EUROPEAN COMMISSION
DIRECTORATE-GENERAL
Joint Research Centre

Institute for Health and Consumer Protection
Toxicology and Chemical Substances (TCS)
European Chemicals Bureau
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2-methoxy-2-methylbutane (TAME)

CAS No: 994-05-8

EINECS No: 213-611-4

Summary Risk Assessment Report

2007 **EUR 22236 EN/2**

The mission of the IHCP is to provide scientific support to the development and implementation of EU polices related to health and consumer protection. The IHCP carries out research to improve the understanding of potential health risks posed by chemical, physical and biological agents from various sources to which consumers are exposed.

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SUMMARY RISK ASSESSMENT REPORT

Final report, 2007

Finland

The summary of the risk assessment of 2-methoxy-2-methylbutane (TAME) has been prepared by the Finnish Environment Institute, in co-operation with the National Product Control Agency for Welfare and Health.

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Date of Last Literature Search:	**2004**
Review of report by MS Technical Experts finalised:	**2005**
Final report:	**2007**

PREFACE

This report provides a summary, with conclusions, of the risk assessment report of the substance 2-methoxy-2-methylbutane (TAME) that has been prepared by Finland in the context of Council Regulation (EEC) No. 793/93 on the evaluation and control of existing substances.

For detailed information on the risk assessment principles and procedures followed, the underlying data and the literature references the reader is referred to the comprehensive Final Risk Assessment Report (Final RAR) that can be obtained from the European Chemicals Bureau[1]. The Final RAR should be used for citation purposes rather than this present Summary Report.

1.1.1.1

[1] European Chemicals Bureau – Existing Chemicals – http://ecb.jrc.it

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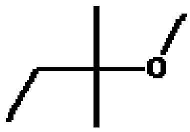
1 GENERAL SUBSTANCE INFORMATION

1.1 IDENTIFICATION OF THE SUBSTANCE

CAS Number:	994-05-8
EINECS Number:	213-611-4
IUPAC Name:	2-methoxy-2-methylbutane
Molecular formula:	$C_6H_{14}O$
Structural formula:	



Molecular weight:	102.18 g/mol
Synonyms:	*tert*-Amyl-methyl ether (TAME), 1,1-dimethylpropyl methyl ether, Butane, 2-methoxy-2-methyl-, Ether methyl *tert*-pentyl, *tert*-Pentyl methyl ether, Methyl 1,1-dimethylpropyl ether, Methyl 2-methyl-2-butyl ether,
SMILES:	COC(C)(C)CC

1.2 PURITY/IMPURITIES, ADDITIVES

Purity:	> 96%	
Impurities:	Cyclohexane	≤ 4%
	Water	< 0.5%
	C_7-ether	< 1%
	2-methyl 2-butanol	1.23%
	$C_5 – C_8$ hydrocarbons	0.50%
	Methanol	0.33%
	methyl tert-butyl ether	0.30%
	tert-butanol	0.17%
	butyl tert-butyl ether	0.06%
	ethyl tert-butyl ether	0.02%
	2 methyl-1-butene	
	2-methyl-2-butene	
	Benzene	
Additives:	none	

1.3 PHYSICO-CHEMICAL PROPERTIES

The physico-chemical properties of TAME are summarised in **Table 1.1**.

Table 1.1 Physico-chemical properties

Property	Value	Reference
Physical state	Liquid	
Melting point	-80°C	Erdölchemie (2000), Fortum (2001), Chemsafe (1994)
Boiling point	86°C	Fortum (2001), Chemsafe (1994)
Density	0.77 g cm^{-3} at 20°C	Erdölchemie (2000), Chemsafe (1994), CRC (1989)
Vapour pressure	90 hPa at 20°C 120 hPa at 25°C	Huttunen et al. (1997), Huttunen (1996)
Water solubility	11 g/l at 20°C	Huttunen et al. (1997), Huttunen (1996), Stephenson (1992)
Partition coefficient n-octanol/water (log value)	1.55 at 20°C	Huttunen et al. (1997), Huttunen (1996)
Granulometry	not relevant	
Conversion factors	1 ppm = 4.24 mg/m^3	
Flash point	- 11°C	Erdölchemie (2000), Chemsafe (1994)
Autoflammability	415°C	Erdölchemie (2000), Chemsafe (1994)
Flammability	Highly flammable	Erdölchemie (2000), Fortum (2001)
Explosive properties	Lower limit 1.0% vol in air; 42 g m-3 and upper limit 7.1% vol in air; 300 g m-3	Chemsafe (1994)
Oxidizing properties	Not oxidising for structural reasons	
Viscosity	0.50 mm^2 s-1 at 40°C	Huttunen et al. (1997), Huttunen (1996), API (1984)
Henry's constant	83 Pa m^3mol-1 at 20°C	calculated (EUSES)

1.4 CLASSIFICATION

The substance is not listed in Annex I of Council Directive 67/548/EEC.

The Meeting of the Technical Committee C&L on the Classification and Labelling of Dangerous Substances in March 2005 agreed on the following classification and labelling of TAME:

<u>Classification</u>

F; R11 Xn R22 R67

Labelling

F; Xn R11-22-67

S(2)-9-16-23-33

2 GENERAL INFORMATION ON EXPOSURE

2.1 PRODUCTION

TAME is manufactured in the petroleum refineries and it is formed by the chemical combination of either of the two reactive C_5 olefins (2-methyl-2-butene and 2-methyl-1-butene) with methanol. Some plants produce TAME from tertiary olefins (C_6-C_7). Only a small fraction (approximately 3%) of the total amount of TAME produced in the EU is isolated as 'pure' TAME (> 96% purity), the majority (97%) is part of a "mixed" refinery stream containing 10-30% of TAME together with other mixed hydrocarbons.

The EU production volume exceeded 175,000 tonnes in the year 2000. A remarkable increase in capacity building and production has happened between 2000 and 2002, since production reached 250,000 tonnes in 2002. The produced TAME is mainly used in the European Union market. There has not been remarkable international marketing of TAME in the 1990's but import and export has increased slightly during the last few years (2000-2002) showing 30,000 tonnes net import to the European Union area in the current reference year 2002.

2.2 USES

The main use of TAME is as an additive/component in petrol and it is the second largest used oxygenate after MTBE. Other uses of the substance are as an intermediate in the production of pure methyl butenes. TAME is blended in petrol alone or often together with other oxygenates (MTBE, ETBE or ethanol) and other octane boosters to meet desired petrol specifications. Typically petrol may contain < 1% – > 10% TAME. The use of TAME is at the moment more or less localised to the market areas of the European TAME producers.

3 ENVIRONMENT

3.1 ENVIRONMENTAL EXPOSURE

3.1.1 Environmental releases

The environmental risk assessment considers the release of TAME to the environment from its production, formulation, its industrial use including storage, transport and delivery of petrol, its private use (consumer use of petrol), its industrial use as chemical intermediate and the release from waste disposal. The emission was estimated using industry specific and use pattern specific information but the default methods from the TGD were also used for some lifecycle stages and environmental compartments. Emissions of TAME into the atmosphere are high in terms of emitted volumes. More than 7,000 tonnes (approximately 2.5% of total volume) are emitted annually into the atmosphere as evaporative and unburnt exhaust emissions. The reasons for high emissions to the atmosphere are high consumption volume and technical issues related to vehicular emissions in road traffic in general.

3.1.2 Environmental fate

TAME is a volatile (vp. 90 hPa at 20°C) liquid which is hydrolytically stable and moderately soluble in water (11 g/l at 20°C). The solubility to water increases as temperature decreases. TAME is very mobile in soil and may easily leach to groundwater (transported with water). TAME is easily volatilised into the atmosphere from top soil and surface water. Static equilibrium partitioning between environmental compartments at 20°C is as follows: air 95.6, water 4.25, sediment 0.001 and soil 0.038 (EQC ver1.1).

Indirect photodegradation in the atmosphere is the primary route of removal in the environment and atmospheric degradation half-life t ½ is approximately 3 – 5 days.

TAME is not readily biodegradable in aquatic environment according to the standardised aerobic ready biodegradation tests. Observed biodegradation in soil, sediment, surface- and groundwater is very slow and TAME may be regarded persistent in these compartments. Some biodegradation studies have shown that at least some microbial species are capable to degrade TAME and to use it even as their sole carbon source. In industrial waste water sewage treatment plants having continuous TAME exposure, adapted microbial population may exist capable of effectively degrade TAME.

Measured log Kow of TAME is 1.55 and calculated BCF in fish is low (4). It is unlikely that TAME would bioconcentrate in high extent to biological material or would accumulate in biota for long time periods. Therefore bioconcentration via the food chain is also unlikely and the monitoring results from environmental samples support these assumptions.

3.1.3 Environmental concentrations

3.1.3.1 Aquatic compartment

Local aquatic Predicted Environmental Concentrations (PECs) were derived for the emission sources mentioned below. It was expected that the surface water assessment would be protective for sediment too.

- Production and formulation (site specific and generic)
  PEC_{local} = 0.0015-0.0001 mg/l
- Intermittent release from storage tank bottom waters (generic calculation)
  $PEC_{local\_intermittent}$ = 35 mg/l (dissolved)
- Boating, emissions to water via exhaust gases
  $PEC_{local\ boating}$ = 0.013 mg/l

In addition, stormwater runoff is a source of TAME to surface water. However, there is not enough monitoring data available to make quantitative PEC calculations for runoff. Known concentrations in runoff are only few micrograms/litre maximum and remain clearly below the current PNEC values, indicating no risk for runoff waters.

3.1.3.2 Terrestrial compartment

Generic local EUSES estimations have been carried out for relevant life-stages of TAME. There are specifically three exposure routes which should be considered when estimating PEC_{local} in soil:

- Direct (point source) release of TAME during petrol storage and refuelling tanks and vehicles;
- STP sludge field application and
- Dry and wet deposition from the atmosphere (infiltration of stormwater runoff and precipitation).

The first issue, soil contamination in petrol stations and storage depots, has not been estimated or expressed quantitatively. Instead, a set of monitoring data from contaminated soil and groundwater observations in Finland is presented in Section 3.1.4.2 of the RAR. It is often, but not always, a question of accidental spillages but continuous slight contamination of storage and delivery area soil. However, in the long term, accidental spillages, like leaking under ground storage tanks (USTs), may have a remarkable contribution on contamination.

The two latter issues were quantified as EUSES modelling results. The EUSES model takes into account both the application of STP sludge on agricultural soil and the deposition from the air.

Table 3.1 Local PECs in soil, concentrations of TAME in agricultural soil and grassland EUSES calculations

Life cycle step	PEC_{local} terrestrial Concentration in grassland > 180 days (mg/kgwwt)	PEC_{local} terrestrial Concentration in agricultural soil > 30 days (mg/kgwwt)
Production 1	0.0038	0.034
Industrial use 1	0.0014	0.028
Industrial use 2	0.0008	0.021

3.1.3.3 Atmospheric compartment

Local atmospheric PECs were derived for the following emission sources: the generic EUSES calculations and site specific calculations for production, formulation and industrial use 1 and 2. In addition a generic local PEC calculation for petrol station, the concentration 100 m from a point source, was carried out. Results can be found in the RAR under the specific sections.

Table 3.2 EUSES calculations, PECs in air from production, formulation and industrial use

Life cycle step	Local concentration in air during emission episode (mg/m^3)	Annual average conc. In air, 100 m from point source (mg/m^3)	Annual PEClocal in air (mg/m^3) (local + regional)
Production 1	0.062	0.059	0.060
Industrial use 1	0.109	0.105	0.105
Industrial use 2	0.002	0.002	0.003

3.1.3.4 Regional concentrations

Table 3.3 shows the calculated regional concentrations $PEC_{regional}$ for air, water and soil.

Table 3.3 Regional PECs in air, water and soil

Compartment	PEC regional
Surface water (total), µg/l	0.52
Surface water (dissolved), µg/l	0.52
Air (total), mg/m^3	0.34
Agricultural soil (total), mg/kg (WWT)	$9.3 \cdot 10^{-6}$
Pore water of agricultural soils, mg/l	$1.7 \cdot 10^{-5}$
Natural soil (total), mg/kg (WWT)	$5.3 \cdot 10^{-6}$
Industrial soil (total), mg/kg (WWT)	0.007
Sediment (total), mg/kg (WWT)	0.0005

3.2 EFFECTS ASSESSMENT

3.2.1.1 Aquatic compartment (fresh and marine water incl. sediment)

There is a complete base set of acute toxicity data for TAME. The acute toxicity value for fish is a LC_{50} of 580 mg/l. The acute toxicity tests for invertebrates show an EC_{50} of 100 mg/l for Daphnia and a LC_{50} of 14 mg/l for *Mysidopsis bahia*, which is a marine invertebrate. The acute E_rC_{50} value for algae is 870 mg/l. The NOEC from this algae test is 77 mg/l. In addition, the chronic test performed on *Americamysis bahia*, formerly known as *Mysidopsis bahia*, gives a 28-day NOEC of 3.39 mg/l.

According to the TGD an assessment factor of 50 applies to the lowest of two NOECs covering two trophic levels when such NOECs have been generated covering that level showing the lowest $L(E)C_{50}$ in the short-term tests. In the case of TAME there is a 72-hour NOEC on algae of 77 mg/l and a NOEC on the invertebrate *Americamysis bahia*, which is the most sensitive species in acute testing. Consequently, an assessment factor of 50 is used for the chronic invertebrate NOEC value of 3.39 mg/l to derive a Predicted No Effect Concentration (PNEC) for aquatic environment

The $PNEC_{aquatic}$ = 0.068 mg/l based on the *Americamysis bahia* chronic test result (AF=50).

The $PNEC_{intermittent}$ = 1.4 mg/l for intermittent release is (AF=10) based on *Americamysis bahia* acute 96-hour LC_{50} = 14 mg/l test result.

In the absence of any ecotoxicological data for sediment-dwelling organisms, the $PNEC_{sediment}$ is calculated using the equilibrium partitioning method. A calculation using $PNEC_{aquatic}$ of 0.0678 mg/l gives a $PNEC_{sediment}$ of 0.0713 mg/kg (WWT)

3.2.1.2 Marine environment

PNEC $_{marine}$ is derived from the lowest chronic aquatic test result (*Americamysis bahia*: 28-day NOEC = 3.4 mg/l) applying the assessment factor 500 (= 10 fold the fresh water assessment factor).

$$PNEC_{marine} = 3.39 \text{ mg/l}: 500 = 0.0068 \text{ mg/l}$$

In the absence of any ecotoxicological data for sediment-dwelling organisms, the $PNEC_{sediment}$ 0.00713 mg/kgwwt is calculated using the equilibrium partitioning method from the $PNEC_{marine}$.

The $PNEC_{marinesediment}$ is 0.00713 mg/kg (WWT)

3.2.1.3 Micro Organisms

PNEC $_{micro\text{-}organisms}$ is derived from a *Pseudomonas putida*, cell multiplication inhibition test (16-hour EC_{10} = 25 mg/l) applying assessment factor 1.

$$PNEC_{micro\text{-}organism} = 25 \text{ mg/l}$$

3.2.1.4 Terrestrial compartment

There are no test results on the effects of TAME to terrestrial compartment. In the absence of any ecotoxicological data for terrestrial organisms, the $PNEC_{soil}$ is calculated using the equilibrium partitioning method. EUSES calculation using $PNEC_{aquatic}$ of 0.0678 mg/l gives:

$$PNEC_{soil} = 0.0354 \text{ mg/kg (WWT)}$$

3.2.1.5 Atmospheric compartment

There is no tested data available on direct effects of TAME on biota through atmospheric exposure. However, read across to general information of known effects of airborne volatile organic compounds on plants has been used to estimate possible direct effects of TAME on vegetation. Based on this evaluation (see Section 3.2.2.3 of the RAR) it is concluded that direct effects on vegetation are unlikely.

Instead, the indirect effects through tropospheric ozone forming potential and formaldehyde (formaldehyde in exhaust gases) are expected to be the most pronouncing atmospheric effects of TAME.

In general, hydrocarbons and vehicular hydrocarbon emissions are contributors to the formation of low level (tropospheric) ozone. As a group, all hydrocarbons (except methane) are considered ozone precursors and TAME has its own role in this general (urban) air quality issue.

3.2.1.6 Secondary Poisoning

Estimated BCF's calculated by EUSES for fish (BCF = 4.1) and earthworm (BCF = 2.7) indicate that secondary poisoning is not likely and there is no need to carry out a detailed risk characterisation for secondary poisoning.

3.2.1.7 PBT–Assessment

According to existing data and assessment of inherent PBT–properties, it can be concluded that TAME can not be regarded as a PBT-substance since it does not meet the toxicity and bioaccumulation criteria.

3.3 RISK CHARACTERISATION

3.3.1 Aquatic compartment (incl. sediment)

Local Site Specific Risk Characterisation

None of the production/formulation sites have a surface water PEC higher than PNEC.

Conclusion (ii).

The PEC_{WWTP} for the production/formulation sites of TAME does not exceed the PNEC for micro-organisms in any cases.

Conclusion (ii).

Regional Risk Characterisation

The regional surface water PEC/PNEC ratio is 0.0077. This ratio indicates that there is no risk at regional level in surface water or sediments.

Conclusion (ii).

3.3.2 Conclusions to the risk assessment for the aquatic compartment

Conclusion (iii).

1. **Conclusion (iii)** applies to intermittent release scenario for storage tank bottom waters at terminal sites. The currently applied risk reduction measures have proved not to be effective enough to reduce the risk for surface waters to an acceptable level.

2. **Conclusion (iii)** applies also to the generic assessment for industrial use 1, terminal sites, under use of default TGD emission factors. (No representative monitoring data is available from these sites since the number of sites at EU level is very high).

It is believed, that terminal site tank bottom waters may still be one of the most pronounced sources of TAME to surface waters from these sites not only as intermittent emission parameter (point 1), but as a more continuous emission source (point 2). In large depot areas with many tanks, bottom water releases may happen monthly or more often or even continuously like in cavern storage. In these cases it is not appropriate to regard emissions as intermittent but rather continuous (PNEC derived from long term tests have to be used in deriving the PEC/PNEC ratio).

If risk reduction measures are applied for intermittent emissions of tank bottom waters, it is believed, that these actions might remove or decrease the expected, intermittent and continuous emission (industrial use 1) risks in many real sites.

Conclusion (ii).

This conclusion applies to the following scenarios (1-4):

1. Boating scenario.

2. Production of TAME in existing production sites in EU. On-site/off-site formulation.

3. Industrial use 2 Scenario: use of TAME as a process intermediate in chemicals production. One of the production sites is the industrial use 2 site and no risks were identified except using the default emission factors. Measured values are used for the risk characterisation according to the TGD.

4. Regional PEC for surface water and sediment.

3.3.3 Conclusions to the risk assessment for micro-organisms in waste water treatment plants

Conclusion (ii).

This conclusion applies to all production/formulation and industrial use 1 and 2 sites.

3.3.4 Terrestrial compartment and groundwater

Conclusion (iii).

Conclusion (iii) applies to overall quality of groundwater. The conclusion is reached because of concern of potability of groundwater in respect to taste and odour as a consequence of exposure arising from leaking underground storage tanks, tank piping and spillage from overfilling the tanks.

Conclusion (iii) is not based on concerns of ecotoxicological endpoints, but more on intrinsic properties of TAME and general groundwater protection. The intrinsic properties of TAME show high persistency in soil and groundwater. TAME is water soluble and has a high mobility in soil and has the tendency to leach to groundwater. TAME is highly odorous and has a low taste threshold in water.

The consumption volume of TAME is expected to increase continuously in the coming years adding risk to the general ground water quality. In that respect, some regions in the EU are more vulnerable areas than others because of their geomorphology.

3.3.5 Atmosphere

Conclusion (ii).

Conclusion (ii) applies to direct effects of atmospheric emissions of TAME from all assessed environmental scenarios.

A PNEC has not been calculated for the atmosphere. Therefore direct PEC/PNEC ratio for the environment can not be derived. Specific endpoints like phytotoxicity have not been tested in this risk assessment process.

Any specific problem regarding TAME emissions into the atmosphere has not been identified in this environmental risk assessment. However, it has been concluded here, that atmospheric TAME emissions should not be handled separately in the ESR (793/93) programme, but in the general scope of air quality issues in the EU.

3.3.6 Secondary poisoning

Conclusion (ii).

This conclusion applies to all environmental compartments and assessment endpoints.

3.3.7 Marine environment

Conclusion (iii).

1. **Conclusion (iii)** applies to intermittent release scenario for storage tank bottom waters at terminal site.

2. **Conclusion (iii)** applies also to generic assessment for transportation, storage and delivery of petrol at terminal sites (see risk characterisation for fresh surface water).

4 HUMAN HEALTH

4.1 HUMAN HEALTH (TOXICITY)

4.1.1 Exposure assessment

4.1.1.1 Occupational exposure

Almost all exposure levels available originate from Finnish studies or industry reports, which make it difficult to evaluate the representativeness of the data for other EU-countries. Exposure assessment is generally evaluated based on studies, in which the average content of TAME in fuels handled was about 5%. In Finland 95 RON gasoline nowadays typically contains 7-8% and in 98 grade about 2%, respectively. Therefore, the use of estimations based on 5% seems justified as the level is below 4% in the other EU member states.

Exposure to TAME occurs almost exclusively as a blending component in fuel. The amount used varies from one brand (95, 98 or 99 RON) to another, with divergences even within the same brand due to production circumstances.

The main route of exposure is inhalation. This conclusion is based on the fact that due to technical developments skin contact to liquid fuel has been minimised in most work tasks. The EASE-estimation of dermal exposure may therefore be unrealistic. An exception to this is manual work tasks like car motor and fuel pump repair, as well as accidental spill in connection with transfer of fuel from small jerry cans to tanks of 2-stroke engines. Evaluating the potential dermal exposure resulting from e.g. splashes (100 mg equals 1-2 droplets depending on drop size) on the skin or clothing the loss due to evaporation should be accounted for. TAME is a medium volatile compound, which means that it will take 8 s for 1 mg/cm² to evaporate from the skin and accordingly the dermal exposure will be reduced because of the shortened retention time of the substance on the skin.

The EASE-estimation of inhalation exposure for the transportation and distribution seemed to be overestimated in comparison with the measured exposure levels. This is supposed to depend on the fact that the main part of these work procedures is supervision with only minor exposure potential.

In the summary table below, the work scenarios identified for occupational exposure to TAME are summarised. The duration and frequency of exposure, numerical values for measured typical inhalation exposure (calculated median value) and reasonable worst case (calculated 90th percentile) are given. Modelled EASE estimation of inhaled and dermal exposure is also presented. For each work scenario except for refuelling the statistical value best representing the exposure was selected. For the selection, one decisive criterion was sampling time in relation to the time of a work day. For refuelling median and RWC-values are average values of all measured refuelling results. The lower exposure level measured at Stage II was excluded, thus the summary result represent only Stage I refuelling.

Table 4.1 Summary of the occupational exposure assessment

				Inhalation				Dermal			
				Reasonable worst case 90th percentile		Typical concentration		Reasonable worst case		Daily dose	
Scenario	Activity [1]	Frequency days/year	Duration hours/day	TWA 8h, mg/m³	Method[2]	TWA 8-hour, mg/m³	Method [2]	mg/cm²/d	Method [2]	mg	Method [2]
Production	Long term	200	2	1.8	Measured	0.46	Measured	Negligible			
Formulation											
Transporting	Long term	50	4	1.2	Measured	0.23	Measured	0.-0.0055 (5 vol %)	EASE	2.1	EASE
Distribution	Long term	200	3	0.6	Measured	0.12	Measured	0-0.005 (5 vol %)	EASE	2.1	EASE
Uses											
Service attendants (refuelling)	Short term Long-term	200	2	14 2.8	Measured Estimated	2.5 0.5	Measured Estimated	0.05-0.25 (5 vol %)	EASE	100	EASE
Car motor repair	Long term	150	3	1.5	Measured*	1.0	Measured*	0.05-0.25 (5 vol %)	EASE	210	EASE
Fuel pump repair	Long-term	100	4	5.5	Measured	0.9	Measured	0.05-0.25 (5 vol %)	EASE	100	EASE
Other	Long- term	150	3	0.21	Measured	0.19	Measured	0.0.005 (5 vol %)	EASE	2.1	EASE

1) Full shift, short term, etc.
2) Measured, EASE, Expert judgment, Calculated, etc.
* Evaluated from benzene exposure of car repair from Laitinen's study

4.1.1.2 Consumer exposure

A reasonable worst-case scenario concerns a person, who is exposed to TAME at the gasoline station during and after refuelling of the car and who also lives near a gasoline station (50 m). Commuting in a car or in a bus is also considered. The total dose for a reasonable worst case scenario is 3.27-17.8 µg/kg of bw/day (see **Table 4.2**). In some cases, the same person might also be exposed to an elevated concentration of TAME in the tap water. It is reasonable to assume that in some cases these two scenarios, i.e. 1) high inhalation exposure due to vicinity to a production or formulation plant or a service station and 2) elevated TAME concentration in contaminated tap water might coincide. The total dose of TAME, which concerns the reasonable worst-case scenario, is based on the currently available data. It is not possible to present an accurate estimate on the percentage of population, which is exposed to this dose level. It is suggested that this percentage of the population is much below 1%.

High concentrations of TAME (5-150,000 µg/l) have been observed in ground water in Finland near petrol stations. Since the higher concentration range is much above the odour and taste threshold of TAME, it is assessed that consumers may only temporarily be exposed to the high concentrations. Therefore, these data are not used in the reasonable worst-case scenario (see **Table 4.2**). However, these measurements do give rise to concern of unacceptable ground-water contamination and will be discussed in the risk characterisation chapter. This conclusion is similar to that drawn in the RAR of MTBE.

Table 4.2 Exposure to TAME via inhalation and via tap water, normal scenario and reasonable worst case scenario

Relevant area/scenario	Source of TAME	Duration of exposure, normal/RWC	Normal Concentration $\mu g/m^3$	Normal Dose µg/day 1)	Concentration used to calculate RWC dose $\mu g/m^3$	RWC Dose µg/day 1)
Inhalation						
Urban background	Car exhausts, rain (?)	22/10 hours/day	0.1	1.8	0.1	0.83
Perimeter of production and formulation plants	Industry	0/12	-	-	1-100	10-996
Perimeter of gasoline stations	Gasoline stations, car exhausts	0/12 hours/day	-	-	0.6-2.1	6.7-20.9
Commuting in car or bus	Car exhausts	2 hours/day	2.3-10.4	3.8-17.3	2.3-10.4	3.8-17.3
Pump area of gas station	Refuelling, leaks, cars	1-5 min./d, 2-3 visits/week	31	0.1-0.9	31	0.1-0.9
Refuelling, Stage I station	Gasoline pistol	1 min./d, 2-3 visits/week	-	-	1,900	7.6-11.4

Table 4.2 continued overleaf

Table 4.2 continued Exposure to TAME via inhalation and via tap water, normal scenario and reasonable worst case scenario

Relevant area/scenario	Source of TAME	Duration of exposure, normal/RWC	Normal Concentration µg/m³	Normal Dose µg/day 1)	Concentration used to calculate RWC dose µg/m³	RWC Dose µg/day 1)
Tap water ingestion						
Urban background in the normal and petrol station in the RWC scenario	Car exhausts, rain, leaks and spills at petrol stations	-	< 0.1µg/l	< 0.2	100µg/l	200
Total exposure µg/kg b.w. day 3)				0.10-0.29	3.27-17.82	

1) Respiratory volume is about 20m³/24 hours=0.83 m³/hour=0.014m³/minute (uptake % not considered). It is assumed that ingestion of tap water is 2 l/day.
2) Dose of an adult (70 kg) is calculated.

4.1.2 Effects assessment: Hazard identification and dose (concentration) - response (effect) assessment

4.1.2.1 Toxicokinetics, metabolism and distribution

TAME is absorbed efficiently from the rat intestine. TAME is rapidly absorbed from lungs; in studies with human volunteers, the respiration net uptake is 50%. The maximum plasma concentration of humans after 50 ppm TAME exposure for 4 hours was 13.2 µmol/L. About one third or less of a percutaneous TAME dose is absorbed. Based on a human volunteer study with, MTBE, a dermal permeation coefficient of 0.028 cm/h was found.

In rat, TAME is distributed evenly throughout the body and is eliminated via respiration, urine and faeces, urine being the main route of elimination while excretion in faeces is only a few percent at maximum.

The elimination from human blood was rapid after the end of inhalation exposure and it occurred in two phases. The blood half-lives were between 1.2 and 6.3 hours with relatively big individual differences between test subjects. The limit of TAME detection was reached after 12 hours. In rat, the removal via respiration increases with higher doses. The primary enzyme responsible for the metabolism of TAME to tert-amyl alcohol in humans is cytochrome 2A6 mainly present in liver. This is the same enzyme which converts MTBE to tert-butyl alcohol and formaldehyde. The main human urine metabolites are 2-methyl-2,3-butanediol, 2-hydroxy-2-methylbutyric acid and 3-hydroxy-3-methylbutyric acid. Free and conjugated TAA and TAME were only minor metabolites in urine.

The absorption percentages to be taken to risk characterisation are 100% for oral, 30% for dermal and 50% for inhalation exposure route.

4.1.2.2 Acute toxicity

The LC_{50} value via inhalation is over 5,400 mg/m³ in rats. No dermal studies were available. The predicted oral LD_{50} in rat was for females 1,602 mg/kg, males 2,417 mg/kg and combined 2,152 mg/kg. TAME can cause slight irritation of eyes and the upper respiratory tract and drying of mouth at air concentrations of 60 mg/m³ but these effects are marginal.

4.1.2.3 Corrosion, irritation and sensitisation

TAME is not corrosive. TAME did not cause skin irritation. In the eye irritation test, slight redness and swelling of the conjunctiva were recorded. However, the effects were reversible after 7 days of instillation of the test substance. The mean 24-48-72-score does not imply classifying TAME as eye irritant. In the human volunteer study with six males described in the toxicokinetics and acute toxicity sections, slight irritation of eyes, throat and nose were reported at an air concentration of 60 mg/m^3. TAME was not considered sensitising in a guinea pig Bühler test.

4.1.2.4 Repeated dose toxicity

A NOAEC of 250 ppm (1,060 mg/m^3) is selected for respiratory exposure based on the organ weight increases seen in the 90-day study with male and female F-344 rats. For the oral route, a LOAEL of 125 mg/kg is selected based on the dose related adrenal weight increase at the dose of 125 mg/kg and higher in male rats in the 28-day study. No classification is warranted based on the effects noted.

4.1.2.5 Mutagenicity

Although a clear positive result was obtained in the *in vitro* CHO clastogenicity assay in the presence of S9 activation, it is probable that the cause for this may have been formaldehyde, which is transiently formed during metabolism. However, formaldehyde is not likely to be a concern in *in vivo* because it is efficiently cleared from the tissues by formaldehyde dehydrogenase. This is supported by the result of a valid mouse micronucleus study, which showed that TAME does not cause chromosome aberrations *in vivo*. Moreover, the compound structure does not give rise to concern for mutagenic activity.

In conclusion, TAME is not considered mutagenic.

4.1.2.6 Carcinogenicity

Results are available from a single oral carcinogenicity study. The dosing regime used to treat the animals was unusual and only two dose levels were used. Moreover, the animals were allowed to live out their natural life span and no adjustment for mortality was available. The neoplasia in this study were of lymphoid origin and derived from cells originating from the bone marrow, however, results from a mouse micronucleus study with TAME, which measure the substance's ability to induce damage in chromosomes of the bone marrow cells, was negative. The publication's reporting was inadequate in many aspects resulting in a low level of confidence of the results. Therefore, an analysis of effective group numbers and tumour incidence were difficult to analyse. Negative results from mutagenicity studies on TAME suggest that mutagenicity is not a contributing mode of action in the formation of tumours. Lack of alert from molecule structure and results of carcinogenicity testing for the related substance MTBE, suggest that carcinogenicity is not an endpoint of concern. Due to lack of confidence in the study results, risk characterisation is not performed on the carcinogenicity end-point.

4.1.2.7 Toxicity for reproduction

2-generation study in rats

The NOAEC for adult systemic toxicity is 250 ppm, for reproductive toxicity 3,000 ppm and for offspring toxicity 250 ppm. The effects seen with TAME were not consistent with those expected for an endocrine disrupting agent.

Developmental study in rats

Maternal toxicity was present at 1,500 and 3,500 pm and it was manifested as reduction of body weight, reduction of weight gain and various clinical signs, especially at the top dose group. The NOAEC for maternal toxicity is 250 ppm. Based on the weight reductions seen in the litters at 3,500 ppm and the absence of embryo-foetal effects at 250 or 1,500 ppm doses, 1,500 ppm is chosen as the NOAEC for developmental toxicity in Sprague-Dawley rat.

Developmental study in mice

Four dams died during the first four days of exposure in the 3,500 ppm dose group. At 1,500 (11%) and 3,500 ppm (20%), the maternal liver absolute and relative weights were significantly increased. The toxicity noted at 1,500 ppm (11% liver weight increase) is likely to represent a slight adaptation of the liver rather than a significant maternal toxicity, which would account for the foetal malformations. Therefore, the maternal toxicity NOAEC is set at 1,500 ppm. The NOAEC for developmental effects is set to 250 ppm based on the malformations (cleft palate) seen at 1,500 and at a higher incidence at 3,500 ppm in CD-1 mice.

4.1.2.8 Conclusion

Toxicity to fertility

NOAEC of 3,000 ppm (12,720 mg/m^3) is selected. Although a statistically significant increase of abnormal sperm counts seen in F0 male rats at 1,500 ppm and 3,000 ppm, the effects on sperm counts occurred together with considerable systemic toxicity at the same dose level and they were within the historical controls. Moreover, no other significant effects on reproductive performance were reported at this level. This end-point will not be considered in the risk characterisation.

Developmental toxicity

A NOAEC of 250 ppm (1,063 mg/m^3) is selected for developmental effects based on the malformations (cleft palate) in mice at 1,500 ppm and 3,500 ppm and based on the reduced body weights seen in the F1-offspring of the 2-generation study. Although slight maternal toxicity is seen at 1,500 ppm, this alone is not seen as sufficient to explain the malformations in mice.

4.2 RISK CHARACTERISATION

4.2.1 Workers

4.2.1.1 Acute toxicity

The smallest MOSs were the service station and fuel pump repair, with MOSs of 15 and 61 when calculated from the 50 ppm air concentration obtained from a volunteer study, where slight irritation was reported. Although the MOS at service station appears quite low it is not considered to be a concern based on the low severity of the effect. When using lethality (rat LD_{50}) as the acute toxicity end-point, the MOSs would be several magnitudes higher. **Conclusion (ii)** is drawn for all scenarios.

4.2.1.2 Repeated dose toxicity

No local effects of concern were noted in the hazard assessment. The smallest MOS in the repeated dose toxicity scenarios was found in the car motor repair (123) in dermal and combined exposure. All other combined or dermal exposure scenarios had MOSs of over 150 not causing concern. In inhalation exposure, the lowest MOS was 303 (fuel pump repair) and it was not considered to cause concern. **Conclusion (ii)** is drawn for all scenarios.

4.2.1.3 Mutagenicity

Mutagenicity is not considered a concern. **Conclusion (ii)** is drawn.

4.2.1.4 Developmental toxicity

The smallest MOS is noted in the car motor repair (128), based on a NOAEL from a developmental toxicity study in mice. This was not considered to cause concern. **Conclusion (ii)** is drawn in all scenarios.

Table 4.3 Overview of the conclusions with respect to occupational risk characterisation

		Acute toxicity		Local toxicity after single or repeated exposure			Sensiti sation	Repeated dose toxicity Systemic			Muta genicity	Reproductive toxicity (combined)
		Dermal	Inhalation	Dermal	Inhalation	Eye		Dermal	Inhalation	Combined		
Production	MOS	n.d.	118	-	-	-	-	-	589	962	-	992
	Concl.	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii
Transportation	MOS	n.d.	177	-	-	-	-	12,500	883	1,250	-	1,290
	Concl.	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii
Distribution	MOS	n.d.	353	-	-	-	-	12,500	1,767	2,500	-	2,580
	Concl.	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii
USES												
Service station	MOS	n.d.	15	-	-	-	-	291	379	198	-	205
	Concl.	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii
Car motor repair	MOS	n.d.	141	-	-	-	-	139	707	123	-	128
	Concl.	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii
Fuel pump repair	MOS	n.d.	61	-	-	-	-	291	303	184	-	190
	Concl.	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii
Other work groups	MOS	n.d.	1,010	-	-	-	-	12,500	5,048	4,167	-	4,300
	Concl.	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii

n.d. no data

4.2.2 Consumers (Humans exposed via the environment)

4.2.2.1.1 Risk characterisation for consumers

Due to their negligible nature, the combined risks from consumer and indirect exposure via the environment were assessed in the consumer Section 4.1.3.3. As no margin of safety lower than 2,120 was obtained, all end points resulted in **Conclusion (ii)**.

4.2.3 Risk characterisation for humans exposed via the environment

These risks are assessed in the consumer section. For combined consumer exposure and exposure via the environment, no margin of safety lower than 2,120 was obtained. Thus, all end points resulted in **Conclusion (ii)**.

4.2.4 Risk characterisation for combined exposure

Because the contribution of consumer exposure or indirect exposure via the environment is negligible compared to the occupational exposure and would practically make no change in the worker MOSs, no assessment of combined exposure is conducted.

4.3 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

4.3.1 Risk characterisation

4.3.1.1 Workers

Flammability could pose a fire and explosion risk in situations, where TAME vapour is generated at high concentrations. This is possible also in the open air if sparks (electric or also static) or open fire are present.

However, the flammability is a well-known feature of neat TAME vapour and necessary precautions are normally taken to prevent ignition during storage and when transferring TAME. Moreover, the professional workers are aware of the characteristics of TAME and the entrance of outsiders to the production area is not allowed. In other scenarios concerning TAME as an additive in petrol, the risk arises from the totality of flammable elements in automotive petrol vapours, where the part of TAME is minor.

Conclusion

Flammability is not considered to cause a significant risk to workers. **Conclusion (ii)** is drawn.

4.3.1.2 Consumers

There are no relevant scenarios.

4.3.1.3 Humans exposed via the environment

TAME has a pronounced taste and odour in water at low concentrations. However, there may be significant differences in the odour and taste thresholds depending on individual sensitivity, which can be affected e.g. by smoking. When the odour and taste thresholds in water are exceeded, the contaminated drinking water is normally not used, but another supply of drinking water is then utilised. When large and important reservoir of ground water serving as drinking water supply is contaminated, the consequences can be remarkable in terms of costs and as well as in terms of a need for temporary arrangements for drinking water. The severity of the consequences of groundwater contamination may vary greatly between countries depending on, e.g. the level of groundwater utilisation for drinking water and the condition of petrol stations' underground storage tanks in important groundwater areas.

The present risk characterisation is formulated keeping in mind that

- TAME is not considered to cause adverse health or ecotoxic effects at taste and odour threshold level.
- Even the relatively small amount of TAME may render large reserves of ground water useless.
- The organoleptic properties of water are also covered by the EU directive on the "Quality of Water Intended for Human consumption" (Council Directive 98/83/EC).

As described in the environmental part of this report the contamination of ground water is mainly caused by leaking underground storage tanks and spillage from overfilling the tanks. Therefore, it is justified to conclude that TAME is causing a risk for the aesthetic quality of drinking water.

Conclusion (iii) is drawn for indirect exposure to humans via drinking water based on the risk on the aesthetic properties of drinking water.

5 RESULTS

5.1 INTRODUCTION

The risk assessment of TAME is based on current practices related to the life-cycle of the substance produced in or imported into the European Community as described in the risk assessment forwarded to the Commission by the Member State Rapporteur.

The risk assessment has, based on the available information, determined that in the European Community the substance is mainly used as a blending component of standard unleaded petrol.

Other uses are as on-site intermediate in neat form.

5.2 ENVIRONMENT

Atmosphere

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

This conclusion is reached because the risk assessment shows that direct risks arising from the use of TAME are not expected. Risk reduction measures already being applied are considered sufficient. However, this conclusion does not apply directly to general air quality issues. Atmospheric TAME emissions should not be handled separately in the ESR (793/93) program, but in the general scope of air quality issues in the EU.

Terrestrial ecosystem

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

This conclusion is reached because the risk assessment shows that risks are not expected. Risk reduction measures already being applied are considered sufficient.

Groundwater

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

This conclusion is reached because of concerns for the potability of ground water in respect of taste and odour as a consequence of exposure arising from leaking underground storage tanks and spillage from overfilling of the storage tanks.

Aquatic ecosystem (incl. sediment and marine environment)

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

This conclusion is reached because of concerns for the aquatic ecosystem as a consequence of exposure arising from releases to surface water from:

- terminal site’s storage-tank bottom waters (intermittent release) and

- transportation, storage and delivery of petrol at terminal sites with direct discharge.

Risk reduction measurements to the aquatic compartment should also cover possible risks to sediment.

Micro-organisms in the sewage treatment plant

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

This conclusion is reached because the risk assessment shows that risks are not expected. Risk reduction measures already being applied are considered sufficient.

Secondary poisoning

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

This conclusion is reached because the risk assessment shows that there is at present no need for further information and/or testing or for risk reduction measures. This conclusion applies to all environmental compartments and assessment endpoints.

5.3 HUMAN HEALTH

5.3.1 Human health (toxicity)

5.3.1.1 Workers

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) applies to acute toxicity, repeated dose toxicity and reproductive toxicity (development). Irritation, sensitisation or mutagenicity were not included in the risk characterisation because these endpoints were assessed not to pose a hazard. Carcinogenicity was not taken forward to the risk characterisation because of the inadequacy of the available data.

5.3.1.2 Consumers

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) applies to acute toxicity, repeated dose toxicity and reproductive toxicity (development). Irritation, sensitisation or mutagenicity were not included in the risk characterisation because these endpoints were assessed not to pose a hazard. Carcinogenicity was not taken forward to the risk characterisation because of the inadequacy of the available data.

5.3.1.3 Combined exposure

No assessment was conducted on combined exposure, due to negligible additional contribution to risk.

5.3.1.4 Humans exposed via the environment

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

The risk assessment shows that risks are not expected. Risk reduction measures already being applied are considered sufficient.

5.3.2 Human health (risks from physico-chemical properties)

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Conclusion (iii) applies to drinking water contamination and concerns for the potability of drinking water in respect of taste and odour as a consequence of exposure arising from leaking underground storage tanks and spillage from overfilling of the storage tanks.

European Commission
DG Joint Research Centre, Institute of Health and Consumer Protection
Toxicology and Chemical Substances (TCS)
European Chemicals Bureau
**EUR 22236 EN/2 European Union Risk Assessment Report Summary
2-methoxy-2-methylbutane (TAME)**

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The summary report provides the comprehensive risk assessment of the substance 2-methoxy-2-methylbutane (TAME). It has been prepared by Finland in the frame of Council Regulation (EEC) No. 793/93 on the evaluation and control of the risks of existing substances, following the principles for assessment of the risks to humans and the environment, laid down in Commission Regulation (EC) No. 1488/94.

Part I - Environment

This part of the evaluation considers the emissions and the resulting exposure to the environment in all life cycle steps. Following the exposure assessment, the environmental risk characterisation for each protection goal in the aquatic, terrestrial and atmospheric compartment has been determined.

The environmental risk assessment concludes that there is concern for the aquatic ecosystem (including marine environment) because of exposure arising from intermittent releases to surface water from storage-tank bottom-waters at terminal sites and from releases to surface water from transportation, storage and delivery of petrol at terminal sites with direct discharge. Risk reduction measurements to the aquatic compartment should also cover possible risks to sediment.

There is concern for groundwater as well, in particular concern of potability of groundwater in respect to taste and odour as a consequence of exposure rising from leaking underground storage tanks and tank piping, as well as spillages from overfilling the tanks.

There is at present no concern for the atmospheric and terrestrial compartments, micro organisms in the sewage treatment plant and secondary poisoning.

Part II - Human Health

This part of the evaluation considers the emissions and the resulting exposure to human populations in all life cycle steps. The scenarios for occupational exposure, consumer exposure and humans exposed via the environment have been examined and the possible risks have been identified.

The human health risk assessment concludes that there is concern arising from the physico-chemical properties of the substance in relation to drinking water contamination and potability of drinking water in respect of taste and odour as a consequence of exposure arising from leaking underground storage tanks and tank piping as well as spillages from overfilling of the storage tanks.

There are no concerns for workers, consumers and humans exposed via the environment with respect to the toxicity of TAME.

The conclusions of this report will lead to risk reduction measures to be proposed by the Commission's committee on risk reduction strategies set up in support of Council Regulation (EEC) N. 793/93.