6. ANALYTICAL METHODS

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

6.1 BIOLOGICAL SAMPLES

Few methods are currently available for analysis of MTBE in biological samples. Some methods have been developed to measure MTBE in blood and various tissues. The primary method of analysis is gas chromatography (GC) with flame ionization detection (FID) or mass spectrometry (MS). Table 6-l is a summary of the applicable analytical methods for determining MTBE in biological fluids and tissues.

Blood can be analyzed by direct injection GC (Li et al. 1991) or by GC/FID analysis of the blood headspace (Savolainen et al. 1985; Streete et al. 1992). Detection limits are in the low ppm range (Li et al. 1991; Savolainen et al. 1985). Otherwise, little performance data are available for these methods. Recently purge-and-trap GC/MS methods have been developed (Bonin et al. 1995; Mannino et al. 1995) for the measurement of MTBE and its metabolite *tert*-butanol in blood. Detection limits are in the sub-ppb range (Bonin et al. 1995; Mannino et al. 1995). Recovery is excellent for both MTBE and *tert*-butanol (>95%) (Bonin et al. 1995) and reproducibility is very good as well (<10% RSD) (Bonin et al. 1995).

A screening method for post-mortem body fluids uses headspace combined with GC/MS for identifying MTBE. Detection limits are in the low ppb range (Schuberth 1994). MTBE has been determined in urine and tissues by GC/FID analysis of urine or by tissue incubation mixture headspace (Streete et al. 1992). No performance data were reported. Fat tissue (rat) has been analyzed by GC after homogenization and

Table 6-1. Analytical Methods for Determining Methyl *tert*-Butyl Ether (MTBE) in Biological Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Blood (MTBE and TBA)	Purge and trap	Capillary GC/MS	0.05 µg/L (MTBE); 0.50 µg/L (TBA)	No data	Mannino et al. 1995
Blood (MTBE and TBA)	Purge and trap	Capillary GC/MS	0.01 µg/mL (MTBE); 0.06 µg/mL (TBA)	97.4 (MTBE); 101.8 (TBA)	Bonin et al. 1995
Blood	Direct analysis from headspace	Capillary GC/FID	1.5 nmol/g	No data	Savolainen et al. 1985
Blood	Direct analysis from headspace	Capillary GC/FID	No data	No data	Streete et al. 1992
Serum (rat)	Direct analysis	GC/FID	0.05 µg/mL	No data	Li et al. 1991
Urine	Direct analysis from headspace	Capillary GC/FID	No data	No data	Streete et al. 1992
Fat	Homogenization; centrifugation	GC/FID	1.5 nmol/g	92	Savolainen et al. 1985
Body fluids	Direct analysis from headspace	Capillary GC/ITD	0.03 µmol/g	No data	Schuberth 1994
Tissues	Direct analysis from headspace	Capillary GC/FID	No data	No data	Streete et al. 1992

CDC = Centers for Disease Control and Prevention; FID = flame ionization detection; GC = gas chromatography; GC = gas chromatography; ITD = ion trap detector; MS = mass spectrometry; TBA = *tert*-butanol

centrifugation (Savolainen et al. 1985). Recovery is very good (>90%) and detection limits are in the low ppb range (Savolainen et al. 1985).

6.2 ENVIRONMENTAL SAMPLES

Methods exist for determining MTBE in air (ambient, occupational, breathing zone, auto exhaust), water, sediments, foods, and gasoline. Environmental methods are primarily based on GC procedures with detection by FID or MS. Many of the methods approved by federal agencies are robust and sensitive. Table 6-2 summarizes methods that have been used for determination of MTBE in environmental samples.

Several methods exist for detecting and measuring MTBE in air. Air samples for MTBE analysis are usually collected in stainless steel canisters (EPA 1984d; Kelley et al. 1993; Lioy et al. 1994; Pate et al. 1992). The samples are analyzed by GC with FID (Pate et al. 1992) or MS (Kelley et al. 1993). The limit of detection is in the very low ppb range (Kelly et al. 1993). Other performance data are not available. MTBE may also be determined in air samples by collection on adsorbent tubes followed by desorption and GUMS analysis (EPA 1984c; Lioy et al. 1994). Performance data for this method is not available. GUMS is more specific, and thus more reliable than GUFID in identifying MTBE in samples containing multiple components which have similar GC elution characteristics. A sophisticated optical method based on infrared (IR) spectral data has been developed for remote measurement of MTBE in air (Grant et al. 1992).

For measuring atmospheric levels of MTBE in the workplace, the air is usually preconcentrated by passing the sample through a trap containing a charcoal adsorbent (NIOSH 1984). The vapors on the charcoal tubes are eluted, then analyzed by GC/FID. This procedure has been modified to measure breathing zone air in the workplace (CDC 1993a; Maninno et al. 1995). A similar method for personal monitoring uses a mixed-bed adsorbent and thermal desorption prior to GC/FID analysis (Coker et al. 1989). Detection limits are in the ppb range (CDC 1993a; Mannino et al. 1995). Little other performance data have been reported. Passive samplers have become available for monitoring occupational or breathing zone air. The adsorbent is desorbed with solvent and analyzed by GC/FID (Harper and Fiore 1995; Mannino et al. 1995). Detection limits are in the ppb range (Harper and Fiore 1995; Mannino et al. 1995); analytical recovery is 97% (Harper and Fiore 1995).

Methods have been developed for analysis of MTBE in automotive exhaust. The auto exhaust is collected in Tedlar bags and analyzed directly by GC/FID (Hoekman 1993; Schuetzle et al. 1991; Siegel et al. 1992).

Table 6-2. Analytical Methods for Determining Methyl *tert*-Butyl Ether (MTBE) in Environmental Samples

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Air (ambient)	Collection on Tenax GC tubes; thermal desorption	GC/MS	No data	No data	EPA 1984c (EPA method TO-1)
Air (ambient)	Collection in passivated stainless steel canisters	GC/MS and other detectors	No data	No data	EPA 1984c (EPA method TO-14)
Air (ambient)	Collection in passivated stainless steel canisters	Capillary GC/MS	0.2 ppb	No data	Kelley et al. 1993
Air (ambient)	Remote sensing	Infrared spectrometry	40 ppb	No data	Grant et al. 1992
Air (occupational)	Collection on adsorbent tubes; desorption with solvent	GC/FID			NIOSH 1984 (NIOSH method 1615)
Air (occupational)	Personal breathing zone air collected on charcoal tubes; desorption in CS_2	GC/FID	0.02 mg/80 L sample	No data	CDC 1993a (modified NIOSH method 1615)
Air (occupational)	Collection on mixed-bed adsorbent; thermal desorption	Capillary GC/FID	No data	100 ±5%	Coker et al. 1989
Air (occupational)	Collection on diffusive samplers; solvent desorption	GC/FID	Sub-ppm	97.4 (analytical recovery)	Harper and Fiore 1995
Air (breathing zone)	Collection on charcoal tubes; solvent desorption	GC/FID	125 µg/m^3 for 400 min	No data	Mannino et al. 1995 (modified NIOSH method 1615)
Air (breathing zone)	Collection on organic vapor badges; solvent desorption	Capillary GC/FID	40 µg/m^3	No data	Mannino et al. 1995
Auto exhaust	Collection in Tedlar bags	Capillary GC/FID	5–10 ppb	No data	Hoekman 1992
Auto exhaust	Collection in Tedlar bags	Capillary GC/FID	30 ppb	89–99	Schuetzle et al. 1991

Table 6-2. Analytical Methods for Determining Methyl *tert*-Butyl Ether (MTBE) in Environmental Samples (continued)

Sample matrix	Preparation method	Analytical method	Sample detection limit	Percent recovery	Reference
Drinking water	Purge and trap method	Capillary GC/MS	0.090 µg/L	95–110	Munch and Eichelberger 1992
Groundwater	Porous probe sampler	Portable GC/PID	3 ppb (vapor) 0.3 ppb (aqueous)	No data	Chiang et al. 1992
Groundwater	Direct analysis of headspace	Capillary GC/FID	44 µg/L	No data	Wang et al. 1991
Waste water	Isotope dilution; purge and trap method	GC/MS	No data	No data	EPA 1984b (EPA Method 1624)
Solid waste	Purge and trap method	Capillary GC/MS	No data	No data	EPA 1994c (EPA Method 8260)
Sediments	Purge and trap method	Capillary GC/dual detector, FID and MS	No data	No data	Bianchi and Varney 1989
Gasoline	None	HPLC/RI	No data	103	Pauls 1985
Gasoline	None	GC/IR	No data	~100	Cochrane and Hillman 1984
Gasoline	None	Capillary multi-dimensional GC/FID	No data	No data	Johansen 1984
Gasoline	Dilution in hexane	Flow analysis; FTIR	0.035%	No data	Gallignani et al. 1994
Gasoline	Pre-cut column with backflushing	Capillary GC/TCD	No data	No data	Annino and Villalobos 1991

CDC = Centers for Disease Control and Prevention; CS_2 = carbon disulfide; *EPA* = Environmental Protection Agency; *FID* = flame ionization detector; FTIR = Fourier transform infrared spectrometry; GC = gas chromatography; HPLC = high performance liquid chromatography; IR = infrared spectrometry; MS = mass spectrometry; NIOSH = National Institute of Occupational Safety and Health; PID = photoionization detector; RI = refractive index detector; TCD = thermal conductivity detector

The sensitivity of the method is sufficient to detect MTBE in the exhaust samples (ppb range); however, care must be taken to assure that the chromatographic column has the resolution necessary to detect MTBE in the multi-component mixture (Siegel et al. 1992).

The most frequently used analytical methods for aqueous samples containing MTBE are GC/MS and GC/FID (EPA 1984b; Munch and Eichelberger 1992; Wang et al. 1991), although GC/photoionization detection (PID) has also been used (Chiang et al. 1992). MTBE is usually isolated from the aqueous media by the purge and trap method (EPA 1984b, Munch and Eichelberger 1992). The purged MTBE is trapped on an adsorbent, and thermally desorbed onto the GC column. Detection limits are in the low-tosub ppb range (Munch and Eichelberger 1992) with excellent recovery >95% (Munch and Eichelberger).
A headspace method has been developed for determining MTBE in gasoline-contaminated groundwater (Chiang et al. 1992; Wang et al. 1991). Detection limits are in the very low ppb range; other performance data were not reported.

Solid wastes, soil, and sediments are most often prepared for analysis using the purge and trap method (Bianchi and Vamey 1989; EPA 1994b). GC/MS is recommended as the separation and detection technique for these analyses, although GC/FID may be used as well (Bianchi and Vamey 1989). No performance data have been reported for these methods.

Methods exist for detection of MTBE in other environmental media such as gasoline and its fumes. These methods include direct analysis by GC/FID (Johansen 1984; Levy and Yancey 1986), GC/IR (Cochrane and Hillman 1984) and HPLC/ refractive index (RI) (Pauls 1985). Gasolines are a complex media, and dual GC columns or multidimensional GC have been used to improve separation (Johansen 1984; Levy and Yancey 1986). Two studies reported quantitative recovery (≈100%) (Cochrane and Hillman 1984; Pauls 1985), but other performance data were not reported. A method has been developed capable of detecting MTBE at the 0.035% level in gasoline (Gallignani et al. 1994). In this method, gasoline is diluted with hexane and analyzed by flow analysis/Fourier transform infrared spectrometry.

6.3 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 MTBE is available. Where adequate information is not available, ATSDR, in conjunction with the 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 MTBE.

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.

6.3.1 Identification of Data Needs

Methods for Determining Biomarkers of Exposure and Effect. Few methods exist for measuring MTBE in breath and most tissues other than blood. Sensitive, reliable methods exist for determining MTBE in blood (Bonin et al. 1995; Mannino et al. 1995). The data on determination of MTBE in urine and tissue samples are very limited, and method performance information is generally not available. Methods that could be used to measure low levels in human urine and tissues are needed to determine the relationship between exposure and effects observed. Few methods are available for determining *tert*-butanol (the major metabolite of MTBE) in blood, urine, and tissues. However, this compound is not unique to MTBE; thus *tert*-butanol would be a less useful biomarker than MTBE itself.

Methods for Determining Parent Compounds and Degradation Products in Environmental Media. Methods for determining MTBE in air (EPA 1984c; Kelley et al. 1993) and water (Munch and Eichelberger 1992; Wang et al. 1991) are sensitive enough to measure background levels in the environment and levels for which health effects might occur, but additional performance are needed. Methods for soil and other solid media are available (Bianchi and Vamey 1989; EPA 1994b). The reliability is limited by the background from the complex matrix. There is little information on methods for determining MTBE in media such as fish, foods, and plants. Improved methods for these media are

needed to better assess the extent of MTBE contamination in the environment and the resulting risk of exposure.

6.3.2 Ongoing Studies

The Environmental Health Laboratory Sciences Division of the National Center for Environmental Health, Centers for Disease Control and Prevention, is developing methods for the analysis of MTBE and other volatile organic compounds in blood. These methods use purge and trap methodology, high resolution gas chromatography, and magnetic sector mass spectrometry which gives detection limits in the low parts per trillion (ppt) range.

The EPA and organizations associated with the fuel industry are currently developing and evaluating methods to measure MTBE in human breath. These methods involve collection of a breath sample in a stainless steel canister with subsequent analysis by GC/MS. Detected limits are in the low-to-sub ppb range.