HHS Public Access

Author manuscript

J Radioanal Nucl Chem. Author manuscript; available in PMC 2020 May 15.

Published in final edited form as:

J Radioanal Nucl Chem. 2020 March 23; 324(2): 887–896.

Determination of ^{237}Np and ^{239}Pu in Urine Using Sector Field Inductively Coupled Plasma Mass Spectrometry (SF-ICP-MS)

Ge Xiao[*,1], **Yongzhong Liu**[2], **Robert L. Jones**[1]

[1]Inorganic and Radiation Analytical Toxicology Branch, Centers for Disease Control and Prevention, 4770 Buford Highway, Mail Stop S110-5, Atlanta, GA 30341, USA

[2]Battelle Memorial Institute, Atlanta Analytical Services, 2987 Clairmont Rd, Atlanta, GA 30329, USA

Abstract

Measuring ^{237}Np and ^{239}Pu in urine at low levels is important for both biomonitoring and radiological emergency response. Here we report a newly developed and validated analytical method used to determine ^{237}Np and ^{239}Pu in urine by selective retention of Np and Pu from 2mL of urine directly onto TEVA® resin followed by SF-ICP-MS (coupled to a membrane desolvating introduction system) detection. The method provides solid phase extraction of Np/Pu with observed recovery ratios ranging from 89% to 113% and rapid results with limits of detection well below recommended detection guidelines for children and pregnant women (NCRP 161 reference).

Keywords

^{237}Np; ^{239}Pu; urine samples; SF-ICP-MS; SPE; TEVA®

Introduction

Neptunium (Np) and plutonium (Pu) are the first and the second transuranic element of the actinide series, respectively. Both Np and Pu are radioactive, metallic elements usually produced by neutron irradiation of uranium (U) in nuclear reactors and primarily generated as a by-product in conventional nuclear power reactors [1, 2]. ^{237}Np and ^{239}Pu were dispersed worldwide as a result of atmospheric tests of nuclear weapons in the 1950s and 1960s, releases from reprocessing plants, nuclear weapons production and testing facilities accidents, and nuclear power plants incidents (e.g. Chernobyl in 1986 [3]).

[*]corresponding author: gxiao@cdc.gov.

Conflict of interest

The authors declare that they have no competing financial and non-financial interest.

The atomic weights of the 25 known isotopes of Np range from 225 to 244 [4]. The most stable Np isotope is ^{237}Np, with a half-life of 2.14 million years. It decays into ^{233}Pa through alpha decay, releasing alpha particles at 4.959 MeV. This series decay chain ends with ^{209}Bi, a nonradioactive element. Of the Pu isotopes, 20 have been characterized, with atomic weights ranging from 228 to 247 [5]. These include ^{239}Pu, an isotope with a half-life of 24,100 years. As ^{239}Pu decays, it releases alpha particles at 5.244 MeV, becoming ^{235}U. This series ends with the stable isotope ^{207}Pb.

^{237}Np and ^{239}Pu are among several priority radionuclides of public health concern because of their toxicity and potential for involvement in a nuclear or radiological incident such as detonation of a dirty bomb or use of a radiological dispersal device. Internal contamination could be caused by inhalation, ingestion or open wounds. Inside the body, the isotopes concentrate in the liver, bones, or other organs inside of the human body. They can remain in the body for decades, continuously exposing the surrounding tissue to radiation. Long-term exposure to ^{237}Np or ^{239}Pu increases the risk for various cancers. Np and Pu are also toxic metals and may lead to kidney damage. Exposure from outside the body poses little health risk [6].

Several techniques are available for measuring long-lived, alpha-emitting transuranium nuclide activity and mass concentrations in environmental and human samples [7–9]. Alpha spectrometry is traditionally used to determine low levels of ^{237}Np and ^{239}Pu. Because of relatively low specific activity and the low concentrations of ^{237}Np and ^{239}Pu in environmental and human samples, time-consuming sample preparation and counting procedures (days to weeks long) are used first to separate interfering radionuclides. Then, it is necessary to pre-concentrate and quantify the analytes ^{237}Np and ^{239}Pu. Since there are relatively small energy difference between alpha emissions from ^{239}Pu and ^{240}Pu (5.16 vs. 5.17 MeV, respectively), alpha spectrometry cannot measure the activity of ^{239}Pu and ^{240}Pu separately [10–12]. The resolution of alpha spectrometry is not adequate, and it is on the order of 0.2 MeV.

Over the past 2 decades, the rapid development of Inductively Coupled Plasma-Mass Spectrometry (ICP-MS) has opened new doors in the field of radioactivity analysis. ICP-MS offers substantial advantages over conventional radiometric counting techniques. It is a fast technique that can be used for simultaneous determination of many nuclides from one measurement. A limit of detection (LOD) of ~0.02 ng/L can be reached with a conventional quadrupole ICP-MS for ^{239}Pu [13]. Detection limits at the picogram per liter level have been reported with Sector Field ICP-MS (SF-ICP-MS) for actinides [14–18]. For a number of radionuclides, these LODs are comparable to those of alpha spectrometry methods.

Because of its high throughput and good sensitivity, SF-ICP-MS has become the most often used mass spectrometry technique for determination of ^{237}Np and ^{239}Pu, as a complement to alpha spectrometry. The main analytical interference issue for ^{237}Np and ^{239}Pu determination on SF-ICP-MS comes from the tailing or hydrides of ^{238}U and polyatomic interferences. Because of the much higher concentration of U in different sample matrices compared with Np and Pu, a chemical separation of ^{237}Np and ^{239}Pu from U is required. This also removes most of the other interfering molecular ions and sample matrix from the

samples [19–21]. Polyatomic interferences of ^{237}Np and ^{239}Pu on ICP-MS for environmental and human samples can result from $^{197}Au^{40}Ar^{+}$, $^{199}Hg^{38}Ar^{+}$, $^{199}Hg^{40}Ar^{+}$, $^{200}Hg^{37}Cl^{+}$, $^{201}Hg^{36}Ar^{+}$, $^{201}Hg^{38}Ar^{+}$, $^{202}Hg^{37}Cl^{+}$, $^{204}Hg^{33}S^{+}$, $^{204}Hg^{35}Cl^{+}$, $^{203}Tl^{34}S^{+}$, $^{203}Tl^{36}Ar^{+}$, $^{205}Tl^{32}S^{+}$, $^{205}Tl^{34}S^{+}$, $^{204}Pb^{33}S^{+}$, $^{204}Pb^{35}Cl^{+}$, $^{206}Pb^{31}P^{+}$, $^{206}Pb^{33}S^{+}$, $^{207}Pb^{32}S^{+}$, or $^{208}Pb^{31}P^{+}$.

In the event of radiological emergency, Centers for Disease Control and Prevention (CDC) is responsible for providing rapid and accurate information on the radionuclide identification and quantification, in order to direct appropriate medical treatment to people that were internally contaminated by radionuclides. CDC is aiming to identify radionuclides in urine at levels well below the action levels for the general population or for special subgroups, such as that of children or pregnant woman (C/P) set by the National Council on Radiation Protection and Measurements [22, 23]. ^{237}Np and ^{239}Pu are among the 22 priority threat radionuclides identified to be possibly released into the environment in various radiological emergency scenarios. Those action levels of ^{237}Np and ^{239}Pu are 812 pg/L (urine output expected at 5 days post intake) and 13.8 pg/L, respectively (using the ^{239}Pu action level scaled to obtain this value based on ^{237}Np to ^{239}Pu. Annual Limits on Intake ratios have been reported [24].

In this study, we report a rapid analytical method for simultaneously determining ^{237}Np and ^{239}Pu in urine samples. The solid phase extraction (SPE) part of the method is based on preliminary studies carried out by Horwitz, et al. [25, 26], Tanner, et al. [21], Maxwell, et al. [19, 20], Pappas, et al. [27], and Qiao, et al. [28]. We further optimized the method by using simple extraction steps to isolate ^{237}Np and ^{239}Pu from other actinides (e.g., U), Pb, Hg, Tl, and Au in a urine matrix. For this method, we use 2 mL of urine, from which we analyze ^{237}Np and ^{239}Pu simultaneously by using a common tracer/internal standard, ^{242}Pu. We used the modified chemical separation procedure on a single TEVA® resin cartridge and a vacuum box separation system, and SF-ICP-MS for detection.

This method is designed to be capable of detecting ^{237}Np and ^{239}Pu at elevated background level with LOD well below the suggested NCRP Guidance for medical follow-up in the non-occupationally exposed population.

Experimental

Reagents and solutions

We purchased TEVA® cartridges (1 mL) and a polycarbonate vacuum box (24 port) from Eichrom Technologies (Darien, IL, USA). All nitric acid (HNO_3) and hydrofluoric acid (HF) solutions were prepared from double-distilled acids (GFS Chemicals Inc. Columbus, OH). Deionized water was used for all solutions (≥18 MΩ·cm, from an Aqua Solutions Ultrapure Water System, Aqua Solutions, Inc., Jasper, GA). “Base urine” was collected through anonymous human donations (following CDC IRB protocol 3994) and acidified to 1% v/v HNO_3. All radioactive source solutions were traceable to the National Institute for Standards and Technology (NIST) (Gaithersburg, MD, USA). We prepared low and high level Quality Control (QC) solutions and all other urine pools for LOD determinations by spiking base urine with dilutions (by volumetric determinations) of ^{237}Np and ^{239}Pu isotope certified

reference materials which are NIST traceable (Eckert & Ziegler Analytics, Inc., Atlanta, GA). We used NIST traceable ^{242}Pu as a tracer/internal standard (U.S. Department of Energy, New Brunswick Laboratory, Argonne, IL). We used iron(II) sulfate ($FeSO_4$) hydrate and sodium nitrite ($NaNO_2$) (Sigma-Aldrich, St. Louis, MO) to adjust the oxidation states. We spiked serial dilutions of U, Pb, Tl, Hg, and Au single-element stock standards (Inorganic Ventures, Christiansburg, VA) into the urine samples to verify high separation factors for those elements from Np and Pu by using this SPE procedure. We prepared different sets of intermediate calibration standards from dilutions of ^{237}Np and ^{239}Pu isotope standard reference materials from the NIST, reference material from Eckert & Ziegler Analytics, Inc. (Atlanta, GA), and reference material from Eckert & Ziegler Isotope Products (Valencia, CA).

Sample preparation

The urine sample volume used for a single analysis is 2 mL. These are the steps we followed for sample preparation (Fig. 1): Allow urine specimens to reach ambient temperature, then shake or vortex them for approximately 5 seconds to mix well before pipetting. Spike 80 μL of 100 ng/L ^{242}Pu solution as tracer/internal standard to every 2 mL of urine patient sample or QC sample. Add 0.5 mL of concentrated HNO_3 (68%–70%), and then add 120 μL of freshly prepared 1 M $FeSO_4$ hydrate aqueous solution to each sample. Shake or vortex for approximately 5 seconds to mix the samples well, then let the reaction occur at room temperature for at least 5 minutes. Add 240 μL of freshly prepared 4 M $NaNO_2$ aqueous solution to each sample. Shake or vortex for approximately 5 seconds to mix the samples well, then let the reaction occur at room temperature for at least 5 minutes. Load each sample on a TEVA® resin cartridge of 1 mL bed volume (cartridge preconditioned with ~15 mL of 5% v/v HNO_3 using a vacuum box) (Fig. 1). Add 5 mL of 5% v/v HNO_3 to each sample tube and shake or agitate for approximately 5 seconds to wash the tube well. Add these washes to the TEVA® cartridges after the initial samples have completely entered the resin bed. Wash the cartridge again twice with ~15 mL of 5 v/v HNO_3 using a vacuum box. If a urine sample has a total U concentration >5 μg/L, use a more aggressive washing procedure by replacing the inner support tubes, outer tips and solution reservoirs that connect cartridges and wash the cartridge four times with ~15 mL of 5% v/v HNO_3. This procedure will improve the U separation by a factor of approximately 2. Strip Np and Pu from the column with 2 mL of 5% v/v HF. Transfer 1 mL of the purified samples into 4 mL polystyrene conical bottom sample cups for analysis (Fig. 1). Prepare external, aqueous-based stock calibrators by spiking 5% v/v HF with dilutions of ^{237}Np and ^{239}Pu isotope standard. Add 40 μL of internal standard solution (100 ng/L ^{242}Pu) to every 1 mL of calibrators to reach the same tracer/internal concentration as the patient and QC samples. Prepare sample blank as 5% v/v HF solution, which matches the elute solution for the column of this method.

Instrumentation

For this method, we used both the Element XR™ and Element 2™ (Thermo Fisher Scientific, Bremen, Germany) sector field ICP-MS instruments to measure ^{237}Np and ^{239}Pu concentrations. Each device is a double-focusing, magnetic sector ICP-MS with a single discrete dynode detector (Mascom, Bremen, Germany). They are equipped with nickel

sampler and skimmer cones and a CD-2 guard electrode in triple and dual mode for Element XR™ and Element 2™, respectively. The sample introduction system consists of a computer-controlled ASX-112 (Cetac, Omaha, NE) autosampler and an Aridus II™ (Cetac, Omaha, NE) desolvation unit. The Aridus II™ setup increases the sensitivity of the SF-ICP-MS by >10 times, enabling measurement of ^{237}Np and ^{239}Pu at the low level of <1 pg/L [17, 29].

Samples self-aspirate from the autosampler into the desolvation apparatus through an Apex perfluoroalkoxy (PFA) 100 μL/minute nebulizer (ESI, Omaha, NE, or equivalent). The desolvation apparatus, equipped with an upgraded PFA spray chamber, operates at 110°C. Aided by argon sweep gas and nitrogen gas for sensitivity enhancement, the sample passes through a semi-permeable membrane coil operating at 160°C. We optimize flow rates as needed, with argon sweep gas at ~3–7 L/min and nitrogen gas at ~3–9 mL/min. The desolvated sample exits the unit into a 1.8 mm (internal diameter) sapphire injector and a standard quartz torch, and then into the mass spectrometer. All experimental instrument parameters are optimized for determination of ^{237}Np and ^{239}Pu concentrations by SF-ICP-MS with respect to maximum ion intensity of ^{238}U and minimum uranium oxide formation rate using a 5 ng/L natural uranium tuning solution. The method parameters were optimized with respect to minimum relative standard deviations for ^{237}Np, ^{239}Pu, and ^{242}Pu in a trade-off with minimal analysis time. Table 1 summarizes the optimized operating conditions.

Results and discussion

Np/Pu chemical yield ratio

Because the chemical behaviors of tetravalent Pu and Np anionic complexes in HNO_3 [25, 26] on TEVA® columns are similar, commercially available and easily produced ^{242}Pu was used as tracer/internal standard for simultaneous determination of ^{237}Np and ^{239}Pu. The oxidation state adjustment of Np and Pu in the loading solution is a crucial step to ensure the same chemical behavior of Pu and Np. We adjusted the oxidation states of both elements to +4 by treatment with $FeSO_4$ and $NaNO_2$ to achieve simultaneous separation and detection in this method. The quantitative spiking experiment yielded consistent chemical recovery within ±25% of the target value. The Np/Pu chemical yield ratio ranged from 89% to 113% for 52 runs over the 5-month experiment period, indicating that the method is well-suited for accurate and precise analysis.

Removal of potential spectral interferences

To test this SPE method's ability to remove ^{238}U from the sample and therefore eliminate its tailing/hydride contribution to the analyte signals, we prepared and tested a series of solutions of natural U spiked into base urine (1–100 μg/L concentrations). When the normal washing procedure was used (Fig. 1), 0.53% to 0.69% of ^{238}U remained in the solutions. That resulted in small interferences at m/z = 237 and m/z = 239 when the separated sample solutions contained levels of ^{238}U >5 μg/L (Fig. 2). When the aggressive washing procedure was used, 0.23% to 0.48% of ^{238}U still remained in the solutions. That resulted in small interferences at m/z = 237 and m/z = 239 when the separated sample solutions contained levels of ^{238}U >10 μg/L (Fig. 2).

The National Health and Nutrition Examination Survey (NHANES) 95th percentile for U in urine of the total U.S. population for year 2015 – 2016 is 0.031 μg/L [30]. The Nuclear Regulatory Commission has recommended intervention if a uranium worker has a total urine U concentration >15 μg/L [31]. Patient urine samples with total U concentrations above 5 μg/L can be treated using this more aggressive preparation procedure (Fig. 1). However, this procedure does not fully eliminate the ^{238}U tailing effect. Because the SPE washing procedures showed good linear correlation for ^{238}U concentration (Fig. 2), if informational concentrations only are needed for ^{237}Np and ^{239}Pu in a radiological emergency, and if high ^{238}U content coexists in patient samples, mathematical correction of the ^{238}U residue's contribution to the concentrations of ^{237}Np and ^{239}Pu is possible.

We performed interference removal experiments using solutions containing the potential interferences spiked into urine matrix. Using the normal SPE sample preparation described above, Pb, Hg, and Tl, spiked into base urine at concentrations of 5 μg/L, 5 μg/L, and 1 μg/L, respectively, did not result in detectable increase of ^{237}Np or ^{239}Pu signals. These spiked concentrations of Pb, Hg, and Tl were well above the NHANES 95th percentile for these elements [30]. Although NHANES survey data is unavailable for Au, analysis of what was otherwise determined [32] to be an elevated concentration (5 μg/L) of Au did not produce detectable increase signal of ^{239}Pu. There was a trace effect on ^{237}Np with ~0.4–0.5 pg/L increased concentration compared with the base urine ^{237}Np concentration, which is far below the target NCRP 161 Clinical Decision Guide for Child/Pregnant woman (C/P) level of 810 pg/L for ^{237}Np.

Limits of detection (LOD)

We determined the LODs for ^{237}Np and ^{239}Pu in urine specimens with this method based on 51 analytical runs of spiked, matrix-matched urine samples from four different low concentration pools close to the LOD (approximately the measured blank concentration plus 3 times the standard deviation of the measured blank concentration). The LODs were calculated according to the following formula:

$$\mathrm{Conc_{LOD}} = [\mathrm{mean}\, b + 1.645(\mathrm{Sb} + \mathrm{int})]/[1 - 1.645(\mathrm{slope})]$$

Where mean b = blank average, Sb = standard deviation of blank average, int = intercept of the equation of standard deviation versus concentration for LOD samples analyzed, and slope = slope of the equation of standard deviation versus concentration.

The LODs of this method were determined to be 0.52 pg/L (1.28E-5 Bq/L) for ^{237}Np and 0.68 pg/L (1.72E-3 Bq/L) for ^{239}Pu (Fig. 3). These LODs are well below 1/3 of the NCRP 161 Clinical Decision Guide for Child/Pregnant woman (C/P) guide level (13.8 pg/L for ^{239}Pu and 810 pg/L for ^{237}Np), and therefore acceptable for an emergency radiobioassay method for determining the concentration of ^{237}Np and ^{239}Pu in urine collected at 5 days post-exposure.

Linearity

The method exhibits good linear signal response between concentrations of LOD and 200 pg/L of ^{237}Np and ^{239}Pu, with a linear fit coefficient >0.999. If a urine ^{237}Np or ^{239}Pu concentration is above the highest calibrator, the urine sample is diluted with base urine to bring the concentration within the validated calibration range. Accuracy test of reference materials and internal methods comparison study show that both ^{237}Np and ^{239}Pu can be analyzed at up to a 1:200 extra dilution without significant effect (< ± 10% error) to the target values.

Precision, accuracy and recovery

To ensure run reproducibility, internal bench QC samples were prepared by spiking base urine with ^{237}Np and ^{239}Pu at low and high concentrations within the calibration range. Table 2 shows the typical precision observed among daily QCs analyzed at the beginning and at the end of each analytical run. The run precision for the low and high QC was within 10% over 52 analytical runs, spanning a period of ~ 5 months. To assess short-term precision/stability, three concentration levels (2.0 pg/L, 100 pg/L, and 200 pg/L) of ^{237}Np and ^{239}Pu were spiked into base urine. Six samples at each concentration level were purified and analyzed sequentially. The results showed relative standard deviations of 1.77% to 4.74% for ^{237}Np and 0.27% to 6.83% for ^{239}Pu (Table 4). The stability and precision of the purified ^{237}Np and ^{239}Pu of low QC and high QC were also monitored in the final extract (5% v/v HF) for 3–4 weeks, stored at room temperature (Table 5). The concentrations were consistent with the freshly purified and analyzed samples and were within established uncertainty limits for the two QC samples.

We analyzed reference materials prepared by Oak Ridge National Laboratory (ORNL) to evaluate the method accuracy for ^{237}Np and ^{239}Pu. We used two sets of calibration standards to analyze six samples for ^{239}Pu and three samples for ^{237}Np. The concentrations of the three ^{237}Np samples were extremely high. We diluted those samples 1:100 or 1:200 with base urine to bring concentrations within the method calibration range, purified them by SPE, and analyzed them using SF-ICP-MS. The average of observed ^{237}Np and ^{239}Pu concentrations closely matched the target values, with an analytical bias of –1.25% to 6.78% (Table 3).

Additionally, 24 urine samples were prepared/spiked in 6 concentration levels in order to evaluate the accuracy using spike recovery. Urine samples spiked with 10.00, 40.00, 100.00, 20.00, 60.00 and 160.00 pg/L for both ^{237}Np and ^{239}Pu, respectively, in different base urine had recoveries that range from 99.4 to 101.9% for ^{237}Np and 100.5 to 101.1% for ^{239}Pu in two analytical runs (Table 6a and 6b) on two different days. The mean recovery is 100.8% with a SD of 1.0% for ^{237}Np, 100.7% with a SD of 0.2% for ^{239}Pu.

Stability

A stability assessment of urine sample quality is necessary to ensure the measured concentrations of ^{237}Np and ^{239}Pu are relatively unaffected by typical storage conditions. Tests were performed with QC materials to evaluate bench top and processed sample stability, short-term room temperature storage stability, stability after three freeze thaw

cycles, and stability for long-term freezer storage at a specified temperature as approximately ≤ −70°C. The results are shown in Table 7a and 7b. All of the mean values from the replicates in stability testing results ranged from −6.6% to −0.3% of the values of initial measurement for each QC material, which are within the acceptable range of +/− 15% required by the Division of Laboratory Sciences in CDC.

Sample turnaround time (TAT)

For a public health emergency response from a radiological incident, when hundreds to thousands of samples need to be analyzed weekly, sample turnaround time is one of the most important considerations in addition to maintaining high quality results. This method provides an excellent solution to the throughput issue. In this method, we need only ~2 hours to pretreat the urine samples, including oxidation state adjustment of Np and Pu isotopes and SPE for a batch of 20 patient urine specimens, urine blank, low and high QC samples. We need additional 4 hours for final analysis on SF-ICP-MS for blanks, calibrators, 20 patient urine specimens, beginning and ending QC samples. In the case of a 24/7 emergency, we can pretreat samples alongside with final SF-ICP-MS determination and achieve a daily throughput of about 100 samples within 24 hours per instrument.

Conclusions

We introduced a method for rapidly determining ultra-low levels of ^{237}Np and ^{239}Pu in urine samples using an SPE purification procedure and a high-sensitivity sample introduction system coupled with SF-ICP-MS. This method provides for analysis of ^{237}Np and ^{239}Pu at very low levels, with LODs of 0.52 pg/L (1.28E-5 Bq/L) and 0.68 pg/L (1.72E-5 Bq/L) for ^{237}Np and ^{239}Pu, respectively (well below the 1/3 of C/P NCRP guidance level) and allows rapid throughput of samples. The results obtained by this method also closely agree with the Oak Ridge National Laboratory target values for reference materials, with biases ranging from –1.65% to 6.78%.

This method successfully eliminates most molecular ion interferences in the process of sample separation. Nonetheless, additional aggressive rinsing procedures are required to further eliminate U from the elution solutions, if the concentration of U is over 5 μg/L in urine samples. A major advantage of this method is that a very small volume (2 mL) of urine sample is required for the analysis, compared with alpha spectrometry and other methods requiring a few hundreds to a few thousands mL of urine. Thus, the successful analysis is more possible especially for young children and infants. Notably, this study demonstrates the established method is appropriate for rapid identification and quantification of ^{237}Np and ^{239}Pu in urine for emergency response involving increased accidental or terrorism-related exposures, or for determining chronic environmental or other non-occupational exposures.

Acknowledgements

The authors thank Ms. Cynthia Ward who assisted in the proof-reading of the manuscript. Specifically, we would like to thank Dr. David Saunders for his guidance and advice throughout this work.

References

1. Hammond CR, CRC Handbook of Chemistry and Physics. 84 ed Elements The. 2004, London: CRC press.
2. Nucleonica: Web Driven Nuclear Science; Available from: https://www.nucleonica.com/wiki/index.php?title=Category:Element_Information. Assessed on March 5th, 2020.
3. IAEA. Radioactive particles in the Environment: Sources, Particle Characterization and Analytical Techniques. 2011; IAEA-TECDOC-1663: Available from: http://www-pub.iaea.org/MTCD/publications/PDF/TE_1663_web.pdf. Assessed on March 5th, 2020.
4. Lehto J and Hou X, Chemistry and Analysis of Radionuclides: 15.15: Neptunium. 2011, Wiley: Hoboken, NJ
5. Laboratory LAN Periodic Table of Elements: LANL 2015 [cited 2019 March 27]; Available from: http://periodic.lanl.gov/94.shtml. Assessed on March 5th, 2020.
6. Morss LR, Edelstein N, Fuger J, Katz JJ (Eds.) The Chemistry of the Actinide and Transactinide Elements: Actinides in Animals and Man 4ed 2011, New York: Springer.
7. Vajda N and Kim C-K, Determination of 241Am isotope: a review of analytical methodology. Journal of radioanalytical and nuclear chemistry, 2010 284(2): p. 341–366.
8. Hou X and Roos P, Critical comparison of radiometric and mass spectrometric methods for the determination of radionuclides in environmental, biological and nuclear waste samples. Analytica Chimica Acta, 2008 608(2): p. 105–139. [PubMed: 18215644]
9. Stricklin D, Tjärnhage Å, and Nygren U, Application of low energy gamma-spectrometry in rapid actinide analysis for emergency preparedness. Journal of radioanalytical and nuclear chemistry, 2002 251(1): p. 69–74.
10. Shultis JK and Faw RE, Fundamentals of Nuclear Science and Engineering 2ed 2007, London: CRC Press.
11. Maxwell SL, et al., Rapid radiochemical method for determination of actinides in emergency concrete and brick samples. Analytica chimica acta, 2011 701(1): p. 112–118. [PubMed: 21763816]
12. Gonzales E, et al., Evaluation of mass spectrometry and radiation detection for the analysis of radionuclides. Journal of radioanalytical and nuclear chemistry, 2005 263(2): p. 457–465.
13. Muramatsu Y, et al., ICP-MS analysis of environmental plutonium. Radioactivity in the Environment, 2001 1: p. 63–77.
14. Truscott JB, et al., Determination of actinide elements at femtogram per gram levels in environmental samples by on-line solid phase extraction and sector-field-inductively coupled plasma-mass spectrometry. Analytica chimica acta, 2001 433(2): p. 245–253.
15. Pointurier F, Baglan N, and Hémet P, Ultra low-level measurements of actinides by sector field ICP-MS. Applied Radiation and Isotopes, 2004 60(2–4): p. 561–566. [PubMed: 14987704]
16. Varga Z, et al., Determination of plutonium and americium in environmental samples by inductively coupled plasma sector field mass spectrometry and alpha spectrometry. Microchemical Journal, 2007 85(1): p. 39–45.
17. Xiao G, et al., Determination of 241Am in urine using sector field inductively coupled plasma mass spectrometry (SF-ICP-MS). Journal of Radioanalytical and Nuclear Chemistry, 2014 301(1): p. 285–291.
18. Röllin S, et al., PU and NP analysis of soil and sediment samples with ICP-MS. Applied Radiation and Isotopes, 2009 67(5): p. 821–827. [PubMed: 19231225]
19. Maxwell SL, et al., Determination of 237Np and Pu isotopes in large soil samples by inductively coupled plasma mass spectrometry. Analytica Chimica Acta, 2010 682(1–2): p. 130–136. [PubMed: 21056724]
20. Maxwell Iii SL and Jones VD, Rapid determination of actinides in urine by inductively coupled plasma mass spectrometry and alpha spectrometry: A hybrid approach. Talanta, 2009 80(1): p. 143–150. [PubMed: 19782204]

21. Tanner SD, et al., Chemical Resolution of Pu+ from U+ and Am+ Using a Band-Pass Reaction Cell Inductively Coupled Plasma Mass Spectrometer. Analytical Chemistry, 2004 76(11): p. 3042–3048. [PubMed: 15167781]
22. Management of Persons Contaminated With Radionuclides: Handbook Report No. 161 II 2008: National Council on Radiation Protection and Measurements.
23. Management of Persons Contaminated With Radionuclides: Handbook Report No. 161 I 2008: National Council on Radiation Protection and Measurements.
24. U.S. NRC Available from: http://www.nrc.gov/reading-rm/doc-collections/cfr/part020/part020-appb.html. Assessed on March 5th, 2020.
25. Horwitz EP, et al., Separation and preconcentration of uranium from acidic media by extraction chromatography. Analytica Chimica Acta, 1992 266(1): p. 25–37.
26. Horwitz EP, et al., Separation and preconcentration of actinides by extraction chromatography using a supported liquid anion exchanger: application to the characterization of high-level nuclear waste solutions. Analytica Chimica Acta, 1995 310(1): p. 63–78.
27. Pappas RS, Ting BG, and Paschal DC, Rapid analysis for plutonium-239 in 1 ml of urine by magnetic sector inductively coupled plasma mass spectrometry with a desolvating introduction system. Journal of Analytical Atomic Spectrometry, 2004 19(6): p. 762–766.
28. Qiao J, et al., Rapid and simultaneous determination of neptunium and plutonium isotopes in environmental samples by extraction chromatography using sequential injection analysis and ICP-MS. Journal of Analytical Atomic Spectrometry, 2010 25(11): p. 1769–1779.
29. Xiao G, et al., Determination of $^{234}U/^{238}U$, $^{235}U/^{238}U$ and $^{236}U/^{238}U$ isotope ratios in urine using sector field inductively coupled plasma mass spectrometry. Radiat Prot Dosimetry, 2014 162(4): p. 618–24. [PubMed: 24563523]
30. The Fourth National Report on Human Exposure to Environmental Chemicals. Jan, 2019; Available from: https://www.cdc.gov/exposurereport/pdf/FourthReport_UpdatedTables_Volume1_Jan2019-508.pdf. Assessed on March 5th, 2020.
31. Regulatory Guide 8.22 (revision 1) Bioassay at Uranium Mills, U.N.R. Commission, Editor 1988.
32. Carson BL, Ellis HV, and McCann JL, Toxicology and Biological Monitoring of Metals in Humans. 1 ed 1986, Chelsea, MI: Lewis Publishers, Inc.

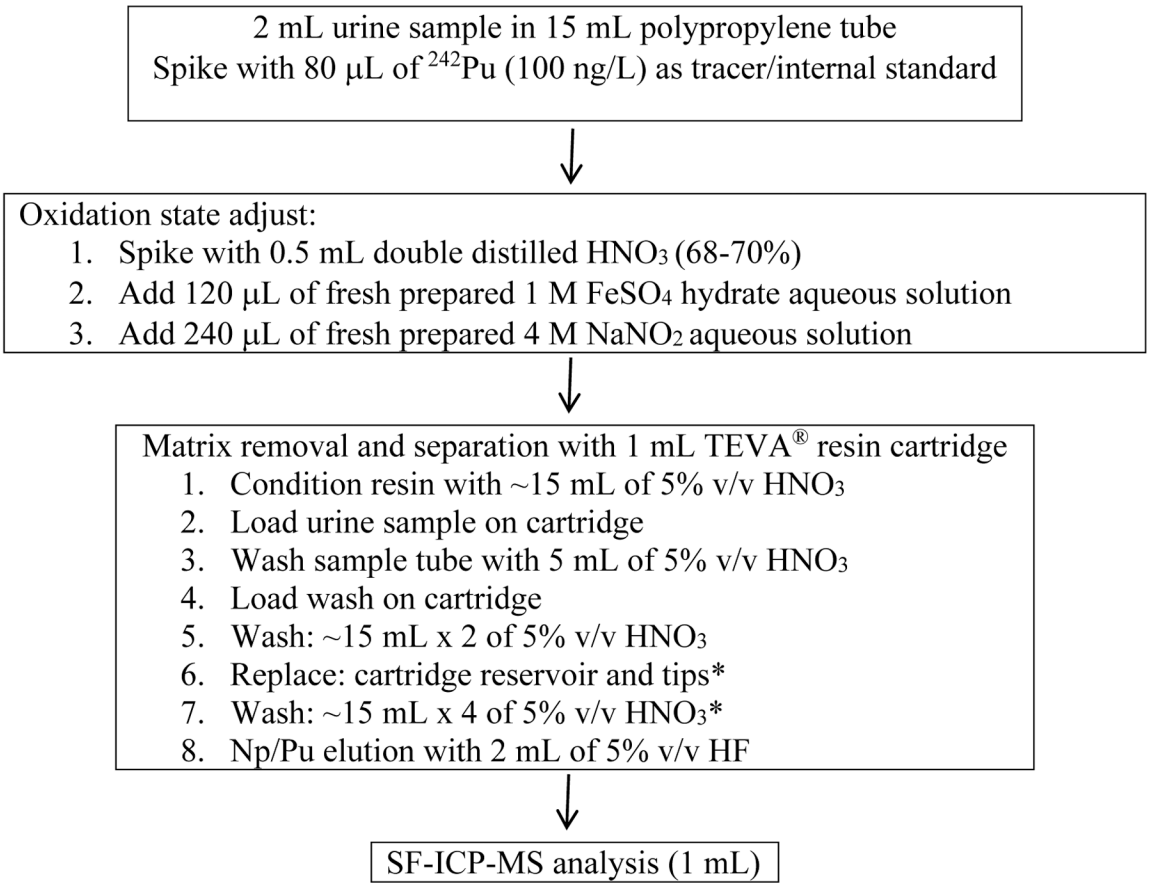


Fig. 1. Sample preparation procedure for ^{237}Np and ^{239}Pu determination.

* Only add steps 6 and 7 if the samples contain U concentrations greater than 5 ug/L.

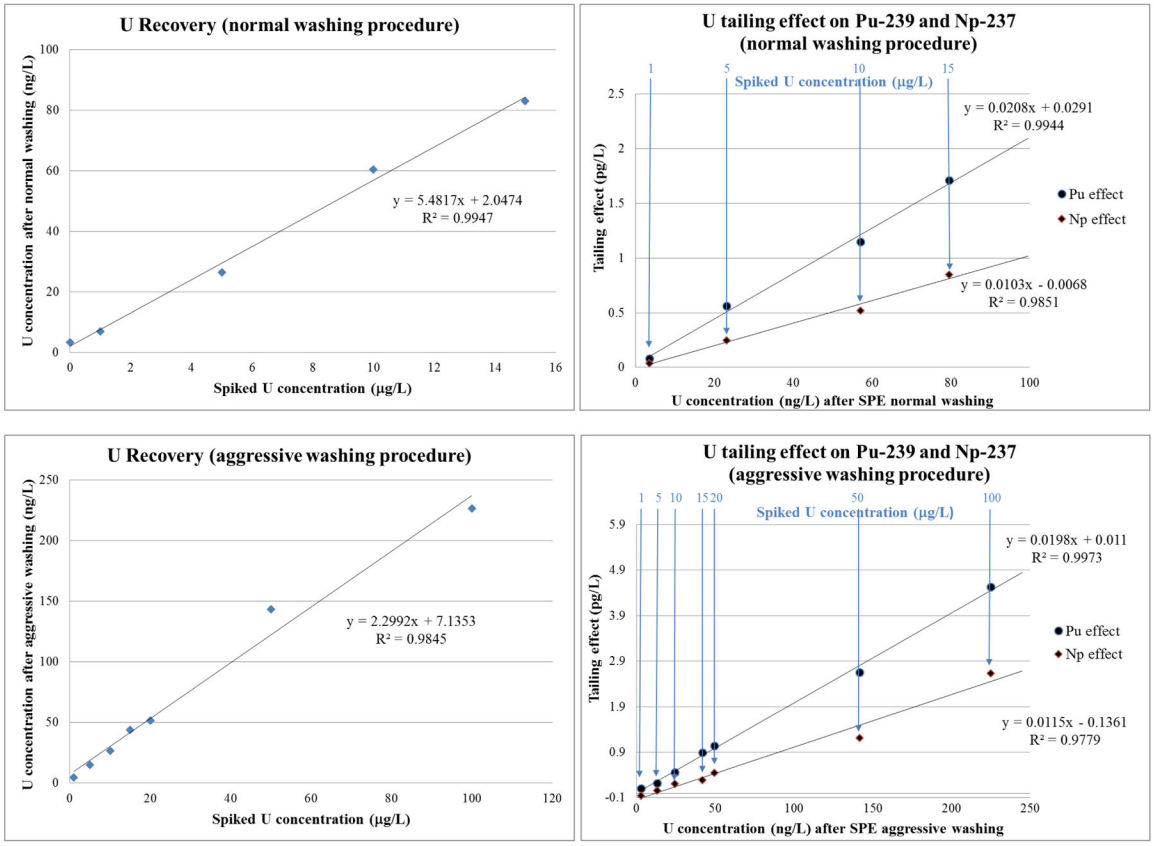
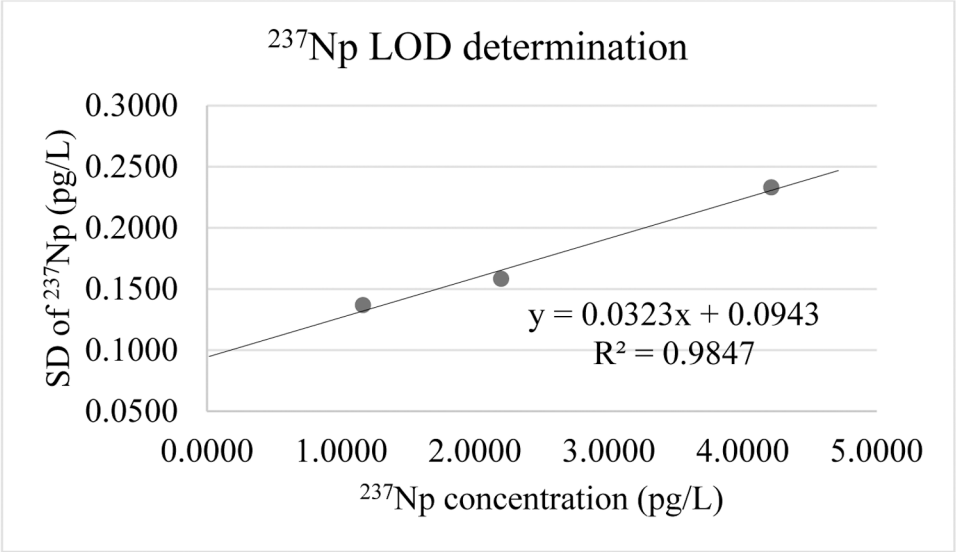


Fig. 2.

Tailing effect of ^{238}U on ^{237}Np and ^{239}Pu determination



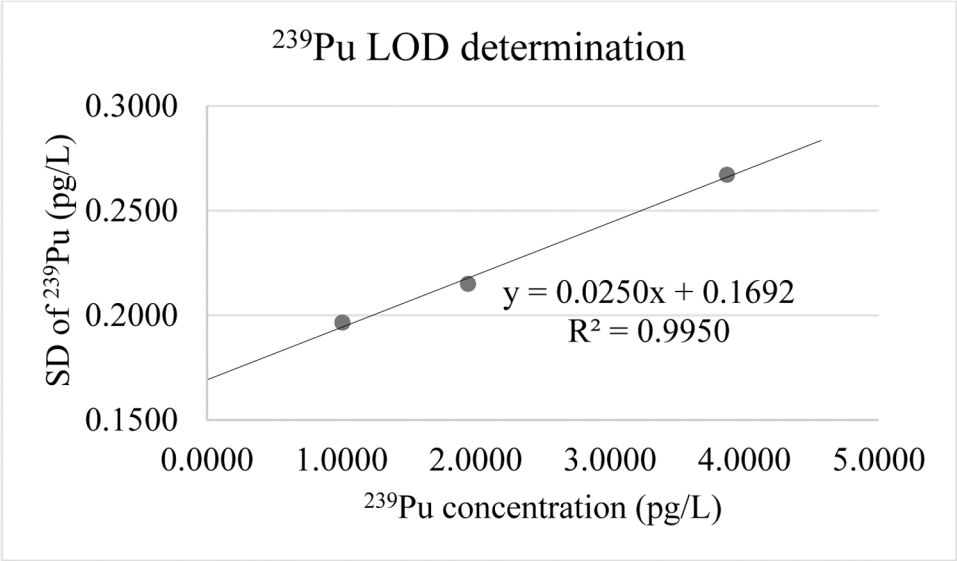


Fig. 3.
Plot for ^{237}Np and ^{239}Pu LOD determination (based on 51 runs per point)

Table 1

Instrumental conditions and data acquisition settings for SF-ICP-MS measurements

RF Power (KW)	1.2 – 1.4
Cooling Gas flow (L/min)	15 – 16
Auxiliary Gas flow (L/min)	0.9
Sample Gas flow (L/min)	0.7 – 0.8
Lenses (V)	Optimized as needed
Sample Take up time (min)	2.1
Wash (min)	3
Pump Speed During Wash (rpm)	1
LR Runs/Passes	3* 60
Detection Mode	Triple/dual
Measurement Units	CPS
Scan Type	ESCAN
Scan Optimization	Speed
Number of Pre-Scans	5
Integration Type	Average
Res. Switch Delay (s)	2
Resolution	Low
Mass Window (%)	25
Setting Time (s)	0.001
Sample Time (s)	0.002
Samples Per Peak	250
Search Window (%)	25
Integration Window (%)	25
Measured Isotopes	^{237}Np, ^{239}Pu, ^{242}Pu, ^{238}U (information only)

Table 2

Observed concentrations of ^{237}Np, ^{239}Pu and among-run precision for reference materials (pg/L)

		^{237}Np				^{239}Pu			
Sample	**N**	**Average**	**SD**	**Target Value**	**Bias (%)**	**Average**	**SD**	**Target Value**	**Bias (%)**
Pool1[a]	52	1.15	0.149	1.00[c]	15.2	1.02	0.192	1.00[c]	2.04
Pool2[a]	46	2.19	0.145	2.00[c]	9.27	1.95	0.223	2.00[c]	−2.61
Low QC[b]	104	4.24	0.247	4.00[c]	6.01	3.88	0.291	4.00[c]	−2.93
High QC[b]	104	156	6.28	150[c]	3.97	142	7.84	150[c]	−5.21

[a] Urine materials made at CDC by spiking certified reference material in pooled urine collected anonymously.

[b] Internal quality control materials made at CDC by spiking certified reference material in pooled urine collected anonymously.

[c] Target values of spiked urine pools using certified reference material from Eckert $ Ziegler (Isotope Products).

Table 3

Comparison of 237Np and 239Pu results with ORNL target values (pg/L)

Sample	N	Dilution Factor	^{239}Pu			
			Average	SD	Target Value	Bias (%)
ORNL09–1	2	1	5.12	0.342	5.052	1.33
ORNL09–2	2	1	79.4	2.96	76.51	3.80
ORNL09–3	2	1	146	4.55	137.1	6.78
ORNL09–4	2	2	197	6.53	199.9	−1.25
ORNL09–5	2	4	412	20.4	401.1	2.69
ORNL14–6	2	1	50.1	2.18	50.29	−0.41
			^{237}Np			
ORNL06–Mix2	2	100	10,600	84.9	10,550	0.50
ORNL06–Mix3	2	200	33,500	348	31,420	6.71
ORNL06–Mix4	2	200	20,800	329	20,350	2.11

Table 4

Short term precision/stability of spiked urine samples (pg/L)

Replicate	Spike1		Spike2		Spike3	
	^{237}Np	^{239}Pu	^{237}Np	^{239}Pu	^{237}Np	^{239}Pu
1	2.23	2.01	100	99.9	206	201
2	2.25	1.73	105	101	210	200
3	2.27	2.02	104	99.9	210	201
4	2.09	1.76	105	100.	209	202
5	2.02	1.84	102	99.8	212	202
6	2.15	2.08	102	99.9	210	200
Average	2.17	1.91	103	100	209	201
SD	0.10	0.13	2.04	0.27	3.71	0.89
RSD (%)	4.74	6.83	1.98	0.27	1.77	0.44

Table 5

Precision/stability of analytes in final extract stored at room temperature (pg/L)

Prepared time	Low QC		High QC	
(days)	^{237}Np	^{239}Pu	^{237}Np	^{239}Pu
Fresh prepared	4.05	3.58	155	143
29	4.20	3.91	155	147
29	4.24	3.79	160	149
28	4.52	3.80	156	146
28	4.26	3.81	157	147
25	4.29	3.62	156	145
25	4.30	3.70	159	148
23	4.26	3.63	163	147
23	4.26	3.76	156	145
22	3.98	3.91	155	147
22	4.03	3.70	159	148
Fresh prepared	4.11	3.68	156	144
Target Value *	4.24	3.88	156	142
Acceptable range *	3.75 – 4.75	3.30 – 4.46	143 – 169	126 – 158

* The Target Value and Acceptable Range was determined internally in CDC by +/− 2SD of the characterized mean over 52 runs as Table 2.

Table 6a

Accuracy using spike recovery for ^{237}Np (pg/L)

		Sample 1					Sample 2				
			Measured concentration					Measured concentration			
	Replicate	Spike concentration	Day 1	Day 2	Mean	Recovery (%)	Spike concentration	Day 1	Day 2	Mean	Recovery (%)
Sample*	1	0.000	<LOD	<LOD			0.000	<LOD	<LOD		
	2		<LOD	<LOD				<LOD	<LOD		
	3		<LOD	<LOD				<LOD	<LOD		
Sample + Spike 1	1	10.0	10.5	10.3	10.4	101.7	20.0	19.9	20.5	20.1	99.4
	2		10.5	10.3				19.2	20.3		
	3		10.3	10.3				19.9	20.6		
Sample + Spike 2	1	40.0	40.1	41.6	40.6	101.0	60.0	59.2	63.8	60.6	100.7
	2		41.3	40.1				58.2	61.6		
	3		40.2	40.4				58.5	62.5		
Sample + Spike 3	1	100	98.2	104	102	101.9	160	155	163	160	100.0
	2		101	102				158	164		
	3		102	105				157	165		

Table 6b

Accuracy using spike recovery for ^{239}Pu (pg/L)

		Sample 1					Sample 2				
			Measured concentration					Measured concentration			
	Replicate	Spike concentration	Day 1	Day 2	Mean	Recovery (%)	Spike concentration	Day 1	Day 2	Mean	Recovery (%)
Sample	1	0.000	<LOD	<LOD			0.000	<LOD	<LOD		
	2		<LOD	<LOD				<LOD	<LOD		
	3		<LOD	<LOD				<LOD	<LOD		
Sample + Spike 1	1	10.0	10.1	10.1	10.2	100.5	20.0	20.1	20.5	20.2	100.6
	2		10.3	10.0				20.1	20.4		
	3		10.2	10.2				20.0	20.3		
Sample + Spike 2	1	40.0	39.9	41.3	40.5	100.9	60.0	61.3	58.2	60.4	100.7
	2		39.7	40.4				59.3	61.6		
	3		40.8	40.6				59.4	62.6		
Sample + Spike 3	1	100	100	102	101	101.1	160	158	162	161	100.7
	2		100	101				157	165		
	3		102	102				158	166		

Table 7a

Stability test for ^{237}Np (pg/L)

Low QC	Initial measurement	Three freeze-thaw Cycles[a]	Bench-top Stability[b]	Processed sample Stability[c]	Long-term Stability[d]
Replicate 1	4.29	4.06	4.25	4.21	3.94
Replicate 2	4.25	4.12	4.16	4.22	4.37
Replicate 3	4.53	4.05	4.30	4.21	4.16
Mean	4.36	4.07	4.24	4.21	4.15
% difference from initial measurement		**−6.6**	**−2.8**	**−3.4**	**−4.7**
High QC					
Replicate 1	152	150	149	148	154
Replicate 2	164	150	150	147	158
Replicate 3	155	149	152	152	157
Mean	157	150	150	149	156
% difference from initial measurement		**−4.6**	**−4.2**	**−5.4**	**−0.3**

[a] Three times frozen at ≤−70°C and then thawed (3 freeze-thaw cycles)

[b] Original samples (not yet prepared for instrument analysis) stored at room temperature for 1 day

[c] Processed samples (ready for instrument analysis) stored at room temperature for 1 day

[d] Samples stored at ≤−70°C for 3 years 5 months

Table 7b

Stability test for ^{239}Pu (pg/L)

Low QC	Initial measurement	Three freeze-thaw Cycles[a]	Bench-top Stability[b]	Processed sample Stability[c]	Long-term Stability[d]
Replicate 1	3.81	3.56	3.97	3.95	3.66
Replicate 2	3.73	3.68	4.04	3.94	3.94
Replicate 3	4.52	3.84	4.08	4.04	4.07
Mean	4.02	3.69	4.03	3.98	3.65
% difference from initial measurement		**−8.2**	**0.3**	**−1.1**	**−3.2**
High QC					
Replicate 1	142	148	145	144	143
Replicate 2	146	150	149	144	142
Replicate 3	150	149	148	145	143
Mean	146	149	147	145	142
% difference from initial measurement		**2.3**	**1.0**	**−0.9**	**−2.3**

a. Three times frozen at ≤−70°C and then thawed (3 freeze-thaw cycles)

b. Original samples (not yet prepared for instrument analysis) stored at room temperature for 1 day

c. Processed samples (ready for instrument analysis) stored at room temperature for 1 day

d. Samples stored at ≤−70°C for 3 years 5 months