KED	0.12-0.80				

7.9. Linearity and Range

7.9.1. The ICP-MS linearity study included standards equivalent to the concentrations shown in Table 15 and encompassed the following standards: (30%, 50%, 100%, 150%, and 200% of the Target Concentration). Each standard was prepared in triplicate and analyzed against the calibration curve described in Section 6.6 to Section 6.8. The average standard recovery for each level of the three replicates was then determined.

7.9.2. Linearity study was performed once as the standard preparation in the protocol is the same regardless of the product analyzed.

7.9.2.1. Acceptance Criteria:

7.9.2.1.1. The mean standard recovery for each element at each of the spike levels, as per USP <233> requirement, must be in the range of 70% - 150%.

TABLE 14: LINEARITY STANDARD PREPARATION

Description	Intermediate Standard (mL)	Acid Mix (mL)	Internal Standard/ Complexing Solution (mL)	Final Volume (mL)
Cal Blank Reference	N/A	4.0	1.0	50
0.3J Standard	0.030	4.0	1.0	50
0.5J Standard	0.050	4.0	1.0	50
1.0J Standard	0.100	4.0	1.0	50
1.5J Standard	0.150	4.0	1.0	50
2.0J Standard	0.200	4.0	1.0	50

TABLE 15: LINEARITY STANDARD CONCENTRATIONS					
Element	**0.3J Standard (µg/L)**	**0.5J Standard (µg/L)**	**1.0J Standard (µg/L)**	**1.5J Standard (µg/L)**	**2.0J Standard (µg/L)**
As	0.90	1.5	3.0	4.5	6.0
Cd	0.12	0.20	0.40	0.60	0.80
Hg	0.18	0.30	0.60	0.90	1.2
Pb	0.30	0.50	1.0	1.5	2.0
Co	0.30	0.50	1.0	1.5	2.0
Ni	1.2	2.0	4.0	6.0	8.0
V	0.60	1.0	2.0	3.0	4.0
Tl	0.48	0.80	1.6	2.4	3.2
Se	4.8	8.0	16	24	32
Ag	0.60	1.0	2.0	3.0	4.0
Au	6.0	10	20	30	40
Pd	0.60	1.0	2.0	3.0	4.0
Ir	0.60	1.0	2.0	3.0	4.0
Os	0.60	1.0	2.0	3.0	4.0
Pt	0.60	1.0	2.0	3.0	4.0
Rh	0.60	1.0	2.0	3.0	4.0
Ru	0.60	1.0	2.0	3.0	4.0
Ba	42	70	140	210	280
Sb	5.4	9.0	18	27	36
Li	15	25	50	75	100
Mo	90	150	300	450	600
Cu	18	30	60	90	120
Sn	36	60	120	180	240
Cr	66	110	220	330	440
Fe	3.0	5.0	10	15	20

TABLE 16: LINEARITY PERCENT RECOVERY RESULTS													
Isotope	**Mode**	**0.3J Mean**	**0.5J Mean**	**1.0J Mean**	**1.5J Mean**	**2.0J Mean**	**Isotope**	**Mode**	**0.3J Mean**	**0.5J Mean**	**1.0J Mean**	**1.5J Mean**	**2.0J Mean**
7Li	STD	107	107	107	101	105	113Cd	KED	99	93	94	97	94
51V	KED	101	104	101	98	101	118Sn	KED	100	99	98	100	98
52Cr	KED	102	101	100	99	100	119Sn	KED	99	99	97	101	99
53Cr	KED	101	101	100	99	99	120Sn	KED	99	99	98	100	97
56Fe	H_2 DRC	96	99	98	97	101	121Sb	KED	101	100	98	100	98
57Fe	KED	99	96	99	101	97	123Sb	KED	100	100	99	100	98
58Ni	KED	99	98	99	100	101	135Ba	KED	101	99	100	99	99
59Co	KED	97	97	99	99	101	137Ba	KED	100	99	99	98	99
60Ni	KED	100	99	99	99	101	138Ba	KED	99	99	99	97	98
62Ni	KED	99	95	98	101	100	188Os	KED	99	100	102	100	103
63Cu	KED	98	98	100	100	101	189Os	KED	103	101	101	102	103
65Cu	KED	98	98	100	100	102	190Os	KED	99	100	100	101	101
75As	H_2 DRC	97	98	97	95	95	191Ir	KED	100	100	101	101	102
75As	KED	99	102	100	97	100	192Os	KED	100	102	101	102	103
77Se	H_2 DRC	100	99	99	99	95	193Ir	KED	99	100	100	100	101
78Se	H_2 DRC	100	99	100	99	97	194Pt	KED	100	100	100	100	101
95Mo	KED	100	100	100	100	99	195Pt	KED	102	100	99	99	100
97Mo	KED	101	101	101	100	100	196Pt	KED	104	100	101	100	101
98Mo	KED	101	101	101	100	100	197Au	KED	101	101	100	100	102
99Ru	KED	99	100	99	100	98	199Hg	KED	105	96	98	97	96
101Ru	KED	99	100	100	101	100	200Hg	KED	103	104	97	95	99
103Rh	KED	99	98	99	102	100	202Hg	KED	101	102	95	94	97
105Pd	KED	99	102	99	100	98	203Tl	KED	100	100	100	101	101
106Pd	KED	99	99	100	101	98	205Tl	KED	101	100	100	100	101
107Ag	KED	100	101	98	101	99	206Pb	KED	99	100	99	99	100
108Pd	KED	102	98	100	101	99	207Pb	KED	102	101	99	101	102
109Ag	KED	100	99	99	101	99	208Pb	KED	101	99	100	100	100
111Cd	KED	91	91	91	96	88							

All elements meet Linearity acceptance criteria of 70% - 150%.

7.10. Accuracy

7.10.1. Three (N=3) unspiked samples were prepared for analysis. The unspiked sample preparations were used for spike recovery calculations. Samples were prepared in triplicate at three spiking levels (50%, 100%, and 150% of the 1.0J Target Concentration) as shown in Table 1. The solutions were analyzed by ICP-MS, as per the protocol, by a single analyst.

$$\% \text{ Recovery} = \frac{(\text{Conc. of spiked replicate} - \text{Average Conc. of 3 unspiked samples}) \times 100}{\text{Expected spiked concentration}}$$

7.10.1.1. Acceptance Criteria

7.10.1.1.1. The mean spike recovery for each element at each of the three spike levels, as per USP <233> requirement, must be in the range of 70% - 150%.

7.10.2. Spiked Reference (Unspiked) Solution Preparation

7.10.2.1. Prepare as per section 6.11.

7.10.3. Spike Recovery Sample Preparation

7.10.3.1. Weighed 100 mg of sample into a 20 mL digestion vessel.

7.10.3.2. Pipetted appropriate intermediate standard spike amount as per Table 17 on top of the solid. All intermediate standards spikes were added prior to acid addition.

7.10.3.3. Pipetted 4.0 mL of Acid Mixture, placed plug on the vessel, properly torqued cap, and placed vessel in microwave carousel. Digested according to Section 6.12

7.10.3.4. After digestion, vessels were placed into ice bath for approximately 40 minutes. Before opening vessel cap, the vessels were turned sideways and slowly rotated to collect condensation on the inside of vessel walls.

7.10.3.5. Quantitatively transferred the contents into a 50 mL Digitube® containing approximately 5 mL of deionized water and 1.0 mL of Internal Standard/ Complexing Solution.

7.10.3.6. Extracted any remaining volatile elements by adding 15 mL of pre-mixed solution of 0.500 mL of 2% Thiourea diluted to 15 mL using deionized water. Transferred to the 50 mL Digitube® after swirling in the vessel.

7.10.3.7. Rinsed the vessel an additional two times with deionized water and transferred each rinse to the Digitube®. Diluted to final volume of 50 mL and mixed well.

TABLE 17: ACCURACY SAMPLE SPIKES

Description	Sample Amount (mg)	Intermediate Standard Spike (mL)	Acid Mix (mL)	Internal Standard/ Complexing Solution (mL)	Final Volume (mL)
Method Blank	N/A	N/A	4.0	1.0	50
Unspiked	100	N/A	4.0	1.0	50
0.3J Spiked Sample	100	0.030	4.0	1.0	50
0.5J Spiked Sample	100	0.050	4.0	1.0	50
1.0J Spiked Sample	100	0.100	4.0	1.0	50
1.5J Spiked Sample	100	0.150	4.0	1.0	50

TABLE 18: ACCURACY RESULTS FOR SODIUM DECANOATE
(Mean percent recovery of triplicate preparations)

Isotope	Mode	0.5J Mean	1.0J Mean	1.5J Mean	Isotope	Mode	0.5J Mean	1.0J Mean	1.5J Mean
7Li	STD	115	108	104	113Cd	KED	113	96	93
51V	KED	89	92	90	118Sn	KED	103	101	96
52Cr	KED	80	86	83	119Sn	KED	102	100	95
53Cr	KED	79	86	83	120Sn	KED	100	100	95
56Fe	H_2 DRC	95	92	94	121Sb	KED	98	102	98
57Fe	KED	101	100	101	123Sb	KED	97	100	97
58Ni	KED	100	91	90	135Ba	KED	114	103	112
59Co	KED	105	95	98	137Ba	KED	112	101	110
60Ni	KED	99	89	89	138Ba	KED	110	101	110
62Ni	KED	107	94	89	188Os	KED	108	98	98
63Cu	KED	91	86	86	189Os	KED	104	96	98
65Cu	KED	90	87	86	190Os	KED	106	98	98
75As	H_2 DRC	92	92	100	191Ir	KED	115	111	108
75As	KED	92	92	93	192Os	KED	103	96	96
77Se	H_2 DRC	85	87	93	193Ir	KED	115	110	108
78Se	H_2 DRC	87	88	93	194Pt	KED	97	84	88
95Mo	KED	85	91	86	195Pt	KED	94	83	86
97Mo	KED	85	91	86	196Pt	KED	95	82	86
98Mo	KED	84	90	84	197Au	KED	101	99	99
99Ru	KED	115	108	99	199Hg	KED	104	98	95
101Ru	KED	110	107	98	200Hg	KED	95	93	95
103Rh	KED	103	98	91	202Hg	KED	90	93	90
105Pd	KED	99	92	84	203Tl	KED	104	102	104
106Pd	KED	93	92	83	205Tl	KED	103	102	103
107Ag	KED	84	83	75	206Pb	KED	106	101	100
108Pd	KED	91	89	80	207Pb	KED	105	100	99
109Ag	KED	83	83	75	208Pb	KED	104	100	99
111Cd[1]	KED	131	92	88					

[1]111Cd did not meet NMT 20% drift criteria during accuracy portion and will be omitted from final test method for analysis. All other elements meet accuracy acceptance criteriaof 70% - 150%.

7.11. Specificity

7.11.1. Specificity was demonstrated by using a method blank and a calibration blank for ICP-MS analysis. A method blank was prepared as per the analytical protocol. The method blank was compared against the calibration blank and high standard for any matrix interference.

7.11.2. The solutions were analyzed as per the analytical method and the counts of the calibration blank, method blank, and high calibration standard are shown below.

7.11.2.1. Acceptance Criteria:

7.11.2.1.1. The lack of a significant interference (as demonstrated by the spike recovery of 70% to 150%, as per the Accuracy requirement from USP <233>) or by any other element in the spiked blank solution or the solution matrix itself will indicate the specificity of the method.

TABLE 19: SPECIFICITY RESULTS

Isotope	Blank (CPS)	Method Blank (CPS)	2.0J STD (CPS)	Isotope	Blank (CPS)	Method Blank (CPS)	2.0J STD (CPS)
7Li	1955	3441	2969131	113Cd	4	5	519
51V	126	139	4165	118Sn	68	93	376983
52Cr	32	879	587647	119Sn	33	45	141787
53Cr	56	155	72209	120Sn	97	152	567530
56Fe	1311	21825	185803	121Sb	5	14	48674
57Fe	12	99	929	123Sb	-35	-17	38803
58Ni	42	1544	23474	135Ba	79	196	126265
59Co	3	42	8824	137Ba	134	308	220734
60Ni	14	648	10249	138Ba	801	2040	1497981
62Ni	7	101	1561	188Os	27	23	14538
63Cu	49	297	412095	189Os	18	22	18444
65Cu	57	176	200775	190Os	44	52	29286
75As	68	84	5860	191Ir	78	47	39752
75As	38	32	2063	192Os	65	58	45547
77Se	63	176	11798	193Ir	153	98	69073
78Se	48	463	37590	194Pt	34	2	23067
95Mo	12	123	856684	195Pt	33	6	23770
97Mo	8	68	533812	196Pt	25	5	17800
98Mo	10	201	1417758	197Au	113	24	327200
99Ru	6	5	6266	199Hg	0	8	883
101Ru	13	9	8732	200Hg	1	10	1154
103Rh	22	19	50190	202Hg	1	5	623
105Pd	71	63	10022	203Tl	99	60	23956
106Pd	7	7	12650	205Tl	12	37	58609
107Ag	27	13	22745	206Pb	274	354	11957
108Pd	5	6	13540	207Pb	233	265	10509
109Ag	27	7	22859	208Pb	574	702	26135
111Cd	2	3	478				

7.12. Precision

7.12.1. Repeatability

7.12.2. All solutions for the Repeatability test were prepared by a single analyst.

7.12.3. The value of the unspiked sample preparations from Section 7.10, "Accuracy," was used for spike recovery calculations. Six sample solutions were prepared at the 1.0J Target Concentration as shown in Table 1. For ICP-MS analysis, the Target Concentration spiked samples and the unspiked samples were used for the accuracy experiment.

7.12.3.1. Acceptance Criteria:

7.12.3.1.1. The %RSD for the spike recovery concentration must be NMT 20% for each element in each sample.

TABLE 20: PRECISION RESULTS FOR SODIUM DECANOATE
(Mean recovery concentration of 6 preparations)

Isotope	Mode	1.0J Mean Recovery Conc. N=6 (µg/kg)	% RSD N=6	Isotope	Mode	1.0J Mean Recovery Conc. N=6 (µg/kg)	% RSD N=6
7Li	STD	26808	5	113Cd	KED	193	6
51V	KED	933	3	118Sn	KED	59510	4
52Cr	KED	92820	3	119Sn	KED	58806	4
53Cr	KED	92611	4	120Sn	KED	58944	4
56Fe	H_2 DRC	5284	3	121Sb	KED	9016	3
57Fe	KED	5690	4	123Sb	KED	8848	3
58Ni	KED	1992	3	135Ba	KED	75167	5
59Co	KED	490	5	137Ba	KED	74034	6
60Ni	KED	1967	2	138Ba	KED	73833	6
62Ni	KED	2008	5	188Os	KED	965	3
63Cu	KED	26068	3	189Os	KED	953	3
65Cu	KED	25998	3	190Os	KED	964	3
75As	H_2 DRC	1439	4	191Ir	KED	1092	3
75As	KED	1407	3	192Os	KED	944	3
77Se	H_2 DRC	7148	2	193Ir	KED	1089	3
78Se	H_2 DRC	7219	3	194Pt	KED	859	3
95Mo	KED	134450	4	195Pt	KED	851	4
97Mo	KED	133727	4	196Pt	KED	849	4
98Mo	KED	131775	4	197Au	KED	9830	2
99Ru	KED	1055	4	199Hg	KED	292	2
101Ru	KED	1033	6	200Hg	KED	283	3
103Rh	KED	951	5	202Hg	KED	272	3
105Pd	KED	893	6	203Tl	KED	822	2
106Pd	KED	885	6	205Tl	KED	817	2
107Ag	KED	804	6	206Pb	KED	505	2
108Pd	KED	856	6	207Pb	KED	501	3
109Ag	KED	802	6	208Pb	KED	504	2
111Cd	KED	184	5				

All elements meet Precision RSD% acceptancecriteria of NMT 20%.

7.13. Intermediate Precision (Ruggedness)

7.13.1. A second analyst, on a different day from the performance of the Repeatability experiment, prepared and analyzed the Intermediate Precision solutions. Six sample solutions were prepared at the 1.0J Target Concentration level found in Table 1 for ICP-MS analysis (this fulfilled two events as "different day" and "different analyst").

7.13.1.1. Acceptance Criteria:

7.13.1.1.1. The %RSD for the spike recovery concentration from both analysts (N=12) must be NMT 25% for each element.

TABLE 21: RUGGEDNESS RESULTS FOR SODIUM DECANOATE
(Mean recovery concentration of 12 preparations)

Isotope	Mode	1.0J Mean Recovery Conc. N=12 (µg/kg)	% RSD N=12	Isotope	Mode	1.0J Mean Recovery Conc. N=12 (µg/kg)	% RSD N=12
7Li	STD	27112	4	113Cd	KED	196	4
51V	KED	949	4	118Sn	KED	60739	4
52Cr	KED	93937	4	119Sn	KED	60128	4
53Cr	KED	93887	4	120Sn	KED	60161	4
56Fe	H_2 DRC	5440	7	121Sb	KED	9161	3
57Fe	KED	5966	8	123Sb	KED	9091	4
58Ni	KED	2003	3	135Ba	KED	76390	5
59Co	KED	502	5	137Ba	KED	74980	4
60Ni	KED	1994	3	138Ba	KED	74789	4
62Ni	KED	2007	5	188Os	KED	976	3
63Cu	KED	26556	4	189Os	KED	967	3
65Cu	KED	26448	3	190Os	KED	971	2
75As	H_2 DRC	1469	4	191Ir	KED	1113	3
75As	KED	1369	5	192Os	KED	957	3
77Se	H_2 DRC	7308	3	193Ir	KED	1107	3
78Se	H_2 DRC	7327	3	194Pt	KED	880	4
95Mo	KED	137795	4	195Pt	KED	876	4
97Mo	KED	136138	4	196Pt	KED	876	4
98Mo	KED	135016	5	197Au	KED	10153	4
99Ru	KED	1076	4	199Hg	KED	299	3
101Ru	KED	1067	5	200Hg	KED	294	5
103Rh	KED	985	5	202Hg	KED	284	6
105Pd	KED	920	5	203Tl	KED	832	2
106Pd	KED	917	6	205Tl	KED	828	2
107Ag	KED	841	6	206Pb	KED	511	3
108Pd	KED	901	7	207Pb	KED	510	3
109Ag	KED	833	6	208Pb	KED	511	2
111Cd	KED	193	8				

All elements meet the Ruggedness %RSD acceptance criteria of NMT 25%.

7.14. Limit of Quantitation (LOQ)

7.14.1. The limit of quantitation (LOQ) is demonstrated from spike recovery performed at the 30% Target Concentration spiking levels as shown in Table 1.

7.14.2. Samples were prepared in triplicate following Section 7.10.3 and using amounts listed for 0.3J spiked samples in Table 17 above.

7.14.2.1. Acceptance Criteria:

7.14.2.1.1. The mean percent spike recovery for each element at the 30% Target Concentration spiking levels, as per the USP <233> accuracy guideline, must be in the range of 70% - 150%.

TABLE 22: LIMIT OF QUANTIFICATION RESULTS
(Mean percent recovery of 3 preparations)

Isotope	Mode	0.3J Mean % Recovery	Isotope	Mode	0.3J Mean % Recovery
7Li	STD	112	113Cd	KED	96
51V	KED	90	118Sn	KED	105
52Cr	KED	82	119Sn	KED	104
53Cr	KED	82	120Sn	KED	102
56Fe	H_2 DRC	97	121Sb	KED	102
57Fe	KED	103	123Sb	KED	102
58Ni	KED	101	135Ba	KED	117
59Co	KED	106	137Ba	KED	115
60Ni	KED	99	138Ba	KED	113
62Ni	KED	100	188Os	KED	102
63Cu	KED	93	189Os	KED	100
65Cu	KED	92	190Os	KED	102
75As	H_2 DRC	97	191Ir	KED	116
75As	KED	94	192Os	KED	102
77Se	H_2 DRC	88	193Ir	KED	115
78Se	H_2 DRC	90	194Pt	KED	104
95Mo	KED	90	195Pt	KED	103
97Mo	KED	89	196Pt	KED	102
98Mo	KED	88	197Au	KED	103
99Ru	KED	114	199Hg	KED	93
101Ru	KED	112	200Hg	KED	95
103Rh	KED	104	202Hg	KED	99
105Pd	KED	97	203Tl	KED	109
106Pd	KED	92	205Tl	KED	110
107Ag	KED	85	206Pb	KED	108
108Pd	KED	89	207Pb	KED	104
109Ag	KED	84	208Pb	KED	105
111Cd	KED	106			

[1]111Cd did not meet NMT 20% drift criteria during LOQ portion and will be omitted from final test method for analysis. All other elements meet the LOQ %RSD acceptance criteria of 70% - 150%.

7.15. Sample and Standard Stability

7.15.1. The 50% and 200% Target Concentration level calibration standards were analyzed as samples against calibration curves constructed from freshly prepared calibration standards at T=1 day from the date of preparation.

7.15.2. A spiked sample solution prepared at the 1.0J Target Concentration level in Table 1 from the Precision experiment was used for sample stability. The spiked sample solution was analyzed against calibration curves constructed from freshly prepared calibration standards at time points T=0 (day of preparation) and T=1 (1 day from the date of preparation).

7.15.2.1. Acceptance Criteria:

7.15.2.1.1. The recovery of each element must be within the range of 80% to 120% recovery of the T = 0 results for the calibration standard.

7.15.2.1.2. The recovery of each element must be within the range of 80% to 120% recovery of the T = 0 results for the spiked sample solution.

TABLE 23: SAMPLE AND STANDARD STABILITY (%RECOVERY)

Isotope	Mode	0.5J Std (%)	2.0J Std (%)	1.0J Spike (%)	Isotope	Mode	0.5J Std (%)	2.0J Std (%)	1.0J Spike (%)
7Li	STD	100	100	94	113Cd	KED	100	101	94
51V	KED	87	92	92	118Sn	KED	96	102	94
52Cr	KED	90	91	91	119Sn	KED	98	101	93
53Cr	KED	91	91	91	120Sn	KED	99	102	96
56Fe	H_2 DRC	94	94	95	121Sb	KED	100	103	98
57Fe	KED	105	100	101	123Sb	KED	100	103	99
58Ni	KED	98	97	104	135Ba	KED	100	97	101
59Co	KED	103	97	98	137Ba	KED	99	97	100
60Ni	KED	102	100	108	138Ba	KED	99	97	100
62Ni	KED	117	99	99	188Os	KED	98	97	96
63Cu	KED	103	98	105	189Os	KED	100	97	99
65Cu	KED	103	98	103	190Os	KED	96	99	99
75As	H_2 DRC	97	91	103	191Ir	KED	98	99	102
75As	KED	106	93	108	192Os	KED	100	97	99
77Se	H_2 DRC	102	98	107	193Ir	KED	97	99	100
78Se	H_2 DRC	101	99	107	194Pt	KED	99	98	102
95Mo	KED	99	101	101	195Pt	KED	101	96	102
97Mo	KED	98	100	101	196Pt	KED	101	96	101
98Mo	KED	98	99	101	197Au	KED	100	99	106
99Ru	KED	99	100	95	199Hg	KED	110	96	92
101Ru	KED	99	100	91	200Hg	KED	95	94	93
103Rh	KED	97	102	97	202Hg	KED	118	100	104
105Pd	KED	94	103	96	203Tl	KED	98	99	98
106Pd	KED	99	102	92	205Tl	KED	100	99	99
107Ag	KED	101	104	96	206Pb	KED	98	98	99
108Pd	KED	99	100	97	207Pb	KED	98	99	98
109Ag	KED	97	102	95	208Pb	KED	99	99	98
111Cd	KED	118	96	104					

All elements met the acceptance criteria of 80% to 120% recovery for stability solutions for standards and samples.

8. DEVIATIONS:

8.1. 111Cd results will be invalidated due to check standard failing above 20% drift during the accuracy/LOQ portion of the validation. 111Cd will not be removed from the final method since it will be used as a correction equation, but values in the calibration and QC tabs will be erased so only counts are monitored. 113Cd meets all acceptance criteria for the validation and will be used for reporting in the final test method.

8.2. Accuracy and Precision was performed a second time due to check standard failure in the final bracketing standard. This was justified since only the system suitability failed and the acceptance criteria was met for all analytes. Similar concentrations were obtained between the two runs.

9. CONCLUSION:

9.1. The test method for Elemental Impurities in Sodium Decanoate has been validated. The Method was found to be:

9.1.1. Specific: The method blank did not show any significant interference for all analyzed masses.

9.1.2. Linear: 30% to 200% of working standard solution corresponding to 0.3J to 2.0J. Mean percent recovery ranged from 88% to 107%.

9.1.3. Sensitive: LOQ recoveries were within 82% to 117% for sodium decanoate.

9.1.4. Accurate: From 50% (0.5J) to 150% (1.5J) of working standard concentration level with mean percent recoveries ranging from 75% to 115%. All masses analyzed met acceptance criteria within the specified range. 111Cd had a recovery of 131% at 0.5J, but the results were disregarded as this analyte did not meet criteria for standard drift.

9.1.5. Precise: Closeness of agreement demonstrated between six sample preparations by percent RSD's ranging from 2% to 6%.

9.1.6. Rugged: Satisfactory precision was demonstrated between two sets of six sample preparations performed on different days and by different analysts. The percent RSD's ranged from 2% to 8%.

9.1.7. Stable: With respect to stability of solutions, the sample solutions for sodium decanoate and the working standards are shown to be stable for 24 hours for all elements analyzed using this protocol.

10. NOTEBOOK REFERENCE:

TABLE 24: NOTEBOOK REFERENCE

STUDY		NOTEBOOK REFERENCE
Specificity		EIV-6/ pages 31-35
Linearity and Range		EIV-6/ pages 27-30
Accuracy/ Precision/LOQ by "Spiked" recovery		EIV-6/ pages 31-40
Intermediate Precision (Ruggedness)		EIV-6/ pages 46-49
Solution Stability	Day-0	EIV-6/ pages 36-40
	Day-1	EIV-6/ pages 41-45