Determination of Pu-239 in Urine by Sector Field Inductively Coupled Plasma Mass Spectrometry (SF-ICP-MS) Using an Automated Offline Sample Preparation Technique

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Abstract

Here we report a new procedure to determine Pu-239 in urine using a custom-made automated pre-analytical processing system (single probe) with Pu-242 as a tracer followed by analysis by SF-ICP-MS. An average Pu-242 recovery rate of 88% was obtained with CF-ThU-1000 columns reused >100 times. Analytical results agree with measurements obtained using the CDC manual method with a R^2 of 0.9994. Results for Oak Ridge National Laboratory (ORNL) reference materials (RM) align with target values with a bias range of −3.44% to 3.05%. The limit of detection for this method is 0.63 pg/L, which is comparable to previous manual methods.

Keywords

automated pre-analytical processing system; SF-ICP-MS; Pu-239; urine

Introduction

Pu-239, with a half-life of 24,100 years, is the most common Pu isotope formed in nuclear power plants when U-238 captures neutrons. Although predominantly man-made for producing nuclear weapons, Pu-239 is environmentally available and is considered a chemically and radiologically toxic substance that represents significant potential health threats from excessive exposure [1]. Pu-239 is one of the 22 priority threat radionuclides that are possibly released into the environment in various radiological emergency scenarios [2]. Because Pu-239 is recognized as the most toxic among the actinides [3], researchers are committed to developing methods to monitor Pu-239 in various environmental and biological matrices using different techniques [4–10].

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The Division of Laboratory Sciences (DLS) in the Centers for Disease Control and Prevention (CDC) develops radionuclide screening and quantitative analytical methods (bioassays) on SF-ICP-MS. These screening and analytical methods can assess the level of threat-radionuclide contamination in human urine during an emergency response. After a national radiological or nuclear incident, public health officials will need to know which radionuclides people have been exposed to or contaminated with, which people have been exposed, and how much exposure or contamination each person has received. After such an incident, CDC may be expected to rapidly analyze tens to hundreds of thousands of clinical samples to determine a dose assessment for medical management or follow-up. The decision to medically treat people will depend on our ability to rapidly and accurately identify and quantify the internal contamination. If the incident involved Pu-239, for example, the process would require extensive staff involvement with gravity/vacuum box column/ cartridge extraction of Pu-239 for SF-ICP-MS. This very labor-intensive process involves the use of concentrated acids, such as hydrofluoric acid (HF) and nitric acid (HNO_3) as reported previously [11–12]. Frequent handling of these acids creates a potential cause of incidents for analysts. Although DLS adheres to and promotes laboratory policies and procedures that assure quality and enhance opportunity to improve quality, safety is always the highest priority.

For over 15 years, we have sought a suitable alternative to the pre-analytical gravity column/ vacuum driven procedure to eliminate the extensive manual labor process and create a safer lab environment during a response requiring 24/7 sample processing for extended periods of time such as weeks or months. Analytical laboratories at CDC that focus on organic compounds have been using automated pre-analytical processing systems for over 20 years, but the analytical systems cannot handle or use acids (dilute or concentrated). Elemental Scientific, Inc. (ESI), a company that produces autosamplers for ICP-MS systems, provides a system that could be used for pre-analytical processing using concentrated acids. In our evaluation of the system, we found that it worked as expected and it allowed us to develop analytical methods that could be optimized to achieve our desired outcomes.

The purposes of this project are to develop and validate a new pre-analytical processing technique (ESI automated pre-analytical processing system [single probe] custom-made for CDC) to purify urine samples and determine the concentrations of Pu-239 by SF-ICP-MS. We evaluated method performance by evaluating variables such as accuracy, precision, specificity, carryover, and stability. Additionally, we verified a limit of detection (LOD) that is low enough to identify Pu-239 in urine at levels that are 1/3 the action levels for the general population or for special subgroups, such as children or pregnant woman (C/P) five days post exposure sample collection. Set by the National Council on Radiation Protection and Measurements (NRCP) [13–14], this action level for subgroups (C/P CDG) is 13.8 pg/L for Pu-239. This method will result in a safer and faster alternative to efficiently identify and quantify Pu-239 in urine. It can be useful for accidental or terrorism-related elevated exposure/contamination situations were rapid analysis is required or for evaluating chronic environmental or other non-occupational exposures. The pre-analytical procedure can also be adaptable for other radio-isotopic applications.

Experimental

Chemicals, reagents, and preparation

We purchased CF-ThU-1000 (Th/U preconcentration column, 1.0 mL bed volume, 100–150 µm TEVA resin columns) from Elemental Scientific, Inc. (Omaha, NE, USA). We prepared all HNO_3 and HF acid solutions as needed from double-distilled acids (GFS Chemicals Inc. Columbus, OH), and used deionized water (18 MΩ·cm, from an Aqua Solutions Ultrapure Water System, Aqua Solutions, Inc., Jasper, GA) for all solutions. We collected "base urine" through anonymous human donations (following CDC IRB protocol 3994) and acidified to 1% v/v HNO_3. All radioactive and non-radioactive source solutions used were traceable to the National Institute for Standards and Technology (NIST) (Gaithersburg, MD, USA).

We prepared low level and high level quality control (QC) solutions and all other urine pools, such as pools to determine LOD, by spiking base urine with dilutions (by volumetric determinations) of NIST ICLN/DHS RDD which is a Pu-239 isotope certified reference material (CRM) (Gaithersburg, MD, USA). We used NIST Standard Reference Material (SRM) 4334I of Pu-242 as a tracer/internal standard (Gaithersburg, MD, USA) and iron(II) sulfate ($FeSO_4$) hydrate and sodium nitrite ($NaNO_2$) (Sigma-Aldrich, St. Louis, MO) to adjust the Pu oxidation states. We performed the interference removal experiments by spiking serial dilutions of uranium, lead, thallium, mercury, and gold single-element stock standards (High Purity Standards, North Charleston, SC; Inorganic Ventures, Christiansburg, VA) into the urine samples to determine schema to efficiently separate those elements from Pu using this automatic pre-analytical procedure. We prepared different sets of intermediate calibration standards from dilutions of the Pu-239 isotope by using the above described CRM and SRM from the NIST, and CRM from Eckert & Ziegler Isotope Products (Valencia, CA, USA).

Sample preparation

We used 2 mL of the urine sample volume for a single analysis. The steps that we followed for sample preparation (Adjusting oxidation states of Pu) before they were loaded on the pre-analytical system have been previously reported [12]. Briefly, after urine specimens reached ambient temperature, we mixed them well before pipetting. Using a 15 mL tube for each sample, we spiked 80 µL of 100 ng/L Pu-242 solution as a tracer/internal standard to 2 mL of urine patient samples and QC samples, as well as a urine blank sample. Next, we added 0.5 mL of concentrated HNO_3 (68%–70%), and 120 µL of freshly prepared 1 M $FeSO_4$ hydrate aqueous solution to each sample and mixed the samples well, letting the reaction occur at room temperature for at least 5 minutes (min). After the reaction, we added 240 µL of freshly prepared 4 M $NaNO_2$ aqueous solution to each sample and mixed the samples well, again letting the reaction occur at room temperature for at least 5 minutes. If we observed cloudy samples, we put them in a sand bath at 85°C for one hour to prolong the life span of those CF-ThU-1000 columns used.

As previously reported [12], we prepared external, aqueous-based stock calibrators by spiking 5% v/v HF with dilutions of Pu-239 isotope CRMs. Then we added 40 µL of 100 ng/L Pu-242 tracer/internal standard solution to every 1 mL of stock calibrators to reach the

same tracer/internal concentration as the urine specimen, urine blank, and QC samples. The calibration blank and calibrators were prepared using 5% v/v HF solution and tracer, which matched the elute solution from the column for this method.

Automated pre-analytical chromatographic separation

For precise Pu-239 analysis, we used a prepFAST MC-4 one probe system (Elemental Scientific, Inc., Omaha, NE, USA) to separate the Pu-239 from other trace elements and the urine matrix using the CF-ThU-1000 (Fig. 1). The prepFAST MC-4 is a fully automatic, low pressure chromatography system equipped with a metal-free (all fluoropolymer flow path), syringe-driven system (4 syringes). This system allows for pre-cleaning, conditioning, and sample loading of the columns, as well as multiple acid washes, elution, and collection cycles on 4 columns simultaneously at user-defined intervals (time, volume, and flow rate) and sequence.

As previously reported [15–16], the computer-controlled software allows the user to define the upload location, volume, and flow rate for the samples and reagents. The columns were operated with in-line switchable valves. Samples were loaded into four separate 15 mL sample loops prior to injection onto the columns concurrently. The flow diagram of this system is illustrated in Fig. 2. Here, ~3 mL of each pretreated urine sample (2 mL of urine sample combined with the oxidation state adjustment additive for a final volume of ~3 mL) was pumped from the autosampler deck via a probe and introduced onto the column. Table 1 describes the experimental solutions and conditions for separating Pu-239 from the trace elements and urine samples matrix on this pre-analytical system. These solutions were sequentially pumped into the system between samples to prevent any potential column carry-over for the analytes of interest. The eluent was collected into user-defined sample containers on the autosampler. One mL of each purified sample was subsequently transferred into 4 mL polystyrene conical bottom sample cups for SF-ICP-MS analysis.

SF-ICP-MS analysis

We employed Element XR™ (Thermo Fisher Scientific, Bremen, Germany) sector field ICP-MS to detect Pu-239 in the elution collected using the ESI prepFAST MC-4. This magnetic sector ICP-MS is equipped with nickel sampler and skimmer cones and a CD-2 guard electrode. All analyses were performed in triple mode. The sample introduction system consists of a computer-controlled ASX-112 (Cetac, Omaha, NE) autosampler and an Aridus II™ (Cetac, Omaha, NE) desolvating nebulizer. The Aridus II™ setup improves the sensitivity of the SF-ICP-MS 10–20x providing the ability to achieve low oxides while detecting Pu-239 at trace levels. All instrument parameters of SF-ICP-MS and Aridus II™ and method parameters for Pu-239 were optimized as described in the previous report [12, 17–18] and are listed in Table 2.

Results and discussion

Specificity

As previously reported [11–12, 19–22], interference of polyatomic species at the same mass of 239 was problematic when analyzing Pu-239 in urine by SF-ICP-MS. The interferences

may come from different sources such as argon plasma, as well as the organic content in the urine matrix and the chemical reagents used for analysis ($^{199}Hg^{40}Ar^+$, $^{201}Hg^{38}Ar^+$, $^{202}Hg^{37}Cl+$, $^{204}Hg^{35}Cl^+$, $^{203}Tl^{36}Ar^+$, $^{205}Tl^{34}S^+$, $^{204}Pb^{35}Cl^+$, $^{206}Pb^{33}S^+$, $^{207}Pb^{32}S^+$, or $^{208}Pb^{31}P^+$, $^{197}Au^{42}Ca^+$, $^{238}UH^+$). To ensure analytical specificity quantifying only the Pu-239, we examined the potential interferences that could be present during SF-ICP-MS analysis.

To determine if the potential interferences were significant, we measured the background equivalent concentrations (BEC) for Pu-239 by analyzing 50 urine samples donated anonymously from different individuals. Each of the 50 urine samples displayed a BEC of Pu-239 far below LOD for this method. We also analyzed urine samples spiked with interferents. The spiked concentrations of interferents' were based on, but well above, the biologically relevant concentration levels of the potential interference expected in human urine - 5 μg/L, 5 μg/L, 1 μg/L and 5 μg/L for Pb, Hg, Tl and Au, respectively, as previously reported [12, 23]. For these spiked samples, we did not observe a detectable increased signal for Pu-239 on SF-ICP-MS measurement. As U is also among the 22 priority threat radionuclides that might coexist in various radiological emergency scenarios [2], we spiked a series of urine samples with high U concentration levels at 1 μg/L, 5 μg/L, 10 μg/L and 15 μg/L. After U spiked urine samples were processed through automatic pre-analytical system, the eluted solutions were checked for both U-238 concentration using an established method [24] and the spectral interferences on mass 239 to determine the U separation efficiency of the automatic pre-analytical procedure. U-spiked samples resulted in elevated BECs on mass of 239, apparently due to the formation of $^{238}UH^+$ and tailing of U-238 peak on SF-ICP-MS. As seen in Fig. 3, when U-238 >1 μg/L (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 [23]), ~5% of U-238 residue still remained in the elutes, and the automated pre-analytical system couldn't eliminate U-238, and U-238 will form spectral interferences at mass 239 on SF-ICP-MS and led to a signal > LOD, but below the action level of 13.8 pg/L for Pu-239, even when U was spiked at 15 μg/L by using this method. Though the automatic prepFAST MC-4 system couldn't efficiently remove the U (~95%) as the manual method as previous reported (~99.5%) [12], we can always mathematically correct the U residue's contribution to the Pu-239 signal if we only need informational concentrations.

Radiochemical tracer yields

To accurately and precisely determine the concentrations of Pu-239 in urine, we added an isotopic Pu-242 as tracer/internal standard for this method. Pu-242 percent recovery is a crucial indicator of separation reproducibility of those multiple re-used columns on the prepFAST MC-4 system and the stability of SF-ICP-MS. For the method validation, data was collected from 22 analytical runs which collectively required ~500 urine samples to be purified and analyzed. The calculated Pu-242 recovery was in a range from 61% to 112%, with an average recovery of 88%.

Linearity and extra sample dilution with base urine

Next, we used 6 calibrators with concentrations of 0, 2, 6, 20, 60, 200 pg/L to quantify Pu-239 concentrations. With a simple linear regression calibration model, the method showed good linearity with correlation coefficients greater than 0.999 in the calibration range. We expected most of the samples analyzed for Pu-239 would fall below the action level of 13.8 pg/L. If a concentration was >200 pg/L, we diluted the urine sample with base urine to bring the measured concentration back into the calibration range of SF-ICP-MS analysis. We conducted experiments that tested extra dilutions of urine samples up to 200x with base urine. We spiked 8 urine samples with NIST CRM of Pu-239; 7 of those with concentrations far beyond the calibration range.

Each sample was prepared for pre-analytical purification/SF-ICP-MS analysis with the following extra dilution factors: 1x (i.e. no extra dilution), 2x, 5x, 10x, 20x, 50x, 100x, and 200x in base urine. The final concentrations were calculated by the dilution factor multiplied by the measured concentrations of samples on SF-ICP-MS with extra dilutions. The average normalized concentration (dilution to no extra dilution) and standard deviation (per extra dilution factor) were calculated and are summarized in Table 3. The final results for Pu-239 with all extra dilutions were very similar to the observed results with no extra dilution (+/− 0.03 of the 1x results).

LOD determination

We determined the LOD of this method uniformly by characterizing the relationship between the standard deviation of the measurement and concentration of the Pu-239 at low concentrations, using the DLS-required method described below. The LOD is based on 22 runs of spiked, matrix-matched urine samples from five different low concentration pools including a urine matrix blank. This LOD determination method was equivalent to the recommendations of Clinical Laboratory Standards Institute (CLSI) and includes considering both Type 1 and Type II error in estimates of LOD [25].

$$\text{conc}_{LOD} = 95^{th}\ \text{percentile}_{blank} + 1.645(s_{LOD})$$

where s_{LOD} is the standard deviation at conc_{LOD}

$$95^{th}\ \text{percentile}_{blank} = \text{mean}_b + 1.645(s_b)$$

where mean_b is the mean of the blank and s_b is the standard deviation of the blank

The relationship between s_{LOD} and conc_{LOD} is quadratic for this method,

$$s_{LOD} = A\left(\text{conc}_{LOD}^2\right) + B(\text{conc}_{LOD}) + C$$

$$0 = 1.645A\text{conc}_{LOD}^2 + [(1.645B) - 1]\text{conc}_{LOD} + [\text{mean}_b + 1.645(s_b + C)]$$

a = 1.645A

b = (1.645B) −1

c = mean$_b$ + 1.645(s$_b$ + C)

then:

$$\mathrm{conc}_{LOD} = \left[-b \pm \mathrm{sqrt}\left(b^2 - 4ac\right) \right] / 2a$$

The calculated LOD for this pre-analytical procedure method was 0.63 pg/L (1.59 E-3 Bq/L) for Pu-239 with a p-value of 0.0033 (Fig. 4). This LOD was comparable to our manual cartridge/vacuum box method of 0.68 pg/L (1.72 E-3 Bq/L) and gravity-driven column method of 1.13 pg/L (2.85 E-3 Bq/L) for Pu-239 [11, 12].

Carryover test

The parameters of this method for the SF-ICP-MS analysis were validated and reported [3] and were adequate to prevent signal carryover from samples. Whereas gravity/vacuum box-driven columns are generally for single use, the columns for prepFAST MC-4 used here were designed for multiple use (>100 separations). Hence, it was important that no potential Pu carryover occurred on the column system from sample to sample for the duration of the analysis.

Accordingly, we monitored the concentration change detected on SF-ICP-MS for urine blanks and high concentration samples on consecutive SPE (on the pre-analytical system) for Pu-239. The sample sequence included 8 cyclic SPE procedures by alternating purification of 4 urine blanks and 4 ORNL09–4 (target value is 199.9 pg/L). As shown in Fig. 5, the resulting concentrations of the urine blanks for Pu-239 after running ORNL09–4 were stable over the full run on the pre-analytical system as well as on the full run on SF-ICP-MS. Using this method, the Pu-239 concentration, though slightly increased over the baseline, remained below the LOD of 0.63 pg/L which is below the action level of 13.8 pg/L. This indicates no significant carryover between samples over the calibration range and intended measurement range during the consecutive sample purification and measurements.

Accuracy

We evaluated method accuracy by analyzing 5 urinary Pu-239 reference material (RM) solutions obtained from Oak Ridge National Laboratory (ORNL). The RMs were analyzed over 6 analytical runs (2 times in each run) from two instruments over roughly two weeks by using two sets of calibrators which were prepared by using standard stock solutions from two different vendors. Pu-239 results for the RMs are listed in Table 4. The average results agreed closely with the target values certified by ORNL with an analytical bias of −3.44% to 3.05%. Additionally, 24 in-house urine samples were prepared/spiked using two different base urine pools to determine recovery for this method. Six concentration levels of samples (3 samples for each level) spiked with 20, 30, 40, 60, 100 and 160 pg/L concentrations of Pu-239 yielded recoveries that ranged from 94.2 – 99.3 % for Pu-239 in 2 analytical runs on two different days (Table 5).

Precision

To ensure run-to-run reproducibility, we prepared pools of spiked internal CDC quality control (QC) materials by spiking ~ 3 liters of urine with Pu-239 for each pool. The spiking target values are 10.0 pg/L and 150 pg/L for low QC and high QC, respectively. The low QC pool was spiked at a level near the action level of 13.8 pg/L. During the characterization process, we rotated two sets of prepared calibrators from two different manufacturing vendors and performed the analysis on two instruments. Table 6 lists the calculated precision and accuracy of these QC samples for 22 analytical runs (44 analyses, both at the beginning and end of a run). The among-run precision for both the low and high QC exhibited a coefficient of variation (CV) <6% over 22 analytical runs that spanned ~ 40 days. To assess in-run producibility and stability of 4 columns for the prepFAST MC-4 system as well as SF-ICP-MS measurement, we treated and purified 12 samples of ORNL09–4 (ORNL) through the pre-analytical system and analyzed sequentially on SF-ICP-MS in the same analytical run as in the carryover experiment. We obtained a CV of 1.82% (Table 6).

Method Comparison

We compared the automated column method described here with the previously reported [5] manual method used at CDC by analyzing the same set of 5 ORNL reference materials for Pu-239 (5.052 – 199.9 pg/L). A correlation plot of results from the two methods resulted in a linear regression of 0.9994 (Fig. 6), thus supporting good agreement between the two methods.

Prepared sample stability test

Stability testing provided information on how the stability of Pu-239 in urine samples over time under varying storage conditions. CDC/DLS required experiments designed here [26] to include conditions samples may encounter during storage. These conditions, such as short-term room temperature storage, long-term freezer storage at a specified temperature, and three freeze-thaw cycles, are ones that can potentially affect the measured concentration of Pu-239 in these samples. Stability was evaluated with both low and high QC materials and summarized in Table 7. The difference of Pu-239 between the mean values of the replicates in stability testing and the mean values of initial measurement ranged from −5.3% to 0.9% and were all in the established acceptable range for QC materials. Long-term prepared sample stability will be accessed for our future study.

Sample Turnaround Time (TAT)

In addition to safety and quality, TAT is also very important, as it is one of the most noticeable parameters of laboratory performance in a radiological emergency. Compared to traditionally used Alpha spectrometry and other techniques with time-consuming sample preparation and counting procedures (usually days and weeks for each sample), the method described here is faster. After adjusting the oxidation state of Pu in urine samples, we loaded the samples directly onto the autosampler of the ESI prepFAST MC-4 system. Fully automated SPE processing took approximately 20 min per sample. The average time for SF-ICP-MS analysis was ~ 7 min per sample. Both sample purification and analysis were

conducted simultaneously by unattended operation, demonstrating that determining Pu-239 concentrations for ~ 70 urine samples per instrument within 24 hours is possible.

Conclusions

In this study, we developed and validated a method for purifying Pu-239 in urine on an automated ESI prepFAST MC-4 followed by SF-ICP-MS analysis to replace the laborious manual column chemistry procedure. Polyatomic interferences are removed by running the pre-analytical system. The resulting LOD and run-to-run precision are comparable to the previous manual purification procedures, and the accuracy of the resulting method agrees well with the target values of ORNL reference materials. This method minimizes human error and human exposure to radioactive samples and improves reproducibility and worker safety through operation of the automation platform.

Acknowledgements

References

1. Toxicological Profile for Plutonium. Available from: https://www.atsdr.cdc.gov/ToxProfiles/tp143.pdf Accessed on 17 April 2020.

2. IAEA Nuclear Security Series No. 6 (2007), Combating Illicit Trafficking in Nuclear and other Radioactive Material. Available from: https://www-pub.iaea.org/MTCD/publications/PDF/Pub1309_web.pdf Accessed on 25 January 2021.

3. Cohen BL (1985) The Myth of Plutonium Toxicity. In: Ott KO, Spinrad BI (eds) Nuclear Energy. Springer, Boston, MA. 10.1007/978-1-4684-4589-3_23

4. Xu Y et al. (2014). Determination of plutonium isotopes (^{238}Pu, ^{239}Pu, ^{240}Pu, ^{241}Pu) in environmental samples using radiochemical separation combined with radiometric and mass spectrometric measurements. Talanta, 119, 590–595. 10.1016/j.talanta.2013.11.061 [PubMed: 24401459]

5. 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]

6. 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.

7. 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]

8. 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.

9. Muramatsu Y, et al., ICP-MS analysis of environmental plutonium. Radioactivity in the Environment, 2001. 1: p. 63–77.

10. 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.

11. Pappas R, Ting B, Paschal D. (2004) Rapid analysis for plutonium-239 in 1 ml of urine by magnetic sector inductively coupled plasma mass spectrometry with a desolvating introduction system. J Anal At Spectrom. 19(6):762–76610.

12. Xiao G, Liu Y, Jones RL (2020) Determination of [237]Np and [239]Pu in Urine Using Sector Field Inductively Coupled Plasma Mass Spectrometry (SF-ICP-MS). J Radioanal Nucl Chem. 324:887–896. DOI 10.1007/s10967-020-07107-7 [PubMed: 32419716]

13. No Report. 161 I – Management of Persons Contaminated With Radionuclides (2008) Bethesda, MD

14. No Report. 161 II. Management of Persons Contaminated With Radionuclides: Handbook (2008) Bethesda, MD

15. Romaniello S et al. (2015) Fully automated chromatographic purification of Sr and Ca for isotopic analysis. J Anal At Spectrom. 30:1906–1912

16. Wylie EM, et al. (2018) An automated micro-separation system for the chromatographic removal of uranium matrix for trace element analysis by ICP-OES. Talanta. 189: 24–30 [PubMed: 30086912]

17. Xiao G, et al. Determination of [241]Am in urine using sector field inductively coupled plasma mass spectrometry (SF-ICP-MS). J Radioanal Nucl Chem. 301(1):285–291 [PubMed: 27375308]

18. Xiao G, et al. (2014) 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. 162(4):618–24 [PubMed: 24563523]

19. Maxwell S, et al. (2010) Determination of 237Np and Pu isotopes in large soil samples by inductively coupled plasma mass spectrometry. Analytica Chimica Acta. 682(1–2):130–136 [PubMed: 21056724]

20. Maxwell S III, Jones V (2009) Rapid determination of actinides in urine by inductively coupled plasma mass spectrometry and alpha spectrometry: A hybrid approach. Talanta. 80(1):143–150 [PubMed: 19782204]

21. Tanner S et al. (2004) Chemical resolution of Pu+ from U+ and Am+ using a band-pass reaction cell inductively coupled plasma mass spectrometer. Anal Chem.76(11):3042–3048 [PubMed: 15167781]

22. Ting B et al. (2003) Rapid analysis for plutonium-239 in urine by magnetic sector inductively coupled plasma-mass spectrometry using Aridus desolvation introduction system. J Anal At Spectrom. 18:795–797

23. [5 March 2020] The Fourth National Report on Human Exposure to Environmental Chemicals. Jan.. 2019. https://www.cdc.gov/exposurereport/pdf/FourthReport_UpdatedTables_Volume1_Jan2019-508.pdf.Accessed

24. Pappas R et al. (2002) Determination of uranium-235, uranium-238 and thorium-232 in urine by magnetic sector inductively coupled plasma mass spectrometry. J. Anal. At. Spectrom 17:131–134

25. Evaluation of Detection Capability for Clinical Laboratory Measurements Procedures; Approved Guideline - Second Edition, Report 1-56238-795-2 (2012). CLSI. Wayne, PA.

26. Centers for Disease Control and Prevention. Division of Laboratory Sciences Policies and Procedures Manual. http://intranet.cdc.gov/nceh-atsdr/dls/pdf/05/DLS_Policies_and_Procedures_Manual.pdf Accessed 11 May 2020
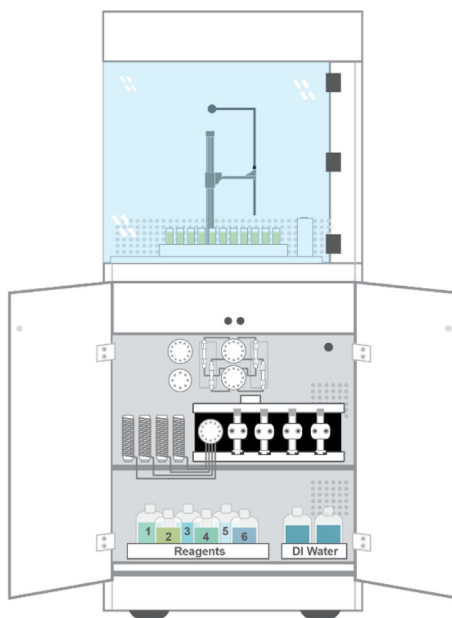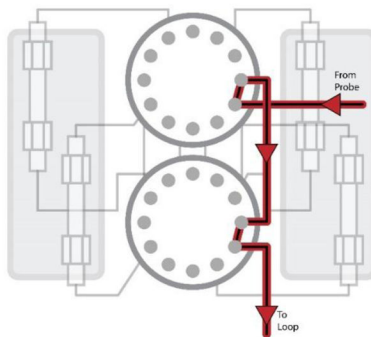
4 Column manifold

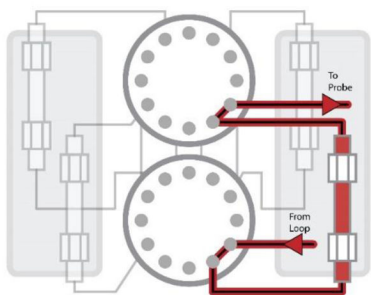- Same chemistry on all 4 columns
- Reuse and regenerate resin
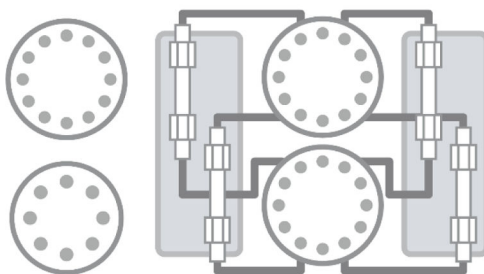
Fig. 1.
Features diagram of 1-probe prepFAST MC-4 automated system (this figure is used with the permission from Elemental Scientific, Inc.)

1. Load Sample into Loop, Bypass Column

2. Load Sample onto Column

3. Elute Sample to Probe

Fig. 2.
Schematic diagram of valves of 1-probe prepFAST MC-4 automated system (this figure is used with the permission from Elemental Scientific, Inc.)
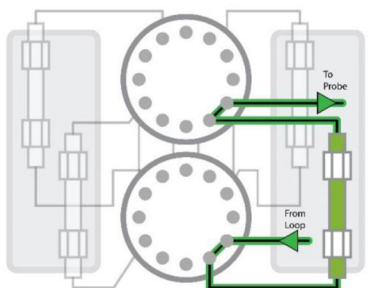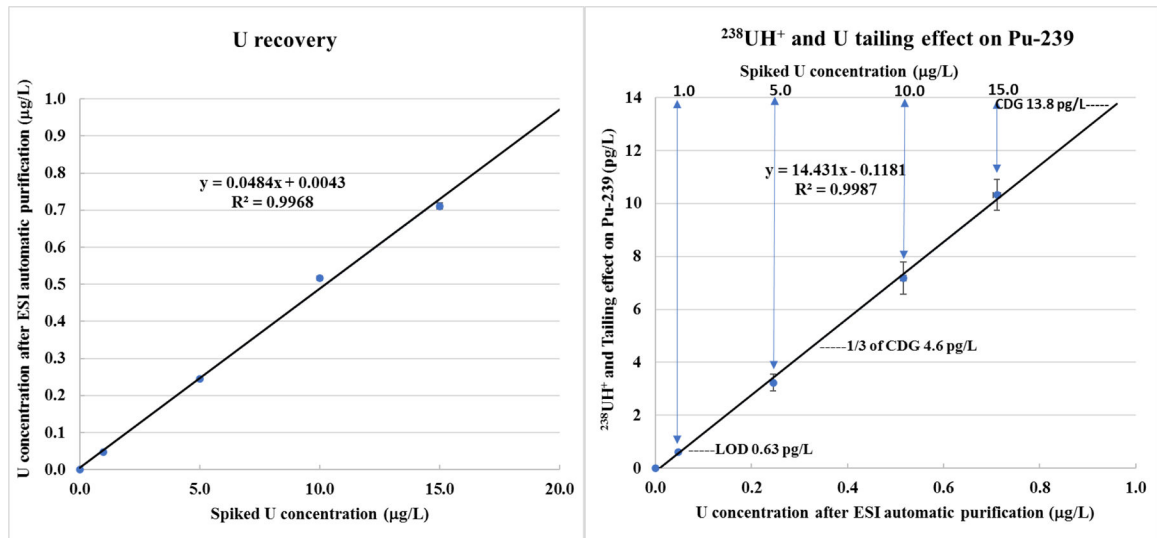
Fig. 3.
Interference of U-238 on mass of 239 after automatic pre-analytical procedure

Fig. 4.
Plot for Pu-239 LOD determination (based on 22 runs per point, N = 44)

Fig. 5.
Carryover experiment for Pu-239 in urine on SF-ICP-MS by ESI pre-analytical system. The sample sequence included cyclic measurements of a urine blank, and a high concentration reference material ORNL09–4.

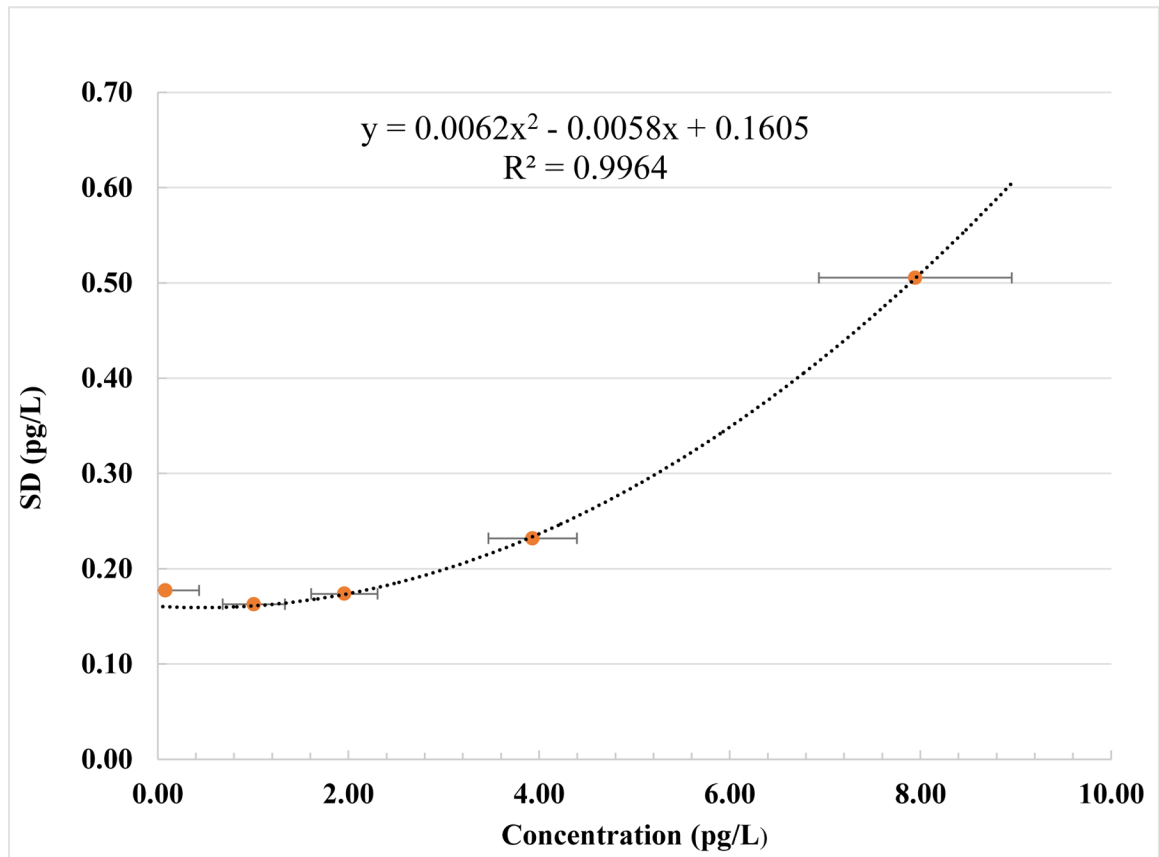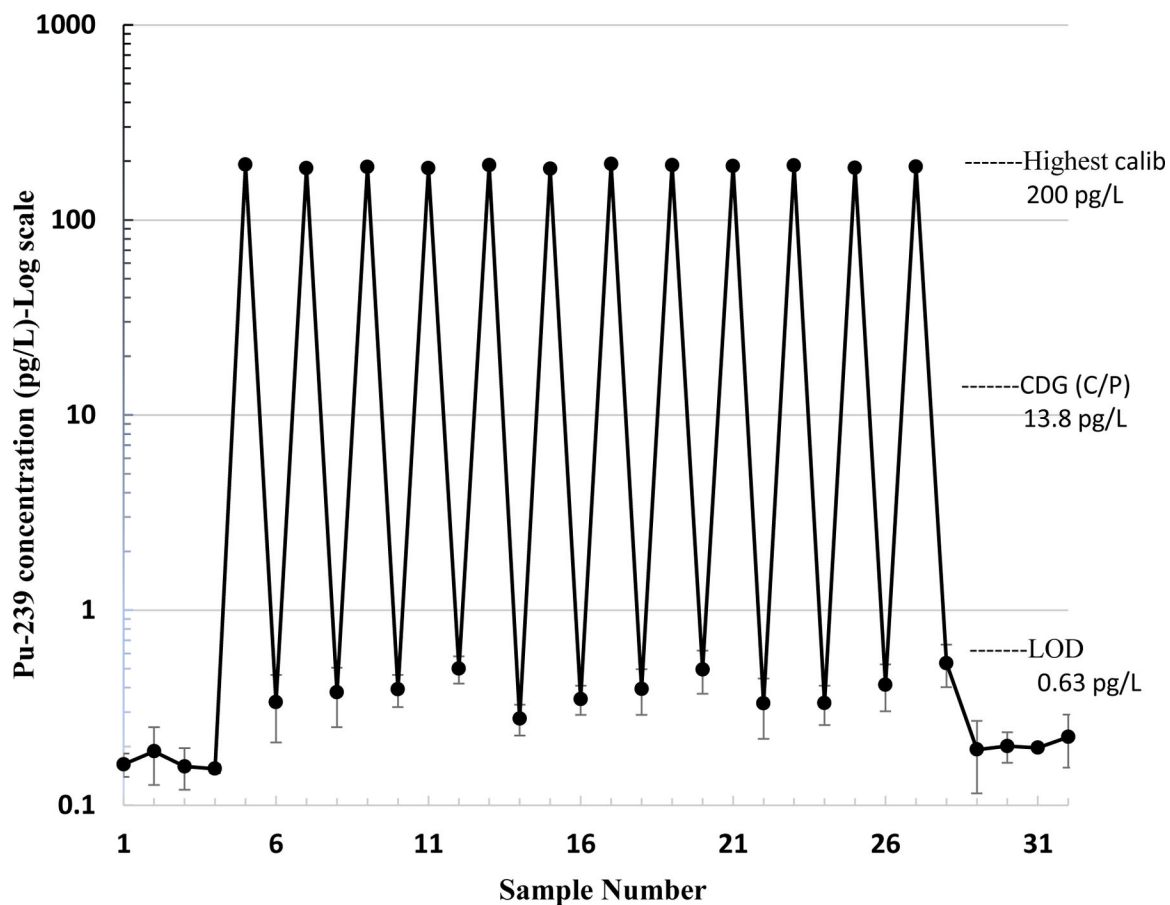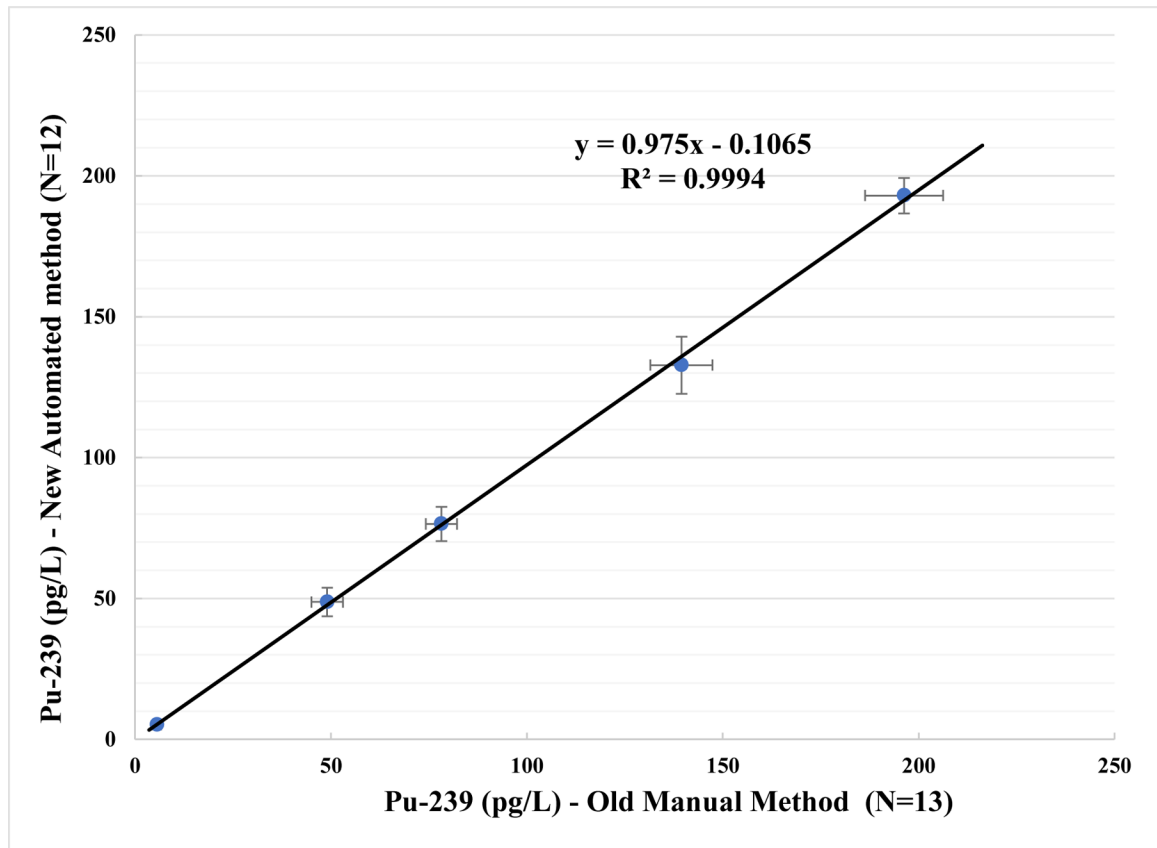**Fig. 6.**
Comparison of ORNL reference materials means between methods

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Table 1

ESI prepFAST MC-4 experimental conditions.

Sequence	Volume (mL)	Eluent	Pathway	Action
Wash columns	10	5% v/v HF	Columns	Sent to waste
Wash columns and Probe	5	5% v/v HF	Columns and Bypass columns	Sent to waste
Condition columns	7.5	5% v/v HNO$_3$	Columns	Sent to waste
Load samples	3	Samples (after adjusted oxidation state)	Sample loop	Sent to waste
Inject the samples into columns	3	Samples	Columns	
Clean plastic loops	10	5% v/v HNO$_3$ and 0.002% v/v Triton X-100	Bypass Column	Sent to waste
Wash columns to remove interferent	20	5% v/v HNO$_3$	Columns	Sent to waste
Air purge	3	Air	Columns	Sent to waste
Elute Pu-239	2	5% v/v HF	Columns	Collected

Table 2

Instrument and method parameters for SF-ICP-MS and Aridus II™

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)	1–2		
LR Runs/Passes	3* 60	Detection Mode	Triple
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	Pu-239, Pu-242, U-238 (information only)		
Nebulizer Flow (µL/min)	100	PFA Spray Chamber (°C)	110
Membrane Coil (°C)	160	Argon Sweep Gas Flow (L/min)	2–8
Nitrogen Gas Flow (mL/min)	2–8		

Table 3

Urine samples dilution test with mean and the normalized results for Pu-239 (N=4)

Dilution factor	Mean observed ± 2SD (pg/L)	Mean Final ± 2SD (pg/L)	Spiking T. V. (pg/L)	Bias (%)	Normalized Extra Dilution Result
1x	190.3 ± 4.1	190.3 ± 4.1	180	5.7	1.00
2x	189.8 ± 4.1	379.6 ± 8.2	360	5.4	1.00
5x	190.1 ± 4.4	950.3 ± 22.0	900	5.6	1.00
10x	190.6 ± 3.3	1906.5 ± 33.4	1800	5.9	1.00
20x	189.6 ± 3.7	3792.0 ± 73.7	3600	5.3	1.00
50x	188.2 ± 4.1	9410.0 ± 204.6	9000	4.6	0.99
100x	187.6 ± 3.9	18762.9 ± 391.0	18000	4.2	0.99
200x	184.2 ± 5.8	36830.6 ± 1158.6	36000	2.3	0.97

Table 4

Accuracy Compared to Reference Material from ORNL for Pu-239

Reference material	Replicate	ORNL T.V. (pg/L)	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Mean ± 2SD	CV (%)	Difference from nominal value (%)
					Measured Concentration for Pu-239 (pg/L)						
ORNL09–1	1	5.05	4.738	5.215	5.148	5.398	5.572	5.413	5.21 ± 0.60	5.80	3.1
	2		4.645	5.126	4.920	5.359	5.502	5.438			
ORNL14–1	1	50.29	45.15	48.13	46.61	51.26	49.89	50.87	48.79 ± 5.04	5.17	–3.0
	2		44.79	49.36	46.17	51.76	50.25	51.20			
ORNL09–2	1	76.51	70.93	76.10	74.55	79.03	78.25	79.14	76.46 ± 6.12	4.00	–0.1
	2		71.97	75.48	74.12	78.66	79.61	79.67			
ORNL09–3	1	137.1	126.8	129.0	127.7	140.1	137.8	136.4	132.84 ± 10.14	3.82	–3.1
	2		126.3	131.7	128.1	136.2	137.3	136.8			
ORNL09–4	1	199.9	187.7	192.9	192.9	194.8	196.1	190.6	193.02 ± 6.30	1.63	–3.4
	2		187.1	195.5	193.6	196.9	195.5	192.5			

Table 5

Accuracy of Pu-239 using spike recovery

| | | Sample 1 | | | | | Sample 2 | | | |
| | Spike concentration | Measured concentration (pg/L) | | | | Spike concentration | Measured concentration (pg/L) | | | |
Replicate		Day 1	Day 2	Mean ± 2SD	Recovery (%)		Day 1	Day 2	Mean ± 2SD	Recovery (%)
Sample										
1	0.000	<LOD	<LOD			0.000	<LOD	<LOD		
2		<LOD	<LOD	<LOD			<LOD	<LOD	<LOD	
3		<LOD	<LOD				<LOD	<LOD		
Sample + Spike 1										
1	20.00	19.42	19.61			30.00	28.49	27.13		
2		19.48	19.74	19.66 ± 0.38	98.3		29.37	28.07	28.52 ± 1.73	95.1
3		19.92	19.78				29.45	28.60		
Sample + Spike 2										
1	40.00	39.56	38.80			60.00	57.01	54.50		
2		40.07	39.86	39.71 ± 0.98	99.3		59.38	55.56	56.52 ± 3.97	94.2
3		40.13	39.82				58.10	54.58		
Sample + Spike 3										
1	100.00	96.39	95.48			160.00	153.56	147.98		
2		100.66	98.95	98.95 ± 5.14	99.0		157.34	151.60	153.71 ± 8.72	96.1
3		102.15	100.09				160.08	151.69		

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Table 6

Among-run and with-in run precision of Pu-239 for reference materials

Sample		Pu-239			
	N	Mean ± 2SD (pg/L)	CV (%)	Target Value (pg/L)	Bias (%)
Low QC	44	9.77 ± 1.16	5.95	10.00	−2.30
High QC	44	150.14 ± 14.56	4.85	150.00	0.09
ORNL09–4	12	188.16 ± 6.86	1.82	199.9	−5.87

Table 7

Stability test

	Initial measurement	Three freeze-thaw cycles[1]	Bench-top stability[2]	Processed sample stability[3]
Low QC	(pg/L)			
Replicate 1	10.20	9.69	10.41	10.13
Replicate 2	9.71	9.78	10.61	9.98
Replicate 3	9.89	9.82	10.34	9.95
Mean ± 2SD	9.93 ± 0.50	9.76 ± 0.13	10.45 ± 0.28	10.02 ± 0.19
Acceptable range[4]	9.77 ± 1.16 (8.61–10.93)			
% difference from initial measurement		**−1.7**	**−5.3**	**0.9**
High QC	(pg/L)			
Replicate 1	155.98	148.24	149.51	153.80
Replicate 2	154.78	147.90	151.43	151.89
Replicate 3	153.53	150.76	153.53	153.48
Mean ± 2SD	154.76 ± 2.45	148.97 ± 3.12	151.49 ± 4.02	153.06 ± 2.05
Acceptable range[4]	150.14 ± 14.56 (135.57–164.70)			
% difference from initial measurement		**−3.7**	**−2.1**	**−1.1**

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

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

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

[4.] Acceptable range were established based on ± 2SD of the characterized mean over 22 runs (N=44)