7. ANALYTICAL METHODS

The purpose of this chapter is to describe the analytical methods that are available for detecting, measuring, and/or monitoring aluminum, its metabolites, and other biomarkers of exposure and effect to aluminum. 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

Because of the ubiquitous nature of aluminum, contamination is a major problem encountered in the analysis of aluminum by all methods except accelerator mass spectroscopy (AMS) using radioactive ^{26}Al. When using the other methods, all items used during collection, preparation, and assay should be checked for aluminum contribution to the procedure. Only by taking these stringent precautions will one be able to produce accurate results. A variety of analytical methods have been used to measure aluminum levels in biological materials, including AMS, graphite furnace atomic absorption spectrometry (GFAAS), flame atomic absorption spectrometry (FAAS), eletrothermal atomic absorption spectrometry (ETAAS), neutron activation analysis (NAA), inductively coupled plasma-atomic emission spectrometry (ICP-AES), inductively coupled plasma-mass spectrometry (ICP-MS), and laser microprobe mass spectrometry (LAMMA) (Roggli et al. 1999; Maitani et al. 1994; Owen et al. 1994; Razniewska and Trzcinka-Ochocka 2003; Van Landeghem et al. 1994) (see Table 7-1). Front-end separation techniques such as chromatography are frequently coupled with analytical methods.

AMS is a technique that can now be used to accurately determine the atomic content in as little as a few milligrams of biological material. AMS has been used in the past for measuring long-lived radionuclides that occur naturally in our environment, but it is suitable for analyzing the ratio of the concentrations of radioactive ^{26}Al to stable ^{27}Al in biological samples. AMS combines a particle accelerator with ion sources, large magnets, and detectors, and is capable of a detection limit of one atom in 10^{15} (1 part per quadrillion [ppq]). This method has biomedical applications regarding the uptake and distribution of aluminum in the body, but is dependent upon the availability of the radioactive ^{26}Al tracer, which is

Table 7-1. Analytical Methods for Determining Aluminum in Biological Materials

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Serum	Direct injection into atomizer	GFAAS	Low µg/L levels	No data	King et al. 1981
Serum	Dilution with water; addition of EDTA	GFAAS	2 µg/L	No data	Alderman and Gitelman 1980
Serum	Centrifugation and injection of supernatant	GFAAS	14.3 µg/L	97–102%	Bettinelli et al. 1985
Serum (Al-organic acid species)	Addition of sodium bicarbonate; direct injection into chromatography column	HPLC/ICP-AES	No data	No data	Maitani et al. 1994
Serum (Al-organic acid species)	Dilution with mobile phase; fractions collected for ETAAS analysis	HPLC/ETAAS	No data	98–100% in spiked and synthetic serum	Wrobel et al. 1995
Serum (Al-organic acid species)	Addition of citrate buffer; direct injection into chromatography column	HPLC/ETAAS	0.12 µg/L	99.2±12.4%	Van Landeghem et al. 1994
Plasma	Dilution	GFAAS	3–39 µg/L	97–105%	Wawschinek et al. 1982
Whole blood, plasma, or serum	Dilution with water	GFAAS	24 µg/L	No data	Gardiner et al. 1981
Whole blood	Addition of sodium citrate; centrifugation; injection of supernatant	GFAAS	Low µg/L levels	No data	Gorsky and Dietz 1978
Whole blood	Dilution with Triton X-100	GFAAS	1.9 µg/L (serum); 1.8 µg/L (plasma); 2.3 µg/L (whole blood)	No data	Van der Voet et al. 1985
Urine	Digestion; ion-exchange clean-up	NAA	50 µg/L	No data	Blotcky et al. 1976
Urine and blood	Dilution with water	GFAAS or ICP-AES	Low µg/L levels	No data	Sanz-Medel et al. 1987
Urine and serum	Dilution with 0.2% nitric acid and water	ETAAS	0.6 µg/L (serum and urine)	No data	Razniewska and Trzcinka-Ochocka (2003)
Urine	Direct injection	GFAAS	Low µg/L levels	No data	Gorsky and Dietz 1978
Urine	Direct injection	GFAAS	Low µg/L levels	No data	Gorsky and Dietz 1978

Table 7-1. Analytical Methods for Determining Aluminum in Biological Materials

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Urine and blood	Dilution with water	ICP-AES	1 µg/L (urine); 4 µg/L (blood)	No data	Allain and Mauras 1979
Biological tissues	Homogenization with EDTA	GFAAS	0.002–10.057 µg/g	95–106%	LeGendre and Alfrey 1976
Biological tissues	Freeze-drying; grinding for homogenization	NAA	8 µg/g	No recovery; RSD <10%	Wood et al. 1990
Biological tissues	Drying; nitric acid digestion; dilution with water	GFAAS	0.5 µg/g	80–117%	Bouman et al. 1986
Biological tissues	Mounting of paraffin sections of formalin fixed tissue on carbon discs; deparaffin sample	SEM/EDXA	0.1% by weight in a detected particle	NA	Abraham and Burnett 1985
Kidney, liver, urine	Acid digestion; dilution with water	ICP-AES	No data	98.8±8.6% in liver	Maitani et al. 1994
Kidney, liver, femur	Microwave nitric acid digestion; addition of internal standard, dilution with eluent	SEC/ICP-MS	0.04 µg/g	100±14% of spiked Al in reference material	Owen et al. 1994
Brain	Freeze drying; acid digestion; dilution with potassium dichromate matrix modifier	GFAAS	0.03 µ/g	No data	Xu et al. 1992a
Brain	Fixing and embedding in polymer matrix; sectioning and staining to visualize Al deposits; laser vaporization of selected sample surface into mass spectrometer	LAMMA	Low µg/g range	No data	Lovell et al. 1993
Hair	Isopropanol wash; nitric acid digestion; dilution with water	GFAAS	0.65 µg/g	84–105%	Chappuis et al. 1988
Human blood, urine, serum, feces	Acid digestion, Parr bomb technique, microwave, or hot plate method	ICP-AES	1 µg/L	>75%	Que Hee and Boyle 1988
Human milk/infant formula	Homogenization; microwave digestion with boiling nitric acid/hydrogen peroxide	ICP-MS	4.8–11 ng/g	No data	de la Flor St. Remy et al. 2004

Table 7-1. Analytical Methods for Determining Aluminum in Biological Materials

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Human milk/cow milk/infant formula	Dilution with ultrapure water	ICP-MS	3 µg/L	No data	Martino et al. 2000
All	None	AMS	1 ppq	NA	Flarend and Elmore 1997

AMS = accelerated mass spectroscopy; EDTA = ethylene diamine tetra acetic acid; EDXA = dispersive x-ray analysis; ETAAS = electrothermal atomic absorption spectrometry; GFAAS = graphite furnace atomic absorption spectrometry; HLPC/ICP-AES = high-performance liquid chromatography/ICP-AES; ICP-AES = inductively coupled plasma - atomic emission spectroscopy; ICP-MS = inductively coupled plasma-mass spectrometry; LAMMA = laser ablution microprobe mass spectrometry; NA = not applicable; NAA = neutron activation analysis; ppq = parts per quadrillion; SEC/ICP-MS = size-exclusion chromatography/ICP-AES/mass spectrometry; SEM = scanning electron microscopy

produced using a cyclotron. The first step in the analysis process is the chemical extraction of aluminum (both stable and radioactive) from the biological sample using a method which is free of aluminum contamination. The extractant is loaded into a holder and inserted through a vacuum lock into the ion source, which then employs ion bombardment to ionize the sample atoms. These are removed from the sample using magnets, and are separated by mass and charge by accelerators, bending magnets, and electron stripper screens. An electrostatic analyzer selects particles based on their energy, and a gas ionization detector counts the ions one at a time using a rate of energy loss assessment that distinguishes between any competing isobars. The amount of ^{26}Al can be calculated from the measured ratio of ^{26}Al to ^{27}Al and the amount of carrier added during the chemical preparation of the sample (Elmore and Phillips 1987; Flarend and Elmore 1997).

GFAAS is the most common technique used for the determination of low-ppb (μg/L) levels of aluminum in serum, plasma, whole blood, urine, and biological tissues (Alder et al. 1977; Alderman and Gitelman 1980; Bettinelli et al. 1985; Bouman et al. 1986; Chappuis et al. 1988; Couri et al. 1980; Gardiner and Stoeppler 1987; Gorsky and Dietz 1978; Guillard et al. 1984; Keirsse et al. 1987; Rahman et al. 1985; Savory and Wills 1986; CEC 1984; van der Voet et al. 1985; Wrobel et al. 1995; Xu et al. 1992a). This is because GFAAS offers the best combination of sensitivity, simplicity, and low cost. When used as a detector for high-performance liquid chromatography (HPLC), GFAAS can analyze for species of complexed or bound aluminum which have been separated into fractions on the chromatography column (Van Landeghem et al. 1994).

NAA has been used to determine low levels of aluminum in biological tissues and urine (Blotcky et al. 1976; Savory and Wills 1986; Wood et al. 1990; Yukawa et al. 1980). NAA involves the bombardment of a sample with neutrons, which transforms some of the stable ^{27}Al atoms into several radioactive aluminum isotopes beginning with ^{28}Al, and measurement of the induced radioactivity. Advantages of NAA include good sensitivity and relative independence from matrix (or media) effects and interferences. Moreover, this technique can be used to detect almost all elements of environmental concern in the same sample (Sheldon et al. 1986). One major problem with using NAA with aluminum is the need to correct for interfering reactions with phosphorus and silicon, which produce the same radioisotope (^{28}Al) of aluminum. Other disadvantages of this technique include its high cost, the limited availability of nuclear reactors for NAA analysis, the short 2.25-minute half-life of ^{28}Al that requires prompt analysis of the sample following bombardment with neutrons, and disposal problems of radioactive waste.

The ICP-AES technique, also referred to as ICP-optical emission spectroscopy (ICP-OES), has been reported for the measurement of aluminum in biological materials and is an excellent alternative to

GFAAS for those laboratories possessing the appropriate instrumentation (Allain and Mauras 1979; Lichte et al. 1980; Maitani et al. 1994; Que Hee and Boyle 1988; Que Hee et al. 1988; Sanz-Medel et al. 1987). ICP-AES is a multi-elemental technique that is relatively free of chemical interferences. The matrix problems that can exist in atomic absorption spectrometry (AAS) are minimized in ICP-AES due to the very high excitation temperature of the sample (Savory and Wills 1986). The limits of detection for the ICP-AES method have been reported to be about 1 and 4 μg aluminum/L of urine and blood, respectively (Allain and Mauras 1979). A major problem with using the ICP-AES technique is the intense and broad emission of calcium, which increases the aluminum background and can raise the detection limit for this element (Allain and Mauras 1979; Que Hee and Boyle 1988; Savory and Wills 1986). Titanium also interferes with aluminum analysis (Que Hee and Boyle 1988). Also, the relatively high cost and complexity of this technique can limit its routine use in many laboratories. However, ICP-AES, especially ICP-MS, technologies have advanced recently largely through the efforts of the Department of Energy, and the cost of analysis has declined considerably.

Inductively coupled plasma-mass spectrometry (ICP-MS) is a powerful technique that uses an inductively coupled plasma as an ion source and a mass spectrometer as an ion analyzer. It can measure the presence of >75 elements in a single scan, and can achieve detection limits down to parts per trillion (ppt) levels for many elements—levels that are two or three orders of magnitude lower than those obtained by ICP-AES (Keeler 1991). It is more expensive than ICP-AES and requires more highly skilled technical operation. Aluminum levels in urine and saliva were detected down to 0.02 μg/mL and in blood serum to 0.001 μg/mL using ICP-MS (Ward 1989). Speciation studies have employed ICP-MS as a detector for aluminum in tissue fractions separated by size-exclusion chromatography (SEC) with detection limits of 0.04 μg/g in femur, kidney, and brain (Owen et al. 1994). ICP-MS has been used to determine metal concentrations, including aluminum, in human milk, cow milk, and infant formulas (de la Flor St. Remy et al. 2004; Martino et al. 2000).

LAMMA has been utilized for the analysis of aluminum in brain tissue affected with Alzheimer's disease (Lovell et al. 1993). This analytical technique of nuclear microscopy can simultaneously image and analyze features in unstained and untreated tissue sections, and therefore avoids contamination problems associated with tissue prepared using conventional chemical techniques. Lovell et al. (1993) reported aluminum concentrations in neurofibrillary tangle (NFT)-bearing neurons and in NFT-free neurons in brain tissue from seven autopsy-confirmed Alzheimer's disease patients. LAMMA was also used in a study that did not detect aluminum in pyramidal neurons in brain tissue from Alzheimer's disease patients (Makjanic et al. 1998). However, in tissue that had been subject to conventional procedures such as

fixation and osmication, aluminum was observed in both neurons and surrounding tissue. The method, however, requires rigorous histological sectioning and preparation prior to analysis, specialized analytical equipment, and highly trained personnel.

Secondary ion mass spectrometry (SIMS) is an analytical method that can be used for the imaging of aluminum and other metals in a variety of materials or biological specimins (Goldsmith et al. 1999; Linton and Goldsmith 1992). This technique uses a primary ion beam to generate secondary ions from the specimen, which are analyzed by mass spectrometry. Spatial resolution is reported to be comparable to that attainable with electron microscopy.

Adequate digestion methods are important in the determination of all metals, including aluminum. Que Hee and Boyle (1988) showed that Parr bomb digestions were always superior to hot plate digestions for many elements, including aluminum, in feces, liver, and testes. Microwaving in closed vessels produced lower aluminum recoveries in liver than Parr bomb digestions. The Parr bomb values for citrus leaves were within 5% of the NBS certified values.

Abraham and Burnett (1983) described a method for quantitative analysis of inorganic particulate burden *in situ* in tissue sections using scanning election microscopy (SEM) with backscattered election (BSE) imaging and energy dispersive x-ray analysis (EDXA). This method can compliment bulk tissue analysis since the analyst can observe the association of certain elements within a particle and the particle size. This information can be correlated to cellular or tissue changes with the types, locations, and concentrations of particles within the tissue. In addition, small samples (<1 µg) can be analyzed. EDXA, which is used to identify the chemical composition of the mineral, allows for separation of particulates into two major classes, endogenous and exogenous. Endogenous particles contain calcium or iron in combination with phosphorus as major constituents along with smaller amounts of sodium, magnesium, and potassium. The remaining particles are considered exogenous, and are divided into three major classes: silica, silicates, and metals. This method has been used to identify aluminum particulates in various human tissues, including lung, kidney, brain, and bone (Baxter et al. 1985; Hull and Abraham 2002; Jederlinic et al. 1990; Perl and Brody 1980; Perl et al. 1982).

Razniewska and Trzcinka-Ochocka (2003) reported a method for the determination of aluminum concentrations in blood serum and urine using ETAAS. Serum and urine samples were analyzed directly following dilution with 0.2% nitric acid and water. The detection limit was reported to be 0.6 µg/L for

serum and urine, with a quantification limit of 1.2 µg/L. This method provided reliable aluminum levels at concentrations observed among non-exposed, healthy individuals.

7.2 ENVIRONMENTAL SAMPLES

A number of analytical techniques have been used for measuring aluminum concentrations in environmental samples. These include GFAAS, FAAS, NAA, ICP-AES, ICP-MS, spectrophotometry using absorbance and fluorescence detection, phosphorimetry, chromatography, and gas chromatography equipped with an electron capture detector (GC/ECD) (Andersen 1987, 1988; AOAC 1990; APHA 1998a, 1998b, 1998c, 1998d; Dean 1989; Fernandez de la Campa et al. 1988; EPA 1983a, 1983b, 1994a, 1994b, 1994c, 2000; Fleming and Lindstrom 1987; Gardiner et al. 1987; NIOSH 1994, 2003a, 2003b, 2003c; OSHA 2001, 2002; USGS 1996). They are summarized in Table 7-2.

There are three NIOSH methods (7300, 7301, and 7303) that analyze elements, including aluminum, in air by ICP-AES; these methods differ only in the digestion method. NIOSH method 7013 analyzes aluminum in air using FAAS. In all of these NIOSH methods, particulate from the air is collected over a filter, either a 0.8-µm cellulose ester membrane or a 5.0-µm polyvinyl chloride membrane. The applicable working ranges are 0.5–10 mg/m^3 for a 100-L air sample by Method 7013, 0.005–2.0 mg/m^3 for a 500-L air sample by Methods 7300 and 7301, and up to 100 mg/m^3 in a 500-L sample for Method 7303. The digestion procedures in Method 7013 (nitric acid) will not dissolve alumina (Al_2O_3); lithium borate fusion is needed. The digestion procedure in Method 7300 (nitric/perchloric acid) may not completely solubilize some species of aluminum; alternative producers are cited in the method (NIOSH 1994, 2003a, 2003b, 2003c).

Method ID-121 (OSHA 2002) can be used to determine the amount of aluminum particulates in the workplace atmosphere. Airborne particulates are collected on filters using calibrated sampling pumps and the samples are analyzed using flame atomic absorption or emission spectrometry. This method can also determine aluminum contained in wipe and bulk samples. Method ID-109-SG (OSHA 2001) determines aluminum oxide in workplace atmospheres. In this method sample filters are fused with a flux containing lithium borate, ammonium nitrate, and sodium bromide in platinum crucibles in order to solubilize the aluminum oxide.

Method 990.08 (AOAC 1990) determines metals, including aluminum, in solid wastes (coal fly ash, industrial and electroplating sludges, mine tailings, river sediment, and soils).

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

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Air	Collect sample on MCE filter, followed by digestion by HNO_3	Method 7013 (FAAS)	2 µg/sample	No data	NIOSH 1994
Air	Collect sample on MCE or PVC filter, followed by nitric/perchloric acid ashing	Method 7300 (ICP-AES)	0.115 µg/filter	101.5–105.4% (MCE) 77.4–92.9% (PVC)	NIOSH 2003a
Air	Collect sample on MCE filter, followed by hot block/HCl/HNO_3 digestion	Method 7303 (ICP-AES)	0.111 µg/mL	No data	NIOSH 2003b
Air	Collect sample on MCE or PVC filter, followed by aqua regia ashing	Method 7301 (ICP-AES)	0.115 µg/filter	99.6–208.1% (MCE) -1.9–112.1% (PVC)	NIOSH 2003c
Air	Collect sample on MCE or PVC filter, followed by HNO_3 digestion or extraction with deionized water	Method ID-121 (FAAS or AES)	0.02 µg/mL	94.5% (average)	OSHA 2002
Air (Al_2O_3)	Collect sample on LAPVC filter, followed by fusion with $LiBO_2/NH_4NO_3$/NaBr	Method ID-109-SG (FAAS)	0.5 µg/mL	96% (average)	OSHA 2001
Water	Filter and acidify filtrate with HNO_3 and analyze	Method 3113 B (GFAAS)	3 µg/L	No data	APHA 1998a
Water	Digest sample with HNO_3/HCl and analyze	Method 3120 B (ICP-AES)	40 µg/L	No data	APHA 1998b
Water	Filter and acidify filtrate with HNO_3 and analyze	Method 3125 (ICP-MS)	0.03 µg/L	98.42% (mean)	APHA 1998c
Water	Acidify with H_2SO_4, add ascorbic acid, buffer and dye (Erichrome cyanine R); measure absorbance at 535 nm	Method 3500-Al B (Spectro-photo-meter)	6 µg/L	No data	APHA 1998d
Water, waste water, and solid wastes	For dissolved constituents: filter, acidify filtrate, and analyze; for samples containing solids: digestion with HNO_3/HCl prior to analysis	Method 200.7 (ICP-AES)	45 µg/L	88–113%	EPA 1994a

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

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Water, waste water, sludges, and soils	For dissolved constituents: filter, acidify filtrate, and analyze; for samples containing solids: digestion with HNO_3/HCl prior to analysis	Method 200.8(ICP-MS)	1.0 µg/L (aqueous) 0.4 mg/kg (solids)	100.4% (average)	EPA 1994b
Water, waste water, sludges, and soils	For dissolved constituents: filter, acidify filtrate, and analyze; for samples containing solids: digestion with HNO_3/HCl prior to analysis	Method 200.9 (GFAAS)	7.8 µg/L	97.1–111.7%	EPA 1994c
Water	For dissolved constituents: filter, acidify filtrate, and analyze; for samples containing solids: digestion with HNO_3/HCl prior to analysis	Method 6010C (ICP-AES)	30 µg/L	No data	EPA 2000
Water	Filter, acidify filtrate, and analyze	Method I-1472-95 (ICP-AES)	5 µg/L	86.1–99.9%	USGS 1996
Water and waste water	For dissolved constituents, filter, acidify filtrate, and analyze; for suspended metals digest with HNO_3 and analyze	Method 202.1 (FAAS)	100 µg/L	No data	EPA 1983a
Water and waste water	For dissolved constituents, filter, acidify filtrate, and analyze; for suspended metals digest with HNO_3 and analyze	Method 202.2 (GFAAS)	3 µg/L	No data	EPA 1983b
Solid wastes	Digest sample in HNO_3/H_2O_2 /HCl, dilute with water; remove particulate matter	Method 990.08 (ICP-AES)	45 µg/L	No data	AOAC 1990
Soil	Filter sample and clean-up on chromatography column	GFAAS	No data	No data	Gardiner et al. 1987
Fly ash	Dry sample in vacuum and irradiate	NAA	No data	Not applicable	Fleming and Lindstrom 1987
Plants	Digest sample with nitric acid and analyze	Spectro-photo-meter	7 µg/L	Not applicable	Dean 1989

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

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Rock, magma, soil, paint, citrus leaves	Acid digest sample using Parr bomb or microwave	ICP-AES	0.001 µg/L	90%	Que Hee and Boyle 1988
Dialysis fluids	Dilute sample with acidic Triton X-100	Phosphor-imetry	3 µg/L	No data	Andersen 1987
Dialysis fluids	Add Ferron and cetyl-trimethylammonium bromide solution to sample and measure phosphorescence at 586 nm	Phosphor-imetry	5.4 µg/L	No data	Fernandez de la Campa et al. 1988
Rock, soil	Digest with acid	AMS	10^{-15} g/g sample	Not applicable	Flarend and Elmore 1997

AMS = accelerated mass spectroscopy; FAAS = flame atomic absorption spectrometry; GC/ED = gas chromatography/electron capture detector; GFAAS : graphite furnace atomic absorption spectrometry; ICP-AES = inductively couples plasma-atomic absorption spectrometry; ICP-MS = inductively couples plasma-mass spectrometry LAPVC = Low Ash Polyvinyl Chloride; MCE = mixed cellulose ester; NAA = neutron activation analysis; PVC = polyvinyl chloride

Method 200.7 (EPA 1994a) provides procedures for determination of metals, including aluminum, in solution in water, wastewater, and solid wastes. Method 200.8 (EPA 1994b) provides procedures for determination of dissolved elements, including aluminum in groundwater, surface water, and drinking water, as well as determination of total recoverable element concentrations in these waters as well as waste waters, sludges and soils samples. Method 200.9 (EPA 1994c) provides procedures for the determination of dissolved and total recoverable elements, including aluminum, by graphite furnace atomic absorption (GFAA) in groundwater, surface water, drinking water, storm runoff, industrial and domestic wastewater, as well as determination of total recoverable elements in sediment, sludges, and soil.

GFAAS and FAAS are the techniques (Methods 202.1 and 202.2) recommended by EPA for measuring low levels of aluminum in water and waste water. Detection limits of 100 and 3 µg of aluminum/L of sample were obtained using the FAAS and GFAAS techniques, respectively (EPA 1983a, 1983b). Spectrophotometry and GC/ECD have also been employed to measure low-ppb (µg/L) levels of aluminum in water (Dean 1989; Ermolenko and Dedkov 1988; Gosink 1975). Flow-injection systems using absorbance (Benson et al. 1990) and fluorescence detection (Carrillo et al. 1992) have been used to monitor aqueous aluminum levels in the field and in the laboratory setting, with detection limits as low as 0.3 µg/L. Ion chromatography using spectrophoto-metric detection and on-line preconcentration gives an effective detection limit <1 µg/L in aqueous samples. GFAAS is the method of choice for measuring low-ppb levels of aluminum in dialysis fluids (Andersen 1987, 1988; Woolfson and Gracey 1988).

The GFAAS and NAA techniques have been employed for measuring aluminum levels in soil and fly ash, respectively (Fleming and Lindstrom 1987; Gardiner et al. 1987). Que Hee and Boyle (1988) employed ICP/AES to measure aluminum in rocks, soils, volcano magma, and print. Aluminum silicate matrices require disruption by hydrofluoric acid/nitric acid digestion in Parr bombs to achieve >90% recoveries of aluminum and other elements in preparation for ICP-AES analysis using wet ashing (Que Hee and Boyle 1988). Aluminum in air particulates and filters has been determined by pressurized digestion and ICP-AES detection (Dreetz and Lund 1992). Microwave digestions in closed polypropylene bottles gave the same concentrations of aluminum for rocks and soils.

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 aluminum 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 aluminum.

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. GFAAS is the method of choice for measuring low-ppb levels of aluminum in whole blood, serum, plasma, urine, and various biological tissues (Alder et al. 1977; Alderman and Gitelman 1980; Bettinelli et al. 1985; Bouman et al. 1986; Chappuis et al. 1988; Couri et al. 1980; Gardiner and Stoeppler 1987; Gorsky and Dietz 1978; Guillard et al. 1984; Keirsse et al. 1987; Rahman et al. 1985; Savory and Wills 1986; CEC 1984; van der Voet et al. 1985). Chromatographic techniques coupled with GFAAS detection have been used to separate various metal species and determine aluminum content in serum (Maitani et al. 1994; Van Landeghem et al. 1994). The NAA and ICP-AES methods have also been used to measure ppb levels of aluminum in biological tissues and fluids (Blotcky et al. 1976; Savory and Wills 1986; Yukawa et al. 1980). ICP-MS has the requisite sensitivity to detect low-ppb levels of aluminum (Ward 1989) in biological and environmental media though it is more expensive than GFAAS. However, the cost of ICP-MS, as well as ICP-AES, analyses has decreased significantly over the last few years. LAMMA can detect aluminum deposits in specific structures of the brain and might be used to correlate the effects of aluminum accumulation (Lovell et al. 1993).

SEM/EDXA allows for quantitative analysis of inorganic particulate burden *in situ* in tissue sections. This method can compliment bulk tissue analysis since the analyst can observe the association of certain elements within a particle and the particle size. This information can be correlated to cellular or tissue

changes with the types, locations, and concentrations of particles within the tissue (Abraham and Burnett 1983).

Although sensitive analytical methods are available for measuring the presence of aluminum in biological tissues and fluids, it is not known whether data collected using these techniques have been used to correlate the levels of aluminum in biological materials to exposure and effect levels. The problem of contamination during tissue preparation (Makjanic et al. 1998) makes this task more challenging.

Razniewska and Trzcinka-Ochocka (2003) noted that there was a need for a simple and sensitive method for the routine measurement of aluminum concentrations in serum and urine. These authors reported a method measuring aluminum concentrations in serum and urine using ETAAS. This method provided reliable results at concentrations observed among non-exposed, healthy individuals. There is a need for additional methods that can measure aluminum concentrations in blood and urine at low concentrations, approximately 1–10 µg/L.

Methods for Determining Parent Compounds and Degradation Products in Environmental Media. FAAS and ICP-AES have been used to measure aluminum in air (Dreetz and Lund 1992; NIOSH 1994, 2003a, 2003b, 2003c; OSHA 2001, 2002). For measuring aluminum in water and waste water, spectrophotometry (Benson et al. 1990; Carrillo et al. 1992; Ermolenko and Dedkov 1988), GC/ECD (Gosink 1975), and FAAS and GFAAS (EPA 1983a, 1983b) have been employed. GFAAS has been used to analyze aluminum in the soil (Gardiner et al. 1987), and GFAAS (Andersen 1987) as well as phosphorimetry (Fernandez de la Campa et al. 1988) have been useful in determining aluminum levels in dialysis fluids. The method used to measure aluminum levels in flyash is NAA (Fleming and Lindstrom 1987). The media of most concern for potential exposure to aluminum are water and dialysis fluids. GFAAS technique is sensitive for measuring background levels of aluminum in water (EPA 1983b) and dialysis fluids (Andersen 1987; Woolfson and Gracey 1988) and levels of aluminum at which health effects might begin to occur. GFAAS and FAAS are the techniques (Methods 202.1 and 202.2) recommended by EPA for detecting aluminum levels in water and waste water (EPA 1983a, 1983b). GFAAS is the method of choice for measuring low-ppb levels of aluminum in dialysis fluids (Andersen 1987; Woolfson and Gracey 1988). ICP-AES has been utilized to detect aluminum in biological media (leaves, feces, serum, blood, liver, spleen, kidney, urine, and testes) and environmental matrices (rocks, soils, water, volcano magma, paint) in addition to other elements (Que Hee and Boyle 1988) and, more recently, ICP-MS has been shown to be useful for even more sensitive analyses of such media. No additional methods for detecting elemental aluminum in environmental media appear to be necessary at

this time. A need exists for developing a range of NIST analytical standards for calibrating instruments and assessing the accuracy and precision of the various analytical methods.

7.3.2 Ongoing Studies

The information in Table 7-3 was found as a result of a search of the Federal Research in Progress database (FEDRIP 2006).

Table 7-3. Ongoing Studies on Aluminum

Investigator	Affiliation	Research description	Sponsor
Mutti, A.	University of Parma, Parma, Italy	The present research project is aimed at applying the most sensitive, selective and specific reference analytical techniques to the study of the composition of exhaled breath condensate in chronic obstructive pulmonary disease patients using ETAAS and ICP-MS.	NIH
Progar, J	Not provided	The goal of the research program is directed toward the development of analytical methodology to determine the quantitative, qualitative, and/or structural identification of inorganic chemical constituents and impurities in drug and biological products through spectrometric means, including FAAS, GFAAS, FES, ICP-AES, and ICP-MS.	NIH
May, JC	Not provided	The research goal is to ensure the safety, purity and potency of vaccines and other biological products through research relating to the development of new or improved accurate, validated, qualitative and/or quantitative methods for the determination and/or characterization of the chemical preservatives, stabilizers, inactivators, adjuvants, residual moisture, protein and other chemical constituents of vaccines and biological products.	NIH

ETAAS = Electro-thermal atomic absorption spectroscopy; FAAS = flame atomic absorption spectrometry; FES = flame emission spectrometry; GFAAS = graphite furnace atomic absorption spectrometry; ; ICP-AES = inductively coupled argon plasma-emission spectrometry ICP-MS = Inductively coupled plasma - mass spectrometry; NIH = National Institutes of Health

Source: FEDRIP 2006