6. ANALYTICAL METHODS

The purpose of this chapter is to describe the analytical methods that are available for detecting and/or measuring and monitoring chloroform in environmental media and in biological samples. The intent is not to provide an exhaustive list of analytical methods that could be used to detect and quantify chloroform. Rather, the intention is to identify well established methods that are used as the standard methods of analysis. Many of the analytical methods used to detect chloroform in environmental samples are the methods approved by federal 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 refine previously used methods to obtain lower detection limits, and/or to improve accuracy and precision.

6.1 BIOLOGICAL SAMPLES

Methods for analyzing chloroform in the biological matrices (breath, blood, urine, and tissues) are listed in Table 6-l. None of these methods has been standardized by an organization or federal agency, although the blood method of Ashley et al. (1992) was developed at the Centers for Disease Control and Prevention (CDC). Sample preparation methods are based on headspace analysis, purgeand-trap, or solvent extraction. Sample preparation for breath samples typically utilizes an adsorbent followed by thermal desorption or direct analysis of an aliquot of breath. These methods all use gas chromatography (GC) with various detection methods as an analytical technique. Cardinali et al. (1994) describe a procedure for the production of blank water for use with analysis of organic compounds in human blood at the parts per trillion (ppt) level; the availability of such blank samples is very important if reliable results are to be obtained. With limits of detection (LODs) in the low-ppt range, these methods are sufficiently sensitive to measure background levels of chloroform in the general population as well as chloroform levels at which health effects might occur after short-term or long-term exposure. However, many studies do not report the method detection limit and/or the recovery percentage for the method. For more information regarding the use of GC methods and detectors, see Section 6.2.

Table 6-1. Analytical Methods for Determining Chloroform in Biological Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Exhaled air (breath)	Collection in Tedlar bag; preconcentration by Tenax-GC; thermal desorption	HRGC/FID and HRGC/MS	No data	No data	Krotoszynski et al. 1979
Alveolar air	Collection of exhaled air using a specially-designed device to provide pure air for inhalation. Breath collected into duplicate evacuated canisters.	GC/MS	0.5 μg/m^3 (0.5 ppt, w/v)	112 (8% RSD) at 5.1 μg/m^3	Raymer et al. 1990
Alveolar air	Collection directly into an evacuated canister	GC/MS	No data	No data	Pleil and Lindstrom 1995
Exhaled air	Collection of whole breath into a sampling bag; collected sample pulled through a Tenax cartridge	GC/Electrolytic conductivity	13 ng on cartridge	63 ± 13	Jo et al. 1990
Alveolar air	Collection onto carbonaceous sorbent; thermal desorption	GC/ITMS	No data	No data	Phillips and Greenberg 1992
Alveolar air	Collection of end-expired air into glass tube	GC/ECD, GC/MS	8.4 nmol/m^3 (1 μg/m^3; 1 ppt, w/v)	No data	Aggazzotti et al. 1993
Whole blood	Purge-and-trap pre-concentration (with isotopically-labelled internal standard)	GC/Isotope dilution MS	0.040 ppb	105 at 0.054 ppb	Ashley et al. 1992
Whole blood	Headspace analysis	GC/FID	0.02 μg/mL (0.02 ppm, w/v)	No data	Seto et al. 1993
Whole blood	Purge-and-trap preconcentration; thermal desorption	GC/MS	<0.5 μg/L	No data	Antoine et al. 1986
Adipose tissue and serum	Purge-and-trap pre-concentration; thermal desorption	GC/Hall with GC/MS confirmation	No data	100 at 0.6 μg/L (serum); No data (tissue)	Peoples et al. 1979

Table 6-1. Analytical Methods for Determining Chloroform in Biological Samples (continued)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Whole blood	Solvent extraction	HRGC/ECD with HRGC/MS confirmation	No data	99 at 50 µg/L	Kroneld 1986
Serum and adipose tissue	Purge-and-trap pre-concentration; thermal desorption	GC/Hall with GC/MS confirmation	0.05 µg/L for serum	No data	Pfaffenberger et al. 1980
Water, serum, and urine	Solvent extraction	HRGC/ECD	1 µg/L for serum and urine	100.3 at 50 µg/L (water); 103 at 2.5 µg/L (serum); 141 at 2.3 µg/L (urine)	Reunanen and Kroneld 1982
Blood, urine	Blood collected into vacutainers containing EDTA. Two-mL aliquots of blood or urine dispensed into headspace vials for analysis	Headspace GC/ECD	No data	No data	Cammann and Hübner 1995
Blood, urine, and tissues	Addition of sample to internal standard; addition of proteolytic enzyme; equilibration at elevated temperature; analysis of headspace gas	GC/ECD	At least 1 ppm	No data	Streete et al. 1992
Blood, urine, and tissue	Purge-and-trap pre-concentration; thermal desorption	GC/HSD or GC/MS	0.10 µg/L (blood and urine)	No data	EPA 1985a

ECD = electron capture detector; FID = flame ionization detector; GC = gas chromatography; Hall = Hall electrolytic conductivity detector; HRGC = high-resolution gas chromatography; HSD = Halogen-specific electrolytic conductivity conductor; MS = mass spectrometry; RSD = relative standard deviation; w/v = weight:volume

6. ANALYTICAL METHODS

Chloroform is transformed by mammalian P-450 enzymes in *vivo* to trichloromethanol which undergoes spontaneous dechlorination to yield phosgene ($COC1_2$) (Pohl et al. 1977), a highly reactive electrophile (Mansuy et al. 1977). Phosgene can react with cysteine to form 2-oxothiazolidine-4-carboxylic acid (Pohl et al. 1977, 1980b), with two molecules of glutathione to form diglutathionyl dithiocarbonate (Pohl et al. 1981), or with water to produce chloride ion and carbon dioxide (Pohl et al. 1980b). Although 2-oxothiazolidine-4-carboxylic acid and diglutathionyl dithiocarbonate have been measured in liver microsomal preparations (Pohl et al. 1977, 1980b, 1981), the applicability of these methods to human tissues is unknown. Phosgene can also be formed from bromotrichloromethane and carbon tetrachloride (Pohl et al. 1981), so the formation of phosgene and any subsequent products cannot be related exclusively to exposure to chloroform.

6.2 ENVIRONMENTAL SAMPLES

Analytical methods for determining chloroform in environmental samples are presented in Table 6-2. As with all extremely volatile chemicals, it is essential to take precautions during sampling, storage, and analysis to avoid loss of chloroform. Methods commonly used for the determination of chloroform concentrations in air are based on either adsorption onto a sorbent column followed by thermal or solvent desorption with subsequent analysis using GC (EPA 1988f; NIOSH 1994; OSHA 1979) or on cryogenic concentration of chloroform directly from a parcel of air (Bureau International Technique des Solvants Chlores 1976; EPA 19888, 19881) followed by GC. The disadvantages of the sorption tubes are that sorption and desorption efficiencies may not be 100%, and that the background impurities in the sorbent tubes may limit the detection limit for samples at low concentrations (Cox 1983). In addition, storage of sorbent tubes before desorption and analysis can result in losses of chloroform (OSHA 1979), and poor retention of chloroform by the sorbent can result in poor LODs (EPA 1988h). Determination of chloroform using isolation methods based on cryogenic trapping can be limited by moisture condensation in the trap (EPA 1988g). Evacuated canisters used to collect air samples in the field for transport to the laboratory must be carefully cleaned to avoid contamination of the sample (EPA 1988i).

Solid phase microextraction (SPME) has been shown to be useful for the determination of chloroform in air (Chai and Pawliszyn 1995). This technique is based upon the absorption of chloroform into a polymer coated on a silica fiber. Following equilibration of the fiber with the atmosphere, chloroform is released via thermal desorption in the injection port of a gas chromatograph. Sample preparation is

Table 6-2. Analytical Methods for Determining Chloroform in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Air	Adsorption onto carbon molecular sieve; thermal desorption	GC/MS (EPA Method TO2)	No data	91 (15% RSD) at 89 ng/L	EPA 1988f
Air	Cryogenic preconcentration; thermal transfer to GC	GC/ECD (EPA Method TO3)	No data	100 (5.8% RSD) at 3.5 ppb	EPA 1988g
Air	Collection into SUMMA polished canister	GC/FID/ECD or GC/MS (EPA Method TO14)	No data	No data	EPA 1988i
Air	Adsorption onto charcoal; desorption with carbon disulfide	GC/FID (OSHA Method 05)	0.11 ppm for 10 L sample	96 (8.5% RSD)	OSHA 1979
Air	Adsorption onto charcoal; desorption with carbon disulfide, containing internal standard if desired	GC/FID (NIOSH method 1003)	0.7 mg/m^3 for 15 L sample	97 at 120–493 mg/m^3	NIOSH 1994
Ambient air and stacks	Adsorption onto Tenax; thermal desorption	GC/FID or ECD	No data	No data	Parsons and Mitzner 1975
Air	Collection in flask; transfer to GC by syringe	GC/ECD	1.5 $\mu g/m^3$	No data	Bureau International Technique des Solvants Chlores 1976
Air	Solid Phase Microextraction; transfer to GC via thermal desorption of fiber.	GC/ion trap MS	2 ppb (v/v); 6% RSD	No data	Chai and Pawliszyn 1995
Air	Exposure of passive sampler (3M 3500 OVM) for four weeks. Extraction with carbon disulfide.	GC/ECD/FID	4 ng/m^3	98 (10.0% inter-day RSD)	Begerow et al. 1995

Table 6-2. Analytical Methods for Determining Chloroform in Environmental Samples (continued)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Air (phosgene)	Phosgene collection in an impinger containing a solution of aniline (forming carbanilide); evaporation of solvent; dissolution of residue in acetonitrile	HPLC/UV (EPA Method TO6)	0.1 ppb (v/v)	100 at 3 ppb (v/v); 15% RSD	EPA 1988n
Air (phosgene)	Phosgene collection onto Chromosorb coated with 1-(2-pyridyl)-piperazine; elution of derivative with acetonitrile	HPLC/UV	0.005 ppm (w/v)	100 over range 0.02–1 ppm (w/v)	Rando et al. 1993
Air (phosgene)	Passage of air through a tube filled with magnesium perchlorate (for water removal); cryogenic trapping	GC/ECD	7 ppt (v/v)	No data	Bächmann and Polzer 1989
Air, water	Solid phase microextraction (from air, water, or headspace over water)	GC/ECD	0.9 ppb (v/v) gas phase; 30 ng/L (30 ppt, w/v) liquid phase	No data	Chai et al. 1993
Drinking water	Direct injection or purge-and-trap pre-concentration	GC/ECD, GC/Hall	1 µg/L (1 ppb, w/v direct); 0.1 µg/L (0.1 ppb, w/v with purge-and-trap)	103–126 at 35–70 µg/L (direct); 91–106 at 35–70 µg/L (purge-and-trap)	Nicholson et al. 1977
Drinking water	Purge-and-trap pre-concentration; thermal desorption	GC/MS	0.1 µg/L (0.1 ppb, w/v)	No data	Coleman et al. 1976
Drinking water	Direct injection	GC/MS	0.1 µg/L (0.1 ppb, w/v)	No data	Fujii 1977

Table 6-2. Analytical Methods for Determining Chloroform in Environmental Samples (continued)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Seawater and freshwater	Solvent extraction with pentane; extract dried with sodium sulfate	GC/ECD	80 ng/L (0.08 ppb, w/v)	No data	Bureau International Technique des Solvants Chlores 1976
Water	Permeation through a silicon polycarbonate membrane into an inert gas stream and into GC port	GC/FID	74.0 µg/L (74 ppb, w/v)	No data	Blanchard and Hardy 1986
Drinking water	Acidification and dechlorination; extraction with methyl-t-butyl ether; direct injection of extract	GC/ECD or GC/MS (EPA Method 551)	0.002 µg/L (0.002 ppm, w/v)	100 (13% RSD) at 0.005 µg/L	EPA 1990g
Drinking water, waste water	Purge-and-trap pre-concentration; thermal desorption	GC/MS (Standard Method 6210)	< 0.1 µg/L (reagent water) using narrow bore capillary column	105 (3% RSD) narrow bore column	Greenberg et al. 1992
Tap water	Solvent extraction	HRGC/ECD with HRGC/MS confirmation	No data	No data	Kroneld 1986
Water	Solvent extraction	HRGC/ECD	1 µg/L (ppb, w/v)	100.3 at 50 µg/L	Reunanen and Kroneld 1982
Drinking water	Purge-and-trap pre-concentration onto Tenax/ silica/charcoal; thermal desorption	GC with PID and Hall in series	0.02 µg/L	98 (2.5% RSD)	Ho 1989
Finished drinking/raw source water	Purge-and-trap pre-concentration onto Tenax/ silica/charcoal; thermal desorption	GC/Hall (EPA method 502.1)	No data	0.90C+3.44 where C = true concentration (µg/L)	EPA 1991a

Table 6-2. Analytical Methods for Determining Chloroform in Environmental Samples (continued)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Finished drinking/raw source water	Purge-and-trap pre-concentration onto Tenax/silica/charcoal; thermal desorption	GC with PID and HSD in series (EPA method 502.2)	0.10 µg/L (0.1 ppb, w/v)	98 (2% RSD)	EPA 1991b
Finished drinking/raw source water	Purge-and-trap pre-concentration onto Tenax/ silica/charcoal; thermal desorption	Subambient programmable HRGC/MS (EPA method 524.1)	0.2 µg/L (0.2 ppb, w/v)	103 at 1.0 µg/L	EPA 1991c
Finished drinking/raw source water	Purge-and-trap pre-concentration onto Tenax/ silica/charcoal; thermal desorption	Cryofocusing (wide or narrow bore); HRGC/MS (EPA method 524.2)	0.03 µg/L (0.03 ppb, w/v) with wide bore column; 0.02 µg/L (0.02 ppb, w/v) with narrow bore column	90 (6.1% RSD) at 0.5–10 µg/L (wide bore); 95 (3.2% RSD) at 0.1 µg/L with narrow bore column	EPA 1992a
Groundwater, liquid, and solid matrices	Direct injection of head-space gas (EPA method 5020) or purge-and-trap pre-concentration and thermal desorption (EPA method 5030)	GC/HSD (EPA method 8010)	0.5 µg/L (ppb, w/v) for groundwater, 0.5 µg/g (ppm, w/w) for low-level soil, 500 µg/L (ppb, w/v) for water-miscible liquid waste, 1,250 µg/g (ppm, w/w) for soil, sludge, and non-water-miscible waste	Water: 0.93C -0.39 where C = true concentration in µg/L.	EPA 1986a
Waste water	Purge-and-trap pre-concentration; thermal desorption	GC/HSD or MS (EPA methods 601 and 624)	0.05 µg/L (for HSD); 1.6 µg/L (for MS)	102 at 0.44–50 µg/L (for HSD); 101 at 10–100 µg/L (for MS)	EPA 19982a

Table 6-2. Analytical Methods for Determining Chloroform in Environmental Samples (continued)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Solid and liquid waste, soil	Dispersion in glycol; purge-and-trap pre-concentration onto Tenax/ silica/charcoal; thermal desorption	GC/ECD and FID in series	No data	105 at 5 µg/L	Lopez-Avila et al. 1987
Sediment	Extraction into methanol; dilution with water; purge-and-trap pre-concentration	GC/FID/ECD	0.1 µg/g (0.1 ppm, w/w)	99 (4% RSD) at 0.8 µg/mL (0.8 ppm, w/v)	Amaral et al. 1994
Bulk oils	Purge-and-trap pre-concentration (with deuterated internal standards) onto Tenax; thermal desorption	GC/MS	1 ppb (w/v)	88 (6.7% RSD) at 93 ppb	Thompson 1994
Food	Extraction of composited, table-ready food with isooctane or acetone-isooctane; micro-Florisil clean-up (if fat content 21–70%); direct injection into GC	GC-ECD/Hall	5 ng/g (ECD); 5 ng/g (Hall)	15–161	Daft 1988a, 1989
Volatile food components	Direct injection of head-space gas	GC/ECD or MS	4.2 µg/kg (4.2 ppb, w/w in beverages); 12.5 µg/kg (12.5 ppb, w/w in dairy products); 18 µg/kg (meats); 28 µg/kg (fats/oils)	No data No data No data No data	Entz et al. 1982

ECD = electron capture detector; EPA = Environmental Protection Agency; FID = flame ionization detector; GC = gas chromatography; Hall = Hall electrolytic conductivity detector; HPLC/UV = high performance liquid chromatography with ultraviolet absorbance detection; HRGC = high-resolution gas chromatography; HSD = halogen-specific electrolytic conductivity detector; MS = mass spectrometry; NIOSH = National Institute for Occupational Safety and Health; OSHA = Occupational Safety and Health Administration; PID = photo-ionization detector; RSD = relative standard deviation; v/v = volume/volume; w/v = weight/volume

very easy and fast (90 seconds for chloroform) with this technique although sample collection conditions and thermal desorption conditions must be carefully controlled for the best precision. Samples containing very volatile analytes, like chloroform, must be analyzed quickly after sample collection to avoid analyte loss with storage.

Phosgene has been identified as an atmospheric decomposition product of several chlorinated compounds, including chloroform (Bachmann and Polzer 1989). Phosgene can be determined in air samples using, for example, capillary GC with electron capture detection (ECD) (Bachmann and Polzer 1989), high-performance liquid chromatography (HPLC) after the conversion of phosgene to carbanilide (EPA 1988n), and HPLC after the reaction of phosgene with 1-(2-pyridyl)-piperazine (Rando et al. 1993). Chloroformates can interfere in the carbanilide analysis (EPA 1988n). In the method of Rando et al. (1993), the apparent recovery of phosgene was nearly quantitative from air at up to 25% relative humidity; this decreased to about 65% at 95% humidity.

The most common method for the determination of chloroform levels in water, sediment, soil, and foods is the purging of the vapor from the sample, or its suspension in a solvent with an inert gas and trapping (purge-and-trap) the desorbed vapors onto a sorbent trap (EPA 1991 a, 1991b, 1991c, 1992; Greenberg et al. 1992; Ho 1989; Lopez-Avila et al. 1987). SPME is a method that combines the ease of headspace analysis with some of the concentration benefits of purge-and-trap (Chai et al. 1993). Subsequent thermal desorption is used for the quantification of chloroform concentrations. Solvent extraction is also used in a number of methods (Amaral et al. 1994; Daft 1988a, 1989; EPA 1990g; Kroneld 1986; Reunanen and Kroneld 1982). No methods were found for phosgene in water, sediment, soil, and foods.

All of the methods listed above for the analysis of environmental samples use GC with various detection methods. The two methods that provide the lowest detection limits are halide-specific detectors (e.g., Hall electrolytic conductivity detector or electron capture detector) and the mass spectrometer (EPA 1986a; Ho 1989; Lopez-Avila et al. 1987; Ramus et al. 1984). The advantage of halide specific detectors is they are not only very sensitive, but are also specific for halide compounds. The mass spectrometer, on the other hand, provides additional confirmation of the presence of a compound through its ionization pattern and is desirable when a variety of compounds are required to be identified and quantified. The disadvantage of halide-specific detectors is their inability to detect and quantify nonhalogen compounds, if nonhalogenated compounds are of interest also; this can be

greatly overcome by using other detectors (e.g., photoionization detector) in series (Lopez-Avila et al. 1987). High-resolution gas chromatography (HRGC) with capillary columns coupled with mass spectrometry (MS) provides better resolution and increased sensitivity for volatile compounds than packed columns. In methods such as EPA method TO14 (EPA 198Si), desorbed compounds are cryogenically trapped onto the head of the capillary column. Such HRGC/MS methods overcome some common problems involved in analyses of excessively complex samples, samples with large ranges of concentrations, and samples that also contain high-boiling compounds (Dreisch and Munson 1983; EPA 1986a). LODs in the sub-parts per billion (ppb) range are routinely possible in both air and liquid/solid matrices. Numerous standard methods exist.

Methods for rapid sample introduction to an ion trap mass spectrometer have been developed for the determination of organic compounds, including chloroform, in aqueous samples. In the method of Bauer and Solyom (1994) a polymeric membrane is placed into contact with the sample, the organics dissolve in the membrane and diffuse to the other side where they are swept directly into the mass spectrometer. This technique, known as membrane introduction mass spectrometry (MIMS) was shown to be sensitive to chloroform in water to 0.025 ppb. Another sample introduction technique known as inertial spray extraction nebulizes an aqueous sample (water, blood) into a small chamber where a countercurrent stream of helium sweeps any released volatile organic compounds (VOCs) into a jet separator at the inlet of an ion trap mass spectrometer (St-Germain et al. 1995). Up to 1 mL of sample can be introduced and the released VOCs are detected by the MS. Although both of these techniques provide for high throughput, no separation step is employed and this can result in interferences from ions formed by compounds other than the target analytes. These methods have great utility in selected applications.

A fiber-optic device has been described that can monitor chlorinated hydrocarbons in water (Gobel et al. 1994). The sensor is based on the diffusion of chlorinated hydrocarbons into a polymeric layer surrounding a silver halide optical fiber through which is passed broad-band mid-infrared radiation. The chlorinated compounds concentrated in the polymer absorb some of the radiation that escapes the fiber (evanescent wave); this technique is a variant of attenuated total reflection (ATR) spectroscopy. A LOD for chloroform was stated to be 5 mg/L (5 ppm). This sensor does not have a high degree of selectivity for chloroform over other chlorinated aliphatic hydrocarbons, but appears to be useful for continuous monitoring purposes.

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The reproducibilities of the methods listed in Table 6-2 are generally acceptable, but will vary, depending on the laboratories doing the analyses. Probable interferences for the methods of analysis include contamination from chloroform vapors in the laboratory. For this reason, it is often recommended that the laboratories doing the analysis should not contain chloroform or any other solvent to be measured in the sample (EPA 1986a). Plastic or rubber system components should be avoided as they can contaminate a sample or result in carryover from one analysis to the next (EPA 1992). The formation of aerosols and foam during purge-and-trap of liquid samples can contaminate the analytical system, so precautions must be taken (Thompson 1994; Vallejo-Cordoba and Nakai 1993). The use of field blanks is extremely important to correct for chloroform that might have diffused into the sample during shipping and storage (EPA 1986a). Other interferences include those volatile compounds that have similar retention times in the various GC columns used. This problem is often eliminated by analyzing the samples with two different types of GC columns such that the retention times will not be coincidental in both columns. Mass spectrometric detection can also help to overcome interferences resulting from incomplete chromatographic resolution. Refer to the references cited in Table 6-2 and the text for specific information regarding reproducibility and potential interferences.

6.3 ADEQUACY OF THE DATABASE

Section 104(i)(5) of CERCLA 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 chloroform 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 chloroform.

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 w,ould reduce or eliminate 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.

6.3.1 Identification of Data Needs

Methods for Determining Biomarkers of Exposure and Effect. Methods are available for the determination of chloroform in breath (Aggazzotti et al. 1993; Jo et al. 1990; Krotoszynski et al. 1979; Phillips and Greenberg 1992; Pleil and Lindstrom 1995; Raymer et al. 1990), blood (Antoine et al. 1986; Ashley et al. 1992; Cammann and Htibner 1995; EPA 1985a; Kroneld 1986; Peoples et al. 1979; Pfaffenberger et al. 1980; Reunanen and Kroneld 1982; Seto et al. 1993; Streete et al. 1992), and other fluids and tissues such as urine and adipose (Cammann and Htibner 1995; EPA 1985a; Peoples et al. 1979; Pfaffenberger et al. 1980; Reunanen and Kroneld 1982; Streete et al. 1992). Sub-ppb limits of detection have been shown (e.g., Ashley et al. 1992; Pfaffenberger et al. 1980) and the methods are adequate for the determination of chloroform concentrations in samples from the general population. No biomarker that can be associated quantitatively with chloroform exposure has been identified (see Sections 2.5.1 and 6.1). Although chloroform levels can be determined in biological samples, the relationship between these levels and the exposure levels has not been adequately studied. In one study, the concentrations of chloroform in alveolar air of people attending activities at an indoor swimming pool were found to be proportional to the concentrations in air (Aggazzotti et al. 1993). Such proportionality was observed, in part, because the alveolar air samples were taken soon after exposure termination. Good correlations have also been measured between chloroform concentrations measured in blood and breath with those in air or water after exposure to water/air during showering (Jo et al. 1990) and swimming (Cammann and Htibner 1995; Lévesque et al. 1994). The studies of Jo et al. (1990) and Lévesque et al. (1994) demonstrated and quantified the uptake of chloroform via dermal absorption. Correlations of alveolar air concentrations with exposure air concentrations based on breath samples at unknown postexposure times will be complicated by metabolism and other factors, such as activity, important in the elimination of chloroform from the body (see PBPK discussion, Chapter 2). Furthermore, the presence of chloroform, or a transformation product of chloroform such as phosgene and reaction products of phosgene, in a biological sample may have resulted from the metabolism of another chlorinated hydrocarbon. If a biomarker of exposure for this compound in a human tissue or fluid was available and a correlation between the level of the biomarker and exposure existed, it could be used as an indication of the extent of chloroform exposure. Further information regarding the accuracy of sample recovery for the methods of chloroform analysis would be useful in interpreting monitoring data.

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No biomarker of effect that can be associated quantitatively and directly to chloroform exposure has been identified (see Section 2.5.2). If biomarkers of effect were available for this compound and a correlation between the level or intensity of the biomarker of effect and the exposure level existed, it could be used as an indication of the levels and extent of chloroform exposure. However, in cases where an exposure to chloroform has been known to occur, measurements of chloroform in breath or blood can indicate body burden.

Methods for Determining Parent Compounds and Degradation Products in Environmental Media. Methods for determining chloroform in the environment are available. These include methods for drinking water (Blanchard and Hardy 1986; EPA 199Og, 1991a, 1991b, 1991c, 1992; Greenberg et al. 1992; Ho 1989; Kroneld 1986; Nicholson et al. 1977), air (Bergerow et al. 1995, Chai and Pawliszyn 1995, EPA 1988f, 1988g, 198831, 19881; NIOSH 1994; OSHA 1979; Parsons and Mitzner 1975), and foods (Daft 1988a, 1989; Entz et al. 1982; Thompson 1994). These three media are of most concern for human exposure. The precision, accuracy, reliability, and specificity of the methods are well documented and well suited for the determination of low levels of chloroform and levels at which health effects occur. For example, the MRL for acute-duration inhalation is 0.1 ppm (weight per volume [w/v] or 0.0099 mg/m^3) so any method used must have a limit of detection equal to or less than this. The methods of Chai et al. (1993), Chai and Pawliszyn (1995), and Bergerow et al. (1995) report limits of detection of 0.9 ppb volume per volume (v/v), 2 ppb, and 4 ng/m^3, respectively, and are adequate for the measurement of chloroform in air. Although no limits of detection were reported for EPA methods TO2 and TO3 (EPA 1988f, 1988g), recoveries were acceptable for low-ppb concentrations of chloroform in air and thus these methods should certainly be applicable to concentrations at the acute-duration inhalation MRL. Similarly, the chronic-duration oral MRL is 0.01 mg/kg/day, which converts to 0.7 mg/day for a 70-kg person. For a 2 L/day water consumption, this translates into a required method limit of detection of 0.35 mg/L. This concentration is easily measured by the methods of EPA (199Og) (limit of detection 0.002 μg/L), Greenberg et al. (1992) (1imit of detection 0.1 μg/L), and Chai et al. (1993) (limit of detection 30 ng/L). Assuming a food intake of 2 kg/day, this oral MRL translates to a needed method limit of detection in food of 0.35 mg/kg. The methods of Entz et al. (1982) and Daft (1988a, 1989) provide limits of detection of less than 0.028 mg/kg and are adequate. Method sensitivities are clearly adequate for matrices in which the higher acute-duration oral MRL is of concern. There is not much information regarding the degradation products of chloroform in the environment. Although phosgene can be produced in the environment and its high reactivity suggests that it would not persist, several

methods were found for the quantification of phosgene in ambient air (Bachmann and Polzer 1989; EPA 1988n; Rando et al. 1993). No methods were found for phosgene in other environmental matrices and it is not likely that it would be found in matrices other than air.

6.3.2 Ongoing Studies

The Environmental Health Laboratory Sciences Division of the Center for Environmental Health and Injury Control, Centers for Disease Control and Prevention, is developing methods for the analysis of chloroform and other VOCs in blood. These methods use purge-and-trap methodology, HRGC, and magnetic sector mass spectrometry which gives detection limits in the low-ppt range (see Ashley et al. 1992).

The following information was obtained form a search of Federal Research in Progress (FEDRIP, 1996). Researchers at Physical Sciences, Inc. are developing an imaging infrared spectrometer that can rapidly screen field sites to detect the presence of VOCs, including chloroform, from remote locations (either in the air or on the ground). The following research projects were identified as having objectives that might require the development or modification of methods to measure chloroform. Researchers at Colorado State University are studying the biodegradation of pollutants, including chloroform, in bioreactors. Researchers at the University of California at Berkeley and Riverside are conducting studies on the biodegradation of organic compounds, including chloroform, in soil.