7. ANALYTICAL METHODS

The purpose of this chapter is to describe the analytical methods that are available for detecting, measuring, and/or monitoring uranium, its metabolites, and other biomarkers of exposure and effect to uranium. The intent is not to provide an exhaustive list of analytical methods. Rather, the intention is to identify well-established methods that are used as the standard methods of analysis. Many of the analytical methods used for environmental samples are the methods approved by federal agencies and organizations such as EPA and the National Institute for Occupational Safety and Health (NIOSH). Other methods presented in this chapter are those that are approved by groups such as the Association of Official Analytical Chemists (AOAC) and the American Public Health Association (APHA). Additionally, analytical methods are included that modify previously used methods to obtain lower detection limits and/or to improve accuracy and precision.

7.1 BIOLOGICAL MATERIALS

Uranium can enter the human body through inhalation, ingestion, or penetration through the skin. Measurement of the quantities of uranium in the body can be performed by two primary methods, *in vivo* measurements and *in vitro* measurements. *In vivo* techniques measure the quantities of internally deposited uranium directly using a whole-body counter, while *in vitro* techniques permit estimation of internally deposited uranium by analysis of body fluids, excreta, or (in rare instances) tissues obtained through biopsy or postmortem tissue sectioning (USTUR 2011). Some of these analytical methods are summarized in Table 7-1.

The accurate and precise quantification of uranium in biological materials by either *in vivo* or *in vitro* methodologies requires that standard, certified sources with known concentrations of appropriate radionuclides be available and used appropriately on properly calibrated equipment. The U.S. national primary standards laboratories for developing and disseminating ionizing radiation standards include DOE laboratories for special nuclear materials standards and the National Institute of Standards and Technology (NIST) for the remaining standards. Also, the Health Physics Society accredits secondary standards laboratories for developing and disseminating NIST-traceable radioactive sources (HPS 2011). DOE does not produce Certified Reference Materials for biological matrices. However, NIST does produce human biological standard reference materials (SRMs) for uranium in two matrices (human lung powder [SRM4351, ^{234}U and ^{238}U each 1.0×10^{-4} Bq/g] and urine [SRM2668, two concentrations, 0.0340 or 13.37 µg/L with 626 or 618 mg creatinine/L, respectively] (NIST 2011).

Table 7-1. Analytical Methods for Determining Uranium in Biological Samples

Sample matrix	Sample preparation	Analytical method	Detection limit	Accuracy	Reference
Urine	Enrichment on an anion exchange column, solvent extraction	α-Counting (total uranium)	Not given	92% at 0.9 dpm spike	Hinton 1983
Urine	Spiked urine wet ashed; sample clean-up by coprecipitation, solvent extraction and electro-deposition	α-Spectrometry (total uranium)	0.02 dpm/L for ^{238}U[a]	78%	Singh and Wrenn 1988
Urine	Sample treated with HCl and H_2O_2, clean-up on anion exchange resin column	Spectro-photometric (total uranium)	5 µg/L	87% at 11 µg/L	Kressin 1984
Urine	Sample wet ashed, enrichment on anion exchange column, purification by solvent extraction	Fluorometric (total uranium)	0.1 µg/L	75% at 0.1–100 µg/L	Dupzyk and Dupzyk 1979
Urine	Sample digestion with $K_2S_2O_8$ and dissolution in water	Laser-induced fluorometry (total uranium)	1 µg/L	86% at 7 µg/L	Hinton and White 1981
Urine	Wet-ashed; solubilized	KPA	~0.050 µg/L	90–110%	Birkenfeld et al. 1995
Urine	Acid digestion, purification by coprecipitation and column chromatography	NAA (isotopic quantification)	<6 µg/L	80% at 2 µg added uranium	Pleskach 1985
Urine	Sample with ^{232}U spike wet ashed, clean-up by anion exchange chromatography	Isotope dilution-MS (isotopic quantification)	5 pg (10^{-6} µg) uranium (total chemical blank)	No data	Kelly et al. 1987
Urine	Acidification; dilution	ICP-MS	3 ng/L	No data	Karpas et al. 1996
Urine	Dilution with acid, triton-X-100	ICP-MS	0.004 µg/L	3.71 RSD (%) at 0.08 µg/L	Caldwell et al. 2005
Urine	Digestion in concentrated HNO_3	ICP-DRC-MS (isotope quantification)	4 ng/L (total uranium); 60 ng/L ($^{235}U/^{238}U$ ratio)	>95%	Todorov et al. 2009
Urine	Compilation from ANSI, DOE, EPA, IAEA, ICRP	Not provided	0.04–1 pCi/L (0.0007–0.07 Bq/L)	Not provided	HPS 1996

Table 7-1. Analytical Methods for Determining Uranium in Biological Samples

Sample matrix	Sample preparation	Analytical method	Detection limit	Accuracy	Reference
Blood	Dilution with deionized water	ICP-DRC-MS (isotope quantification)	0.0001 µg/L (total U); 0.003 µg/L ($^{235}U/^{238}U$ ratio)	97–99% at 0.005–0.5 µg/L	Ejnik et al. 2005
Soft tissue	Spiked tissues wet ashed; clean-up by coprecipitation, solvent extraction and electro-deposition	α-Spectrometry (total uranium)	0.03 µg/ sample	85–92%	Singh and Wrenn 1988
Soft tissue	Spiked sample wet digested; purification by anion exchange; loaded into a single ion-exchange bead as a point source for MS	Isotope dilution-MS (isotopic quantification)	<5 pg/L	77%	Kelley and Fassett 1983
Bones	Spiked sample dry ashed; clean-up by coprecipitation, solvent extraction and electrodeposition	α-Spectrometry (isotopic quantification)	0.03 µg/ sample	60–93%	Singh and Wrenn 1988; Singh et al. 1984
Bone ash	Spiked sample wet ashed; clean-up by solvent extraction and electrodeposition	α-Spectrometry (isotopic quantification)	0.4 µg/kg for ^{238}U	>95%	Fisenne et al. 1980
Feces	Spiked sample dry and wet ashed; clean-up by coprecipitation, solvent extraction and electro-deposition	α-Spectrometry (isotopic quantification)	0.03 µg/ sample	58%	Singh and Wrenn 1988
Bone ash	Sampled dried; wet-ashed; homogenization; dissolution in acid	ICP-MS	3 ng/g	No data	Twiss et al. 1994
Feces	Sample wet or dry ashed, irradiation	^{3}He neutron analyzer	0.04 ng/ sample	No data	Gonzales et al. 1988

[a]This detection limit was reported by Melgard 1988.

ANSI = American National Standard Institute; DOE = Department of Energy; DRC = dynamic reaction cell; EPA = Environmental Protection Agency; IAEA = International Atomic Energy Agency; ICP = inductively coupled plasma; ICRP = International Commission on Radiological Protection; KPA = kinetic phosphorescence analysis; MS = mass spectrometry; NAA = neutron activation analysis

Ough et al. (2006) conducted an interlaboratory comparison of analytical methods of synthetic urine samples containing natural and depleted uranium. The laboratories used ICP-sector field-MS (ICP-SF-MS), quadrupole ICP-MS (ICP-Q-MS), thermal ionization mass spectrometry (TIMS), and instrumental and delayed neutron activation analysis (I/DNAA) methods. The study showed that the ICP-SF-MS and ICP-Q-MS had the greatest accuracy and precision in measuring total uranium; the TIMS method also had a high precision, but lower accuracy. In tests of the $^{238}U/^{235}U$ isotope ratio, the TIMS results had the lowest accuracy, but the highest precision. The ICP-SF-MS and ICP-Q-MS had high accuracy and precision in the isotope ratio tests; I/DNAA method was not analyzed for the isotope tests. The relative sensitivity of the instrument detection limits was TIMS>ICP-SF-MS>ICP-Q-MS>I/DNAA.

7.1.1 Internal Uranium Measurements

In vivo or direct measurements of uranium in the body are made with radiation detector systems and associated electronics called whole-body counters that measure radiation as it leaves the body from internally deposited uranium. *In vivo* assays are the most direct method of quantifying internally deposited radioactive materials. However, not all radionuclides emit radiations than may be detected with sufficient accuracy outside the body (^{234}U and ^{238}U due to low-energy, low-intensity gamma emissions, for example) (NCRP 1978).

The most commonly used detectors for uranium *in vivo* counting are sodium iodide, phoswich (NaI and CsI sandwich), and hyperpure germanium, which measure the gamma rays emitted during uranium decay (DOE 1988, 2009). Since the gamma radiations emitted from uranium and a number of its progeny are the same as those emitted by uranium in the environment, shielded rooms are normally used to house the uranium internal monitoring equipment to ensure that background radiation is as low as possible (DOE 1999b; MARLAP 2004; Parrington et al. 1996). Although whole-body counters may be made in many configurations, a chest counter is usually used for inhaled uranium. *In vivo* analysis is widely used throughout the nuclear industry, both commercial and government, for quantifying levels of insoluble uranium in the body. *In vitro* analysis (see Section 7.1.2) is often used in conjunction with whole-body counting for monitoring workers handling uranium (DOE 2009).

In vivo counting systems are calibrated using tissue-equivalent phantoms. These phantoms have shapes similar to the human torso and are made of polystyrene or other tissue equivalent material. Standard uranium sources of known activity are inserted into the phantom at locations where uranium would be expected to accumulate in a human body (DOE 1988). Relationships are determined between the

uranium activity measured by the detection system and the known activity in the phantom (DOE 1988; HPS 1996).

There are limitations associated with *in vivo* counting uranium measurements. First, soluble uranium is readily excreted, with fractions retained for varying periods in the bone and kidney, so detectability depends on factors such as intake quantity, chemical and physical form, biodistribution fraction, time since intake, background uranium contribution, analysis time, and detection system efficiency. Second, only the ^{235}U isotope is typically evaluated using sodium iodide or hyperpure germanium detector systems, since ^{234}U and ^{238}U decay results in the emission of gamma rays of such low intensity and energy that they are difficult for these systems to quantify (NCRP 1987). In such cases, indirect *in vitro* methods can be used for measuring uranium in urine or feces (DOE 2009). Analytical equipment and procedures vary widely among laboratories and often require individual-specific input (NCRP 1987). Routine bioassay monitoring is recommended for uranium processing facility workers at high risk of incurring an intake when the quantity of uranium handled reaches 0.5 kg (320 μCi), 5 kg (3,200 μCi), or 50 kg (32,000 μCi), respectively, when the process occurs in an open room or on a bench top with possible escape from a process vessel, in a fume hood, or in a glove box (DOE 2009). The Minimum Testing Level (amount of radioactive material a test laboratory should be able to measure in a performance test) for laboratories engaged in biomonitoring is 0.81 nCi (30 Bq) for *in vivo* lung monitoring (HPS 1996). The radiological limit is based on 50-rem to bone surfaces for class F uranium (formerly class D uranium), 5-rem to the whole body for class M uranium (formerly class W uranium), and 50-rem to the extrathoracic portion of the respiratory tract for class S uranium (formerly class Y uranium) (DOE 2009).

7.1.2 External Measurements

In vitro uranium analyses are routinely performed in support of a personnel monitoring program, or in cases where the size of an operation does not justify the cost of whole-body counter facilities. These analyses are usually done on urine samples, but other types of body materials may also be used (e.g., feces or blood). Urinalysis is effective for analysis of transportable or soluble uranium. A fraction of insoluble uranium also appears in the urine (DOE 2009).

The excretion of uranium in fecal material results primarily from intakes by ingestion, and includes uranium swallowed after inhalation. Uranium will usually appear in feces within hours after intake, thus providing a rapid means of determining whether an intake has occurred. Fecal analysis requires prechemistry preparation that includes ashing of the sample, cleaning by co-precipitation, and solvent

extraction followed by electrodeposition. Alpha spectroscopy is then performed (Singh and Wrenn 1988). In the other methods, electrodeposition is replaced with an equipment-specific step, such as direct injection for ICP-MS and mixing with a scintillation cocktail for liquid scintillation. Urinalysis is typically favored over both fecal and blood analysis because it is generally more sensitive and less costly, and because fecal analysis provides no uptake or retention information and blood analyses is invasive.

The analysis of uranium is rarely performed in favor of modeling using biokinetic and biodynamic parameters linked to bioassay results, unless it is conducted as part of an autopsy. The U.S. Transuranium and Uranium Registries (USTUR) maintains the bodies and tissues of uranium workers who donated their bodies to scientific research. USTUR has developed methods for accepting, handling, storing, preparing, analyzing, and disposing of donated human tissues. Tissues analyzed for uranium content are prepared by ashing, anion exchange, and electrodeposition followed by alpha spectroscopy (USTUR 2011).

Several methods that do not require chemical separation are available for measuring uranium in urine (in units of total mass or total activity). These methods include spectrophotometric (total mass), fluorometric (total mass), kinetic phosphorescence analysis (KPA) (total mass), and gross alpha (total activity) analyses (DOE 2009; Elliston et al. 2001, 2005; MARLAP 2004; Wessman 1984). Photometric techniques such as fluorometry and phosphorometry are not frequently used, but kinetic phosphorescence analysis is widely used. Measurements of total uranium do not provide the relative isotopic abundance of the uranium isotopes, but this may only be important when converting between activity and mass when the isotopic ratios are uncertain, or when differentiating between natural and depleted uranium (Magnoni et al. 2001; Roth et al. 2003).

If quantification of an individual uranium isotope is needed (e.g., ^{234}U, ^{235}U, or ^{238}U), the most commonly used methods require chemical separation followed by α-spectrometry, or chemical separation and electrodeposition followed by α-spectrometry (see Table 7-1). Mass spectrometers are more expensive, but provide sensitive, accurate, low-level analysis of uranium isotopes in much less time and with greater throughput than other methods due to greatly reduced sample preparation and analysis times (Twiss et al. 1994; MARLAP 2004; MARSSIM 2000).

The Minimum Testing Level for laboratories engaged in *in vitro* analysis of ^{234}U, ^{235}U, and ^{238}U in biological samples using α-spectroscopy is 0.54 pCi (0.02 Bq) per liter or per sample (HPS 1996). An acceptable minimum testing level of 20 μg/L of urine has also been established for natural uranium based on mass determination (HPS 1996).

7.2 ENVIRONMENTAL SAMPLES

Two types of methods are commonly used for measurement of uranium in environmental samples. The first are field surveys using portable survey instruments, and the second is analysis of samples procured in the field that are returned to the laboratory for quantification.

Accurately measuring the uranium in the field and in environmental samples requires that standard, certified radioactive sources with known concentrations of uranium, or other appropriate radionuclides, be available and used properly. The U.S. national primary standards laboratories for developing and disseminating ionizing radiation standards are the DOE (for special nuclear materials only) and the NIST for the remainder. Also, the Health Physics Society accredits secondary standards laboratories for calibrating portable radiation meters and developing and disseminating NIST-traceable radioactive sources (HPS 2011). DOE can provide environmental uranium standards for metal (natural and depleted uranium), compounds (hexafluoride, oxide, nitrate, and octaoxide), isotopic mixtures, and minerals (phosphate rock, carnotite, pitchblende, monazite, and octaoxide) (DOE 2011b). NIST produces environmental uranium standards in 4 matrices (aqueous solution [SRM3164, SRM4321c] and natural water [SRM1640a], coal [SRMs 1632c and 1635], glass [SRMs 610 and 612–617], and urban particulate matter [SRM1648]) (NIST 2011). Specifics for these include: SRM3164 (natural uranium aqueous solution; 9.994 mg/g), SRM 4321b (natural uranium aqueous solution; $^{234,\ 235,\ \text{and}\ 238}$U; 6.5, 0.3, 6.3 nCi/g; 242.0, 11.14, 233.1 Bq/g, respectively), SRM 617 (trace elements in glass, 0.02 ppm uranium), SRM1635 (trace elements in coal, uranium, 0.24 mg/kg) (NIST 2011).

7.2.1 Field Measurements of Uranium

Uranium measurements in the field are typically qualitative in nature in that the instruments simply respond to alpha emissions, regardless of their isotopic origin. However, the levels can be measured quantitatively if key parameters are known, such as relative abundances of all alpha-emitting isotopes present, thickness of the layer being assessed, and detection efficiency of the instrument for the type of surface being assessed. Measurements in the past have typically been made using a portable, hand-held alpha scintillation detector (e.g., ZnS) equipped with a count rate meter, which detects alpha radiation while discriminating against beta-emitters in the same area. However, the need for low detection limits in radiological remediation efforts has found a more suitable and sensitive instrument in the large-area gas-flow proportional counter. These instruments can be carried by an individual or attached to a holder for maintaining a selected surface-to-detector distance. The latter method can be integrated into a system

which moves along a surface at a predetermined velocity recording spatially-related real-time data for later graphical imaging of absolute surface activity distributions (DOE 1988). These surveys can also be performed on people whose skin or clothing is contaminated. Survey instruments can provide a quick estimate or a measure of the level of activity that might be present. However, more accurate measurement of uranium activity may require that samples be taken for laboratory analyses. Under normal usage, the lowest level of uranium that can be reliably detected using an alpha scintillation survey meter is 200–500 disintegrations per minute/100 cm^2 (0.09–0.23 nCi/100 cm^2) (DOE 1988); however, detection of levels several time lower is practical with gas flow proportional counters, especially when used in the integrate mode. Detection capability varies with the type of detector used, the active area of the probe, the electronics, etc.

Several limitations are associated with the measurement of uranium by portable survey instruments. First, the uranium must be present on the surface of the material being surveyed. Since uranium decays by emission of α particles, which travel only short distances in materials, any uranium that is imbedded in the surface being surveyed will be partially or completely masked. Secondly, when performing surveys, it must be possible to place the detector very close to the surface being surveyed (i.e., approximately one-quarter of an inch) (DOE 1988, 1994a), and uneven surfaces that are unintentionally touched can tear the detector window, disabling the instrument. Additional information is available in MARSSIM (2000) on the use and usefulness of field survey instruments.

7.2.2 Collection of Environmental Samples

The Multi-Agency Radiological Laboratory Analytical Protocols Manual (MARLAP 2004) recommends that a field sampling plan be developed to provide comprehensive guidance for collecting, preparing, preserving, shipping, and tracking field samples and recording field data. The principal objective is to provide representative samples of the proper size for analysis. The design should address input and recommendations of representatives from the field sampling team, health physics professional staff, analytical laboratory, statistical and data analysts, quality assurance personnel, and end-users of data. Field organizations conduct operations according to standard operating procedures that may include but should not be limited to the following:

- Developing a technical basis for defining the size of individual samples;
- Selecting field equipment and instrumentation;
- Using proper sample containers and preservatives;

- Using consistent container labels and sample identification codes;
- Documenting field sample conditions and exceptions;
- Documenting sample location;
- Tracking, accountability, custody, and shipment forms;
- Providing legal accountability, such as chain-of-custody record, when required;
- Selecting samples for field quality control (QC) program;
- Decontaminating equipment and avoiding sample cross-contamination;
- Specifying sample packaging, radiological surveys of samples, shipping, and tracking; and
- Documenting the health and safety plan.

The *in situ* high purity germanium (HPGe) gamma spectrometry system is used to assess concentrations of radioactive materials in undisturbed soils (MARSSIM 2000). The detector is able to discriminate among different radionuclides on the basis of characteristic gamma and x-ray energies. Another in situ technology, laser ablation-ICP-atomic emission spectrometry or MS (LA-ICP-AES/MS), sends a probe to various soil depths where a laser ablates a 1 m^3 sample (MARSSIM 2000). The material is then passed through a plasma torch where it becomes ionized and electrically excited, producing an ionic emission spectrum. As with the *in situ* HPGe system, the surface material is not consumed during the operation and results can be obtained in real-time.

7.2.3 Laboratory Analysis of Environmental Samples

Analytical methods for measuring uranium in environmental samples are summarized in Table 7-2. The available methods can be divided into two groups: chemical methods to determine the total mass of uranium in a sample, and radiological methods to determine amounts of individual isotopes. Environmental media that have been tested for uranium include air filters, swipes, biota, water, soil, and others; a full range of laboratory analysis methods has been used to quantify the total uranium or its individual isotopes. The equipment and methods tend to improve over time. The radiological analysis methods include alpha counting (with ionization, proportional, scintillation, or other solid state detectors), alpha spectroscopy, beta counting (with thin-window GM, ionization, proportional, and solid state detectors), beta spectrometry, or gamma spectroscopy (with NaI or HPGe systems). The equipment and method selection depends on the results needed and the non-uranium radionuclides that may be present

Table 7-2. Analytical Methods for Determining Uranium in Environmental Samples

Sample matrix	Sample preparation	Analytical method	Sample detection limit	Accuracy	Reference
Air	Air particulate collection on glass fiber filter; digestion in HNO_3	ICP-MS (total uranium)	0.1 µg/L in final solution	No data	Boomer and Powell 1987
Air	Spiked air particulate dry and wet ashed; dissolution; coprecipitation with iron hydroxide and Ca oxalate, purification by solvent extraction and electrodeposition onto platinum	α-Spectrometry (isotope quantification)	0.02 dpm/L[b] for ^{238}U in solution	No data	Singh and Wrenn 1988
Air	Sample collection on cellulose filters; ashing; extraction with triisooctylamine; purification by anion exchange chromatography and coprecipitation.	α-Spectroscopy	0.015 pCi	No data	EPA 1984b
Air	Collection on cellulose filters	INAA	0.03 µg per filter	No data	Querol et al. 1997
Rainwater	Coprecipitation with iron hydroxide, radiochemical, ion-exchange and solvent extractive purification, and electrodeposition on steel	α-Spectrometry (isotope quantification)	0.02 dpm/L for ^{238}U in solution[a]	68%	Jiang et al. 1986
Drinking water	Direct analysis or concentration by co-precipitation and solvent extraction; fusion	Fluorometry (total uranium)	<20 µg/L (direct); 0.1 µg/L (cleaned)	104% (cleaned)	EPA 1980c (EPA Method 908.1)
Drinking water	Concentrated by co-precipitation; separation; clean-up by ion-exchange	Gross α-counting (total uranium)	1 pCi/L	92.6%	EPA 1980c (EPA Method 908.0)
Drinking water	Sample chelation in EDTA; addition of Fluron	Laser-induced fluorometry	0.08 µg/L	100% at 1 µg/L	EPA 1984e (EPA Method 908.2)
Natural waters	Sample concentration by cation-exchange resin, separation by ion-exchange resin and complexation with Arsenazo III	Spectro-photometry (total uranium)	0.1 µg/L	80%	Paunescu 1986

Table 7-2. Analytical Methods for Determining Uranium in Environmental Samples

Sample matrix	Sample preparation	Analytical method	Sample detection limit	Accuracy	Reference
Water	Sample fusion with NaF and LiF	Fluorometry (total uranium)	5 µg/L	117.5% at 6.3 µg/L	ASTM 1986 (ASTM Method D2907-83)
Water	Coprecipitation with iron hydroxide; purification by ion-exchange chromatography and electrodeposition	α-Spectrometry (isotope quantification)	0.02 dpm/L	97.7–108% at 0.028–0.044 Bq/L	ASTM 1986 (EPA Method D3972-82)
Water	Solvent extraction; coprecipitation with $BaSO_4$; dissolution in $HClO_4$; reprecipitation with TiF_3; filtration	α-Spectrometry (isotope quantification)	0.02 dpm/L[b] for ^{238}U	No data	Stewart et al. 1988
Water	Preconcentration by complexation with oxine and adsorption on activated carbon	NAA (total uranium)	3 µg/L	>80%	Holzbecher and Ryan 1980
Water	Preconcentration by ion-exchange chromatography; purification by ion-exchange and solvent extraction	NAA (^{235}U and ^{238}U)	No data	No data	Gladney et al. 1983
Water	Extraction by ion-exchange; dissolution in low oxygen solvent; irradiation	Delayed neutron analysis (total uranium)	0.4 µg/L	No data	Zielinski and McKown 1984
Water	Wet-ashed; reaction with complexant	Pulsed-laser phosphorimetry	0.05 ppb	103% (average)	ASTM 1994 (Method 5174-91)
Water (uranyl nitrate)	Solvent extraction	Fluorescence spectroscopy	6.1–10.5 ppm	No data	ASTM 1994 (Method D4763-88)
Ground-water	Separation on resin; automated	FI-ICP-MS (isotope quantification)	0.3 ng/L for ^{238}U	±1.8%	Aldstadt et al. 1996
Ground-water	Separation and concentration on two HPLC columns; complexation with Arsenazo III	Spectro-photometry (total uranium)	1–2 µg/L	No data	Kerr et al. 1988
Water and wastes	Acid digestion; filtration (dissolved); acid digestion (total recoverable)	ICP-MS (total uranium)	0.1 µg/L	105–110%	EPA 1991a (EPA Method 200.8)

Table 7-2. Analytical Methods for Determining Uranium in Environmental Samples

Sample matrix	Sample preparation	Analytical method	Sample detection limit	Accuracy	Reference
Seawater	Uranium enriched by chelation with APDC in the presence of Fe^{+2}, complexation with APDC followed by adsorption on activated carbon	X-ray fluorescence (total uranium)	0.56–0.64 µg/L	No data	Nagj et al. 1986
Seawater	Oxine addition	Cathodic stripping voltametry (total uranium)	0.02–0.2 nM	No data	Van den Berg and Nimmo 1987
Sediment	Sediment dried and well-mixed; dissolution in HCl-$HClO_4$-HF; purification by coprecipitation, ion exchange and electrodeposition	α-Spectrometry (isotope quantification)	No data	No data	Anderson and Fleer 1982
Soil	Soil leached with HCl-HNO_3-HF; purification by ion-exchange, and solvent extraction, and electrodeposition	α-Spectrometry (isotope quantification)	No data	No data	Golchert et al. 1980
Soil	Dissolution in HCl-HNO_3-HF; purification by coprecipitation, solvent extraction and electrodeposition	α-Spectrometry (isotope quantification)	0.03 µg/ sample	67%	Singh and Wrenn 1988
Soil, sediment, and biota	Ashing; fusion with KF and $K_2S_2O_7$; purification by extraction with triisooctylamine, anion exchange chromatography and coprecipitation.	α-Spectroscopy	No data	No data	EPA 1984b
Soil, sediment, and biota	Ashing; extraction into triisooctylamine, strip from triisooctylamine with HNO_3 and coprecipitation with lanthanum.	gross α-Spectroscopy or α-spectroscopy	No data	No data	EPA 1984b
Minerals	Dissolution in HNO_3-HF-$HClO_4$; purification by solvent extraction	Laser fluorometry (total uranium)	No data	No data	Veselsky et al. 1988
Low level radioactive waste	Dissolution; purification by coprecipitation, ion-exchange and electro-deposition	α-Spectrometry (isotope quantification)	0.03 dpm	No data	Wessman 1984

Table 7-2. Analytical Methods for Determining Uranium in Environmental Samples

Sample matrix	Sample preparation	Analytical method	Sample detection limit	Accuracy	Reference
Building materials and lichen	Wet ashing with HNO_3-H_2O-HF; purification by coprecipitation, solvent extraction and electro-deposition	α-Spectrometry (isotope quantification)	0.03 µg/ sample	54–73%	Singh and Wrenn 1988
Vegetation	Sample dried and homogenized; dry and wet ashing	ICP-MS (total uranium)	0.1 µg/L in final solution	No data	Boomer and Powell 1987
Vegetation	Sample dried and homogenized; wet ashing and purification by solvent extraction	Laser fluorometry (total uranium)	0.05 mg/kg in plant ash	No data	Harms et al. 1981
Process water	Dilution and filtration water	Laser fluorometry (total soluble uranium)	0.01 µg/L[b]	No data	Hinton and White 1981
Process water	Direct analysis	Ion chromatography spectrophoto-metric detection (U^+6)	0.04 mg/L	No data	Byerley et al. 1987
Field survey	None	Scintillation detector and count rate meter	200–500 dpm/ 100 cm^2 (scintillation detector)	No data	ANSI 1978 (ANSI Standard N323)

[a]This detection limit was reported by Melgard 1988.
[b]This detection limit was reported by Wessman 1984.

APDC = ammonium pyrrolidine dithiocarbamate; Bq = Bequerel and 1 pCi = 0.37 Bq; dpm = disintegration per minute and 1 pCi = 2.22 dpm; EDTA = ethylenediaminetetraacetic acid; FI = flow injection; HPLC = high performance liquid chromatography; ICP = inductively coupled plasma spectrometry; INAA = instrumental neutron activation and analysis; MS = mass spectrometry; NAA = neutron activation analysis; nM = nanomole or 10^{-9} of a mol

(DOE 2009). The use of high resolution α-spectroscopy is common, although gamma spectroscopy is usable with great care. The chemical methods which are often used include spectrophotometry, fluorometry, and kinetic phosphorescence, with the addition of various mass spectrometer applications (ICP-MS, AES-MS, and accelerator-MS). If conversions between mass and activity are to be made accurately, prior knowledge of the relative abundance of the various uranium isotopes must be available or measured radiologically. A few media-specific methods that have been used successfully for measuring uranium concentrations in environmental samples are described below. The current trend, however, is away from prescriptive methods and toward performance-based methods which enable the user to optimize their available analytical tools.

A cornerstone of this method is the development of Data Quality Objectives and the use of Data Quality Assessment to ensure that the selected method is properly developed and the results are of the appropriate quality (DOE 2010; EPA 2000, 2006a, 2006b). Field sampling quality assurance (QA) addresses a range of practices aimed at minimizing errors and evaluating sampling performance, and is a responsibility of all individuals involved. Aspects of field QA/QC include the use of standard operating procedures for sample collection and analysis; chain-of-custody and sample-identification procedures; instrument standardization, calibration, and verification; technician and analyst training; sample preservation, handling, and decontamination; and QC samples such as field and trip blanks, duplicates, and equipment rinses (ORNL 2011).

DOE's method for analyzing environmental materials is based on the methods of Hindman (1983), Sill and Williams (1981), and Welford et al. (1960) and involves preparing vegetation, soft tissue, and water samples by concentrating or isolating uranium from the media prior to separation in an anion exchange column, followed by alpha spectrometry (DOE 2000).

In one analytical method for air filters, the air filters are ashed, silica content is volatilized with hydrogen fluoride, and uranium is extracted with triisooctylamine, purified by anion exchange chromatography and co-precipitated with lanthanum as fluoride. The precipitated uranium is collected by filtration, dried, and α-spectroscopy is performed (EPA 1984b). The activities of ^{234}U, ^{235}U, and ^{238}U are determined based on the number of counts that appear in the α energy region unique to each isotope. This method is used by the EPA National Air and Radiation Environmental Laboratory for measurement of uranium in air as part of the Environmental Radiation Ambient Monitoring System (see Chapter 6).

Singh and Wrenn (1988) describe a method for uranium isotopic analysis of air filters. Air filters are ashed, redissolved, and co-precipitated with iron hydroxide and calcium oxalate. The uranium is further purified by solvent extraction and electrodeposition. An alpha spectroscopy detection level of 0.02 dpm/L for ^{238}U in solution was reported (Singh and Wrenn 1988).

Considerable work has been done to develop methods for analysis of uranium in water. In 1980, the EPA published standardized procedures for measurement of radioactivity in drinking water, which included uranium analysis by both radiochemical and fluorometric methods (EPA 1980c), and more recently developed an ICP-MS method. An example of each is provided below.

The radiochemical method quantifies gross α activity utilizing either a gas flow proportional counter or a scintillation detection system following chemical separation. In the EPA radiochemical method, the uranium is co-precipitated with ferric hydroxide, purified through anion exchange chromatography, and converted to a nitrate salt. The residue is transferred to a stainless steel planchet, dried, flamed, and counted for α particle activity (EPA 1980c).

For the fluorometric method, uranium is concentrated by co-precipitation with aluminum phosphate and dissolved in diluted nitric acid containing magnesium nitrate as a salting agent, and the co-precipitated uranium is extracted into ethyl acetate and dried. The uranium is dissolved in nitric acid, sodium fluoride flux is added, and the samples are fused over a heat source (EPA 1980b).

The ICP-MS method was developed for measuring total uranium in water and wastes. The sample preparation is minimal—filtration for dissolved uranium and acid digestion for total recoverable uranium. Recovery is quantitative (near 100%) for a variety of aqueous and solid matrices and detection limits are low, 0.1 μg/L for aqueous samples and 0.05 mg/kg for solid samples (EPA 1991a).

The EPA developed two methods for the radiochemical analysis of uranium in soils, vegetation, ores, and biota, using the equipment described above. The first is a fusion method in which the sample is ashed, the silica is volatilized, the sample is fused with potassium fluoride and pyrosulphate, a ^{236}U tracer is added, and the uranium is extracted with triisooctylamine, purified on an anion exchange column, coprecipitated with lanthanum, filtered, and prepared in a planchet. Individual uranium isotopes are separately quantified by high resolution α-spectroscopy and the sample concentration calculated using the ^{236}U yield. The second is a nonfusion method in which the sample is ashed, the silica is volatilized, a ^{236}U tracer is added, and the uranium is extracted with triisooctylamine, stripped with nitric acid, co-

precipitated with lanthanum, transferred to a planchet, and analyzed in the same way by high resolution α-spectroscopy (EPA 1984).

The detection capability of any measurement process is an important performance characteristics, along with precision and accuracy. The lower limit of detection (LLD) has been adopted to refer to the intrinsic detection capability of the measurement process (sampling through data reduction and reporting. Factors that influence the LLD include background count rate, sensitivity of detector, and, particularly, the length of time a sample and background are counted. Because of these variables, LLDs between laboratories, employing the same or similar chemical separation procedures, will vary. Additional examples of the techniques for quantification of uranium (as described above) are available, as well as examples of less frequently used techniques. These are identified in Table 7-3.

7.3 ADEQUACY OF THE DATABASE

Section 104(i)(5) of CERCLA, as amended, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of uranium is available. Where adequate information is not available, ATSDR, in conjunction with NTP, is required to assure the initiation of a program of research designed to determine the health effects (and techniques for developing methods to determine such health effects) of uranium.

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that if met would reduce the uncertainties of human health assessment. This definition should not be interpreted to mean that all data needs discussed in this section must be filled. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

7.3.1 Identification of Data Needs

Methods for Determining Biomarkers of Exposure and Effect. Analytical methods with satisfactory sensitivity and precision are available to determine the levels of uranium in human tissues and body fluids. However, improved methods are needed to assess the biological effects of uranium in tissues.

Table 7-3. Additional Analytical Methods for Determining Uranium in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Rocks, minerals, nuclear fission products, biological material	Solvent extraction as MHFA complex; optional purification by back-extraction	Spectro-photometric	0.0062 mg/L (with back-extraction)	99–103%	Abbassi 1989
Ore leachates	Separation as arsenazo III complex	Flow injection; spectro-photometric	6.6 µg/L	No data	Perez et al. 1990
Aqueous solutions	Complexation with o-hydroxy-propiophenone isonicotinoyl-hydrazone	Spectro-photometric	No data	No data	Ramachandraiah et al. 1993
Natural waters	Co-precipitation with $Fe(OH)_3$; selective separation by precipitation; determined as dibenzoyl methane complex	Laser fluorometry	5 ppb	No data	Eral 1989
Rocks, minerals, nuclear fission products and biological material	Solvent extraction as MHFA complex; optional purification by back-extraction	Atomic absorption spectrometry	<0.08 mg/L	No data	Abbassi 1989
Phosphate rock and phosphoric acid	Wet digestion; separation by extraction with trioctylphosphine oxide; destruction of complex prior to analysis	Argon plasma emission spectrometry	No data	98–100%	Woodis et al. 1980
Uranium tailings (U_3O_8)	Wet digestion; solvent extraction	ICP-OES	No data	101%	Feeney et al. 1983
Phosphate rock	Wet digestion; extraction with trioctylphosphine oxide; back-extraction with stripping solution	dc argon ICP	<1 ppm	99–106%	Norman et al. 1983
Ground, mine waters	Direct analysis	ICP	low ppm	No data	Greene et al. 1985
Coal ash	Acid digestion; separation with s-thenoyltrifluoric acetone; back-extraction	ICP	29 µg/L	98%	Kamata et al. 1987

Table 7-3. Additional Analytical Methods for Determining Uranium in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Seawater	Separation on chelate fiber	ICP-OES	5 µg/L	No data	Chang et al. 1990
Apatite minerals	Extraction with 3-phenyl-4-benzoyl-s-isoxazolone	ICP-AES	0.02 mg/L	No data	Fujino et al. 1994
Natural waters	Extraction with s-thenoyltrifluoric acetone and tri-n-butyl phosphate	Stripping voltametry	10^{-10} mol/dm^3	≈90%	Mlakar and Branica 1989
Groundwater, soil	Separation as propyl gallate complex	Stripping voltametry	subnanomolar	No data	Wang et al. 1994
Surface soils	*in situ*	Gamma spectrometry	0.1 Bq/g	No data	Miller et al. 1994
Ceramic and plastic semiconductor packaging material	None	NAA with fission track counting	0.02 ppb	No data	Riley 1982
River sediments	None	Instrumental NAA	No data	≈70% (certified materials)	Labrecque et al. 1986
Air samples	Sample collection on filters	Instrumental NAA	2 ng/sample	95%	Landsberger and Wu 1993
Sediment, pore water	Dilution	ICP-MS	40 pg/mL	99%	Toole et al. 1991
Soil	None	Proton induced fluorescent x-rays	No data	No data	Lazo et al. 1991
Soil		Isotope dilution MS			Wessman 1984
Biological and environmental samples	Complexation with phosphoric acid	Laser phosphori-metry	Sensitivity 10^{-12} g	No data	Bushaw 1984

AES = atomic emission spectrometry; Bq = Bequerel; ICP = inductively coupled plasma (spectrometry); MHFA = N-p-methoxyphenyl-2-furylacrylohydroxamic acid; MS = mass spectrometry; NAA = neutron activation analysis; OES = optical emission spectrometry

Uranium is in essentially all food, water, and air, so everyone is exposed to some levels. In a study reported by NIOSH (1981) and Thun et al. (1985), enhanced levels of β_2-microglobulin levels were observed in the urine of uranium workers. It was postulated that enhanced excretion of β_2-microglobulin might be used as an indication of uranium exposure; however, NIOSH (1981) and Thun et al. (1985) were unable to establish a dose-response correlation between level of exposure and excretion of the β_2-microglobulin. Limson Zamora et al. (1998) identified changes in several potential biomarkers of effect following exposure to uranium, in which each individual biomarker could be affected by a range of chemicals, but the results suggested that it may be possible to identify a series of biomarkers whose combined responses could serve as a single uranium-specific biomarker of effect. Development of new or combination biomarkers for high uranium exposures would be useful.

Methods for Determining Parent Compounds and Degradation Products in Environmental Media. Analytical methods with the required sensitivity and accuracy are available for quantification of uranium, both total and isotopic, in environmental matrices (Table 7-2). Knowledge of the levels of uranium in various environmental media, along with the appropriate modeling (see Chapters 3 and 5), can be used to evaluate potential human exposures through inhalation and ingestion pathways.

Whether in the environment or in the human body, uranium will undergo radioactive decay to form a series of radioactive nuclides that end in a stable isotope of lead (see Chapter 4). Examples of these include radioactive isotopes of the elements thorium, radium, radon, polonium, and lead. Analytical methods with the required sensitivity and accuracy are also available for quantification of these elements in the environment where large sample are normally available (EPA 1980b, 1984), but not necessarily for the levels from the decay of uranium in the body. More sensitive analytical methods are needed for accurately measuring very low levels of these radionuclides.

7.3.2 Ongoing Studies

No ongoing studies were identified.

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