7. ANALYTICAL METHODS

The purpose of this chapter is to describe the analytical methods that are available for detecting, measuring, and/or monitoring 1-bromopropane, its metabolites, and other biomarkers of exposure and effect to 1-bromopropane. 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

Table 7-1 lists the methods used for determining 1-bromopropane in biological materials. Biological exposure to the general population and workers can be assessed by measurement of bromide ion, 1-bromopropane, and its metabolite, N-acetyl-S-(n-propyl)-L-cysteine (AcPrCys), in urine or blood (NTP 2013). Direct analysis of 1-bromopropane in urine samples by gas chromatography (GC) equipped with an electron capture detector (ECD) was accomplished at a detection limit of 2 ng/mL (B'hymer and Cheever 2005).

The longer physiological half-lives of the metabolites of volatile organic compounds, such as those of 1-bromopropane, in urine compared to blood give monitoring urinary metabolites an advantage over blood sampling (Alwis et al. 2012). One method to measure the urinary metabolite of 1-bromopropane, AcPrCys, involves ultra-high performance liquid chromatography (UPLC) with electrospray ionization tandem mass spectrometry (ESI/MS/MS). Sample preparation involved collection of urine, where a 1.8 mL aliquot was stored at -70°C until the time of the assay. When assayed, the samples were diluted 1:10 with 425 µL of 15 mM ammonium acetate (pH 6.8), followed by washing with acetonitrile to obtain a mobile phase for detection. The limit of detection was reported to be 1.2 ng/mL (Alwis et al. 2012). Another method to measure the urinary metabolite, AcPrCys, involves solid-phase extraction (SPE) from urine samples by washing with a 40:60 solution of methanol and water followed by elution with acetone

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

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Urine	50 µL urine diluted with 425 µL 15 mM ammonium acetate pH 6.8; washed with acetonitrile solvent to create mobile phase; analysis for AcPrCys	UPLC-ESI/MS/MS	1.2 ng/mL (AcPrCys)	95 (mean)	Alwis et al. 2012
Urine	Urine samples diluted with water (1:4) and fortification with 1-bromobutane, which was used as an internal standard; each sample then sealed in a headspace vial and placed in the analyzer	GC/ECD	2 ng/mL	104–121	B'hymer and Cheever 2005
Urine	Urine sample was extracted 4 times with 4.0 mL of ethyl acetate using a vortex mixer for 1 minute for each extraction; analysis for metabolite, 3-BPA	GC/MSD	0.01 µg/mL (3-BPA)	93–98	B'hymer and Cheever 2004
Urine	Urine sample extracted by SPE; washed with 40% methanol/60% water followed by elution with acetone; analysis for AcPrCys	HPLC/MS	0.01 µg/mL (AcPrCys)	96–103	Cheever et al. 2009
Urine	SPE of urine samples with addition of 1 mL ammonium formate buffer (50 mmol/L, pH 2.5) and 40 µL formic acid; sample vortex-mixed and centrifuged	LC/MS	2.0 µg/mL (PrMA)	99.5	Eckert and Goen 2014
Blood	Blood collected from laboratory animals by cardiac puncture using a heparinized syringe; plasma separated by centrifugation at 4°C and stored at -80°C until analysis	GC/MS	No data	No data	Ishidao et al. 2002

3-BPA = 3-bromopropionic acid; AcPrCys = N-acetyl-S-(n-propyl)L-cysteine; ECD = electron capture detector; ESI = electrospray ionization; GC = gas chromatography; HPLC = high-performance liquid chromatography; LC = liquid chromatography; MS = mass spectrometry; MSD = mass selective detector; PrMA = n-propyl mercapturic acid; SPE = solid phase extraction; UPLC = ultra high performance liquid chromatography

and analysis using high performance liquid chromatography (HPLC) and mass spectrometry (MS) (Cheever et al. 2009). 3-Bromopropionic acid (3-BPA) is also a metabolic product of 1-bromopropane in human urine. B'hymer and Cheever (2004) discuss a GC method to quantify this metabolite in human urine. A method for the simultaneous determination of four short-chain alkyl mercapturic acids, including 1-bromopropane metabolite n-propyl mercapturic acid (PrMA), in human urine by SPE and detection by column-switching liquid chromatography and MS/MS has been discussed (Eckert and Goen 2014).

7.2 ENVIRONMENTAL SAMPLES

Table 7-2 lists the methods used for determining 1-bromopropane in environmental samples. Due to its volatility, 1-bromopropane released to the environment is expected to partition mostly to air (HSDB 2013).

The principal separation and detection methods for 1-bromopropane in air samples include GC in conjunction with flame ionization detection (FID). NIOSH Method 1025 and OSHA Method PV2061 have both been fully validated for use in occupational settings where regulatory exposure limits are of concern (NIOSH 2003b; OSHA 1999). Both of these methods draw air samples through a solid coconut shell charcoal (CSC) sorbent tube. The sample is then desorbed with carbon disulfide or a 99/1 (v/v) carbon disulfide/dimethylformamide mixture followed by GS/FID analysis. The limit of detection for NIOSH Method 1025 is 1.0 µg/sample, while the detection limit for OSHA Method PV2061 is reported as 0.007 ppm (0.037 mg/m^3) at a 12-L air volume using a sampling rate of 0.1 L per minute.

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 1-bromopropane 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 1-bromopropane.

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

Table 7-2. Analytical Methods for Determining 1-Bromopropane in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Air	Air drawn through a solid sorbent tube lined with Anasorb CSC; desorbed with addition of 1.0 mL of carbon disulfide for 30 minutes	GC/FID (Method 1025)	1.0 µg/sample	96.8 (RSD= 0.015)	NIOSH 2003b
Air	Air drawn through CSC tube; desorbed with a mixture of 99/1 (v/v) carbon disulfide/dimethylformamide	GC/FID (Method PV2061)	0.007 ppm (0.037 mg/m^3)	97.5	OSHA 1999
Air	Air sampled at 530 mL/minute to lithium ionization chamber	SCF/MS	52 pptv	No data	Fujii 1992

CSC = coconut shell charcoal; FID = flame ionization detector; GC = gas chromatography; MS = mass spectrometry; RSD = relative standard deviation; SCF = super critical fluid chromatography

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.

Exposure. Exposure to 1-bromopropane is typically assessed by measuring its metabolites such as AcPrCys, 1-bromopropionic acid, or released bromine in urine or blood (NTP 2013). Field studies indicated that urinary levels of N-acetyl-S-(n-propyl)-L-cysteine and bromide were significantly correlated with 8–12-hour TWA breathing zone air concentrations of 1-bromopropane in several groups of workers (Hanley et al. 2006, 2009, 2010). Methods of determining biomarkers of exposure are well characterized by urine analysis. Additional studies on the direct detection of 1-bromopropane biomarkers in human blood would be useful in determining exposure.

Effect. There are no specific biomarkers to characterize effects caused by 1-bromopropane. Nervous system effects caused by inhalation of 1-bromopropane can be caused by many other substances as well. See Section 3.8.2 for more details. Identification and additional studies of specific biomarkers would be useful in characterizing the effects caused by 1-bromopropane.

Methods for Determining Parent Compounds and Degradation Products in Environmental Media. Human exposure to 1-bromopropane may occur through inhalation of ambient air and dermal uptake through occupational contact and consumer products containing 1-bromopropane. Methods have been reported for the detection of 1-bromopropane in air. The methods of NIOSH (2003b) (LOD 1.0 µg/sample) and OSHA (1999) (LOD 0.007 ppm [0.037 mg/m^3]) are adequate for the determination of 1-bromopropane in air. Methods for detection of 1-bromopropane in other environmental media are not needed, as it is rarely found in environmental compartments other than air. Additional studies do not seem necessary at this time.

7.3.2 Ongoing Studies

No ongoing studies were located for 1-bromopropane.