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Methyl *tert*-butyl ether – Determination of methyl *tert*-butyl ether in blood and urine using headspace gas chromatography mass spectrometry

Biomonitoring Method – Translation of the German version from 2018

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Methyl tert-butyl ether – Determination of methyl tert-butyl ether in blood and urine using headspace gas chromatography mass spectrometry

Biomonitoring Methods

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Abstract

The working group "Analyses in Biological Materials" of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area verified the present biomonitoring method. The described analytical method allows the specific and sensitive determination of methyl tert-butyl ether (MTBE) in blood and urine of persons occupationally exposed to this substance. The volatile MTBE is determined using static headspace GC-MS. Before analysing an aliquot of the headspace, the urine and blood samples are diluted 1:10 with water, spiked with internal standard and incubated for 45 min at 60 °C. The isotope-labelled d_3-MTBE serves as internal standard. Aqueous standard solutions are used for calibration.
The method was extensively validated and the reliability data were confirmed by an independent laboratory, which has established and cross-checked the whole procedure.

Keywords

methyl tert-butyl ether; MTBE; urine; blood; biomonitoring; Analyses in Biological Materials; headspace-gas chromatography mass spectrometry; HS-GC-MS

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Methyl *tert*-butyl ether (MTBE) – Determination of methyl *tert*-butyl ether (MTBE) in blood and urine using headspace gas chromatography mass spectrometry

Matrix:	Blood and urine
Hazardous substance:	Methyl *tert*-butyl ether
Analytical principle:	Headspace gas chromatography with mass spectrometry (HS-GC-MS)
Completed in:	October 2013

Overview of the parameters that can be determined with this method and the corresponding hazardous substances:

Hazardous substance	CAS	Parameter	CAS
Methyl *tert*-butyl ether	1634-04-4	Methyl *tert*-butyl ether	1634-04-4

Summary

The described analytical method allows the specific and sensitive determination of methyl *tert*-butyl ether (MTBE) in blood and urine of persons occupationally exposed to this substance. The volatile MTBE is determined using static headspace GC-MS. Before analysing an aliquot of the headspace volume, the urine and blood samples are diluted 1:10 with water, spiked with internal standard and incubated for 45 min at 60 °C. The isotope-labelled d_3-MTBE serves as internal standard. Aqueous standard solutions are used for calibration.

Reliability data of the method

Methyl *tert*-butyl ether (MTBE) in urine

Within-day precision:	Standard deviation (rel.)	s_w = 1.8%, 2.1% or 0.6%
	Prognostic range	u = 4.1%, 4.8% or 1.3%
	at a spiked concentration of 0.10, 0.75 or 2.5 mg MTBE per litre urine and where n = 10 determinations	

Day-to-day precision:	Standard deviation (rel.)	s_w = 7.1% or 5.9%
	Prognostic range	u = 18.3% or 15.2%
	at a spiked concentration of 0.25 or 2.5 mg MTBE per litre urine and where n = 6 determinations	
Accuracy:	Recovery rate (rel.)	r = 95.5–97.6%
	at a spiked concentration of 0.5 mg MTBE per litre urine and where n = 10 determinations	
Detection limit:	1.8 µg MTBE per litre urine	
Quantitation limit:	6 µg MTBE per litre urine	

Methyl *tert*-butyl ether (MTBE) in blood

Within-day precision:	Standard deviation (rel.)	s_w = 1.5%, 1.4% or 0.8%
	Prognostic range	u = 3.5%, 3.1% or 1.8%
	at a spiked concentration of 0.10, 0.75 or 2.5 mg MTBE per litre blood and where n = 10 determinations	
Day-to-day precision:	Standard deviation (rel.)	s_w = 6.7% or 5.2%
	Prognostic range	u = 17.2% or 13.4%
	at a spiked concentration of 0.25 or 2.5 mg MTBE per litre blood and where n = 6 determinations	
Accuracy:	Recovery rate (rel.)	r = 98.1–102%
	at a spiked concentration of 0.5 mg MTBE per litre blood and where n = 10 determinations	
Detection limit:	1.2 µg MTBE per litre blood	
Quantitation limit:	4 µg MTBE per litre blood	

General information on methyl *tert*-butyl ether

Methyl *tert*-butyl ether (MTBE) is a colourless, volatile liquid with a characteristic, ether-like odour. For humans, the mean odour threshold in air is given as 0.32–0.47 mL/m³. Its solubility in water is 42 g/L.

MTBE is almost exclusively used as an additive in vehicle fuels. It improves combustion and thus reduces CO_2 emission. In petrol, MTBE concentrations generally vary between 2 and 5% (w/w) although up to 15% (w/w) may occur [Römpp 2017]. This substance is manufactured in or imported into the European Economic Area in quantities of 1 000 000–10 000 000 tonnes per year [ECHA 2017].

Methyl *tert*-butyl ether is readily absorbed after inhalation exposure and ingestion, whereas dermal absorption in the case of direct contact with the skin may be relatively low due to the substance's high vapour pressure. At the workplace, inhalation is thus the most important route of exposure [Greim 2000, translated]. The pulmonary retention of methyl *tert*-butyl ether in man during exposure to concentrations of 5, 25 or 50 mL/m³ with light-intensity physical activity (2 h, 50 watts) is about 40% [Nihlén et al. 1998].

For the most part, the absorbed MTBE is subject to oxidative demethylation. The resulting metabolites are exhaled or renal eliminated. Tertiary butyl alcohol is the most important metabolite. This compound can be further metabolised to form various other products, such as 2-methyl-1,2-propanediol, α-hydroxy-isobutyric acid, and formaldehyde [Brady et al. 1990; Nihlen et al. 1999]. About 20% of methyl *tert*-butyl ether is exhaled unchanged. The half-life for its elimination in the first phase via exhaled air varies between 1.3 and 2.9 min [Lindstrom and Pleil 1996]. A small part of the absorbed MTBE is also excreted unchanged via the kidneys [Johanson et al. 1995; Nihlén et al. 1998].

Less than 1% of the absorbed amount of MTBE is eliminated unchanged or in the form of *tert*-butyl alcohol with the urine [Amberg et al. 1999; Johanson et al. 1995; Nihlén et al. 1998]. After single exposure the excretion of methyl *tert*-butyl ether and its metabolites is more or less complete within 24 h. In volunteers exposed for 2 h to 5, 25 or 50 mL/m^3, three-phase [Johanson et al. 1995] or four-phase [Nihlén et al. 1998] elimination of methyl *tert*-butyl ether from the blood with half-lives of about 10 and 90 min and 20 h, or 1, 10 and 90 min and 19 h, respectively, was observed. In volunteers exposed for 4 h to methyl *tert*-butyl ether concentrations of 4 or 40 mL/m^3, other authors determined total elimination half-lives from plasma of about 1.8 and 2.6 h [Amberg et al. 1999]. Elimination with the urine was found to involve two phases with half-lives of 0.3 and 3 h [Johanson et al. 1995; Nihlén et al. 1998].

Due to the rapid elimination and metabolism of the substance, accumulation is not to be expected after repeated exposure to MTBE.

Occupational exposure to MTBE can primarily be expected in work areas where MTBE-containing fuels are refined, handled or transported, especially on refilling and unloading petrol stations. A Finnish study in twelve tank drivers yielded mean MTBE concentrations of 10 ± 6.7 µg/L in post shift urine samples [Saarinen et al. 1998]. Vainiotalo et al. [1998] also examined the exposure of tank drivers to MTBE. The mean MTBE concentrations in the blood were 18.8 µg/L in August and 12.6 µg/L in October, whereas the mean MTBE concentrations in urine samples were 9.8 µg/L in August and 4.1 µg/L in October. Due to the different study design as regards exposure level, exposure duration, parameters and sampling time, a BAT Value could not be evaluated from these or other field and laboratory studies.

A comparative overview and an extensive discussion of the individual field and laboratory studies can be found in the BAT Value Documentation [Drexler and Greim 2006, translated]. Generally, no background exposure could be determined either for MTBE or its metabolites in blood and urine samples of occupationally unexposed persons [Drexler and Greim 2006, translated].

An extensive review of the toxicity of MTBE can be found in the Concawe Report No. 97/54 [McKee et al. 1997], in the TLV Documentation on MTBE [ACGIH 2001], in the ECETOC Documentation [1997], and in the WHO report [1998].

The current MAK Value Documentation for MTBE is based on these reviews of toxicological data and has been supplemented with more recent data [Greim 2000, translated]. The MAK Value for MTBE established by the Commission is 50 mL/m^3 or 180 mg/m^3. Moreover, MTBE has been classified in Carcinogen Category 3B of

Section III of the List of MAK and BAT Values [DFG 2017]. Table 1 gives an overview of the toxicological classification of the substance by the Commission.

Table 1 Classification of methyl-*tert*-butyl ether by the Commission [DFG 2017].

Substance	MAK Value	Designation with "H", "S"	Carcinogen category	Pregnancy risk group	Germ Cell Mutagen category	BW
Methyl tert-butyl ether	50 mL/m³ (ppm)	–	3B	C	–	–

BW: assessment values in biological material (BAT/EKA/BLW/BAR)
H: danger of percutaneous absorption
S: danger of sensitisation
3B, C: see List of MAK and BAT Values [DFG 2017]

Contents

1 General principles

The described analytical method allows the specific and sensitive determination of methyl *tert*-butyl ether (MTBE) in blood and urine of persons occupationally exposed to this substance. The volatile MTBE is determined using static headspace GC-MS. Before analysing an aliquot of the headspace, the urine and blood samples are diluted 1:10 with water, spiked with internal standard and incubated for 45 min at 60 °C. The isotope-labelled d_3-MTBE serves as internal standard. Aqueous standard solutions are used for calibration.

2 Equipment, chemicals and solutions

2.1 Equipment

- Gas chromatograph with mass selective detector, headspace autosampler and data processing system
- Gas chromatographic column: stationary phase: 5% diphenyl-95% dimethylpolysiloxane; length: 60 m; inner diameter: 0.32 mm; film thickness 1 µm (e.g. Rtx-5, Restek, No. 10257)
- Vortex mixer (e.g. VTX-3000 L Mixer UZUSIO, LMS, Japan)
- Microlitre pipettes, adjustable between 10 and 100 µL or between 100 and 1000 µL with suitable pipette tips (e.g. Eppendorf)
- Motor driven pipette (e.g. Eppendorf Multipette®)
- 20-mL Headspace vials (e.g. Macherey-Nagel)
- Aluminium crimp caps with teflon-coated butyl rubber septa (e.g. Macherey-Nagel)
- Crimpers and decappers (e.g. Macherey-Nagel)
- 10-mL volumetric flasks (e.g. Brand)
- Analytical balance (e.g. Sartorius)
- 10-mL urine tubes (e.g. Sarstedt Urine-Monovette®)
- 10-mL EDTA blood collection tubes (e.g. Sarstedt S-Monovette®)

2.2 Chemicals

Unless stated otherwise, the quality of all used chemicals must be at least p.a.

- Methyl *tert*-butyl ether (e.g. Merck, No. 101995)
- d_3-Methyl *tert*-butyl ether (e.g. Aldrich, No. 434132)
- Methanol (e.g. Merck, No. 106009)
- Ultrapure water for chromatography (e.g. Merck, No. 115333)
- Helium 4.6 (e.g. Linde)
- Urine of persons with no known exposure to MTBE
- Blood of persons with no known exposure to MTBE
- Bovine blood, defibrinated, sterile (e.g. ACILA, No. 2201025)

2.3 Solutions

Internal standard

- d_3-MTBE stock solution (5 g/L)
  50 mg d_3-MTBE are weighed into a 10-mL volumetric flask containing approx. 8 mL methanol. The solution is made up to the mark with methanol and mixed. The stock solution is stored in sealed vials at –18 °C. Under these conditions, it can be kept for at least six months.
- d_3-MTBE spiking solution (2.5 mg/L)
  5 µL of the d_3-MTBE stock solution are pipetted to 10 mL of ultrapure water. The prepared solution is thoroughly mixed.

Calibration standards

- MTBE stock solution (10 g/L)
  Approx. 8 mL methanol are placed into a 10-mL volumetric flask. Then 100 mg MTBE are weighed into the flask. The solution is made up to the mark with methanol and thoroughly mixed. This solution is stable for at least 6 months when stored at –18 °C.
- MTBE working solution (100 mg/L)
  Approx. 8 mL methanol are placed into a 10-mL volumetric flask. Then 100 µL of the MTBE stock solution are pipetted into the flask. The solution is made up to the mark with methanol and thoroughly mixed. This solution is stable for at least 6 months when stored at –18 °C.
- MTBE spiking solution I (1 mg/L)
  100 µL of the working solution are pipetted into a 10-mL volumetric flask containing water. The solution is made up to the mark with water and thoroughly mixed. This MTBE spiking solution I is stable for two days when stored at room temperature.
- MTBE spiking solution II (0.1 mg/L)
  1 mL of the MTBE spiking solution I is pipetted into a 10-mL volumetric flask. The flask is made up to the mark with water and the solution is thoroughly mixed. This MTBE spiking solution II is stable for two days when stored at room temperature.

Calibration solutions

The calibration solutions are freshly prepared in water. For this, the MTBE spiking solutions are mixed with ultrapure water in 20-mL headspace vials according to the pipetting scheme in Table 2. After adding 50 µL of the internal standard spiking solution, the calibration solutions are incubated in the headspace autosampler and analysed by HS-GC-MS (see Section 3.2).

Table 2 Pipetting scheme for the preparation of aqueous calibration standards. The given MTBE concentrations already take into account the 1:10 dilution of the sample material (see Section 3.2).

Calibration solution	Spiked conc. [mg/L]	Volume of spiking solution [µL]		Volume of water [µL]
		I	II	
0	0	–	–	2000
1	0.010	–	20	1980
2	0.025	–	50	1950
3	0.050	–	100	1900
4	0.10	–	200	1800
5	0.25	50	–	1950
6	0.50	100	–	1900
7	0.75	150	–	1850
8	1.0	200	–	1800
9	1.5	300	–	1700
10	2.5	500	–	1500
11	5.0	1000	–	1000

3 Specimen collection and sample preparation

3.1 Specimen collection

Due to rapid elimination of the unmetabolised MTBE, urine and blood samples of occupationally exposed workers should be taken immediately after exposure.

For urine sampling sealable containers are used. If necessary, urine samples may be drawn from urine into monovettes for shipping. The urine samples are stable for one week at room temperature and for two weeks if stored at 5–8 °C in the fridge. The storage of the urine samples at –18 °C was not tested during method development. For blood sampling EDTA-monovettes are used to draw 5 mL of whole blood by venipuncture. The monovettes prepared with EDTA anticoagulant are mixed thoroughly. The taken blood samples are stable for one week at room temperature and for two weeks if stored at 5–8 °C in the fridge, but must not be deep-frozen.

3.2 Sample preparation

Prior to analysis, the samples were allowed to reach room temperature and were mixed thoroughly. 0.2 mL of the sample (blood or urine) and 50 µL of the spiking solution of the internal standard are pipetted into a 20-mL headspace vial containing 1.8 mL water. The vial is sealed and the sample is thoroughly mixed using a Vortex

mixer. The prepared sample is stable for at least 48 h at room temperature. The sample is then analysed using static headspace GC-MS. For this, the sample is incubated in the headspace autosampler for 45 min at 60 °C in order for the gas phase of the analyte being in equilibrium with the liquid phase.

4 Operational parameters

4.1 Headspace autosampler

Equilibration time:	45 min at 60 °C
Transfer line:	130 °C
Pressure build-up:	125 kPa for 30 s
Injection time:	0.08 min

4.2 Gas chromatography

Capillary column:	Material:	Fused Silica
	Stationary phase:	Rtx-5 (5% diphenyl-95% dimethylpolysiloxane)
	Length:	60 m
	Inner diameter:	0.32 mm
	Film thickness:	1 µm
Detector:	Mass selective detector (MSD)	
Temperatures:	Column:	initial temperature 75 °C, 3 min isothermal, increase at 20 °C/min to 190 °C, then at 40 °C/min to 250 °C, 4 min isothermal at the final temperature
	Injector:	130 °C
	Interface:	230 °C
Carrier gas:	Helium 4.6	
Flow:	1.4 mL/min (initial pressure: 58 kPa)	
Injection:	Split ratio 2	

4.3 Mass spectrometry

Ionisation type:	Electron ionisation (EI)
Ionisation energy:	70 eV

Source temperature:	200 °C
Quadrupole temperature:	150 °C
Dwell time:	30 ms
Electron multiplier:	1.0 kV
Detection mode:	Selected Ion Monitoring (SIM)

All the other parameters need to be individually adjusted by the user. The parameters given above can therefore be used as a rough guide only.

5 Analytical determination

For the analytical determination of the samples, prepared according to Section 3, 1 mL of the headspace vapour phase is injected into the GC-MS system.

The resulting retention times of the analyte and the internal standard as well as the characteristic ion traces for the analytes are given in Table 3.

Table 3 Retention times and detected ions.

Analyte	Retention time [min]	Detected ions [m/z]
MTBE	5.60	73[a] 74
d_3-MTBE	5.58	76[a] 77

[a] Ion trace used for quantitation

The retention times given in Table 3 are intended to be a rough guide only. Users of the method must ensure proper separation performance of the column used influencing the resulting retention behaviour of the analytes.

Figure 1 (in the Appendix) shows a chromatogram of a pooled urine sample spiked with 3.7 µg MTBE/L. Figure 2 (in the Appendix) shows a chromatogram of a human blood sample spiked with 3.7 µg MTBE/L.

6 Calibration

For the calibration of the method, the calibration solutions described in Section 2.3 are prepared in water, spiked with internal standard and analysed using HS-GC-MS. The calibration graph is obtained by plotting the quotient of the peak area of the analyte and the peak area of the isotope-labelled internal standard against the concentration of the calibration solution. Under the analytical conditions described, the

calibration graph is linear in the concentration range between the limit of detection and 5 mg/L. As an example, Figure 3 (in the Appendix) shows calibration graphs in a concentration range between 0.01 mg MTBE/L and 5 mg MTBE/L prepared in water, human urine and human blood, respectively. In everyday routine, calibration is performed using aqueous calibrations solutions.

7 Calculation of the analytical results

To calculate the analyte concentration in a urine or blood sample, the calibration function corresponding to the analytical run is used (Section 6). Using the quotient obtained by dividing the peak area of the analyte by the peak area of the corresponding internal standard d_3-MTBE, the GC-MS-data processing software calculates the analyte level automatically. Any reagent blank values have to be subtracted from the analytical results of the measured samples.

If the analytical result is outside the calibration range, the respective sample is diluted appropriately and reanalysed.

8 Standardisation and quality control

Quality control of the analytical results is carried out as stipulated in the guidelines of the Bundesärztekammer (German Medical Association) and in a general chapter of the MAK-Collection for Occupational Health and Safety Part IV: Biomonitoring Methods [Bundesärztekammer 2008; Bader et al. 2010]. To check precision two quality control samples with a constant low (Q_{low}) and high analyte concentration (Q_{high}) are analysed within each analytical run. As material for quality control is not commercially available, it must be prepared in the laboratory. The concentration of this control material should lie within the relevant concentration range.

For preparation of the quality control sample Q_{low}, human urine or bovine blood was spiked with 0.25 mg MTBE/L. To prepare the quality control material Q_{high}, 2.5 mg MTBE/L were spiked to human urine or bovine blood. 200-µL aliquots of this material were stored in headspace vials at −18 °C until use. The quality control material and a reagent blank, consisting in 2 mL of ultrapure water, are analysed within each analytical run. The nominal value and the tolerance ranges of this quality control material are determined in a pre-analytical period [Bader et al. 2010].

9 Evaluation of the method

The reliability of the method was proved by comprehensive validation and by implementation and validation of the procedure in a second independent laboratory.

9.1 Precision

For determining the within-day precision, pooled urine samples and human blood samples were spiked with MTBE at 0.10 mg/L, 0.75 mg/L and 2.5 mg/L, prepared and analysed. MTBE background levels were determined to be < 0.003 mg/L in urine and < 0.03 mg/L in blood. Based on the tenfold determination of these samples the within-day precision was calculated as given in Table 4.

Day-to-day precision was determined by preparing and analysing the QC samples Q_{low} and Q_{high} on six different days. The obtained precision data are presented in Table 5.

Table 4 Within-day precision for the determination of methyl *tert*-butyl ether in urine and blood (n = 10).

Analyte	Spiked concentration [mg/L]	Recovery (rel.) [%]	Standard deviation (rel.) s_w [%]	Prognostic range u [%]
MTBE in urine	0.10	102–107	1.8	4.1
	0.75	96.4–121	2.1	4.8
	2.5	97.6–99.4	0.6	1.3
MTBE in blood	0.10	99.0–104	1.5	3.5
	0.75	102–105	1.4	3.1
	2.5	101–103	0.8	1.8

Table 5 Day-to-day precision for the determination of methyl *tert*-butyl ether in urine and blood (n = 6).

Analyte	Spiked concentration [mg/L]	Standard deviation (rel.) s_w [%]	Prognostic range u [%]
MTBE in urine	0.25	7.1	18.3
	2.5	5.9	15.2
MTBE in blood	0.25	6.7	17.2
	2.5	5.2	13.4

9.2 Accuracy

Recovery tests were carried out in order to determine the accuracy of the method. Therefore, ten individual urine and blood samples were spiked with the analyte at 0.5 mg/L, prepared and analysed. The relative and absolute recovery rates are given in Table 6 and 7, respectively.

Table 6 Relative recovery for the determination of methyl *tert*-butyl ether in urine and blood (n = 10).

Analyte	Spiked concentration [mg/L]	Recovery (rel.)	
		Standard deviation (rel.) [%]	Mean (range)
MTBE in urine	0.5	0.7	98.9 (95.5–97.6)
MTBE in blood	0.5	1.2	99.7 (98.1–102)

Table 7 Absolute recovery for the determination of methyl *tert*-butyl ether in urine and blood (n = 10).

Analyte	Spiked concentration [mg/L]	Recovery (abs.)	
		Standard deviation (rel.) [%]	Mean (range)
MTBE in urine	0.5	2.3	103.6 (101–108)
MTBE in blood	0.5	5.3	91.7 (88–96.8)

9.3 Detection and quantitation limits

The detection and quantitation limit of MTBE were determined according to DIN 32645 [1994]. To this end, calibration curves with ten equidistant points in the range between 5 and 50 µg/L were prepared in pooled urine and pooled blood, respectively, and analysed. The determined detection and quantitation limit of the analyte are shown in Table 8.

Table 8 Detection and quantitation limit of methyl *tert*-butyl ether according to DIN 32645 [1994] (n = 3).

Analyte	Detection limit [µg/L]	Quantitation limit [µg/L]
MTBE in urine	1.8	6
MTBE in blood	1.2	4

9.4 Sources of error

When using solvents and reagents of the stated reagent grade, no interference occurs in the detection of MTBE. It has been established that there is no interference with diethyl ether, diisopropyl ether, tetrahydrofuran, 1,4-dioxane, methanol, ethanol, n-propanol and isopropanol, isobutanol, 1-butanol, 2-butanol, acetone, methyl ethyl ketone, methyl butyl ketone and methyl isobutyl ketone. Routine analyses of highly volatile halogenated hydrocarbons and BTX compounds in blood are carried out using the described method. Cross-interferences were not observed. As MTBE is a solvent commonly used in analytical laboratories, consistent testing for blank values is mandatory.

10 Discussion of the method

MTBE, a highly volatile aliphatic ether, can easily be analysed using static headspace GC-MS. Due to the absence of liquid extraction and purification steps, the sample preparation is reduced to a minimum. The highly sensitive MS detection enables the analysis of samples at a 1:10 dilution. This reduces the required sample volume to 200 µL and minimises potential matrix effects. Linearity ranges from at least 0.005 to 5 mg/L. The method has been developed for occupational medicine. Detection sensitivity can be increased approximately five- to ten-fold by using 2 mL instead of 0.2 mL biological material.

For both matrices, calibration is carried out using aqueous standards. Simultaneously recorded calibration curves of standards in water and human blood were linear and the graphs run parallel (see Figure 3; in the Appendix). That means that matrix effects do not play a significant role. The high relative and absolute recovery in individual blood and urine samples confirms this observation (see Table 6 and 7).

d_3-MTBE has proved successful as an internal standard. In particular, the very high recovery rate and good precision of the method can be attributed to this fact. Figure 4 (in the Appendix) shows the mass spectra of native and deuterated MTBE. Selective masses are thus m/z 73 (quantifier) and m/z 74 (qualifier) for MTBE as well as m/z 76 for d_3-MTBE. If additional masses are required for MTBE identification, the sample has to be reanalysed without the addition of d_3-MTBE.

The GC-MS method is highly selective. Rtx-5 (5% diphenyl-95% dimethylpolysiloxane) has proved its worth as a separating column. Comparable results can also be achieved on Rtx-1701 (14% cyanopropylphenyl-84% dimethylpolysiloxane) and Rtx-624 (6% cyanopropylphenyl-94% dimethylpolysiloxane). Under routine conditions, however, the Rtx-5 separating column will be preferred due to the very low level of column bleed and the higher thermal resistance. The method can readily be extended to include other ethers (i.a. THF, diisopropyl ether, diethyl ether), alcohols and ketones.

Environmental MTBE background levels in humans are in the lower ng/L range and cannot be detected with this method. For reliable detection of these very low concentrations, dynamic headspace [Bonin et al. 1995] or HS-SPME [Scibetta et al. 2007] methods are recommended.

Instruments used:

Headspace autosampler Turbomatrix (Perkin-Elmer) and GC-MS-System QP2010+ (Shimadzu)

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12 Appendix

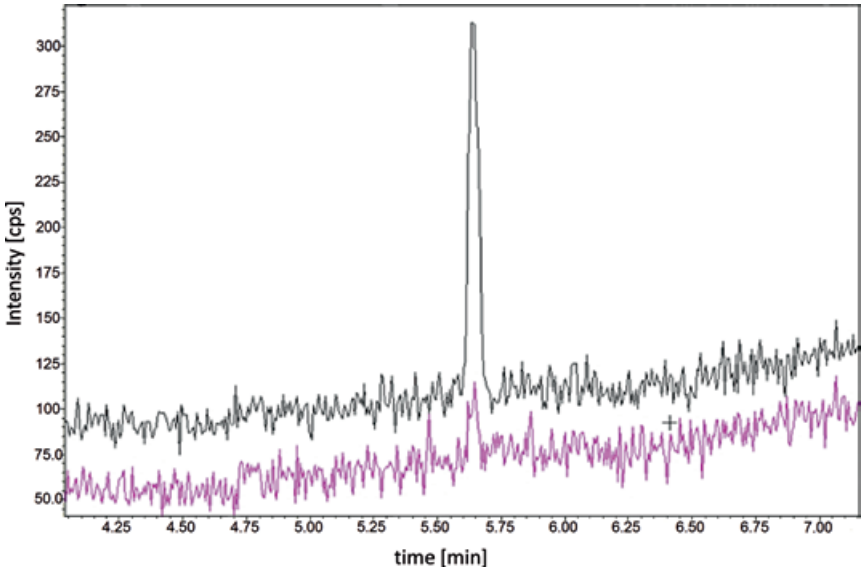

Figure 1 GC-MS chromatogram of a spiked (3.7 µg/L) and a native pooled urine sample on the ion trace m/z 73.

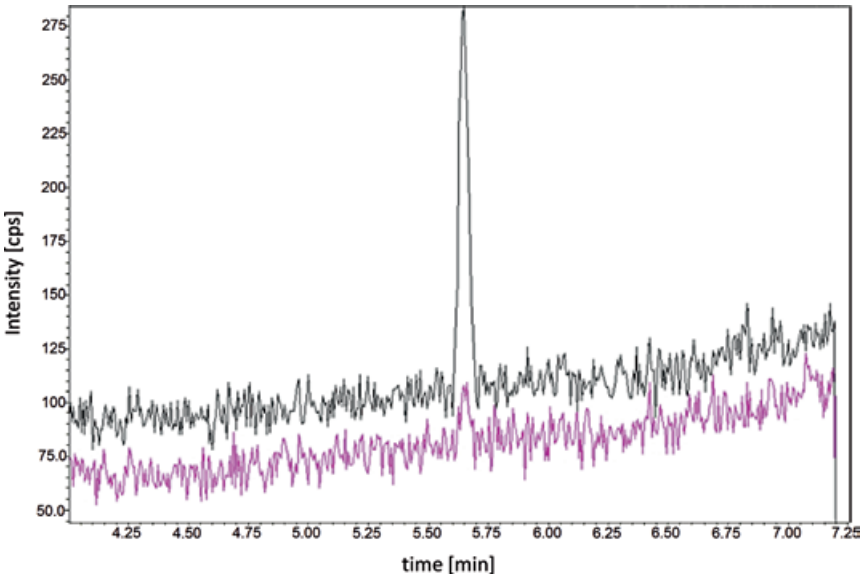

Figure 2 GC-MS chromatogram of a spiked (3.7 µg/L) and a native pooled human blood sample on the ion trace m/z 73.

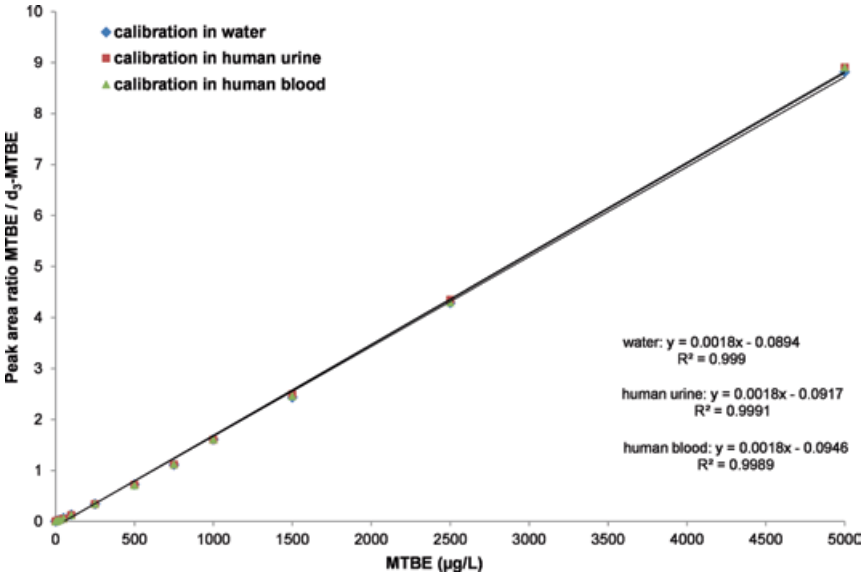

Figure 3 Comparison of calibration graphs prepared in water, human urine and human blood.

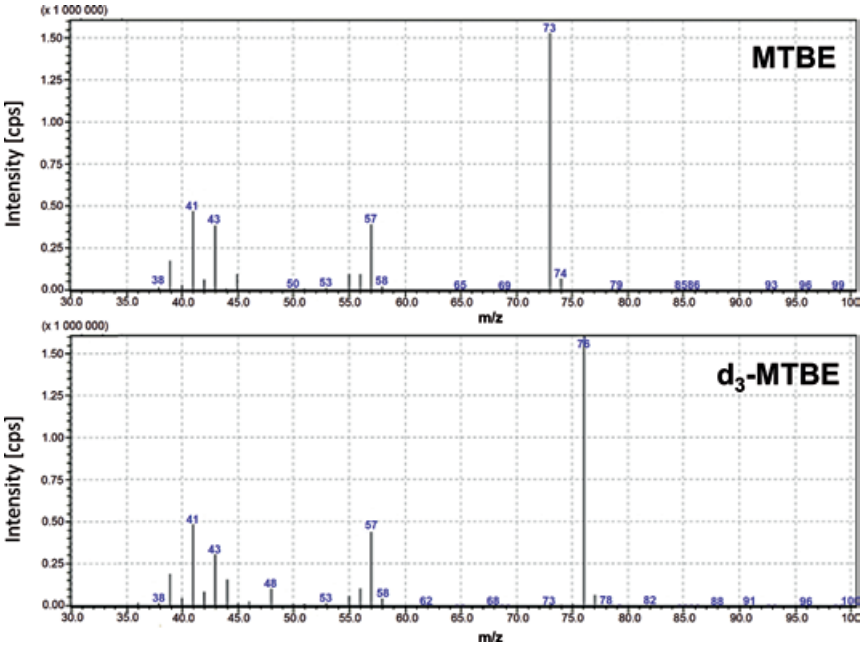

Figure 4 EI mass spectra of MTBE and d_3-MTBE.