7. ANALYTICAL METHODS

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

Entry of cobalt and its radioisotopes into the human body can be gained through ingestion, inhalation, or penetration through skin. The quantities of cobalt within the body can be assessed through the use of bioassays that are comprised of either *in vivo* and/or *in vitro* measurements. *In vivo* measurements can be obtained through techniques that directly quantitate internally deposited cobalt using, for example, whole body counters. These *in vivo* measurement techniques are commonly used to measure body burdens of cobalt radioisotopes (i.e., ^{60}Co), but cannot be used to assess the stable isotope of cobalt (^{59}Co). Instead, *in vitro* measurements provide an estimate of internally deposited cobalt (both the stable and radioactive isotopes), utilizing techniques that measure cobalt in body fluids, feces, or other human samples. Examples of these analytical techniques are given in NRCP Report No. 87 (1987) and are also listed in Tables 7-1 and 7-2.

7.1.1 Internal Cobalt Measurements

In vivo measurement techniques are the most direct and widely used approach for assessing the burden of cobalt radioisotopes within the body. The *in vivo* measurement of these radioisotopes within the body is

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

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Urine	Direct injection	GF-AAS with Zeeman background correction	0.3 µg/L	101% at 40µg/L	Bouman et al. 1986
	Addition of magnesium nitrate and nitric acid matrix modifiers and equal volume dilution of sample with water	GF-AAS with Zeeman background correction	2.4 µg/L	107.6% at 50 µg/L	Kimberly et al. 1987
	Sample chelated with dithiocarbamic acid derivative, solvent extracted	GF-AAS with Zeeman background correction	0.1 µg/L	No data	Alexandersson 1988; Ichikawa et al. 1985
	Sample wet digested with acid and chelated with 2,3-butanedion dioxide and complex preconcentrated at hanging mercury drop electrode	DPCSV	0.2 µg/L	No data	Heinrick and Angerer 1984
	Direct injection	GF-AAS with Zeeman background correction	0.1 µg/L	No data	Sunderman et al. 1989
Whole blood	Sample diluted with a homogenizer	GF-AAS with D_2 background correction	2 µg/L	No data	Heinrick and Angerer 1984
	Sample wet digested with acid and chelated with 2,3-butanedion dioxine and complex preconcentrated at hanging mercury drop electrode	DPCSV	0.8 µg/L	No data	Heinrich and Angerer 1984
	Sample acid digested, complexed with thiocyanate and N-phenylcinnamo-hydroxamic acid and extracted into ethyl acetate	Colorimetric	0.15 mg/L	No data	Afeworki and Chandravanshi 1987
Serum	Direct injection	GF-AA with Zeeman background correction	0.02 µg/L	No data	Sunderman et al. 1989

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

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Blood or tissue	Acid digestion	ICP-AES (NIOSH method 8005)	10 µg/g (blood); 0.2 µg/g (tissue)	81% at 110 µg/L (blood)	NIOSH 1984

D_2 = deuterium; DPCSV = differential pulse cathodic stripping voltammetry; GF-AAS = graphite furnace atomic absorption spectrometry; ICP-AES = inductively coupled plasma-atomic emission spectrometry; NIOSH = National Institute for Occupational Safety and Health

Table 7-2. Analytical Methods for Determining Radioactive Cobalt in Biological Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit[a]	Percent recovery	Reference
Urine	Direct count of sample	γ-spectrometry with NaI detector	No data (<MDL)	No data	Miltenberger et al. 1981
Soft tissue	Sample wet-ashed	γ-spectrometry (NaI)	No data	No data	Baratta et al. 1969
	Sample directly counted in detector	γ-spectrometry	5 pCi/g	No data	Rabon and Johnson 1973
	Sample digested in acid, oxidized with $HClO_4$, concentrated by precipitation with AMP, purified by resin column, precipitated with hexachloroplatinic acid	-counter	0.1 pCi/g	40–85%	Nevissi 1992
Feces	Direct count of sample	γ-spectrometry	No data	No data	Smith et al. 1972
Blood	Red cells separated from plasma and washed	γ-spectrometry with NaI detector	No data	No data	Smith et al. 1972

[a]1 Bq=2.7×10^{-11} Ci=27 pCi

AMP = ammonium molybdophosphate; MDL = minimum detectable level; NaI = sodium iodide

performed with various radiation detectors and associated electronic devices that are collectively known as whole body counters. These radiation detectors commonly utilize sodium iodide (NaI), hyperpure germanium, and organic liquid scintillation detectors to measure the 1,172 and 1,332 keV gamma rays from the decay of ^{60}Co. Because of the relatively low attenuation of the high energy gamma rays emitted from ^{60}Co by most tissues, cobalt radioisotopes can easily be detected and quantified using whole body counting techniques (Lessard et al. 1984; NCRP 1987; Raghavendran et al. 1978; Smith et al. 1972; Sun et al. 1997). Many configurations of the whole body counter and scanning methods have been utilized, ranging from unshielded single-crystal field detectors to shielded, multi-detector scanning detectors (IAEA 1962, 1970, 1972, 1976, 1985; NCRP 1987). Where appropriate, shielding of the room that houses the whole body counter and/or the detector is often used to increase the detection sensitivity of the equipment by minimizing background radiation. Additionally, care must be exercised to insure that external contamination with radioactive cobalt or other gamma-emitting radioisotopes on the clothing or skin of the individual to be scanned has been removed. Also, *in vitro* measurements of cobalt (see Section 7.1.2) are often used in conjunction with whole body counting when monitoring individuals working with cobalt, especially in conjunction with the assessment of individuals who have experienced accidental exposures to cobalt (Bhat et al. 1973).

Calibration of whole body counters is achieved through the use of tissue-equivalent phantoms. These phantoms are constructed to mimic the shape and density of the anatomical structure using tissue equivalent materials such as water-filled canisters or masonite (Barnaby and Smith 1971; Bhat et al. 1973; Sun et al. 1997). For example, the bottle mannequin absorber (BOMAB) consists of a series of water-filled polyethylene canisters constructed into seated or reclined human forms (Sun et al. 1997). ^{60}Co standards are measured either as point sources along the phantom or dissolved within the water-filled canisters. Comparisons of the actual counts obtained from the phantom to the known activity of the cobalt standards are used to determine the efficiency of the counting technique and, thus, provide the basis for calibrating the technique. Even so, differences in whole body measurement techniques, calibration methods, and background radiation count calculations between different laboratories can complicate the direct comparisons of body burden measurements and clearance rates for cobalt radioisotopes and should be taken into consideration when comparing data obtained from independent laboratories.

7.1.2 External Measurements

In vitro analyses of cobalt are routinely performed in situations where *in vivo* analyses can not be obtained or in support of an *in vivo* monitoring program. Urine and feces are the preferred samples for *in vitro* analyses of cobalt, although other sample types, such as tissue, bone, or blood, can also be used on a more limited basis. Urine provides for an analysis of soluble (inorganic) cobalt, fecal analysis can be used to assess the cobalt (organic) that is eliminated into the gut or the fraction of ingested cobalt not absorbed by the gut, and tissue/blood/bone are used to assess whole or regional body burdens of cobalt (NCRP 1987; Smith et al. 1972).

The analytical methods for determining the stable cobalt isotope, ^{59}Co, in biological matrices are given in Table 7-1. For accurate determination of cobalt, contamination of samples during sample collection, storage, and treatment must be avoided, particularly for biological samples containing low levels of cobalt. Cobalt contamination in blood samples has been reported from disposable syringes and technical-grade anticoagulants. Menghini needles, often used for liver biopsy, and mortar, pestles, and grinding devices used for homogeneous mixing may contaminate samples. Other sources of contamination may be collection and storage containers and chemical reagents used for preparing samples. In fact, sample contamination was responsible for erroneous reports in the earlier literature of grossly high levels of cobalt in biological specimens of unexposed persons. Therefore, blanks should always be run with the samples.

The commonly used classical methods for determining stable cobalt in biological samples are polarographic and colorimetric methods. Details about these methods are given by Saltzman and Keenan (1957). Since these older methods have interference problems and are unsuitable for determining low levels of cobalt in many biological samples, the samples are pretreated before quantification. Precipitation, chelation, chromatography, and ion-exchange are some of the methods used for this purpose. In recent years, the two single-element instrumental techniques most frequently used methods for determining cobalt are graphite furnace-atomic absorption spectrometry (GF-AAS) (also called electrothermal atomic absorption spectrometry) and differential pulse anodic stripping voltammetry (DPAVS). Multi-element techniques commonly used for cobalt determination are neutron activation analysis and inductively coupled plasma-atomic emission spectrometry (ICP-AES). Several other methods are available for determining stable cobalt in biological samples; these include x-ray fluorescence and Spark source mass spectrometry (Adeloju et al. 1985; Smith and Carson 1981).

For the *in vitro* analysis of cobalt radioisotopes in human samples, the majority of the analytical methods measure the cobalt radioisotopes directly in the samples, without the requirement for an extensive sample preparation procedure, using gamma spectrometry techniques. Of the cobalt radioisotopes that have been detected in the environment (e.g., ^{57}Co, ^{58}Co, and ^{60}Co), ^{60}Co is the most common. Consequently, most of the analytical methods that will be described in this chapter are those developed for the detection and quantitation of ^{60}Co in biological (see Table 7-2) and environmental samples (see Table 7-4).

The radiochemical analysis of ^{60}Co in urine has been used in conjunction with whole body scanning methods to assess acute and long-term body burdens of this isotope. The analysis of ^{60}Co in urine is the same as that described for a standardized method of analysis of cesium radioisotopes in urine (Gautier 1983). A urine sample of approximately 2 L is collected (either over 24 hours or before and after bedtime) and a 1-L aliquot is transferred to a Marinelli beaker for counting in a gamma-ray spectrometer (Gautier 1983). This simple procedure offers high recoveries of cobalt (98%) and the minimum detection sensitivity (100 pCi/L [3.7 Bq/L]) that is required to evaluate individuals for exposures to radioactive cobalt (Gautier 1983). Direct counting methods are also used for the analysis of cobalt radioisotopes in tissues, feces, and blood (Smith et al. 1972, Table 7-2). However, some of these methods may require sample preparation to reduce volume or increase concentration.

Accuracy of *in vivo* and *in vitro* measurements of cobalt is determined through the use of standard, certified solutions or radioactive sources with known concentrations or activities of cobalt. Certified standards for stable cobalt can be obtained through a number of commercial sources. The primary source of certified cobalt radioisotope standards is the National Institute of Standards and Technology (NIST). Gamma ray point sources for ^{60}Co (SRM 4200, 60,000 Bq [1.6 μCi] and SRM 4207, 300,000 Bq [56 μCi]) and standard solutions of ^{60}Co (SRM 4233, 600,000 Bq/g [16 μCi/g]) are available from NIST. Also, the determination of accuracy of a method often requires standard reference materials (SRMs). Unfortunately, very few biological SRMs are available. An SRM for cobalt in animal muscle is available from the International Atomic Energy Agency (IAEA), Vienna; an SRM for bovine liver (SRM-1577) is available from NIST (formerly the National Bureau of Standards) (Adeloju et al. 1985; Smith and Carson 1981).

7.2 ENVIRONMENTAL SAMPLES

There are two common approaches for measuring cobalt in the environment. Cobalt radioisotopes can either be measured directly in the field (*in situ*) using portable survey instruments or samples can be procured from the field and returned to the laboratory for quantitation. However, quantitation of the stable cobalt isotope ^{59}Co in environmental samples is generally conducted in the laboratory.

7.2.1 Field Measurements of Cobalt

In situ measurement techniques are extremely useful for the rapid characterization of radionuclide contamination in the environment, such as soils, sediments, and vegetation, or when monitoring personnel for exposure to radionuclides. The measurement of gamma-ray-emitting radionuclides, like cobalt, in the environment is conducted with portable survey instruments such as Gieger-Mueller detectors, sodium iodide scintillation detectors, and gamma-ray spectrometers. However, the use of gamma-ray spectrometers in field survey equipment is preferred for measuring cobalt in the field because of its selectivity and sensitivity. The relatively high energy and penetrability of the gamma ray that is emitted during the decay of ^{60}Co provides an advantage for assessing the level of cobalt both on and below the surface using portable field survey instruments such as the gamma-ray spectrometer. These gamma-ray spectrometers are equipped with a high purity germanium detector that is able to selectively and sensitively differentiate the 1,173 and 1,332 keV gamma rays emitted from ^{60}Co from the gamma-rays emitted from other radionuclides, for example ^{40}K or ^{137}Cs (USNRC 1997). Minimum detectable activities (MDAs) of 0.005 Bq/g (0.05 pCi/g) for ^{60}Co are routinely achieved using p-type germanium gamma-ray spectrometers with 10-minute counting times (USNRC 1997). However, counting errors can occur where the simultaneous detection of the 1,173 and 1,332 keV gamma rays produces a sum peak at 2,505 keV or a count in the continuum between the individual peaks and the sum peak (APHA 1998; USNRC 1997). These errors can be minimized by changing the geometry of the detector or the distance of the detector from the source of radioactivity. Computational methods have been derived to aid in determining the concentrations and distributions of ^{60}Co in different soil types and depths (USNRC 1997). The concentrations and distributions of ^{60}Co that have been derived from the computational analysis of the survey data are often verified by laboratory-based analyses of soil samples procured from the survey area.

7.2.2 Laboratory Analysis of Environmental Samples

Analytical methods for quantifying stable cobalt and cobalt radioisotopes in environmental samples (e.g. air, water, soil, and biota) are summarized in Tables 7-3 (^{59}Co) and 7-4 (^{60}Co). The methods that are commonly used in the analysis of stable cobalt are based on instrumental analytical techniques, such as atomic absorption spectrometry (AAS), instrumental neutron activation analysis (INAA), and mass spectrometry (MS). The analysis of ^{60}Co can be determined either as total mass or total activity, depending on the analytical technique that is used. Typically, radiochemical methods of analysis employing gamma-ray spectrometry techniques are used to quantitate ^{60}Co in environmental samples.

Analytical methods for determining stable cobalt in environmental samples are given in Table 7-3. Since cobalt exists in the particulate form in the atmosphere, it is sampled by drawing air through a metal-free filter (usually cellulose ester membrane), and the metal is quantified in the collected particles. Sample treatment prior to quantification is important for environmental samples. For example, the use of sodium carbonate for dry ashing plant materials results in poor cobalt recovery. Low-temperature ashing may be inadequate for some samples, and losses may occur during rigorous dry ashing. Wet ashing is the preferred method when sample treatment is necessary. Wet extraction with dilute nitric acid is most suitable for analyzing cobalt in dust samples. In some samples, the determination of soluble and insoluble cobalt is important, and analytical methods used to determine cobalt in filtered and unfiltered samples are available for this purpose.

As in the case of biological samples, contamination of environmental samples during sample collection, storage, and treatment should be avoided. Loss of cobalt from aqueous samples due to adsorption on storage containers should be avoided by using polyethylene or similar containers and acidifying the solution to the proper pH (Smith and Carson 1981). Because of its rapidity, accuracy, and low detection limit, GF-AAS with Zeeman background correction is the most commonly used method for quantifying cobalt in environmental samples. To meet the detection limits of the available analytical methods, preconcentration prior to quantification may be necessary for some samples (e.g., seawater). A few commonly used methods for determining cobalt in environmental samples are given in Table 7-3. Other less frequently used methods are inductively coupled plasma-mass spectrometry (ICP-MS) (Henshaw et al. 1989; McLaren et al. 1985), gas, liquid, and ion chromatography with colorimetric, electron capture, and electrochemical detection (Bond and Wallace 1984; Carvajal and Zienius 1986; Cheam and Li 1988; King and Fritz 1987; Schaller and Neeb 1987), photoacoustic spectroscopy with colorimetry (Kitamori

Table 7-3. Analytical Methods for Determining Stable Cobalt in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Air (workplace)	Weighed filter irradiated in a reactor	INAA	0.17 µg/m^3	No data	Haddad and Zikovsky 1985
	Sample filter digested by wet acid ashing	Flame-AAS with background correction (NIOSH method 7027)	0.4 µg/m^3	98% with 12–96 µg spiked filter	NIOSH 1984
	Sample filter digested by wet acid ashing	ICP-AES (NIOSH method 7300)	0.5 µg/m^3	95–100% with 2.5–1,000 spiked filter	NIOSH 1984
Water (low ionic strength)	Direct injection	GF-AAS with Zeeman or deuterium back-ground correction	<0.5 µg/L	93–115% at 8.5–30 µg/L	Fishman et al. 1986
Lake water	Sample complexed with 8-hydroxyquinoline absorbed on a column, desorbed and digested with acid	ICP-AES	<0.004 µg/L	No data	Nojiri et al. 1985
Rainwater	Sample preconcentrated onto polystyrene films by spray-drying	PIXE	0.08 µg/L	No data	Hansson et al. 1988
Seawater	Sample complexed with 8-hydroxyquinoline absorbed on a column, desorbed and digested with acid	GF-AAS with Zeeman back-ground correction	0.0002 µg/L	90%	Nakashima et al. 1988
Water and waste water	Direct aspiration of sample	Flame-AAS (EPA method 219.1)	0.05 mg/L	97–98% at 0.2–5.0 mg/L	EPA 1983
	Direct injection	GF-AAS with background correction (EPA method 219.2)	1 µg/L	No data	EPA 1983
Groundwater or leachate	Direct aspiration	Flame-AAS with background correction (EPA method 7200)	0.05 mg/L	97–98% at 0.2–5.0 mg/L	EPA 1986b
Groundwater or leachate	Direct injection	GF-AAS with background correction (EPA method 7201)	1 µg/L	No data	EPA 1986b

Table 7-3. Analytical Methods for Determining Stable Cobalt in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Food	Sample digested with acid	GF-AAS with background correction	1.88 µg/L in dissolved extract	100–107% at 0.2–0.6 mg/kg (leaves, liver)	Barbera and Farre 1988
Milled Wheat	Wet ashing (HNO_3), preconcentration and chelation	ET-AAS	20 ng/L	approximately 100%	González et al. 2000

AAS = atomic absorption spectrometry; EPA = Environmental Protection Agency; ET-AAS = electrothermal atomic absorption spectrometry; GF-AAS= graphite furnace atomic absorption spectrometry; ICP-AES = inductively coupled plasma-atomic emission spectrometry; INAA = instrumental neutron activation analysis; NIOSH = National Institute for Occupational Safety and Health; PIXE = photon induced x-ray emission

Table 7-4. Analytical Methods for Determining Radioactive Cobalt in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit[a]	Percent recovery	Reference
Air	Direct count of sample collected on paper filter	γ-spectrometry with Ge/Li detector	0.001 pCi/m^3	No data	USAEC 1974a
Air	Sample filter ashed	Scintillation counter with NaI detector	No data	No data	De Franceschi et al. 1974
Drinking water	Direct count of sample	γ-spectrometry with Ge detector	<2 pCi/L	99%	APHA 1998
Drinking water	Direct count of sample	γ-spectrometry	2 pCi/L	No data	USAEC 1974b
Water	Direct count of sample	γ-spectrometry with Ge/Li detector	2 pCi/L	No data	ASTM 1999
Water	Direct count of sample	γ-spectrometry	10 pCi/L	No data	Cahill et al. 1972
Seawater	Sample concentrated using continuous-flow coprecipitation-flotation separation technique	Scintillation detector	50 fCi/L	92–95%	Hiraide et al. 1984
Sediments	Sample dried and ground	γ-spectrometry	0.04 pCi/g	No data	Cahill et al. 1972
Fish	Samples dried and ashed	γ-spectrometry	0.001 pCi/g (DW)	No data	Cushing et al. 1981
Mollusc	Samples dried and ashed	γ-spectrometry	<0.01 pCi/g	No data	De Franceschi et al. 1976

[a]1 Bq=2.7×10^{-11} Ci=27 pCi

DW = dry weight; Ge/Li = lithium drifted geranium; NaI = sodium iodide

et al. 1986), electrothermal vaporization with ICP-AES (Malinski et al. 1988) and chemiluminescence with spectrofluorimetry (Jones et al. 1989).

Analytical methods for determining cobalt radioisotopes in the environment are shown in Table 7-4. The analysis of cobalt in air is based on quantifying cobalt within aerosols or particles that become trapped on cellulose (paper) or glass fiber filters after a calibrated amount of air is passed through the filters. Since the cobalt radioisotopes do not occur naturally, but may be released as a result of nuclear weapons testing (which has been discontinued for several years), neutron-activation of specific materials (e.g., cobalt containing alloys used in piping of nuclear reactors), or a severe core damage accident in a nuclear plant, the amounts of these isotopes within the ambient environment are near or below the minimum detectable levels for these isotopes (DOE 1995). However, trace amounts of ^{60}Co can be detected in air, water, and sediments within or near nuclear weapons or fuel production facilities, nuclear reactors, and nuclear waste storage sites (DOE 1995; Boccolini et al. 1976; USAEC 1973). Analysis of cobalt radioisotopes in air filters, water, sediments, vegetation, and biota can be performed directly using gamma-ray spectrometry, or following some sample preparation (e.g., drying, ashing, or extraction) (Boccolini et al. 1976; Cahill et al. 1972; Cushing 1981; Hiraid et al. 1984; Windham and Phillips 1973).

The detection limits, accuracy, and precision of any analytical methodology are important parameters in determining the appropriateness of a method for quantifying a specific analyte at the desired level of sensitivity within a particular matrix. The Lower Limit of Detection (LLD) has been adopted to refer to the intrinsic detection capability of a measurement procedure (sampling through data reduction and reporting) to aid in determining which method is best suited for the required sample quantitation (USNRC 1984). Several factors influence the LLD, including background, size or concentration of sample, detector sensitivity and recovery of desired analyte during sample isolation and purification, level of interfering contaminants, and, particularly, counting time. Because of these variables, the LLDs between laboratories, utilizing the same or similar measurement procedures, will vary.

The accuracy of a measurement technique in determining the quantity of a particular analyte in environmental samples is greatly dependent on the availability of standard reference materials. Several SRMs for cobalt in environmental samples are also available. Some of these are coal, fly ash, diet, and orchard leaf SRMs available from NIST. The Community Bureau of Reference, European Communities offers SRMs for cobalt in sludges, and an SRM for cobalt in thin polymer films is available from NIST for x-ray fluorescence analysis in aerosol particle samples (Dzubay et al. 1988; Miller-Ihli and Wolf

1986; Schramel 1989; Smith and Carson 1981; Tinsley et al. 1983). Gamma ray point sources for ^{60}Co (SRM 4200, 60,000 Bq [1.6 μCi] and SRM 4207, 300,000 Bq [56 μCi]) and standard solutions of ^{60}Co (SRM 4233, 600,000 Bq/g [16 μCi/g]) are available from NIST.

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 cobalt is available. Where adequate information is not available, ATSDR, in conjunction with the National Toxicology Program (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 cobalt.

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. Cobalt concentrations in blood or urine can serve as exposure indicator (Alexandersson 1988; Ichikawa et al. 1985; Scansetti et al. 1985). The available analytical methods are capable of determining the levels of cobalt in both the blood and urine of normal and occupationally exposed persons (Table 7-1). For the quantitation of cobalt radioisotopes, whole body counters can be used to assess radioactive cobalt body burdens that have occurred both from acute and chronic exposures to cobalt radioisotopes (Bhat et al. 1973; NCRP 1987). *In vitro* analytical methods are available for analyzing cobalt radioisotopes in urine, feces, and tissues obtained from normal and occupationally exposed persons (Table 7-2).

Sensitive serum protein responses were found in animals exposed to cobalt at levels below those that produce hematopoietic effects. This unique serum protein response to cobalt exposure includes an increase in alpha globulin fractions of serum proteins and associated serum neuraminic acid. Details of this effect are given in Chapters 2 and 3. If similar changes occur in humans, this measurement may provide the earliest indications of effects of cobalt exposure. The available analytical methods are capable of determining these effects of cobalt exposure.

Methods for Determining Parent Compounds and Degradation Products in Environmental Media. Analytical methods with good sensitivity and specificity are available for determining cobalt in air, water, soil, and other environmental media (Table 7-3). Analytical methods for cobalt, like those for most metals, measure total metal content rather than the particular compound. Therefore, analytical methods do not generally differentiate between the parent compound and a transformation product as would be the case, for example, were cobalt oxide to be converted to cobalt sulfate. (An exception to this would be the case of radioactive decay in which the parent could be readily distinguished from the decay product.) Analytical methods with the capability of distinguishing between different cobalt species would be important an important tool for assessing the fate of cobalt compounds in the environment. However, methods for quantifying specific cobalt compounds were not found in the literature.

The levels of the parent compound or its reaction products in different environmental media can be used to assess the exposure to cobalt by humans through the inhalation of air and ingestion of food and drinking water. In the case of cobalt, a correlation between its levels in environmental media (e.g., occupational air) and in biological tissues and body fluids has been found (Alexandersson 1988; Ichikawa et al. 1985; Scansetti et al. 1985). Therefore, it is possible to estimate the total body burden of cobalt in workers exposed to airborne cobalt vapor and fumes from its concentration in workplace air.

For cobalt radioisotopes, analytical methods also exist that have good sensitivity and specificity for determining radioactive cobalt in air, water, soil, and other environmental media are available (Table 7-4). Because ^{60}Co decays to the stable element ^{60}Ni, there is no need to develop methods to detect and quantify the decay products.

7.3.2 Ongoing Studies

Two studies involving analytical techniques for cobalt was listed in the Federal Research in Progress database (FEDRIP 2002, 2004). N.J. Miller-Ihli and co-workers of the Agricultural Research Service in Beltsville, Maryland are developing single and multielement methods for the determination of trace elements of nutritional and health concern. This work will develop new/improved methods permitting direct analysis of solids by GF-AAS and ICP-MS, as well as methods for the determination of different chemical forms of these elements by coupling capillary zone electrophoresis with inductively coupled plasma mass spectrometry (ICP-MS). This research is supported by the U.S. Department of Agriculture (USDA) Agricultural Research Service. B.T. Jones of Wake Forest University in Winston-Salem, North Carolina along with C. Calloway of Winthrop College, South Carolina, are working to develop a novel, low-cost, portable instrument for the simultaneous determination of trace radioactive elements in nuclear forensic samples. The instrument to be developed is expected to provide analytical figures comparable to ICP-MS, but the instrument is much lower cost and more portable. The specific objectives of the project include determination of the analytical figures of merit for elements including cobalt, cesium, and strontium, and analysis of real samples such as soil, urban dust, water, and agricultural materials.