

# I U C L I D

# D a t a s e t

Existing Chemical            Substance ID: 108-10-1  
CAS No.                      108-10-1  
EINECS Name                4-methylpentan-2-one  
EINECS No.                 203-550-1  
Molecular Formula         C6H12O

Dataset created by:        EUROPEAN COMMISSION - European Chemicals Bureau

This dossier is a compilation based on data reported by the European Chemicals Industry following 'Council Regulation (EEC) No. 793/93 on the Evaluation and Control of the Risks of Existing Substances'. All (non-confidential) information from the single datasets, submitted in the IUCLID/HEDSET format by individual companies, was integrated to create this document.

The data have not undergone any evaluation by the European Commission.

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**1.0.1 OECD and Company Information**

**Name:** Atochem  
**Street:** 4, Cours Michelet  
**Town:** 92080 Paris la Defense  
**Country:** France

**Name:** Cheminova Agro A/S  
**Street:** P.O. Box 9  
**Town:** 7620 Lemwig  
**Country:** Denmark

**Name:** Huels AG  
**Street:** Postfach  
**Town:** D-45764 Marl  
**Country:** Germany

**Name:** Petrasol B.V.  
**Street:** P.O.Box 222  
**Town:** 4200 AE Gorinchem  
**Country:** Netherlands  
**Phone:** +31 183 630555  
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**Name:** PPG Industries  
**Street:** 3, Z.A.E Les Dix Muids B.P.89  
**Town:** F 59583 MARLY Cedex MARLY Cedex  
**Country:** France  
**Phone:** +33 3 27 19 35 00  
**Telefax:** +33 3 2719 3513

**Name:** SHELL FRANCE  
**Street:** 89 bld Franklin Roosevelt  
**Town:** 92564 Rueil Malmaison  
**Country:** France  
**Phone:** 33 1 47.14.71.00  
**Telefax:** 33 1 47.14.82.99  
**Telex:** SHELL 615013F

**Name:** Shell Nederland Chemie B.V.  
**Street:** P.O. Box 3030  
**Town:** 3190 GH Hoogvliet-Rotterdam  
**Country:** Netherlands  
**Phone:** +31-10-2317005  
**Telefax:** +31-10-2317125

**Name:** Union Carbide Benelux  
**Street:** Norderlaan 147  
**Town:** 2030 Antwerpen  
**Country:** Belgium

**Name:** ZENECA Specialties  
**Street:** PO Box 42  
**Town:** M9 3DA Manchester  
**Country:** United Kingdom

### **1.0.2 Location of Production Site**

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### **1.0.3 Identity of Recipients**

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## **1.1 General Substance Information**

**Substance type:** organic  
**Physical status:** liquid

### **1.1.1 Spectra**

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## **1.2 Synonyms**

2-Methylpentan-4-on

**Source:** Huels AG Marl

2-Pentanone, 4-methyl

**Source:** Cheminova Agro A/S Lemwig

2-Pentanone, 4-methyl-

**Source:** Huels AG Marl

4-Methyl-2-oxopentan

**Source:** Huels AG Marl

4-Methylpentan-2-on

**Source:** Huels AG Marl

4-méthyl-2-pentanone

**Source:** PPG Industries MARLY Cedex

hexanone

**Source:** Union Carbide Benelux Antwerpen

Hexon

**Source:** Huels AG Marl

Isobutylmethylketon

**Source:** Huels AG Marl

Isopropylacetone

**Source:** Huels AG Marl

Methyl isoButyl Ketone

**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

methyl isobutyl ketone

**Source:** Union Carbide Benelux Antwerpen

Methyl Isobutyl Ketone

**Source:** ZENECA Specialties Manchester

Methyl isobutyl ketone

**Source:** Cheminova Agro A/S Lemwig

Methylisobutyl ketone; 4-methyl-pentan-2-on

**Source:** ISIS/RISKLINE, release VI, 1997, Haskoning  
Petrasol B.V. Gorinchem

Methylisobutylketon

**Source:** Huels AG Marl

MIBK

**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam  
Union Carbide Benelux Antwerpen  
Huels AG Marl

MIBK ; Methylisobutylketone-Isopropylacetone-Hexanone.

**Source:** SHELL FRANCE Rueil Malmaison

MIBK; Methylisobutylcetone

**Source:** Atochem Paris la Defense

MIK

**Source:** Huels AG Marl

méthylisobutylcétone

**Source:** PPG Industries MARLY Cedex**1.3 Impurities**

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**1.4 Additives**

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**1.5 Quantity****Quantity** 100 000 - 500 000 tonnes

### 1.6.1 Labelling

**Labelling:** as in Directive 67/548/EEC  
**Symbols:** F  
Xn  
D  
**Specific limits:** no data  
**R-Phrases:** 1  
**S-Phrases:** (2) Keep out of reach of children  
(9) Keep container in a well-ventilated place  
(16) Keep away from sources of ignition - No smoking  
(29) Do not empty into drains

### 1.6.2 Classification

**Classification:** as in Directive 67/548/EEC  
**Class of danger:** corrosive  
**R-Phrases:** (20) Harmful by inhalation

**Classification:** as in Directive 67/548/EEC  
**Class of danger:** highly flammable  
**R-Phrases:** (11) Highly flammable

**Classification:** as in Directive 67/548/EEC  
**Class of danger:** irritating  
**R-Phrases:** (36/37) Irritating to eyes and respiratory system

**Classification:** as in Directive 67/548/EEC  
**Class of danger:**  
**R-Phrases:** 6

### 1.7 Use Pattern

**Type:** type  
**Category:** Non dispersive use

**Type:** type  
**Category:** Use in closed system

**Type:** type  
**Category:** Use resulting in inclusion into or onto matrix

**Type:** type  
**Category:** Wide dispersive use

**Type:** industrial  
**Category:** Basic industry: basic chemicals

**Type:** industrial  
**Category:** Chemical industry: used in synthesis

**Type:** industrial  
**Category:** Paints, lacquers and varnishes industry

**Type:** use  
**Category:** Adhesive, binding agents

**Type:** use  
**Category:** Intermediates

**Type:** use  
**Category:** Pesticides

**Type:** use  
**Category:** Pharmaceuticals

**Type:** use  
**Category:** Solvents

**Type:** use  
**Category:** other: dewaxing agent for lubricating oils

**Type:** use  
**Category:** other: extraction solvent for pharmaceuticals

**Type:** use  
**Category:** other

### 1.7.1 Technology Production/Use

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### 1.8 Occupational Exposure Limit Values

**Type of limit:** BAT (DE)  
**Limit value:** 3500 µg/l  
**Country:** Germany  
**Remark:** To be determined in urine at the end of exposure / shift  
**Source:** Huels AG Marl

**Type of limit:** MAC (NL)  
**Limit value:** 240 mg/m<sup>3</sup>  
**Remark:** Skin notation  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

(1)

**Type of limit:** MAK (DE)  
**Limit value:** 400 mg/m<sup>3</sup>  
**Short term expos.**  
**Limit value:** 2000 mg/m<sup>3</sup>  
**Schedule:** 30 minute(s)  
**Frequency:** 2 times  
**Source:** Atochem Paris la Defense

(2)

Type of limit: MAK (DE)  
Limit value: 400 mg/m3  
Short term expos.  
Limit value: 1600 mg/m3  
Schedule: 15 minute(s)  
Frequency: 4 times  
Country: Germany  
Source: Huels AG Marl

Type of limit: MAK (DE)  
Limit value: 100 ml/m3  
Short term expos.  
Limit value: 100 ml/m3  
Schedule: 15 minute(s)  
Frequency: 4 times  
Country: Germany  
Source: Huels AG Marl

Type of limit: TLV (US)  
Limit value: 205 mg/m3  
Short term expos.  
Limit value: 307 mg/m3  
Schedule: 15 minute(s)  
Source: Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

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Type of limit: TLV (US)  
Limit value: 205 mg/m3  
Short term expos.  
Limit value: 307 mg/m3  
Schedule: 8  
Source: Union Carbide Benelux Antwerpen

(4)

Type of limit: TLV (US)  
Limit value:  
Remark: 100 ppm PEL-TWA (OSHA)  
Source: Union Carbide Benelux Antwerpen

Type of limit: TLV (US)  
Limit value: 205 mg/m3  
Short term expos.  
Limit value: 307 mg/m3  
Schedule: 15 minute(s)  
Frequency: 8 times  
Source: Atochem Paris la Defense

(2)

**Type of limit:** other: VME  
**Limit value:** 205 mg/m3  
**Country:** France  
**Source:** Atochem Paris la Defense

(5)

**Type of limit:** other: VME  
**Limit value:** 205 mg/m3  
**Short term expos.**  
**Limit value:** 307 mg/m3  
**Remark:** Use local exhaust ventilation.  
 Hand protection : neoprene or nitrile gloves.  
 Eye protection : safety monogoggles.  
 Body protection : standard issue work protection.  
 safety shoes or boots-chemicals resistant  
**Source:** SHELL FRANCE Rueil Malmaison

**Type of limit:**  
**Limit value:** 205 mg/m3  
**Country:** VME France  
**Source:** PPG Industries MARLY Cedex

### 1.9 Source of Exposure

**Remark:** As the quantities of this substance placed on the EU market by Union Carbide Benelux N.V. are normally sourced from the manufacturing facilities of its U.S. parent company, no exposure can arise within the EU from the manufacture of these quantities. The comments below on exposure are restricted to uses for which Union Carbide believes its customers use this substance.

Major use(s): As a solvent for paints and chemical processes, and as a chemical intermediate.

Sources of human exposure: Some human exposure in consumer uses via inhalation and/or skin contact. Quantitative estimates are not available. Negligible human exposure in industrial uses, assuming appropriate industrial hygiene and personal protective precautions are observed.

Sources of environmental exposure: Releases to the atmosphere occur from consumer uses of products containing this substance, and certain industrial applications. Releases to water can occur from consumer applications. Industrial uses release negligible quantities to water, as the substance readily biodegrades in waste water treatment systems. Quantitative estimates of releases to air and water are not available.

**Source:** Union Carbide Benelux Antwerpen

**Remark:** Continuous closed process.  
Hydrogenation of mesityl oxide. Formation of methylisobutylcarbinol and methylisobutylketone.  
Purification by distillation.  
One production site.  
Explosivity detectors  
Fumes detectors  
Protective measures: goggles; gloves and glasses  
Losses in air: < 0.0001% of the production  
Losses in effluents: very low

**Source:** Atochem Paris la Defense

**Remark:** Inhalation or skin contact when loading, unloading, using the product.  
In case of accidental release, product may contaminate the environment.

**Source:** SHELL FRANCE Rueil Malmaison

### **1.10.1 Recommendations/Precautionary Measures**

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### **1.10.2 Emergency Measures**

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### **1.11 Packaging**

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### **1.12 Possib. of Rendering Subst. Harmless**

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### **1.13 Statements Concerning Waste**

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#### **1.14.1 Water Pollution**

**Classified by:** KBwS (DE)  
**Labelled by:** KBwS (DE)  
**Class of danger:** 1 (weakly water polluting)  
**Country:** Germany  
**Remark:** Katalog-Nr. 137  
**Source:** Huels AG Marl

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**1.14.2 Major Accident Hazards**

**Legislation:** Stoerfallverordnung (DE)  
**Substance listed:** yes  
**Country:** Germany  
**Remark:** Anhang IV Kat. 6: leichtentzuendliche Fluessigkeit  
**Source:** Huels AG Marl

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**1.14.3 Air Pollution**

**Classified by:** TA-Luft (DE)  
**Labelled by:** TA-Luft (DE)  
**Number:** 3.1.7 (organic substances)  
**Class of danger:** III  
**Country:** Germany  
**Remark:** Appendix E  
**Source:** Huels AG Marl

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**1.15 Additional Remarks**

**Remark:** TRANSPORT INFORMATION

UN Number: 1245  
Class: 3  
Packing Group: II  
Proper Shipping Name: Methyl isobutyl ketone

Sea (IMO)  
Class: 3.2  
Packing Group: II  
Symbol: Flammable liquid  
Marine Pollutant (Y/N): No

Rail/Road (RID/ADR)  
Class: 3  
Item: 3(b)  
Symbol: Flammable liquid  
Kemler Plate: 33/1245

Air (IATA/ICAO)  
Class: 3  
Packing Group: II  
Symbol: Flammable liquid

**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

**Remark:** Disposal: Incinerate in a furnace where permitted under national and local regulations. At very low concentrations in water, this product is biodegradable in a biological wastewater treatment plant.

Transport: 4-methyl-pentane-4-one is a class 3 product

according the ADR/RID/IMDG/ICAO regulations.  
This products is shipped in road/rail tankcars,  
tankcontainers/ISOtanks and smaller packages (e.g. drums)  
**Source:** Union Carbide Benelux Antwerpen

**Remark:** Recover or recycle if possible. Otherwise : incineration.  
Avoid electrostatic discharge generation.  
Earth all equipment.  
Avoid naked flames. Remove ignition sources. Avoid sparks.  
Do not smoke.  
Transport Information

UN number : 1245  
Class : 3  
Packing Group : II  
Proper Shipping Name : Methylisobutylketone

Sea (IMO)  
Marine Pollutant : No  
Symbol : Flammable liquid

Rail/Road (ADR/RID)  
Class : 3  
Item : 3 (b)  
Symbol : Flammable liquid  
Kemler Plate : 33/1245

Air (IATA/IACO)  
Class : 3  
Symbol : Flammable liquid  
**Source:** SHELL FRANCE Rueil Malmaison

### 1.16 Last Literature Search

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### 1.17 Reviews

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### 1.18 Listings e.g. Chemical Inventories

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### 2.1 Melting Point

**Value:** = -84 degree C  
**Decomposition:** no  
**Sublimation:** no  
**Method:** other  
**Year:** 1986  
**GLP:** no  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam  
**Test condition:** Method ASTM D 97 (7) (8)

**Value:** = -84 degree C  
**Source:** Huels AG Marl (9)

### 2.2 Boiling Point

**Value:** 114 - 117 degree C at 101.3 hPa  
**Decomposition:** no  
**Method:** other  
**Year:** 1993  
**GLP:** no  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam  
**Test condition:** Method ASTM D 1078 (8)

**Value:** 114 - 117 degree C at 1013 hPa  
**Source:** Huels AG Marl (9)

### 2.3 Density

**Type:** density  
**Value:** = .802 g/cm<sup>3</sup> at 20 degree C  
**Source:** Huels AG Marl (9)

**Type:** density  
**Value:** 799 - 802 kg/m<sup>3</sup> at 20 degree C  
**Year:** 1992  
**GLP:** no  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam  
**Test condition:** Method ASTM D 4052 (8)

#### 2.3.1 Granulometry

-

### 2.4 Vapour Pressure

**Value:** = 20 hPa at 20 degree C  
**GLP:** no  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam (8)

**Value:** = 21.5 hPa at 20 degree C  
**Source:** Huels AG Marl (9)

### 2.5 Partition Coefficient

**log Pow:** = 1.19  
**Method:** other (calculated): Leo, Hansch: Modifiziert, CLOPG3 computer program nach Leo und Weininger (1985).  
**Year:**  
**Source:** Huels AG Marl (10)

**log Pow:** = 1.25  
**Method:** other (calculated): Leo, Hansch: "Fragment constant method" nach Hansch und Leo (1979).  
**Year:**  
**Source:** Huels AG Marl (11)

**log Pow:** = 1.31 at 20 degree C  
**Method:** other (measured)  
**Year:** 1986  
**GLP:** no data  
**Remark:** Shaking Flask, Ponomona peer reviewed.  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam (12)

**log Pow:** = 1.31  
**Method:** other (measured): Messung, Gas-Fluessigkeits-Chromatographie  
**Year:**  
**Source:** Huels AG Marl (13)

**log Pow:** = 1.39  
**Method:** OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"  
**Year:**  
**Source:** Huels AG Marl (14)

### 2.6.1 Water Solubility

**Value:** = 20 g/l at 20 degree C  
**Qualitative:** of low solubility  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam (8)

**Value:** = 20 g/l at 20 degree C  
**Qualitative:** soluble  
**Source:** Huels AG Marl

(9)

### 2.6.2 Surface Tension

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### 2.7 Flash Point

**Value:** = 14 degree C  
**Type:** closed cup  
**Method:** other  
**Year:**  
**GLP:** no  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam  
**Test condition:** Method is IP 170

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**Value:** = 14 degree C  
**Type:** closed cup  
**Method:** other: DIN 51755  
**Year:**  
**Source:** Huels AG Marl

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**Value:** = 16 degree C  
**Type:** closed cup  
**Method:**  
**Year:**  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

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### 2.8 Auto Flammability

**Value:** = 460 degree C  
**Method:** other  
**Year:** 1990  
**GLP:** no  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam  
**Test condition:** Method is ASTM D 2155

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### 2.9 Flammability

**Result:** highly flammable  
**Method:** other  
**GLP:** no  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

**2.10 Explosive Properties**

**Result:** not explosive  
**Remark:** Vapour can form explosive mixtures in air  
Elf Atochem 1.4 - 7.5%  
Shell 1.3 - 8.0%  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam (15) (8)

**2.11 Oxidizing Properties**

**Result:** no oxidizing properties  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

**2.12 Additional Remarks**

**Remark:** Viskositaet bei 20 Grad C: 0.61 mPa x s.  
Zuendtemperatur : 460 Grad Celsius (DIN 51794)  
Explosionsgrenzen in Luft: 1,7 - 9,0 Vol.-%  
Bei Normaldruck ohne Zersetzung destillierbar.  
**Source:** Huels AG Marl (9)

### 3.1.1 Photodegradation

Type: air  
INDIRECT PHOTOLYSIS  
Sensitizer: OH  
Conc. of sens.: 500000 molecule/cm3  
Rate constant: = .00000000000141 cm3/(molecule \* sec)  
Degradation: = 50 % after 1.1 day  
Method: other (measured): AOP Computer Program, Vers. 1.53, Syracuse  
Research Center (based on Reference)  
Year: 1994 GLP:  
Test substance:  
Remark: Half-life refers to 24 hour-days  
Source: Huels AG Marl

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Type: air  
INDIRECT PHOTOLYSIS  
Sensitizer: OH  
Conc. of sens.: 1000000 molecule/cm3  
Rate constant: = .00000000000142 cm3/(molecule \* sec)  
Degradation: = 50 % after 13.6 hour(s)  
Method: OECD Guide-line draft "Photochemical Oxidative Degradation in  
the Atmosphere"  
Year: 1987 GLP: no data  
Test substance: as prescribed by 1.1 - 1.4  
Source: Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

### 3.1.2 Stability in Water

Type: abiotic  
Method:  
Year: GLP:  
Test substance:  
Remark: MIBK is not susceptible to hydrolysis under environmental  
conditions.  
Source: Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

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### 3.1.3 Stability in Soil

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### 3.2 Monitoring Data (Environment)

Type of  
measurement: concentration at contaminated site  
Medium: air  
Result: MIBK found in air space of 3 municipal waste treatment  
plants in Cincinnati, Ohio in 1982 (range <0.5-13 ppm).  
Source: Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

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**Type of measurement:** concentration at contaminated site  
**Medium:** ground water  
**Result:** During 1981-1982, MIBK was detected in leachate from municipal landfill at Granby, CT (range 25-150 ppb) Leachate from Southington, CT municipal landfill during 1982-1983 contained MIBK (range 172-263 microgram/litre)  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam (19) (20)

**Type of measurement:** concentration at contaminated site  
**Medium:** other: discharge water  
**Result:** MIBK detected in water discharged from an offshore (Shell Oil) production in Gulf of Mexico (concentration 190 ppb)  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam (21)

### 3.3.1 Transport between Environmental Compartments

**Type:** volatility  
**Media:** water - air  
**Method:** other  
**Year:** 1982  
**Result:** The volatilisation half-life of MIBK in the model river system according to Lyman et al (current 1m/s; wind 3 m/s; depth 1m) is calculated to be 10.8 hours. This is based on a calculated Henry's law constant of 11.1 Pa\*m<sup>3</sup>/mol.  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam (22)

### 3.3.2 Distribution

**Media:** air - biota - sediment(s) - soil - water  
**Method:** Calculation according Mackay, Level I  
**Year:** 1981  
**Remark:** Compartment distribution after equilibration.  
**Result:**  
Air: 79.60 %  
Water: 20.34 %  
Soil: 0.03 %  
Sediment: 0.03 %  
-----  
100.00 %  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam (23)

**Media:** air - biota - sediment(s) - soil - water  
**Method:** Calculation according Mackay, Level I  
**Year:**  
**Result:** Air: 71.048 %  
 Soil: 0.043 %  
 Water: 20.868 %  
 Sediment: 0.040 %  
 Biota: 0.000 %  
**Source:** Huels AG, Marl  
 Huels AG Marl  
**Test condition:** Data used:  
 Molar mass: 100.20 g/mol  
 Log Pow: 1.39  
 Vapour pressure: 2150 Pa  
 Water solubility: 20.0 g/l

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 Equations used for additional data:  
 $\log K_{oc} = 0.989 \log Pow - 0.346$   
 -----

Volumes used:  
 Air: 6 000 000 000  
 Soil: 45 000  
 Water: 7 000 000  
 Sediment: 35 + 21 000  
 Biota: 7

### 3.4 Mode of Degradation in Actual Use

**Remark:** In air MIBK is very rapidly degraded by reaction with OH-radicals. MIBK will disappear from the aquatic environment by evaporate and biodegradation.  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

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### 3.5 Biodegradation

**Type:** aerobic  
**Inoculum:** predominantly domestic sewage  
**Concentration:** 10 mg/l related to DOC (Dissolved Organic Carbon)  
**Degradation:** 99 % after 7  
**Result:** readily biodegradable  
**Method:** OECD Guide-line 301 E "Ready biodegradability: Modified OECD Screening Test"  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Source:** Huels AG Marl

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**Type:** aerobic  
**Inoculum:** activated sludge  
**Concentration:** 10 mg/l related to DOC (Dissolved Organic Carbon)  
**Degradation:** = 100 %  
**Result:** readily biodegradable  
**Method:** OECD Guide-line 303 A "Simulation Test - Aerobic Sewage Treatment: Coupled Unit Test"  
**Year:** 1981 **GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4  
**Remark:** Der Abbaugrad von 100 +/- 1 % bezieht sich auf eine mittlere Verweilzeit von 3 Stunden.  
**Source:** Huels AG Marl

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**Type:** aerobic  
**Inoculum:** domestic sewage, non-adapted  
**Concentration:** mg/l related to Test substance  
**Degradation:** = 76 % after 5 day  
**Result:** readily biodegradable  
**Method:** other  
**Year:** 1971 **GLP:** no data  
**Test substance:** as prescribed by 1.1 - 1.4  
**Remark:** Test Method: APHA No.: 219.  
Standard Methods for the Examination of Water and Wastewater, American Public Health Association, Inc., New York, 1971.  
The test substance is weighted into the test system in order to obtain the concentration needed (2-3 mg/l).  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

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**Type:** aerobic  
**Inoculum:** other bacteria: Salzwassermikroorganismen, nicht adaptiert  
**Degradation:** 53 % after 20  
**Method:** other: BSB-Methode nach Standard Methods for the Examination of Water and Wastewater, APHA (1971)  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Remark:** Einsatzkonzentration: 3-10 mg Methylisobutylketon/l  
Abbaugrad bezogen auf "Biooxidation" (Sauerstoffaufnahme x 100/ Testkonzentration x theoretischer Sauerstoffbedarf (2.70 g O2/g Methylisobutylketon)).  
Abbaugrad: 5 d 15 %  
                  10 d 46 %  
                  15 d 50 %  
**Source:** Huels AG Marl

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**Type:** aerobic  
**Inoculum:** other bacteria: aus ueberwiegend kommunalem Abwasser, nicht adaptiert  
**Degradation:** 69 % after 20  
**Method:** other: BSB-Methode nach Standard Methods for the Examination of Water and Wastewater, APHA (1971)  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Remark:** Einsatzkonzentration: 3-10 mg Methylisobutylketon/l  
Abbaugrad bezogen auf "Biooxidation" (Sauerstoffaufnahme x 100/ Testkonzentration x theoretischer Sauerstoffbedarf (2.70 g O2/g Methylisobutylketon)).  
Abbaugrad: 5 d 56 %  
                  10 d 66 %  
                  15 d 69 %  
**Source:** Huels AG Marl

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**Type:** aerobic  
**Inoculum:** other bacteria: Abwasser  
**Concentration:** 2.3 mg/l related to Test substance  
**Degradation:** = 64.8 % after 50 day  
**Kinetic:** 5 day = 4.4 %  
                  10 day = 49.3 %  
                  15 day = 55.9 %  
                  20 day = 56.6 %  
                  30 day = 64.8 %  
**Method:** other: BSB-Methode, keine weiteren Angaben  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Remark:** Abbaugrad bezogen auf theoretischen BSB  
nach 5 d 4.4 %  
                  etc ...  
                  40 d 64.8 %  
**Source:** Huels AG Marl

(28)

**Type:** aerobic  
**Inoculum:** activated sludge, non-adapted  
**Concentration:** 100 mg/l related to Test substance  
**Degradation:** ca. 70 % after 20  
**Method:** other: Elektrolytischer Respirometer-Test  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Remark:** Abbaugrad: BSB bezogen auf ThSB; nach 4 d ca. 60 %.  
**Source:** Huels AG Marl

(29)

**Type:** aerobic  
**Inoculum:** activated sludge, non-adapted  
**Degradation:** 76 % after 5  
**Method:** other: Standard Method for the Examination of Water and Wastewater, No. 219, APHA (1971)  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Remark:** Abbaugrad: BSB (2.06 g O<sub>2</sub>/g Methylisobutylketon) bezogen auf ThSB (2.72 g O<sub>2</sub>/g Methylisobutylketon).  
**Source:** Huels AG Marl

(30)

**3.6 BOD5, COD or BOD5/COD Ratio**

-

**3.7 Bioaccumulation**

-

**3.8 Additional Remarks**

-

**AQUATIC ORGANISMS****4.1 Acute/Prolonged Toxicity to Fish**

**Type:** flow through  
**Species:** Pimephales promelas (Fish, fresh water)  
**Exposure period:**  
**Unit:** mg/l **Analytical monitoring:** no data  
**NOEC:** = 57  
**Method:** other: Durchfluss-Verfahren  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Remark:** Testdauer: 31-33 d; kontinuierliche Exposition von Fischlaich, geschluepften Larven und Jungfischen; Testparameter: Schlupffaehigkeit, Missbildungsrate und Mortalitaet der Larven, Koerpergewicht und -laenge sowie Mortalitaet der Jungfische.  
**Source:** Huels AG Marl

(31)

**Type:** static  
**Species:** Carassius auratus (Fish, fresh water)  
**Exposure period:** 24 hour(s)  
**Unit:** mg/l **Analytical monitoring:** yes  
**LC50:** = 450  
**Method:** other  
**Year:** 1971 **GLP:** no data  
**Test substance:** as prescribed by 1.1 - 1.4  
**Remark:** Test method: APHA No.: 231. Standard Methods for the Examination of Water and Wastwater. American Public Health Association Inc., New York, 1971. This data point is the result of a comprehensive appraisal of all available data. The selection criteria are: the methodology, analysis and end point.  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

(32)

**Type:** static  
**Species:** Leuciscus idus (Fish, fresh water)  
**Exposure period:** 48 hour(s)  
**Unit:** mg/l **Analytical monitoring:** no  
**LC50:** = 900  
**Method:** other: Bestimmung der Wirkung von Wasserinhaltsstoffen auf Fische, DIN 38412 Teil15  
**Year:** **GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4  
**Source:** Huels AG Marl

(14)

**Type:**  
**Species:** Carassius auratus (Fish, fresh water)  
**Exposure period:** 24  
**Unit:** mg/l **Analytical monitoring:** no data  
**LC50:** = 460  
**Method:** other: Statisches Verfahren nach Standard Method for the Examination of Water and Wastewater, No. 231, APHA (1971)  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Source:** Huels AG Marl (33)

**Type:**  
**Species:** Leuciscus idus (Fish, fresh water)  
**Exposure period:** 48  
**Unit:** mg/l **Analytical monitoring:** no data  
**LC50:** = 672  
**Method:** other: Bestimmung der Wirkung von Wasserinhaltsstoffen auf Fische, DIN 38412 Teil15  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Source:** Huels AG Marl (34)

**Type:**  
**Species:** Leuciscus idus (Fish, fresh water)  
**Exposure period:** 48  
**Unit:** mg/l **Analytical monitoring:** no data  
**LC50:** = 744  
**Method:** other: Bestimmung der Wirkung von Wasserinhaltsstoffen auf Fische, DIN 38412 Teil15  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Source:** Huels AG Marl (34)

**Type:**  
**Species:** Pimephales promelas (Fish, fresh water)  
**Exposure period:** 96  
**Unit:** mg/l **Analytical monitoring:** no data  
**LC50:** = 505  
**Method:** other: Durchfluss-Verfahren  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Source:** Huels AG Marl (35)

**Type:**  
**Species:** Pimephales promelas (Fish, fresh water)  
**Exposure period:** 96  
**Unit:** mg/l **Analytical monitoring:** no data  
**LC50:** = 509  
**Method:** other: Durchfluss-Verfahren  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Source:** Huels AG Marl (36)

**Type:**  
**Species:** Pimephales promelas (Fish, fresh water)  
**Exposure period:** 96  
**Unit:** mg/l **Analytical monitoring:** no data  
**LC50:** = 540  
**Method:** other: Durchfluss-Verfahren  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Source:** Huels AG Marl (37)

**Type:**  
**Species:** Pimephales promelas (Fish, fresh water)  
**Exposure period:** 96  
**Unit:** mg/l **Analytical monitoring:** no data  
**LC50:** = 537  
**Method:** other: Durchfluss-Verfahren nach Standard Methods for the Examination of Water and Wastewater, APHA (1980)  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Source:** Huels AG Marl (38)

**Type:**  
**Species:** Pimephales promelas (Fish, fresh water)  
**Exposure period:** 24  
**Unit:** mg/l **Analytical monitoring:** no data  
**LC50:** = 780  
**Method:** other: Statisches Verfahren nach Standard Methods for the Examination of Water and Wastewater, APHA (1971)  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Source:** Huels AG Marl (39)

**Type:**  
**Species:** Pimephales promelas (Fish, fresh water)  
**Exposure period:** 48  
**Unit:** mg/l **Analytical monitoring:** no data  
**LC50:** = 780  
**Method:** other: Statisches Verfahren nach Standard Methods for the Examination of Water and Wastewater, APHA (1971)  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Source:** Huels AG Marl (39)

**Type:**  
**Species:** Pimephales promelas (Fish, fresh water)  
**Exposure period:** 96  
**Unit:** mg/l **Analytical monitoring:** no data  
**LC50:** = 780  
**Method:** other: Statisches Verfahren nach Standard Methods for the Examination of Water and Wastewater, APHA (1971)  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Source:** Huels AG Marl (39)

**Type:**  
**Species:** Salmo gairdneri (Fish, estuary, fresh water)  
**Exposure period:** 96  
**Unit:** mg/l **Analytical monitoring:**  
**LC50:** = 600  
**Method:** other: Semistatisches Verfahren  
**Year:** **GLP:**  
**Test substance:** as prescribed by 1.1 - 1.4  
**Source:** Huels AG Marl (40)

#### 4.2 Acute Toxicity to Aquatic Invertebrates

**Species:** Artemia salina (Crustacea)  
**Exposure period:** 24  
**Unit:** mg/l **Analytical monitoring:** no data  
**EC50:** = 1230  
**Method:** other: Statisches Verfahren  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Source:** Huels AG Marl (27)

**Species:** Daphnia magna (Crustacea)  
**Exposure period:** 48 hour(s)  
**Unit:** mg/l **Analytical monitoring:** yes  
**EC50:** = 170  
**Method:** other  
**Year:** 1983 **GLP:** yes  
**Test substance:** as prescribed by 1.1 - 1.4  
**Remark:** The tests were carried out in a way that evaporation of the test substance was avoided. The precise methodology is described in the reference.  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam (41)

**Species:** Daphnia magna (Crustacea)  
**Exposure period:** 24  
**Unit:** mg/l **Analytical monitoring:** no data  
**EC50:** = 862  
**Method:** other: Daphnien-Kurzzeitest, DIN 38412 Teil 11, Bestimmung der Wirkung von Wasserinhaltsstoffen auf Kleinkrebse  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Source:** Huels AG Marl (14)

**Species:** Daphnia magna (Crustacea)  
**Exposure period:** 24  
**Unit:** mg/l **Analytical monitoring:** no data  
**EC0:** = 930  
**EC50:** = 3682  
**Method:** other: Daphnien-Kurzzeitest, DIN 38412 Teil 11, Bestimmung der Wirkung von Wasserinhaltsstoffen auf Kleinkrebse  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Source:** Huels AG Marl (42)

**Species:** Daphnia magna (Crustacea)  
**Exposure period:** 24  
**Unit:** mg/l **Analytical monitoring:** no data  
**EC0:** = 474  
**EC50:** = 1550  
**EC100:** = 5000  
**Method:** other: Schwimmunfaehigkeitstest, statisches Verfahren  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Source:** Huels AG Marl (43)

**Species:** Daphnia magna (Crustacea)  
**Exposure period:** 24  
**Unit:** mg/l **Analytical monitoring:** no data  
**EC0:** = 2280  
**EC50:** = 4280  
**EC100:** = 5000  
**Method:** other: Schwimmunfaehigkeitstest, statisches Verfahren  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Source:** Huels AG Marl

(44)

**Species:** Daphnia magna (Crustacea)  
**Exposure period:** 24  
**Unit:** mg/l **Analytical monitoring:** no data  
**EC50:** = 240  
**Method:** other: Statisches Verfahren, geschlossenes System  
(Testparameter: Immobilitaet)  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Source:** Huels AG Marl

(45)

**Species:** Daphnia magna (Crustacea)  
**Exposure period:** 48  
**Unit:** mg/l **Analytical monitoring:**  
**EC50:** > 1000  
**Method:** other: Statisches Verfahren, offenes System (Testparameter:  
Immobilitaet)  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Huels AG Marl

(45)

**Species:** Daphnia magna (Crustacea)  
**Exposure period:** 21  
**Unit:** mg/l **Analytical monitoring:**  
**NOEC:** = 78  
**Method:** other: Verlaengerter Toxizitaetstest bei Daphnia magna  
(Bestimmung der NOEC fuer Reproduktionsrate, Mortalitaet und  
den Zeitpunkt des ersten Auftretens von Nachkommen),  
Umweltbundesamt (1984)  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Source:** Huels AG Marl

(42)

**4.3 Toxicity to Aquatic Plants e.g. Algae**

**Species:** Microcystis aeruginosa (Algae, blue, cyanobacteria)  
**Endpoint:**  
**Exposure period:** 8  
**Unit:** mg/l **Analytical monitoring:**  
**EC0:** = 136  
**Method:** other: Zellvermehrungshemmtest, statisches Verfahren  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** Niedrigste Konzentration, bei der eine beginnende Hemmung der Zellvermehrung zu beobachten war.  
**Source:** Huels AG Marl (46)

**Species:** Scenedesmus quadricauda (Algae)  
**Endpoint:**  
**Exposure period:** 8  
**Unit:** mg/l **Analytical monitoring:**  
**EC0:** = 725  
**Method:** other: Zellvermehrungshemmtest, statisches Verfahren  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** Niedrigste Konzentration, bei der eine beginnende Hemmung der Zellvermehrung zu beobachten war.  
**Source:** Huels AG Marl (47)

**Species:** Scenedesmus subspicatus (Algae)  
**Endpoint:**  
**Exposure period:** 48  
**Unit:** mg/l **Analytical monitoring:**  
**EC10:** = 310  
**EC50:** = 980  
**Method:** other: Modifizierter Scenedesmus-Zellvermehrungs-Hemmtest, DIN 38412 Teil 9  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** EC10 = niedrigste Konzentration, bei der eine beginnende Hemmung der Zellvermehrung zu beobachten war.  
**Source:** Huels AG Marl (48)

**Species:** Selenastrum capricornutum (Algae)  
**Endpoint:** growth rate  
**Exposure period:** 96 hour(s)  
**Unit:** mg/l **Analytical monitoring:** yes  
**EC50:** = 400  
**Method:** other  
**Year:** 1983 **GLP:** yes  
**Test substance:** as prescribed by 1.1 - 1.4  
**Remark:** See remark item 4.2  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam (49)

**Species:** Selenastrum capricornutum (Algae)  
**Endpoint:**  
**Exposure period:** 96  
**Unit:** mg/l **Analytical monitoring:**  
**EC50:** = 400  
**Method:** other: Zellvermehrungshemmtest  
**Year:** **GLP:**  
**Test substance:**  
**Source:** Huels AG Marl (45)

#### 4.4 Toxicity to Microorganisms e.g. Bacteria

**Type:** aquatic  
**Species:** Pseudomonas putida (Bacteria)  
**Exposure period:** 16 hour(s)  
**Unit:** mg/l **Analytical monitoring:** no data  
**NOEC :** = 275  
**Method:** other  
**Year:** 1980 **GLP:** no data  
**Test substance:** as prescribed by 1.1 - 1.4  
**Remark:** Method described in reference.  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam (50)

**Type:** aquatic  
**Species:** Pseudomonas putida (Bacteria)  
**Exposure period:** 18 hour(s)  
**Unit:** mg/l **Analytical monitoring:** no  
**EC10:** = 413  
**Method:** other: Pseudomonas-Zellvermehrungs-Hemmtest, DIN 38412 Teil 8, zum Gelbdruck verabschiedet, Bestimmung der Hemmwirkung von Wasserinhaltsstoffen auf Bakterien  
**Year:** **GLP:** yes  
**Test substance:** as prescribed by 1.1 - 1.4  
**Source:** Huels AG Marl (51)

**Type:**  
**Species:** activated sludge, domestic  
**Exposure period:** 30  
**Unit:** **Analytical monitoring:**  
**Method:** other: Modifizierter Activated Sludge, Respiration Inhibition Test, OECD Guideline 209, adopted April 4, 1984  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** 1000 mg Testsubstanz/l hemmte den O2-Verbrauch um 26 % im Vergleich zur Kontrolle.  
**Source:** Huels AG Marl (52)

**Type:**  
**Species:** activated sludge, domestic  
**Exposure period:** 60  
**Unit:** **Analytical monitoring:**  
**Method:** other: RIKA (Respiration Inhibition Kinetic Analysis)-Screening-Test  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** 1000 mg Testsubstanz/l hemmte den O2-Verbrauch um 34 % im Vergleich zur Kontrolle.  
**Source:** Huels AG Marl (53)

**Type:**  
**Species:** Photobacterium phosphoreum (Bacteria)  
**Exposure period:**  
**Unit:** mg/l **Analytical monitoring:** no data  
**EC50:** = 80  
**Method:** other: Bioassay mit "microtox toxicity analyzer" (Beckman Instruments)  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Remark:** Konzentration, die nach 5 min Testdauer 50 %ige Hemmung der Biolumineszenz bewirkte.  
**Source:** Huels AG Marl (54)

**Type:**  
**Species:** Pseudomonas putida (Bacteria)  
**Exposure period:** 16  
**Unit:** mg/l **Analytical monitoring:** no data  
**EC0:** = 275  
**Method:** other: Zellvermehrungshemmtest, statisches Verfahren  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Remark:** Niedrigste Konzentration, bei der eine beginnende Hemmung der Zellvermehrung zu beobachten war.  
**Source:** Huels AG Marl (47)

**Type:**  
**Species:** other bacteria: Anaerobe fettsaeurebildende Bakterien  
**Exposure period:**  
**Unit:** **Analytical monitoring:** no data  
**Method:** other: Gaschromatographischer Nachweis der Fettsaeureproduktion waehrend des Gaerungsprozesses.  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Remark:** 53 g Methylisobutylketon/l hemmte die Fettsaeureproduktion von aus dem Faulraum fuer Schweinemist isolierten Bakterien um ca. 66 %.  
**Source:** Huels AG Marl (55)

**Type:**  
**Species:** other bacteria: Anaerobe saeurebildende Bakterien  
**Exposure period:** 75  
**Unit:** **Analytical monitoring:**  
**Method:** other: Batch-Fermentation-Bioassay  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** Eine Konzentration von ca. 2500 mg Testsubstanz/l fuehrte in einer Mischkultur aus anaeroben saeurebildenden Bakterien (isoliert aus Rinderpansen) zu einer 99 %igen Hemmung der Gasproduktion (zu 73 % CO<sub>2</sub>).  
**Source:** Huels AG Marl (56)

**Type:**  
**Species:** other bacteria: Fakultativ anaerobe saeurebildende Bakterien  
**Exposure period:** 75  
**Unit:** **Analytical monitoring:**  
**Method:** other: Batch-Fermentation-Bioassay  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** Eine Konzentration von ca. 250 mg Testsubstanz/l fuehrte in einem kommerziellen Inokulum (Methanobac: u.a. Bacillus cereus, Bacillus pantothenicus, Bacillus coagulans, Pseudomonas aeruginosa, Lactobacillus plantarum, Coryne bacterium sp.) zu einer um 44 % gehemmten Gasproduktion (zu 73 % CO<sub>2</sub>). Bei 25 ul Testsubstanz/ml Medium war die Gasproduktion um 97 % gehemmt.  
**Source:** Huels AG Marl (56)

#### 4.5 Chronic Toxicity to Aquatic Organisms

##### 4.5.1 Chronic Toxicity to Fish

**Species:** Pimephales promelas (Fish, fresh water)  
**Endpoint:** weight of young fish  
**Exposure period:** 31 day  
**Unit:** mg/l **Analytical monitoring:** yes  
**NOEC:** = 57  
**LOEC:** = 105  
**MATC :** = 77.4  
**Method:** other  
**Year:** 1985 **GLP:** no data  
**Test substance:** as prescribed by 1.1 - 1.4  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam (57)

**4.5.2 Chronic Toxicity to Aquatic Invertebrates**

**Species:** Daphnia magna (Crustacea)  
**Endpoint:** reproduction rate  
**Exposure period:** 21 day  
**Unit:** mg/l **Analytical monitoring:** no  
**NOEC:** = 78  
**Method:** other  
**Year:** 1989 **GLP:** no data  
**Test substance:** as prescribed by 1.1 - 1.4  
**Remark:** Reference contains method  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

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**TERRESTRIAL ORGANISMS****4.6.1 Toxicity to Soil Dwelling Organisms**

-

**4.6.2 Toxicity to Terrestrial Plants**

-

**4.6.3 Toxicity to other Non-Mamm. Terrestrial Species**

-

**4.7 Biological Effects Monitoring**

-

**4.8 Biotransformation and Kinetics**

-

**4.9 Additional Remarks**

**Remark:** Photochemische Abbaubarkeit:  
 $k_{OH} = 12.4 \times 10E-12 \text{ cm}^3/\text{Molekuel} \times \text{s}$  bei 27 Grad C  
 somit errechnet sich eine Halbwertszeit  $t_{1/2}$  von 15.5 h bei  
 einer angenommenen OH-Radikal-Konzentration von  $10E6$   
 Molekuele/cm<sup>3</sup>.

**Source:** Huels AG Marl

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**Remark:**  $k_{OH} = 13 \times 10E-12 \text{ cm}^3/\text{Molekuel} \times \text{s}$  bei 22 Grad C  
 somit errechnet sich eine Halbwertszeit  $t_{1/2}$  von 14.8 h bei  
 einer angenommenen OH-Radikal-Konzentration von  $10E6$   
 Molekuele/cm<sup>3</sup>.

**Source:** Huels AG Marl

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- Remark:**  $k_{OH} = 14.9 \times 10^{-12} \text{ cm}^3/\text{Molekuel} \times \text{s}$  bei 32 Grad C  
somit errechnet sich eine Halbwertszeit  $t_{1/2}$  von 12.9 h bei  
einer angenommenen OH-Radikal-Konzentration von  $10E6$   
Molekuele/cm<sup>3</sup>.
- Source:** Huels AG Marl (61)
- Remark:** 2 ppm Methylisobutylketon wurde in einer Smogkammer in  
Gegenwart von NO<sub>x</sub> (anfängliche Konzentration = 1 ppm NO<sub>x</sub>)  
bei 6stuendiger UV-Bestrahlung (Photodissoziationskonstante  
NO<sub>2</sub> = 0.33 min<sup>-1</sup>) bei 30 Grad C zu 30 % abgebaut. Als  
Reaktionsprodukte wurden Peroxyacetylnitrat und Formaldehyd  
nachgewiesen.
- Source:** Huels AG Marl (62)
- Remark:** Als Reaktionsprodukt bei der Photooxidation von  
Methylisobutylketon mit HONO wurde Aceton (68 %) neben  
Peroxyacetylnitrat und Methylnitrat nachgewiesen.
- Source:** Huels AG Marl (59)
- Remark:** In einer weiteren Studie zur Photooxidation von  
Methylisobutylketon mit HONO wurden nur Aceton (90 %) und  
Peroxyacetylnitrat als Reaktionsprodukte nachgewiesen.
- Source:** Huels AG Marl (60)
- Remark:** Bei der Photolyse (UV-Licht) von Methylisobutylketon mit NO  
(Anfangskonzentration: 5 ppm) bei 27 Grad C wurde eine  
Halbwertszeit von  $t_{1/2} = 3.5 \text{ h}$  ermittelt.
- Source:** Huels AG Marl (63)
- Remark:** Entosiphon sulcatum (Geisseltierchen):  
Niedrigste Konzentration, die die Zellvermehrung hemmt:  
EC<sub>0</sub> = 447 mg/l, Zellvermehrungshemmtest, statisch,  
72 h, 25 Grad C.
- Source:** Huels AG Marl (64)
- Remark:** Uronema parduczi (Wimpertierchen):  
Niedrigste Konzentration, die die Zellvermehrung hemmt:  
EC<sub>0</sub> = 941 mg/l, Zellvermehrungshemmtest, statisch,  
20 h, 25 Grad C.
- Source:** Huels AG Marl (65)
- Remark:** Chilomonas paramecium (Geisseltierchen):  
Niedrigste Konzentration, die die Zellvermehrung hemmt:  
EC<sub>0</sub> > 800 mg/l, Zellvermehrungshemmtest, statisch,  
48 h, 25 Grad C.
- Source:** Huels AG Marl (66)

**Remark:** Pimephales promelas (Dickkopfritze):  
Befruchtete Eier (maximal 24 h alt) und die daraus  
schluepfenden Larven wurden fuer insgesamt 31 - 33 Tage  
gegenueber 57, 105, 169, 246 bzw. 418 mg  
Methylisobutylketon/l im Durchfluss-Verfahren exponiert.  
Das Wasser der Kontrollgruppe enthielt 0.525 mg  
Methylisobutylketon/l als Verunreinigung. Die Schlupfrate  
sowie der Anteil toter bzw. missgebildeter Larven lag im  
Bereich der Kontrolle. Ab einer Konzentration von  $\geq 105$   
mg/l waren Koerpergewicht und -laenge der Fische  
signifikant reduziert. Die Mortalitaet der Fische war bei  
418 mg/l signifikant erhoehrt.

**Source:** Huels AG Marl

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## 5.1 Acute Toxicity

### 5.1.1 Acute Oral Toxicity

**Type:** LD50  
**Species:** rat  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Value:** = 4600 mg/kg bw  
**Method:** other  
**Year:** 1973 **GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4  
**Remark:** When administered as an emulsion, MIBK has an LD50 of 2.08 g/kg.  
Source: Krasavage, W.J., O'Donoghue, J.L., Divinzeno, G.D., Chapter 56 in Patty's Industrial Hygiene and Toxicology, Vol. 2C : Toxicology , Clayton, G.D. & F.E. Editors, Wiley-Interscience, 1982.  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam (68)

**Type:** LD50  
**Species:** rat  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Value:** = 2080 mg/kg bw  
**Method:** other: see reference  
**Year:** 1951 **GLP:** no  
**Test substance:** no data  
**Remark:** range of values: 1910 - 2270 mg/kg  
**Source:** Huels AG Marl (69)

**Type:** LD50  
**Species:** rat  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Value:** ca. 4570 mg/kg bw  
**Method:**  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Remark:** no further details reported;  
**Source:** Huels AG Marl (70)

## 5. Toxicity

date: 18-FEB-2000  
Substance ID: 108-10-1

**Type:** LD50  
**Species:** rat  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Value:** = 4600 mg/kg bw  
**Method:**  
**Year:** **GLP:** no  
**Test substance:** no data  
**Remark:** range of values: 3932 - 5382 mg/kg  
no further details reported;  
**Source:** Huels AG Marl (71)

**Type:** LD50  
**Species:** rat  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Value:** = 3200  
**Method:**  
**Year:** **GLP:** no  
**Test substance:**  
**Remark:** the test substance was administered undiluted to male albino rats;  
range of values: 2735 - 3744 mg/kg  
**Source:** Huels AG Marl (72)

**Type:** LD50  
**Species:** mouse  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Value:** = 1900 mg/kg bw  
**Method:**  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Remark:** no further details reported;  
**Source:** Huels AG Marl (73)

**Type:** LD50  
**Species:** mouse  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Value:** = 2850 mg/kg bw  
**Method:**  
**Year:** **GLP:** no  
**Test substance:** no data  
**Remark:** range of values: 2638 - 3078 mg/kg  
no further details reported;  
**Source:** Huels AG Marl

(71)

**Type:** LD50  
**Species:** mouse  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Value:** ca. 2671 mg/kg bw  
**Method:** other: see reference  
**Year:** 1986 **GLP:** no data  
**Test substance:** no data  
**Remark:** male mice were used in this study, no further details reported;  
range of values: 2113 - 3376 mg/kg  
**Source:** Huels AG Marl

(13)

### 5.1.2 Acute Inhalation Toxicity

**Type:** LC50  
**Species:** rat  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Exposure time:** 4 hour(s)  
**Value:** ca. 8.2 - 16.4 mg/l  
**Method:** other  
**Year:** 1951 **GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4  
**Source:** ECETOC 1987, Joint Assessment of Commodity Chemicals Report,  
No. 8. Brussels, Belgium.  
Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

**Type:**  
**Species:** rat  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Exposure time:**  
**Value:**  
**Method:**  
**Year:** GLP: no data  
**Test substance:** no data  
**Remark:** Exposition gegenueber gesaettigter Atmosphaere;  
Mortalitaet:  
Expositionsdauer 15 min: 0 von 6 Tieren  
Expositionsdauer 30 min: 6 von 6 Tieren  
**Source:** Huels AG Marl

(70)

**Type:**  
**Species:** rat  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Exposure time:**  
**Value:**  
**Method:** other: see reference  
**Year:** 1951 GLP: no  
**Test substance:** no data  
**Remark:** Mortalitaet:  
8.32 mg/l/4 h: 0 von 6 Tieren  
16.64 mg/l/4 h: 6 von 6 Tieren  
**Source:** Huels AG Marl

(69)

**Type:** LC100  
**Species:** mouse  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Exposure time:** 1 hour(s)  
**Value:** = 89 mg/l  
**Method:**  
**Year:** GLP: no  
**Test substance:** no data  
**Remark:** no details reported  
**Source:** Huels AG Marl

(74)

**Type:** LC50  
**Species:** mouse  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Exposure time:** 1.23 hour(s)  
**Value:** = 83.1 mg/l  
**Method:**  
**Year:** **GLP:** no  
**Test substance:** no data  
**Remark:** no details reported  
**Source:** Huels AG Marl (74)

**Type:** LC50  
**Species:** mouse  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Exposure time:** 2  
**Value:** = 23.3 mg/l  
**Method:**  
**Year:** **GLP:** no  
**Test substance:** no data  
**Source:** Huels AG Marl (71)

**Type:**  
**Species:** mouse  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Exposure time:**  
**Value:**  
**Method:**  
**Year:** **GLP:** no  
**Test substance:** no data  
**Remark:** Mortalitaet:  
81 mg/l/0.5 h: 0 von 10 Tieren  
**Source:** Huels AG Marl (74)

### 5.1.3 Acute Dermal Toxicity

Type: LD50  
Species: rabbit  
Sex:  
Number of  
Animals:  
Vehicle:  
Value: > 16000 mg/kg bw  
Method:  
Year: GLP: no data  
Test substance: no data  
Source: Huels AG Marl

(70)

Type:  
Species:  
Sex:  
Number of  
Animals:  
Vehicle:  
Value:  
Method:  
Year: GLP:  
Test substance:  
Remark: The percutaneous toxicity of MIBK has not been determined.  
However, based on data from skin irritancy tests, it is  
expected to be low.  
Source: Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

### 5.1.4 Acute Toxicity, other Routes

Type: LD50  
Species: rat  
Sex:  
Number of  
Animals:  
Vehicle:  
Route of admin.: i.p.  
Value: ca. 914 mg/kg bw  
Method: other: see reference  
Year: 1976 GLP: no data  
Test substance: no data  
Remark: groups of six male rats were used for this study;  
Source: Huels AG Marl

(75)

**Type:** LD50  
**Species:** guinea pig  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Route of admin.:** i.p.  
**Value:** ca. 735 mg/kg bw  
**Method:** other: see reference  
**Year:** 1976 **GLP:** no data  
**Test substance:** no data  
**Remark:** groups of six male guinea pigs were used in this study;  
**Source:** Huels AG Marl

(75)

**Type:** other: LD20  
**Species:** rat  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Route of admin.:** i.p.  
**Value:** = 584 mg/kg bw  
**Method:**  
**Year:** **GLP:** yes  
**Test substance:** other TS: purity 99.56%  
**Source:** Huels AG Marl

(76)

**Type:**  
**Species:** rat  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Route of admin.:** other  
**Value:**  
**Method:**  
**Year:** **GLP:** no  
**Test substance:** no data  
**Remark:** Nach intratrachealer Verabreichung von 0.2 ml Testsubstanz (ca. 160 mg) an männliche Albino-Ratten starben innerhalb weniger Minuten 3 von 5 Tieren (keine weiteren Angaben).  
**Source:** Huels AG Marl

(77)

**Type:**  
**Species:** rat  
**Sex:**  
**Number of Animals:**  
**Vehicle:**  
**Route of admin.:** other  
**Value:**  
**Method:**  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Remark:** Nach intratrachealer Verabreichung von 1 ml Testsubstanz/kg (ca. 800 mg/kg) starben 6 von 6 Tieren sofort.  
**Source:** Huels AG Marl

(78)

## **5.2 Corrosiveness and Irritation**

### **5.2.1 Skin Irritation**

**Species:** rabbit  
**Concentration:**  
  
**Exposure:**  
**Exposure Time:**  
**Number of Animals:**  
**PDII:**  
**Result:** moderately irritating  
**EC classificat.:** irritating  
**Method:** Estimation  
**Year:** 1982 **GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4  
**Source:** ECETOC,1987. Joint Assessment of Commodity Chemicals Report, no. 8, Brussels, Belgium.  
Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

**Species:** rabbit  
**Concentration:**  
  
**Exposure:**  
**Exposure Time:**  
**Number of Animals:**  
**PDII:**  
**Result:**  
**EC classificat.:**  
**Method:** other: according to Draize  
**Year:** 1959 **GLP:** no  
**Test substance:** no data  
**Remark:** 24 h Einwirkzeit, intakte bzw. skarifizierte Rueckenhaut, Applikationsvolumen: 0.5 ml; primaerer Reizindex von 0.75 (kombinierter Durchschnittswert fuer intakte und skarifizierte Haut) bei einem maximalen Reizindex von 8. (Methode nach Draize)  
not classifiable according to current EEC directives;

**Source:** Huels AG Marl (79)

**Species:** rabbit  
**Concentration:**

**Exposure:**  
**Exposure Time:**  
**Number of  
Animals:**

**PDII:**

**Result:**

**EC classificat.:**

**Method:** other: Patch-Test

**Year:** **GLP:** no

**Test substance:** no data

**Remark:** Ueber 24 h andauernde Erythembildung (keine weiteren Angaben).

not classifiable according to current EEC directives;

**Source:** Huels AG Marl (74)

**Species:** rabbit  
**Concentration:**

**Exposure:**  
**Exposure Time:**  
**Number of  
Animals:**

**PDII:**

**Result:**

**EC classificat.:**

**Method:**

**Year:** **GLP:** no

**Test substance:** no data

**Remark:** Applikationsvolumen: 10 ml, Applikationsdauer: taeglich ueber 7 Tage; Austrocknung und Abschuppung der Haut nach 7 Tagen (keine weiteren Angaben).

not classifiable according to current EEC directives;

**Source:** Huels AG Marl (74)

**Species:** rabbit  
**Concentration:**

**Exposure:**  
**Exposure Time:**  
**Number of  
Animals:**

**PDII:**

**Result:**

**EC classificat.:**

**Method:**

**Year:** **GLP:** no

**Test substance:** no data

**Remark:** Das Eintauchen des Ohres in unverduenntes Methylisobutylketon fuer 2 h verursachte deutlich

ausgepraegte Entzuendungen mit Gewebsnekrosen (keine weiteren Angaben).  
not classifiable according to current EEC directives;  
**Source:** Huels AG Marl (71)

**Species:** rabbit  
**Concentration:**

**Exposure:**  
**Exposure Time:**  
**Number of Animals:**  
**PDII:**  
**Result:**  
**EC classificat.:**  
**Method:**

**Year:** **GLP:** no  
**Test substance:** no data  
**Remark:** Applikationsmenge: 500 mg, 24 h Einwirkzeit.  
no further details reported;  
not classifiable according to current EEC directives;  
**Source:** Huels AG Marl (80)

**Species:** rabbit  
**Concentration:**

**Exposure:**  
**Exposure Time:**  
**Number of Animals:**  
**PDII:**  
**Result:** irritating  
**EC classificat.:**

**Method:** OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"  
**Year:** 1981 **GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4  
**Remark:** irritation index: 3.7/8  
redness: x=2.00  
edema : x=1.67  
**Source:** Huels AG Marl (81)

**Species:** guinea pig  
**Concentration:**

**Exposure:**  
**Exposure Time:**  
**Number of  
Animals:**  
**PDII:**  
**Result:**  
**EC classificat.:**

**Method:** other: Patch-Test, okklusiv  
**Year:** **GLP:** no data

**Test substance:** no data

**Remark:** Applikationsvolumen: 5 bzw. 10 ml, 24 h Einwirkzeit,  
depilierte Rueckenhaut; leicht reizend ohne klinische  
Anzeichen fuer eine Resorption (keine weiteren Angaben).  
not classifiable according to current EEC directives;

**Source:** Huels AG Marl

(82)

**Species:** guinea pig  
**Concentration:**

**Exposure:**  
**Exposure Time:**  
**Number of  
Animals:**  
**PDII:**  
**Result:**  
**EC classificat.:**

**Method:**  
**Year:** **GLP:** no

**Test substance:** no data

**Remark:** Wiederholtes Auftragen (ueber 3 Monate) der Testsubstanz auf  
die Haut fuehrte zu geringfuegigen Hautveraenderungen  
(Einwirkzeit jeweils < 2 h; keine weiteren Angaben).  
not classifiable according to current EEC directives;

**Source:** Huels AG Marl

(71)

**Species:** mouse  
**Concentration:**

**Exposure:**  
**Exposure Time:**  
**Number of  
Animals:**  
**PDII:**  
**Result:**  
**EC classificat.:**

**Method:**  
**Year:** **GLP:** no

**Test substance:** no data

**Remark:** Das Eintauchen des Schwanzes in unverduenntes  
Methylisobutylketon fuer 2 h verursachte deutlich  
ausgepraegte Entzuendungen mit Gewebsnekrosen (keine  
weiteren Angaben).

**Source:** not classifiable according to current EEC directives;  
Huels AG Marl

(71)

### 5.2.2 Eye Irritation

**Species:** rabbit

**Concentration:**

**Dose:**

**Exposure Time:**

**Comment:**

**Number of**

**Animals:**

**Result:** irritating

**EC classificat.:** irritating

**Method:** other

**Year:** 1982

**GLP:** no

**Test substance:** as prescribed by 1.1 - 1.4

**Remark:** Appraisal is an estimation only, not a formal classification.

**Source:** ECETOC, 1987. Joint Assessment of Commodity Chemicals report, no. 8, Brussels, Belgium.  
Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

**Species:** rabbit

**Concentration:**

**Dose:**

**Exposure Time:**

**Comment:**

**Number of**

**Animals:**

**Result:**

**EC classificat.:**

**Method:**

**Year:**

**GLP:** no

**Test substance:** no data

**Remark:** Applikationsvolumen: 0.1 ml; Entzuendungsreaktion, Schwellung und Exsudat-Bildung innerhalb von 8 bis 24 h nach Instillation (keine weiteren Angaben).

**Source:** not classifiable according to current EEC directives;  
Huels AG Marl

(74)

**Species:** rabbit

**Concentration:**

**Dose:**

**Exposure Time:**

**Comment:**

**Number of**

**Animals:**

**Result:** not irritating

**EC classificat.:**

**Method:** OECD Guide-line 405 "Acute Eye Irritation/Corrosion"

**Year:** 1981

**GLP:** no

**Test substance:** as prescribed by 1.1 - 1.4

**Remark:** irritation index: 8.4/110

cornea: x=0.33  
iris : x=0  
conjunctivae  
-----  
redness : x=1.89  
chemosis: x=0.78  
**Source:** Huels AG Marl (83)

**Species:** rabbit  
**Concentration:**  
**Dose:**  
**Exposure Time:**  
**Comment:**  
**Number of Animals:**  
**Result:**  
**EC classificat.:**  
**Method:**  
**Year:** GLP: no  
**Test substance:** no data  
**Remark:** application volume: 40 mg = 'severe'  
no further details reported;  
not classifiable according to current EEC directives;  
**Source:** Huels AG Marl (84)

**Species:** rabbit  
**Concentration:**  
**Dose:**  
**Exposure Time:**  
**Comment:**  
**Number of Animals:**  
**Result:**  
**EC classificat.:**  
**Method:**  
**Year:** GLP: no  
**Test substance:** no data  
**Remark:** Applikationsmenge: 500 mg, 24 h Einwirkzeit = 'mild'  
no further details reported;  
not classifiable according to current EEC directives;  
**Source:** Huels AG Marl (80)

**Species:** rabbit  
**Concentration:**  
**Dose:**  
**Exposure Time:**  
**Comment:**  
**Number of Animals:**  
**Result:** not irritating  
**EC classificat.:**  
**Method:** other: according to Draize  
**Year:** 1959 GLP: no  
**Test substance:** no data

**Remark:** Applikationsvolumen: 0.1 ml; voruebergewende Reizung der Konjunktiven bei 6 von 6 Tieren (Roetung, Chemosis, Sekret-absonderung: Reizindex 2 bei einem maximalen Reizindex von 3 bzw. 4) bzw. der Iris bei 1 von 6 Tieren (Reizindex 1 bei einem maximalen Reizindex von 2), die innerhalb von 3 bis 4 Tagen vollstaendig abgeklungen waren. Die Kornea blieb ohne Befund. (Methode nach Draize)  
cornea: x=0  
iris : x=0  
conjunctivae

-----  
redness : x=1.06  
chemosis: x=0.11

**Source:** Huels AG Marl

(85)

**Species:** rabbit

**Concentration:**

**Dose:**

**Exposure Time:**

**Comment:**

**Number of**

**Animals:**

**Result:** not irritating

**EC classificat.:**

**Method:** other: according to Draize

**Year:** 1959

**GLP:** no data

**Test substance:** other TS: purity > 97%

**Remark:** Applikationsvolumen: 0.1 ml unverduennt, 24 h Einwirkzeit; Reizindex von 5 bei einem maximalen Reizindex von 110.  
Applikationsvolumen: 0.1 ml einer 30 %igen Loesung in Poly-ethylenglykol, 24 h Einwirkzeit; Reizindex von 2 bei einem maximalen Reizindex von 110 (Methode nach Draize).

**Source:** Huels AG Marl

(86)

**Species:** rabbit

**Concentration:**

**Dose:**

**Exposure Time:**

**Comment:**

**Number of**

**Animals:**

**Result:**

**EC classificat.:**

**Method:** other: according to Draize

**Year:** 1959

**GLP:** no data

**Test substance:** no data

**Remark:** Applikationsvolumen: 0.1 ml, 24 h Einwirkzeit = 'mild' (Methode nach Draize).

no further details reported;

**Source:** Huels AG Marl

(87)

### 5.3 Sensitization

**Type:** Guinea pig maximization test  
**Species:** guinea pig  
**Number of Animals:**  
**Vehicle:**  
**Result:** not sensitizing  
**Classification:**  
**Method:** OECD Guide-line 406 "Skin Sensitization"  
**Year:** 1981 **GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4  
**Remark:** No sensitisation was observed in any of 20 animals.  
**Source:** Huels AG Marl

(88)

**Type:**  
**Species:**  
**Number of Animals:**  
**Vehicle:**  
**Result:**  
**Classification:**  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** No data available.  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

### 5.4 Repeated Dose Toxicity

**Species:** rat **Sex:** male/female  
**Strain:** Fischer 344  
**Route of admin.:** inhalation  
**Exposure period:** 6 hours per day, 90 days.  
**Frequency of treatment:** daily, 5 days per week  
**Post. obs. period:** none  
**Doses:** 50, 250, 1000 ppm  
**Control Group:** yes  
**NOAEL:** = 250 ppm  
**LOAEL:** = 1000 ppm  
**Method:**  
**Year:** 1983 **GLP:** yes  
**Test substance:** as prescribed by 1.1 - 1.4  
**Source:** ECETOC Joint Assessment of Commodity Chemicals No. 8, Brussels, 1987.  
Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

**Species:** rat **Sex:** male/female  
**Strain:** Fischer 344  
**Route of admin.:** inhalation  
**Exposure period:** 11 days (9 exposures)  
**Frequency of treatment:** 6 h/day, 5 days/week  
**Post. obs. period:** none  
**Doses:** 416, 2080 and 8320 mg/m<sup>3</sup> (100, 500 and 2000 ppm)  
**Control Group:** yes  
**NOAEL:** = 100 ppm  
**Method:** other: see reference  
**Year:** 1982 **GLP:** yes  
**Test substance:** other TS: purity > 99%  
**Remark:** 6 rats/dose/sex were exposed six hours per day, five days per week, for eleven days (nine exposures) to vapors of MIBK.  
**Result:** The only consistent clinical observations was that of periocular wetness observed in the 2000 ppm group. No ophthalmologic lesions or alterations in body weight gain were found in the treated animals. Relative liver weights were increased in both sexes of the 2000 ppm group and in the males of the 500 ppm dose group. Kidney weights were increased in the males of the 2000 and, to a lesser extent of the 500 ppm group. In addition to organ weight changes were histopathologic findings in the kidneys. Male rats of the 2000 and of the 500 ppm dose groups had hyaline droplet nephropathy coupled with epithelial regeneration of the proximal convoluted tubules. No histopathologic findings were observed in animals exposed to 100 ppm.  
**Source:** Huels AG Marl

(89)

**Species:** rat **Sex:** male/female  
**Strain:** Fischer 344  
**Route of admin.:** inhalation  
**Exposure period:** 90 days  
**Frequency of treatment:** 6 h/day, 5 days/week  
**Post. obs. period:** none  
**Doses:** 208, 1040 and 4160 mg/m<sup>3</sup> (50, 250 and 1000 ppm)  
**Control Group:** yes  
**NOAEL:** = 50 ppm  
**Method:** other: see reference  
**Year:** 1983 **GLP:** yes  
**Test substance:** other TS: purity > 99%  
**Remark:** 14 Tiere/Geschlecht/Substanz- und Kontrollgruppe  
**Result:** Die Koerpergewichtsentwicklung lag im Bereich der Kontrolle. Der Wasserverbrauch blieb unbeeinflusst. 1 von 14 m der 1040 mg/m<sup>3</sup>- Gruppe starb waehrend der 11. Versuchswoche, der Todesfall war jedoch nicht substanzbedingt. Die haematologische Untersuchung ergab eine signifikant erhoehte Anzahl Thrombozyten bei den m der 4160 mg/m<sup>3</sup>-Gruppe und eine signifikant verringerte Anzahl eosinophiler Granulozyten bei den w der 4160 mg/m<sup>3</sup>-Gruppe. Die biochemische Untersuchung ergab lediglich einen signifikant erhoehten

Cholesteringehalt im Serum bei den m der 1040 und 4160 mg/m<sup>3</sup>-Gruppe. Bei der Untersuchung der Harnparameter war der Glukosegehalt bei den m der 1040 und 4160 mg/m<sup>3</sup>-Gruppe und den w der 4160 mg/m<sup>3</sup>-Gruppe signifikant erhoeht, bei den m der 4160 mg/m<sup>3</sup>- Gruppe war der Proteingehalt signifikant erhoeht. Bei den m der 208 mg/m<sup>3</sup>-Gruppe war das absolute Lebergewicht signifikant erhoeht, bei den w der 1040 mg/m<sup>3</sup>-Gruppe war das absolute Nierengewicht signifikant erhoeht und bei den m der 4160 mg/m<sup>3</sup>-Gruppe war das absolute und relative Lebergewicht signifikant erhoeht. Das Herz-, Lungen- bzw. Testisgewicht lag im Bereich der Kontrolle. Keine substanzbedingten makroskopischen bzw. histopathologischen Veraenderungen (in der 4160 mg/m<sup>3</sup>-Gruppe und der Kontrollgruppe ca. 26 Organe untersucht, in der 208 und 1040 mg/m<sup>3</sup>-Gruppe 5 Organe untersucht), mit Ausnahme einer Zunahme der Inzidenz schwer detektierbarer "hyaline droplets" in den Nieren der m der 4160 und 1040 mg/m<sup>3</sup>-Gruppen.

**Source:** Huels AG Marl

(90)

**Species:** rat **Sex:** no data  
**Strain:** Wistar  
**Route of admin.:** inhalation  
**Exposure period:** 2 weeks  
**Frequency of treatment:** 24 h/day  
**Post. obs. period:** none  
**Doses:** ca. 410 and 820 mg/m<sup>3</sup> (100 and 200 ppm)  
**Control Group:** yes  
**Method:** other: see reference  
**Year:** 1970 **GLP:** no  
**Test substance:** no data  
**Remark:** 25 Tiere/Substanz- und Kontrollgruppe  
**Result:** Die Koerpergewichtsentwicklung blieb unbeeinflusst. Ab 410 mg/m<sup>3</sup> war das relative und absolute Nierengewicht signifikant erhoeht, bei den Tieren der 820 mg/m<sup>3</sup>-Gruppe war das relative und absolute Lebergewicht signifikant erhoeht. Das relative und absolute Herz-, Lungen- bzw. Milzgewicht lag im Bereich der Kontrolle. Die histopathologische Untersuchung ergab toxische Nephrose in den proximalen Nierentubuli bei den Tieren beider Substanzgruppen. Keine weiteren Angaben.

**Source:** Huels AG Marl

(91)

**Species:** rat **Sex:** male  
**Strain:** Wistar  
**Route of admin.:** inhalation  
**Exposure period:** 90 days  
**Frequency of treatment:** 24 h/day  
**Post. obs. period:** yes (see remark)  
**Doses:** 410 mg/m<sup>3</sup>  
**Control Group:** yes  
**Method:** other: see reference  
**Year:** 1970 **GLP:** no  
**Test substance:** no data  
**Remark:** 100 Tiere/Substanz- und Kontrollgruppe  
2 Tiere/Substanz- und Kontrollgruppe wurden woeentlich bzw. 14taegig seziert. Nach 2woechiger Exposition wurden 10 Ratten/ Substanz- und Kontrollgruppe nicht weiter exponiert und je 14taegig wurden 2 Tiere/Substanz- und Kontrollgruppe seziert. Nach 90taegiger Inhalation wurden 10 Ratten/Substanz- und Kontrollgruppe nachbeobachtet und zu verschiedenen Zeiten seziert.  
**Result:** Die Koerpergewichtsentwicklung blieb unbeeinflusst. Das relative und absolute Nieren- bzw. Lebergewicht war signifikant erhoeht, das Herz-, Lungen- bzw. Milzgewicht lag im Bereich der Kontrolle bei Sektion nach 90taegiger Exposition. Die histopathologische Untersuchung ergab keine substanzbedingten Veraenderungen bis auf eine Degeneration (hyaline Tropfenbildung) der proximalen Nierentubuli mit vereinzelt auftretenden Foci tubulaerer Nekrose nach 15, 22, 28, 71, 85 und 90taegiger Exposition. Bei Tieren, die bereits nach 15taegiger Exposition aus der Inhalationskammer entfernt wurden, waren die histologischen Veraenderungen in den Nieren bei einer bis zu 60taegigen Nachbeobachtungsperiode vollstaendig reversibel. Nach 90taegiger Exposition war dieser Reversionsprozess verzoegert. Keine weiteren Angaben.  
**Source:** Huels AG Marl

(91)

**Species:** rat **Sex:** male/female  
**Strain:** other: Charles River  
**Route of admin.:** inhalation  
**Exposure period:** 4 weeks  
**Frequency of treatment:** 6 h/day, 5 days/week (20 exposures)  
**Post. obs. period:** none  
**Doses:** 4210 mg/m<sup>3</sup>  
**Control Group:** yes  
**Method:** other: see reference  
**Year:** 1968 **GLP:** no  
**Test substance:** no data  
**Remark:** 10 Tiere/Geschlecht/Substanz- und Kontrollgruppe  
Histopathologische Untersuchung bei 3 Tieren/Geschlecht/  
Substanz- und Kontrollgruppe  
**Result:** Koerpergewichtsentwicklung unbeeinflusst, keine  
substanzbedingten haematologischen, makroskopischen (16  
Organe untersucht) bzw. histopathologischen (5 Organe  
untersucht) Befunde. Das absolute und relative Lungen-,  
Leber-, Milz-, Nieren- bzw. Nebennierengewicht von m und w  
der Substanzgruppe lag im Bereich der Kontrolle, lediglich  
das relative Nebennierengewicht der w der Substanzgruppe war  
signifikant verringert im Vergleich zur Kontrolle.  
**Source:** Huels AG Marl

(92)

**Species:** rat **Sex:** no data  
**Strain:** no data  
**Route of admin.:** inhalation  
**Exposure period:** 5 months  
**Frequency of treatment:** 6 h/day, 5 days/week  
**Post. obs. period:** none  
**Doses:** 6240 mg/m<sup>3</sup> (1500 ppm)  
**Control Group:** yes  
**Method:** other: see reference  
**Year:** 1974 **GLP:** no  
**Test substance:**  
**Remark:** 6 Tiere/Substanzgruppe  
3 Tiere/Kontrollgruppe  
Es wurden mehrere Proben des zentralen und des peripheren  
Nervensystems licht- und elektronenmikroskopisch untersucht.  
Testsubstanz enthielt ca. 3 % Methyl-n-Butylketon.  
**Result:** Koerpergewichtsentwicklung normal, leichte Narkose waehrend  
der Exposition; keine Anzeichen von neurologischen  
Funktionsstoerungen. Nervengewebsproben des zentralen  
Nervensystems und des proximalen peripheren Nervensystems  
zeigten keine Auffaelligkeiten, die distalen Bereiche des  
Nervus tibialis und des Nervus ulnaris zeigten Anzeichen von  
Schaedigung.  
**Source:** Huels AG Marl

(93)

**Species:** rat **Sex:** no data  
**Strain:** no data  
**Route of admin.:** inhalation  
**Exposure period:** 4.5 months  
**Frequency of treatment:** 4 h/day, 5 days/week  
**Post. obs. period:** 2 months  
**Doses:** 115 mg/m<sup>3</sup> (86 - 127 mg/m<sup>3</sup>)  
**Control Group:** yes  
**Method:**  
**Year:** **GLP:** no  
**Test substance:** no data  
**Remark:** insgesamt 70 Tiere (keine weiteren Angaben)  
**Result:** Die Anzahl der eosinophilen Granulozyten im Blut war bei den Tieren der Substanzgruppe verringert. 2 Monate nach Versuchsbeginn, am Versuchsende sowie 1 - 2 Monate nach Versuchsende waren das Leber- und Nebennierengewicht verringert im Vergleich zur Kontrollgruppe. Die histopathologische Untersuchung ergab dystrophische Veraenderungen des parenchymatoesen Gewebes bis hin zur Nekrobiose im Zentralnervensystem und der wichtigsten inneren Organe (keine weiteren Angaben). Bei Untersuchungen zur Neurotoxizitaet zeigten die Tiere der Substanzgruppe eine verlaengerte Laufzeit und eine hoehere Fehlerquote im Labyrinthverhaltenstest. Es trat eine leichte Hemmung des Abwehrreflexes auf. Keine weiteren Angaben.  
**Source:** Huels AG Marl

(71)

**Species:** rat **Sex:** no data  
**Strain:** no data  
**Route of admin.:** drinking water  
**Exposure period:** 7 days  
**Frequency of treatment:**  
**Post. obs. period:** none  
**Doses:** 396 and 652 mg/kg b.w./day (0.5 and 1.0 %)  
**Control Group:** yes  
**Method:** other: see reference  
**Year:** 1977 **GLP:** no data  
**Test substance:** no data  
**Remark:** 5 Tiere/Dosis- und Kontrollgruppe  
**Result:** Koerpergewichtsentwicklung in der hohen Dosisgruppe signifikant gehemmt, Futter- und Wasserverbrauch im Bereich der Kontrolle. Keine substanzbedingten makroskopischen Befunde. Keine weiteren Angaben.  
**Source:** Huels AG Marl

(94)

**Species:** rat **Sex:** female  
**Strain:** Wistar  
**Route of admin.:** drinking water  
**Exposure period:** 120 days  
**Frequency of treatment:**  
**Post. obs. period:** none  
**Doses:** 1040 mg/kg b.w./day (1.3 %)  
**Control Group:** yes  
**Method:** other: see reference  
**Year:** 1977 **GLP:** no data  
**Test substance:** no data  
**Remark:** 5 Tiere/Dosis- und Kontrollgruppe  
**Result:** Koerpergewichtsentwicklung, Futter- und Wasserverbrauch lagen im Bereich der Kontrolle. Das absolute und relative Nierengewicht war signifikant erhoehrt, das absolute und relative Lebergewicht lag im Bereich der Kontrolle. Es traten keine substanzbedingten makroskopischen bzw. histopathologischen (ca. 30 Organe untersucht) Befunde auf. Die Evaluierung neurologischer Parameter (verschiedene Verhaltenstests) nach 46, 57, 80 und 110 Versuchstagen ergab keine substanzbedingten Befunde.  
**Source:** Huels AG Marl

(94)

**Species:** rat **Sex:** male/female  
**Strain:** Sprague-Dawley  
**Route of admin.:** gavage  
**Exposure period:** 13 weeks  
**Frequency of treatment:** daily  
**Post. obs. period:** none  
**Doses:** 50, 250, 1000 mg/kg/day  
**Control Group:** yes  
**NOAEL:** = 50 mg/kg  
**LOAEL:** = 250 mg/kg  
**Method:**  
**Year:** 1986 **GLP:** yes  
**Test substance:** as prescribed by 1.1 - 1.4  
**Source:** WHO Enviromental Health Criteria 117 Methyl Isobutyl Ketone, World Health Organisation, Geneva, 1990.  
Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

**Species:** rat **Sex:** male/female  
**Strain:** Sprague-Dawley  
**Route of admin.:** gavage  
**Exposure period:** 13 weeks  
**Frequency of treatment:** daily  
**Post. obs. period:** none  
**Doses:** 0, 50, 250 and 1000 mg/kg  
**Control Group:** yes, concurrent vehicle  
**NOAEL:** = 50 mg/kg  
**Method:**  
**Year:** **GLP:** no data

**Test substance:** no data  
**Remark:** 30 rats/dose/sex were used;  
 Body weight, food consumption, organ weight, morbidity, clinical chemistry, haematology, and histopathology evaluations were performed. All surviving animals were killed after 90 days and 10 animals of each sex per group were examined.

**Result:** Nephrotoxicity was seen as a general nephropathy for both male and female rats administered 1000 mg/kg/day. Although increased liver and kidney weights were observed for males and females at 1000 mg/kg/day, there were no corresponding histopathological lesions present in the liver. The effects seen at 1000 mg/kg/day were present to a significantly lesser extent in the animals of both sexes of the 250 mg/kg dose group. No effects were observed at 50 mg/kg.

**Source:** Huels AG Marl

(95)

**Species:** rat **Sex:** male  
**Strain:** Sprague-Dawley  
**Route of admin.:** i.p.  
**Exposure period:** 35 weeks (165 injections)  
**Frequency of treatment:** 5 days/week  
**Post. obs. period:** none  
**Doses:** 20, 60 and 200 mg/kg b.w./day (see remark)  
**Control Group:** yes  
**Method:** other: see reference  
**Year:** 1977 **GLP:** no data

**Test substance:** no data  
**Remark:** Die Dosierung wurde nach 2 Versuchswochen von 10, 30 und 100 mg/ kg Kgw./Tag auf 20, 60 und 200 mg/kg Kgw./Tag erhoeht. 12 Tiere/Dosisgruppe (Testsubstanz unverduennt) 13 Tiere/Kontrollgruppe (Maiskeimoel bzw. Aq. dest.)  
**Result:** Nach 17.5 Wochen Hemmung der Koerpergewichtsentwicklung in der hoechsten Dosisgruppe, voruebergewende Sedierung waehrend des 1. Versuchsmonats in der hoechsten Dosisgruppe. Die Mortalitaet lag im Bereich der Kontrolle (1 von 12, 4 von 12 bzw. 5 von 12 Tieren in der 20, 60 bzw. 200 mg/kg-Dosisgruppe; Kontrolle 4 von 13 Tieren). Bei 1 bzw. 2 Tieren der niedrigen bzw. hoechsten Dosisgruppe traten chronische Veraenderungen der Atmungsorgane auf und bei jeweils einem Tier der niedrigen bzw. mittleren Dosisgruppe

eine Veraenderung des Nucleus gracilis im Nachhirn, bei 4 Tieren der hoechsten Dosisgruppe Peritonitis und bei je einem Tier zusaetzlich Hyperplasie des Knochenmarks bzw. gesteigerte Haemopoese in der Milz. Im zentralen und peripheren Nervengewebe traten keine substanzbedingten neuropathologischen Befunde auf.

**Source:** Huels AG Marl

(96)

**Species:** mouse **Sex:** male/female  
**Strain:** B6C3F1  
**Route of admin.:** inhalation  
**Exposure period:** 6 hours per day, 90 days  
**Frequency of treatment:** daily, 5 days per week  
**Post. obs. period:** none  
**Doses:** 50, 250, 1000 ppm  
**Control Group:** yes  
**NOAEL:** = 250 ppm  
**LOAEL:** = 1000 ppm  
**Method:**  
**Year:** 1983 **GLP:** yes  
**Test substance:** as prescribed by 1.1 - 1.4  
**Source:** ECETOC Joint Assessment of Commodity Chemicals, No.8, Brussels, 1987.  
Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

**Species:** mouse **Sex:** male/female  
**Strain:** B6C3F1  
**Route of admin.:** inhalation  
**Exposure period:** 11 days (9 exposures)  
**Frequency of treatment:** 6 h/day, 5 days/week  
**Post. obs. period:** none  
**Doses:** 416, 2080 and 8320 mg/m<sup>3</sup> (100, 500 and 2000 ppm)  
**Control Group:** yes  
**NOAEL:** = 500 ppm  
**Method:** other: see reference  
**Year:** 1982 **GLP:** yes  
**Test substance:** other TS: purity > 99%  
**Remark:** 6 mice/dose/sex were exposed 6 h/day, 5 days/week for eleven days (nine exposures) to vapors of MIBK.  
**Result:** The only clinical signs of significance were scattered incidence of lethargy and lacrimation in the high dose group animals. No treatment-related differences in body weight change during the study period was observed. Females of the high exposure group had significant imcreases in absolute and relative liver weights and absolute kidney weight compared to control. Males of the high exposure group had a significant decrease in relative kidney weight. No other significant differences in organ weights were noted. At necropsy, no macroscopic or microscopic lesions were observed.  
**Source:** Huels AG Marl

(89)

**Species:** mouse **Sex:** male/female  
**Strain:** B6C3F1  
**Route of admin.:** inhalation  
**Exposure period:** 90 days  
**Frequency of treatment:** 6 h/day, 5 days/week  
**Post. obs. period:** none  
**Doses:** 208, 1040 and 4160 mg/m<sup>3</sup> (50, 250 and 1000 ppm)  
**Control Group:** yes  
**NOAEL:** = 50 ppm  
**Method:** other: see reference  
**Year:** 1983 **GLP:** yes  
**Test substance:** other TS: purity > 99%  
**Remark:** 14 Tiere/Geschlecht/Substanz- und Kontrollgruppe  
**Result:** Die Koerpergewichtsentwicklung blieb unbeeinflusst. Die haematologischen Parameter lagen im Bereich der Kontrolle. In der 4160 mg/m<sup>3</sup>-Gruppe starb 1 von 14 m. Bei den m der 1040 mg/m<sup>3</sup>- Gruppe war das absolute Lebergewicht signifikant erhoehrt, bei den m der 4160 mg/m<sup>3</sup>-Gruppe war das absolute und relative Lebergewicht signifikant erhoehrt. Das Herz-, Lungen-, Nieren- bzw. Testisgewicht lag im Bereich der Kontrolle. Keine substanzbedingten makroskopischen bzw. histopathologischen Veraenderungen (26 Organe untersucht in der 4160 mg/m<sup>3</sup>-Gruppe und in der Kontrollgruppe; 5 Organe untersucht in der 208 und 1040 mg/m<sup>3</sup>- Gruppe).  
**Source:** Huels AG Marl

(90)

**Species:** mouse **Sex:** no data  
**Strain:** no data  
**Route of admin.:** inhalation  
**Exposure period:** 2 weeks  
**Frequency of treatment:** 24 h/day  
**Post. obs. period:** none  
**Doses:** ca. 410 and 820 mg/m<sup>3</sup> (100 and 200 ppm)  
**Control Group:** yes  
**Method:** other: see reference  
**Year:** 1970 **GLP:** no  
**Test substance:** no data  
**Remark:** 20 Tiere/Substanz- und Kontrollgruppe  
**Result:** Die Koerpergewichtsentwicklung blieb unbeeinflusst. Die makroskopische bzw. histopathologische Untersuchung ergab keine substanzbedingten Veraenderungen. Das relative und absolute Herz-, Lungen-, Leber-, Milz- bzw. Nierengewicht lag im Bereich der Kontrolle. Keine weiteren Angaben.  
**Source:** Huels AG Marl

(91)

**Species:** mouse **Sex:** no data  
**Strain:** no data  
**Route of admin.:** inhalation  
**Exposure period:** 15 days  
**Frequency of treatment:** 20 min/day  
**Post. obs. period:** none  
**Doses:** 83200 mg/m3 (20000 ppm)  
**Control Group:**  
**Method:**  
**Year:** **GLP:** no  
**Test substance:** no data  
**Remark:** 10 Tiere/Substanzgruppe  
**Result:** Mortalitaet:  
Jeweils 1 Tier starb nach 1 bzw. 6 Tagen, 3 Tiere nach 9  
Tagen und 1 nach 10 Tagen. 4 Tiere ueberlebten die 15  
Expositionen. Keine weiteren Angaben.  
**Source:** Huels AG Marl

(74)

**Species:** cat **Sex:** no data  
**Strain:** no data  
**Route of admin.:** s.c.  
**Exposure period:** 8.5 months  
**Frequency of treatment:** twice daily, 5 days/week  
**Post. obs. period:** none  
**Doses:** 150 mg/kg b.w. (undiluted)  
**Control Group:** yes  
**Method:** other: see reference  
**Year:** 1976 **GLP:** no  
**Test substance:** other TS: purity 98.79%  
**Remark:** 4 Tiere/Dosis- und Kontrollgruppe  
Kontrolle: isot. Kochsalzloesung  
Histologische Untersuchung des Nervengewebes des  
Hinterpfotenballens.  
**Result:** Die Substanz war lokal gut vertraeglich. Das untersuchte  
Gewebe erschien normal. Keine weiteren Angaben.  
**Source:** Huels AG Marl

(97)

**Species:** dog **Sex:** no data  
**Strain:** Beagle  
**Route of admin.:** inhalation  
**Exposure period:** 2 weeks  
**Frequency of treatment:** 24 h/day  
**Post. obs. period:** none  
**Doses:** ca. 410 and 820 mg/m<sup>3</sup> (100 and 200 ppm)  
**Control Group:** yes  
**Method:** other: see reference  
**Year:** 1970 **GLP:** no  
**Test substance:** no data  
**Remark:** 4 Tiere/Substanz- und Kontrollgruppe  
**Result:** Die Koerpergewichtsentwicklung blieb unbeeinflusst. Vergiftungssymptome traten nicht auf. Die Untersuchung biochemischer und haematologischer Parameter, eine Blutgasanalyse sowie die makroskopische bzw. histopathologische Untersuchung ergaben keine substanzbedingten Veraenderungen. Das relative und absolute Herz-, Lungen-, Leber-, Milz- bzw. Nierengewicht lag im Bereich der Kontrolle. Keine weiteren Angaben.  
**Source:** Huels AG Marl

(91)

**Species:** dog **Sex:** male  
**Strain:** Beagle  
**Route of admin.:** inhalation  
**Exposure period:** 90 days  
**Frequency of treatment:** 24 h/day  
**Post. obs. period:** 60 days  
**Doses:** 410 mg/m<sup>3</sup>  
**Control Group:** yes  
**Method:** other: see reference  
**Year:** 1970 **GLP:** no  
**Test substance:** no data  
**Remark:** 8 Tiere/Substanz- und Kontrollgruppe  
2 der 8 Tiere/Substanz- und Kontrollgruppe wurden am Ende der Exposition ueber 60 Tage nachbeobachtet.  
**Result:** Keine substanzbedingten Veraenderungen der biochemischen und haematologischen Parameter bzw. der Leberfunktion (Bromsulfaleinretentionsprobe). Die histopathologische Untersuchung (8 Organe untersucht) ergab eine hyaline Tropfenbildung in der Niere bei jeweils 1 von 8 Tieren der Substanz- bzw. Kontrollgruppe sowie eine Fettverteilung in einigen Nierentubuli am kortikomedullaeren Uebergang bei den Tieren der Substanzgruppe. Diese Veraenderung tritt gewoehnlich auch bei unbehandelten Tieren auf. Keine weiteren Angaben.  
**Source:** Huels AG Marl

(91)

**Species:** guinea pig **Sex:** male  
**Strain:** Hartley  
**Route of admin.:** dermal  
**Exposure period:** 31 weeks  
**Frequency of treatment:** 5 days/week  
**Post. obs. period:** none  
**Doses:** up to 5940 mg/kg b.w./day (see remark)  
**Control Group:** no  
**Method:** other: see reference  
**Year:** 1978 **GLP:** no data  
**Test substance:** no data  
**Remark:** 15 Tiere erhielten Methylisobutylketon in einem Volumen von bis zu ca. 4 ml/Tier/Tag (ca. 5940 mg Methylisobutylketon/kg Kgw./Tag bei einem durchschnittlichen Koerpergewicht von 674 g) auf die Haut aufgetragen (keine weiteren Angaben). 5 der 15 Tiere erhielten 3 ml Dimethylsulfoxid (DMSO) + Methylisobutylketon (2.5 : 7.5) fuer die letzten 50 - 70 Applikationen 2 x/Tag auf die Haut aufgetragen. 4 Tiere der Substanzgruppe wurden am Ende der Applikationsperiode histopathologisch (bei 1 der 4 Tiere einschliesslich Medulla oblongata und Nervus tibialis; keine weiteren Angaben) untersucht.  
**Result:** Koerpergewichtsentwicklung unbeeinflusst.  
Mortalitaet: 1 von 10 Tieren der Substanzgruppe sowie 3 der 5 Tiere der Substanzgruppe, die Methylisobutylketon in DMSO erhielten, starben spontan.  
Im Applikationsbereich traten lokale Reizerscheinungen auf (leichte bis mittelstarke Desquamation); bei Applikation von Methylisobutylketon in DMSO starke Desquamation mit Erythembildung und leichter Alopezie. Keine substanzbedingten klinischen bzw. histopathologischen neurotoxischen Befunde.  
**Source:** Huels AG Marl

(98)

**Species:** hen **Sex:** female  
**Strain:** Leghorn  
**Route of admin.:** inhalation  
**Exposure period:** 90 days  
**Frequency of treatment:** 24 h/day  
**Post. obs. period:** 30 days  
**Doses:** 4160 mg/m<sup>3</sup> (1000 ppm)  
**Control Group:** yes  
**Method:** other: see reference  
**Year:** 1984 **GLP:** no data  
**Test substance:** other TS: purity 99.95%  
**Remark:** 5 Tiere/Substanz- und Kontrollgruppe  
Reinheitsgrad 99.95 %  
weitere 5 Gruppen wurden gegen 100, 250, 500 oder 1000 ppm und zusaetzlich gegen 1000 ppm n-Hexan bzw. gegen 1000 ppm n-Hexan allein exponiert;  
**Result:** Koerpergewichtsreduktion waehrend der 90taegigen Exposition, Koerpergewichtszuwachs waehrend der 30taegigen

Nachbeobachtungsperiode (leichte Koerpergewichtsreduktion der Kontrolltiere waehrend des gesamten Versuchs). Nach ca. 44taegiger Exposition trat bei den Tieren der Substanzgruppe eine Muskelschwaeche der hinteren Extremitaeten auf, bei Abbruch der Exposition erholten sich die Tiere wieder. Es traten keine substanzbedingten histopathologischen Befunde (Rueckenmark, periphere Nerven) auf. In den Gruppen, die zusaetzlich gegen 1000 ppm n-Hexan exponiert worden waren, traten dosisabh?ngig Zeichen von Neurotoxizit?t auf. Keine weiteren Angaben.

**Source:** Huels AG Marl

(99)

**Species:** monkey **Sex:** no data

**Strain:** other: Macacus mulatta

**Route of admin.:** inhalation

**Exposure period:** 2 weeks

**Frequency of treatment:** 24 h/day

**Post. obs. period:** none

**Doses:** ca. 410 and 820 mg/m3 (100 and 200 ppm)

**Control Group:** yes

**Method:** other: see reference

**Year:** 1970

**GLP:** no

**Test substance:** no data

**Remark:** 2 Tiere/Substanzgruppe  
3 Tiere/Kontrollgruppe

**Result:** Die Koerpergewichtsentwicklung blieb unbeeinflusst. Die Untersuchung biochemischer und haematologischer Parameter, eine Blutgasanalyse sowie die makroskopische bzw. histopathologische Untersuchung ergab keine substanzbedingten Veraenderungen. Das relative und absolute Herz-, Lungen-, Leber-, Milz- bzw. Nierengewicht lag im Bereich der Kontrolle. Eine Elektroenzephalographie, durchgefuehrt bei 1 Tier/Substanz- und Kontrollgruppe, zeigte am Ende der 2woechigen Exposition keine substanzbedingten Veraenderungen.

**Source:** Huels AG Marl

(91)

**Species:** monkey **Sex:** male  
**Strain:** other: Macacus mulatta  
**Route of admin.:** inhalation  
**Exposure period:** 90 days  
**Frequency of treatment:** 24 h/day  
**Post. obs. period:** none  
**Doses:** 410 mg/m<sup>3</sup>  
**Control Group:** yes  
**Method:** other: see reference  
**Year:** 1970 **GLP:** no  
**Test substance:** no data  
**Remark:** 2 Tiere/Substanz- und Kontrollgruppe  
**Result:** Keine substanzbedingten Veraenderungen der biochemischen und haematologischen Parameter. Die histopathologische Untersuchung (8 Organe untersucht) ergab eine fokale chronische Entzuendung der Niere bei 1 von 2 Tieren der Substanzgruppe. Keine weiteren Angaben.  
**Source:** Huels AG Marl

(91)

### 5.5 Genetic Toxicity 'in Vitro'

**Type:** Ames test  
**System of testing:** Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538  
**Concentration:** up to 5000 ug/plate  
**Metabolic activation:** with and without  
**Result:** negative  
**Method:** Directive 84/449/EEC, B.14 "Other effects - Mutagenicity (Salmonella typhimurium - reverse mutation assay)"  
**Year:** 1984 **GLP:** yes  
**Test substance:** as prescribed by 1.1 - 1.4  
**Remark:** solvent: DMSO  
**Source:** Huels AG Marl

(100)

**Type:** Ames test  
**System of testing:** Salmonella typhimurium  
**Concentration:** 0.04-0.4 ug/plate  
**Metabolic activation:** with and without  
**Result:** negative  
**Method:** other  
**Year:** 1988 **GLP:** no data  
**Test substance:** as prescribed by 1.1 - 1.4  
**Source:** WHO Enviromental Health Criteria 117, Methyl Isobutyl Ketone, Geneva, 1990.  
 Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

**Type:** Ames test  
**System of testing:** Escherichia coli  
**Concentration:** up to 8000 ug/plate  
**Metabolic activation:** with  
**Result:** negative  
**Method:** other  
**Year:** 1988 **GLP:** no data  
**Test substance:** as prescribed by 1.1 - 1.4  
**Source:** WHO Environmental Health Criteria 117, Methyl Isobutyl Ketone, Geneva, 1990.  
Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

**Type:** Ames test  
**System of testing:** Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538  
**Concentration:** up to 2000 æg/plate  
**Metabolic activation:** with and without  
**Result:** negative  
**Method:** other: according to Ames et al., Mut. Res. 31, 347  
**Year:** 1975 **GLP:** no data  
**Test substance:** no data  
**Remark:** 0.1-2000 ug/Platte; 3 Platten/Konzentration; keine Angaben zum zytotoxischen Bereich.  
**Source:** Huels AG Marl

(101)

**Type:** Ames test  
**System of testing:** Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538  
**Concentration:** up to 5000 æg/plate  
**Metabolic activation:** with and without  
**Result:** negative  
**Method:** other: according to Ames et al., Mut. Res. 31, 347-364  
**Year:** 1975 **GLP:** no  
**Test substance:** as prescribed by 1.1 - 1.4  
**Remark:** solvent: DMSO  
**Source:** Huels AG Marl

(102)

**Type:** Ames test  
**System of testing:** Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538; Escherichia coli WP2 and WP2 uvr A  
**Concentration:** up to 8000 µg/ml  
**Metabolic activation:** with and without  
**Result:** negative  
**Method:** other: see reference  
**Year:** 1988 **GLP:** no data  
**Test substance:** other TS: purity > 98.5%  
**Remark:** Praeinkubationstest; 3 Platten/ Konzentration; 1 unabhaengige Wiederholung;  
**Source:** Huels AG Marl

(103)

**Type:** Ames test  
**System of testing:** Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538  
**Concentration:** 32, 80, 320, 800 and 3200 µg/plate  
**Metabolic activation:** with and without  
**Result:** negative  
**Method:** other: see reference  
**Year:** 1984 **GLP:** yes  
**Test substance:** other TS: purity 99.6%  
**Remark:** preincubation assay; solvent: DMSO  
**Source:** Huels AG Marl

(104)

**Type:** Ames test  
**System of testing:** Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538  
**Concentration:** 8 to 8000 µg/plate  
**Metabolic activation:** with and without  
**Result:** negative  
**Method:** other: see reference  
**Year:** 1978 **GLP:** no data  
**Test substance:** no data  
**Remark:** solvent: DMSO  
**Source:** Huels AG Marl

(105)

**Type:** Ames test  
**System of testing:** Salmonella typhimurium  
**Concentration:** no data  
**Metabolic activation:** no data  
**Result:** negative  
**Method:**  
**Year:** **GLP:** no data  
**Test substance:** no data  
**Remark:** no details reported;  
**Source:** Huels AG Marl

(106)

**Type:** Cytogenetic assay  
**System of testing:** rat liver cells (RL4 assay)  
**Concentration:** up to 1000 µg/ml  
**Metabolic activation:** without  
**Result:** negative  
**Method:** other: see reference  
**Year:** 1988 **GLP:** no data  
**Test substance:** other TS: purity > 98.5%  
**Remark:** S9 mix was not used in the experiment owing to the fact that RL4 cells are metabolically competent; no further details reported;  
**Source:** Huels AG Marl

(103)

**Type:** Mitotic recombination in Saccharomyces cerevisiae  
**System of testing:** Saccharomyces cerevisiae JD1  
**Concentration:** 5000 µg/ml  
**Metabolic activation:** with and without  
**Result:** negative  
**Method:** other: see reference  
**Year:** 1988 **GLP:** no data  
**Test substance:** other TS: purity > 98.5%  
**Remark:** no details reported;  
**Source:** Huels AG Marl

(103)

**Type:** Mouse lymphoma assay  
**System of testing:** L51784 TK+/-  
**Concentration:** 0.4 - 6.0 µl/ml  
**Metabolic activation:** with and without  
**Result:** negative  
**Method:** other  
**Year:** 1988 **GLP:** no data  
**Test substance:** as prescribed by 1.1 - 1.4  
**Source:** WHO Environmental Health Criteria 117, Methyl Isobutyl Ketone, Geneva, 1990.  
 Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

**Type:** Mouse lymphoma assay  
**System of testing:** L5178Y TK +/-  
**Concentration:** up to 3368 µg/ml  
**Metabolic activation:** with and without  
**Result:** ambiguous  
**Method:** other: see reference  
**Year:** 1984 **GLP:** yes  
**Test substance:** other TS: purity 99.6%  
**Remark:** The non-activated and activated cultures that were cloned were treated with a range of test article concentrations which produced 3% to 95% and 23% to 95% total growth, respectively.  
Three non-activated cultures exhibited mutant frequencies which were significantly greater than the mean mutant frequency of the solvent (DMSO) controls, but there was no evidence of a dose-response relationship. None of the S-9 activated cultures exhibited mutant frequencies which were greater than the mean mutant frequency of the solvent controls.

**Source:** Huels AG Marl

(104)

**Type:** Mouse lymphoma assay  
**System of testing:** L5178Y TK +/-  
**Concentration:** up to 2967 µg/ml  
**Metabolic activation:** with and without  
**Result:** ambiguous  
**Method:** other: see reference  
**Year:** 1984 **GLP:** yes  
**Test substance:** other TS: purity 99.6%  
**Remark:** The non-activated and activated cultures that were cloned were treated with a range of test article concentrations which produced 1% to 80% and 28% to 63% total growth, respectively.  
Four non-activated cultures exhibited mutant frequencies which were more than twice the mean mutant frequency of the solvent (DMSO) controls, but no clear dose-dependent response was noted. None of the S-9 activated cultures exhibited mutant frequencies which were greater than the mean mutant frequency of the solvent controls.

**Source:** Huels AG Marl

(104)

**Type:** Unscheduled DNA synthesis  
**System of testing:** Primary rat hepatocytes  
**Concentration:** 0.1 - 100 ul/ml  
**Metabolic activation:** no data  
**Result:** negative  
**Method:** other  
**Year:** 1988 **GLP:** no data  
**Test substance:** as prescribed by 1.1 - 1.4  
**Source:** WHO Environmental Health Criteria 117, Methyl Isobuyl Ketone, Geneva, 1990.  
 Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

**Type:** Unscheduled DNA synthesis  
**System of testing:** rat primary hepatocytes  
**Concentration:** 8.02, 80.2, 802, 8020 and 80200 æg/ml  
**Metabolic activation:**  
**Result:** negative  
**Method:** other: see reference  
**Year:** 1984 **GLP:** yes  
**Test substance:** other TS: purity 99.6%  
**Source:** Huels AG Marl

(104)

**Type:** Yeast gene mutation assay  
**System of testing:** Saccharomyces cerevisiae  
**Concentration:** up to 5 mg/ml  
**Metabolic activation:** with and without  
**Result:** negative  
**Method:** other  
**Year:** 1988 **GLP:** no data  
**Test substance:** as prescribed by 1.1 - 1.4  
**Source:** WHO Environmental Health Criteria 117, Methyl Isobutyl Ketone, Geneva, 1990.  
 Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

**Type:** other: cell transformation assay  
**System of testing:** mouse embryo cells (BALB/3T3 clone A31)  
**Concentration:** up to 4 mg/ml  
**Metabolic activation:** with and without  
**Result:** ambiguous  
**Method:** other: see reference  
**Year:** 1984 **GLP:** yes  
**Test substance:** other TS: purity 99.56%  
**Remark:** The original assay was conducted with three concentrations (1.92, 2.88 and 3.84 mg/ml in the non-activated study and 0.8, 1.6 and 3.2 mg/ml in the S-9 activated study). A confirmatory study was conducted with four concentrations (3.2, 4, 4.8 and 5.6 mg/ml in the non-activated study and 1.6, 2.4, 3.2 and 4 mg/ml in the S-9 activated study). Under

the conditions of the study, the original assay was positive while the confirmatory assay was negative.  
**Source:** Huels AG Marl (104)

**Type:** other  
**System of testing:** rat liver cell chromosomal damage assay (RL4 cells)  
**Concentration:** up to 1000 ug/ml  
**Metabolic activation:** without  
**Result:** negative  
**Method:** other  
**Year:** 1988 **GLP:** no data  
**Test substance:** as prescribed by 1.1 - 1.4  
**Source:** WHO Environmental Health Criteria 117, Methyl Isobutyl Ketone, Geneva, 1990.  
Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

**Type:** other  
**System of testing:** cell transformation using Balb/3T3 cells  
**Concentration:** 2-5 ul/ml without S9, 1-7 ug/ml with S9.  
**Metabolic activation:** with and without  
**Result:** ambiguous  
**Method:** other  
**Year:** 1988 **GLP:** no data  
**Test substance:** as prescribed by 1.1 - 1.4  
**Source:** WHO Environmental Health Criteria 117, Methyl Isobutyl Ketone, Geneva, 1990.  
Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

### 5.6 Genetic Toxicity 'in Vivo'

**Type:** Micronucleus assay  
**Species:** mouse **Sex:** male/female  
**Strain:** no data  
**Route of admin.:** i.p.  
**Exposure period:** Once  
**Doses:** 0.73 ml/kg  
**Result:**  
**Method:** other  
**Year:** 1988 **GLP:** no data  
**Test substance:** as prescribed by 1.1 - 1.4  
**Remark:** Results were negative.  
**Source:** WHO Environmental Health Criteria 117, Methyl Isobutyl Ketone, Geneva, 1990.  
Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

**Type:** Micronucleus assay  
**Species:** mouse **Sex:** male/female  
**Strain:** CD-1  
**Route of admin.:** i.p.  
**Exposure period:** once  
**Doses:** 585 mg/kg  
**Result:**  
**Method:** other: see reference  
**Year:** 1984 **GLP:** yes  
**Test substance:** other TS: purity 99.56%  
**Remark:** 5 mice/sex/group;  
time of sacrifice: 12, 24 and 48 hours after treatment;  
1000 polychromatic erythrocytes were scored;  
**Result:** Methyl isobutyl ketone did not induce micronucleated  
erythrocytes in male or female mice.  
**Source:** Huels AG Marl

(104)

### 5.7 Carcinogenicity

**Species:** **Sex:**  
**Strain:**  
**Route of admin.:**  
**Exposure period:**  
**Frequency of treatment:**  
**Post. obs. period:**  
**Doses:**  
**Result:**  
**Control Group:**  
**Method:**  
**Year:** **GLP:**  
**Test substance:**  
**Remark:** No studies available.  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

### 5.8 Toxicity to Reproduction

-

**5.9 Developmental Toxicity/Teratogenicity**

**Species:** rat **Sex:** female  
**Strain:** Fischer 344  
**Route of admin.:** inhalation  
**Exposure period:** 6 hours per day.  
**Frequency of treatment:** During organogenesis (days 6-15).  
**Duration of test:** Sacrifice on day 21  
**Doses:** 300, 1000, 3000 ppm  
**Control Group:** yes  
**NOAEL Maternalt.:** = 1000  
**NOAEL Teratogen.:** = 3000  
**Method:**  
**Year:** 1987 **GLP:** yes  
**Test substance:** as prescribed by 1.1 - 1.4  
**Source:** WHO Environmental Health Criteria 117, Methyl Isobutyl Ketone, Geneva, 1990.  
Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

**Species:** rat **Sex:** female  
**Strain:** Fischer 344  
**Route of admin.:** inhalation  
**Exposure period:** gestation day 6 through 15  
**Frequency of treatment:** 6 hours/day  
**Duration of test:**  
**Doses:** 0, 300, 1000 or 3000 ppm  
**Control Group:** yes  
**NOAEL Maternalt.:** = 1000 ppm  
**NOAEL Teratogen.:** >= 3000 ppm  
**Method:** other: see reference  
**Year:** 1984 **GLP:** yes  
**Test substance:** other TS: purity > 99.5%  
**Remark:** Timed-pregnant Fischer-344 rats (23-26 dams/group) were exposed to methyl isobutyl ketone by inhalation on gestational day (gd) 6 through 15 and were sacrificed on gd 21. Live fetuses were examined for external, visceral and skeletal alterations.  
**Result:** Exposure to 3000 ppm resulted in maternal toxicity (clinical signs, decreased body weight and body weight gain, increased relative kidney weight and decreased food consumption) and fetotoxicity (reduced fetal body weight per litter and reductions in skeletal ossification). No increase in fetal malformations was observed in any exposure group relative to controls. At 1000 or 300 ppm, there was no maternal, embryo, or fetal toxicity. Reduced fetal body weight was observed at 300 ppm which was confounded by litter size; this finding was apparently not treatment-related.  
**Source:** Huels AG Marl

(107)

**Species:** mouse **Sex:** female  
**Strain:** CD-1  
**Route of admin.:** inhalation  
**Exposure period:** organogenesis (days 6-15).  
**Frequency of treatment:** 6 hours per day  
**Duration of test:** Sacrificed on day 18.  
**Doses:** 300, 1000, 3000 ppm  
**Control Group:** yes  
**NOAEL Maternalt.:** = 1000  
**NOAEL Teratogen.:** = 3000  
**Method:**  
**Year:** 1987 **GLP:** yes  
**Test substance:** as prescribed by 1.1 - 1.4  
**Source:** WHO Environmental Health Criteria 117, Methyl Isobutyl Ketone, Geneva, 1990.  
Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

**Species:** mouse **Sex:** female  
**Strain:** CD-1  
**Route of admin.:** inhalation  
**Exposure period:** gestation day 6 through 15  
**Frequency of treatment:** 6 hours/day  
**Duration of test:**  
**Doses:** 0, 300, 1000 or 3000 ppm  
**Control Group:** yes  
**NOAEL Maternalt.:** = 1000 ppm  
**NOAEL Teratogen.:** >= 3000 ppm  
**Method:** other: see reference  
**Year:** 1984 **GLP:** yes  
**Test substance:** other TS: purity > 99.5%  
**Remark:** Timed-pregnant CD-1 mice (22-25 dams/group) were exposed to methyl isobutyl ketone by inhalation on gestational day (gd) 6 through 15 and were sacrificed on gd 18. Live fetuses were examined for external, visceral and skeletal alterations.  
**Result:** Exposure to 3000 ppm resulted in maternal toxicity (apparent exposure-related increases in deaths [12 %; 3/25 dams], clinical signs and increased absolute and relative liver weight), and fetotoxicity (increased incidence of dead fetuses, reduced fetal body weight per litter and reductions in skeletal ossification). No treatment-related embryotoxicity was seen.  
No treatment-related increases in fetal malformations were seen at any exposure concentration tested. There was no evidence of treatment-related maternal, embryo, or fetal toxicity at 1000 or 300 ppm.  
**Source:** Huels AG Marl

(107)

### 5.10 Other Relevant Information

- Type:** adsorption  
**Remark:** Absorption occurs following oral, dermal and inhalational administration. In man, pulmonary absorption in volunteers was reported to be about 60%. Total uptake was linear with increasing concentration and blood concentrations did not reach a plateau. In the guinea pig, a dermal exposure over 2.5 hours resulted in a maximum blood level after 10-45 minutes, followed by a decline (despite continued exposure to MIBK).  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam (108) (109)
- Type:** Biochemical or cellular interactions  
**Remark:** Bei maennlichen Meerschweinchen war die Ornithin-Carbamoyl-Transferase-Aktivitaet im Serum als Testparameter fuer eine Schaedigung der Leber 24 h nach einer einmaligen intraperitonealen Verabreichung von 500 bzw. 1000 mg Methylisobutylketon/kg Kgw. leicht erhoelt (nicht signifikant). In der hohen Dosisgruppe starb 1 von 4 Tieren. Die histopathologische Untersuchung der Leber ergab keine Hinweise fuer eine Schaedigung bzw. Verfettung (keine weiteren Angaben).  
**Source:** Huels AG Marl (110)
- Type:** Biochemical or cellular interactions  
**Remark:** 48 h nach 4stuendiger Ganzkoerperexposition von je 5 maennlichen Sprague-Dawley Ratten gegenueber 595, 1280 bzw. 3020 ppm Methylisobutylketon (ca. 2475, 5325 bzw. 12563 mg/m<sup>3</sup>/4 h) waren der Cytochrom P-450 Gehalt sowie die Glutathion-S-Transferase-Aktivitaet in der Leber signifikant erhoelt im Vergleich zur Kontrolle, die Glutamat-Dehydrogenase-Aktivitaet im Serum blieb unbeeinflusst.  
**Source:** Huels AG Marl (111)
- Type:** Biochemical or cellular interactions  
**Remark:** Nach einmaliger oraler Verabreichung von 1.5, 5.0, 7.5, 15.0 und 30.0 mmol Methylisobutylketon/kg Kgw. (150, 500, 750, 1500 und 3000 mg/kg Kgw.) an je 6-8 maennliche Sprague-Dawley Ratten wurde nach 24 h ein Lebermikrosomenassay durchgefuehrt: Der Cytochrom P-450 Gehalt war in der 7.5 und 15.0 mmol/kg-Dosis- gruppe signifikant erhoelt, die Anilin-Hydroxylase-Aktivitaet und die 7-Ethoxycumarin O-Desethylaseaktivitaet war ab 7.5 mmol/kg Kgw. signifikant erhoelt und die Aminopyrin N-Desmethylase-Aktivitaet lag bei allen Dosierungen im Bereich der Kontrolle.  
**Source:** Huels AG Marl (112)

- Type:** Biochemical or cellular interactions  
**Remark:** 5 Leghorn-Hennen/Substanz- und Kontrollgruppe wurden gegen 1000 ppm MIBK fuer 50 Tage (24 h/d) exponiert; Der Cytochrom P-450 Gehalt bzw. die Aktivitaet der Anilin-Hydroxylase in der Leber waren signifikant um das 5.6 bzw. 3.6 fache erhoeht im Vergleich zur Kontrolle. Keine weiteren Angaben.  
**Source:** Huels AG Marl (99)
- Type:** Biochemical or cellular interactions  
**Remark:** The effects of MIBK administration on the activity of the mixed function oxidase system (MFOS) in male New Zealand rabbits was determined. The administration of MIBK (5 mmol/kg, once daily on three consecutive days) by gavage resulted in an increase of the activities of the 7-ethoxycoumarin-dealkylase, the aniline-hydroxylase and the aminopyrine-N-demethylase in vitro, as well as an increased concentration of total cytochrome P-450. In another experiment the effect of MIBK treatment (same regimen as above) on plasma concentration of warfarin (given on the fourth day) was examined in vivo. No effects on warfarin plasma concentrations was observed.  
**Source:** Huels AG Marl (113)
- Type:** Biochemical or cellular interactions  
**Remark:** The ability of methyl isobutyl ketone (MIBK) and its two major metabolites, 4-methyl-2-pentanol (4MPOL) and 4-hydroxymethyl isobutyl ketone (4-OHMIBK) to potentiate the liver injury induced by CHCl<sub>3</sub> was assessed in male Sprague-Dawley rats. The parent compound and both metabolites significantly increased the liver damage induced by CHCl<sub>3</sub>, as demonstrated by the elevation of the plasma activity of alanine aminotransferase and ornithine carbamoyl transferase and by the severity of the morphological changes. The minimally effective dosage needed to potentiate CHCl<sub>3</sub>-induced hepatotoxicity was approximately 5 mmol/kg for the three compounds. In addition, the inducing properties of MIBK (cytochrome P-450 content and the activity of aniline hydroxylase, 7-ethoxycoumarin O-deethylase, and aminopyrine N-demethylase) were determined. Cytochrome P-450 content and the oxidation of aniline and 7-ethoxycoumarin were significantly increased with either a single (7.5 mmol/kg or greater) or a multiple (5.0 and 7.5 mmol/kg/day for 5 days) administration of MIBK. An increase in the activity if the aminopyrine demethylase was also elicited by the repetitive administration of MIBK.  
**Source:** Huels AG Marl (112)

**Type:** Biochemical or cellular interactions  
**Remark:** Groups of hens (*Gallus gallus domesticus*) were exposed for 29 days in inhalation chambers to 1000 ppm n-hexane in combination with 10, 100, 250, 500 or 1000 ppm methyl isobutyl ketone (MIBK). Other groups received either 1000 ppm n-hexane, 1000 ppm MIBK, or ambient air and served as controls. A dose-dependent decrease in body weight and an increase in clinical effects were noted for the highest exposure groups (1000 ppm n-hexane combined with 1000, 500 or 250 ppm MIBK). There was a MIBK dose-dependent increase in cytochrome P450 content and benzphetamine N-demethylase activity, but there was no distinct pattern for ethoxyresorufin O-deethylase or cytochrome c reductase activities. Mixed-function oxidase levels and activities (P450 content and benzphetamine N-demethylase) were elevated significantly over controls even in the lowest MIBK group, although there were no clinical signs of neurotoxicity. Four different isozymes of cytochrome P450 were measured immunologically. There was a dose-dependent increase in three of the isozymes, two of which were phenobarbital inducible and one of which was induced by naphthoflavone. Quantitatively, the largest increase was in the PB-A isozyme, a phenobarbital-inducible isozyme which accounted for approximately 70% of the P450 present in animals treated with MIBK.

**Source:** Huels AG Marl

(114)

**Type:** Biochemical or cellular interactions  
**Remark:** Potential toxic interaction between hexachlorobenzene (HCB) and methyl isobutyl ketone (MIBK) was investigated in female Sprague-Dawley rats using two different schedules of toxicant administration [1: simultaneous p.o. administration of 50 mg/kg/d HCB 5 d/week and 7.5 mmol/kg/d 3 d/week, for 6 weeks; 2: initial dosing of 25 or 50 mg HCB/kg/d for 12 consecutive days, followed by the administration of 7.5 mmol MIBK/kg/every other day for 27 days;]. When administered simultaneously, MIBK reduced the severity of HCB-induced porphyria, but when given sequentially after HCB accumulation, it enhanced the porphyrinogenic response.

**Source:** Huels AG Marl

(115)

**Type:** Biochemical or cellular interactions  
**Remark:** The mechanism of methyl isobutyl ketone (MIBK) potentiated intrahepatic cholestasis induced by taurochenodeoxycholate and the combination of manganese-bilirubin was investigated using the lithocholate-induced cholestasis model. Male rats were given MIBK 7.5 mmol/kg on three consecutive days. MIBK potentiated lithocholate-induced cholestasis and reduced significantly bile salt, phospholipid and cholesterol secretion rates as well as the transport maximum of taurochenodeoxycholic acid.

**Source:** Huels AG Marl

(116)

- Type:** Biochemical or cellular interactions  
**Remark:** The potentiation of experimental cholestasis after inhalation or oral administration of methyl isobutyl ketone was investigated in male Sprague-Dawley rats. Rats exposed to MIBK orally or by inhalation exhibited an enhanced diminution in bile flow that was dose-dependent. With dosages of 3 mmol/kg p.o. or 400 ppm by inhalation or more, diminution in bile flow was significantly different from control values. Comparisons between maximal bile flow decrease and MIBK plasma concentration showed that the severity of the hepatotoxic response was dependent on the plasma MIBK concentration, irrespective of the route of administration.  
**Source:** Huels AG Marl (117)
- Type:** Distribution  
**Remark:** Following constant infusion in guinea pig, a high blood clearance value was obtained indicating a high metabolising capability. Different infusion rates indicated linear kinetics. Following accidental exposure in man, MIBK is widely distributed about the body. Following inhalation (of 500 ppm for 2 hours), distribution of MIBK was divided equally between red blood cells and plasma. A similar distribution was obtained in vitro in both rat and human blood. MIBK is reported to cross the placenta.  
**Source:** Dutch Expert Committee for Occupational Standards Health based recommended occupational exposure limit for methyl isobutyl ketone. Dutch Directorate General of Labour, The Hague, September, 1991. Shell Nederland Chemie B.V. Hoogvliet-Rotterdam (118) (119)
- Type:** Excretion  
**Remark:** Volunteer studies, in which 8 males involved in light exercise were exposed on 4 occasions to 10, 100 or 200 mg/m<sup>3</sup> for 2 hours indicate that very little unchanged MIBK (0.04%) is excreted in the urine within 3 hours post-exposure. The amount of unchanged MIBK was proportional to the total dose. The apparent blood clearance was 1.6 l/hr/kg at all exposure levels with no evidence of saturation kinetics. Elimination was faster within the first 30 minutes after exposure, from 30-180 minutes blood levels fell more slowly. Urinary metabolites were below the limit of detection.  
**Source:** Shell Nederland Chemie B.V. Hoogvliet-Rotterdam (120)
- Type:** Metabolism  
**Remark:** Two metabolites have been identified in guinea pig and rat serum following ip injection. The major metabolite 4-hydroxy-4-methyl-2-pentanone was formed by oxidation, the other, 4-methyl pentanol by reduction. The serum half life of MIBK was calculated as 66 minutes and the clearance time of 6 hours compared to a clearance time of 16 hours for the major metabolite.  
**Source:** WHO Environmental Health Criteria 117, Methyl Isobutyl Ketone, Geneva, 1990.

Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

**Type:** Metabolism  
**Remark:** Nach einmaliger intraperitonealer Verabreichung von 450 mg Methylisobutylketon/kg Kgw. an maennliche Meerschweinchen betrug die Eliminationshalbwertszeit im Serum 66 min. Als Hauptmetabolit im Serum wurde 4-Hydroxy-4-methyl-2-pentanon innerhalb von 16 h vollstaendig eliminiert. Ein weiterer qualitativ nachgewiesener Metabolit im Serum war 4-Methyl-2-pentanol.  
**Source:** Huels AG Marl (121)

**Type:** Neurotoxicity  
**Remark:** Work in rodents and primates suggests a depressive effect of MIBK on the central nervous system. MIBK does not induce peripheral neuropathy. MIBK does enhance the neurotoxic effects of n-Hexane, probably by induction of liver cytochrome P-450.  
**Source:** Dutch Expert Committee for Occupational Standards Health based recommended occupational exposure limit for methyl isobutyl ketone. Dutch Directorate General of labour, The Hague, 1991.  
Shell Nederland Chemie B.V. Hoogvliet-Rotterdam

**Type:** Neurotoxicity  
**Remark:** Methylisobutylketonkonzentration, die die Atemfrequenz von maennlichen Swiss OF1-Maeusen waehrend einer 5minuetigen Exposition um 50 % herabsetzte RD50 = 13291 mg/m<sup>3</sup> Luft.  
**Source:** Huels AG Marl (122)

**Type:** Neurotoxicity  
**Remark:** Bei Sprague-Dawley Ratten, die ein um 20 % reduziertes Koerpergewicht hatten, fuehrte die 3stuendige Ganzkoerperexposition gegenueber 25 ppm Methylisobutylketon (ca. 104 mg/m<sup>3</sup>) bei 2 von 7 Tieren in einem operanten Verhaltenstest zu einer erhoekten Frequenz bei der Betaetigung eines Hebels zur Futterspende (Fluessigfutter) waehrend der Exposition sowie bis zu 12 Tage nach der Exposition. Die Testdauer 2, 5, 6, 7, 8 und 12 Tage nach der Exposition betrug jeweils 3 h/Tag, waehrend der die durchschnittliche Anzahl der Hebelbetaetigungen zur Futterspende/min ermittelt wurde.  
**Source:** Huels AG Marl (123)

**Type:** Neurotoxicity  
**Remark:** Waehrend einstuendiger kontinuierlicher intravenoeser Verabreichung von 30 umol Methylisobutylketon/kg Kgw./min (ca. 3 mg/kg Kgw./min) wurden weibliche Sprague-Dawley Ratten alle 5 min Drehbeschleunigung ausgesetzt und der resultierende Nystagmus registriert (Elektronystagmographie). Die Methylisobutylketon-Blutkonzentration betrug waehrend des Versuches 0.2 mmol/l (ca. 20 mg/l); der Nystagmus war waehrend der Verabreichung vermindert im Vergleich zum Wert

**Source:** vor der Verabreichung.  
Huels AG Marl (124)

**Type:** Neurotoxicity  
**Remark:** Bei Katzen lag die Reizschwelle fuer Speichelsekretion aus der Ohrspeicheldruese bei 15minuetiger Inhalation zwischen 0.25 und 0.50 mg Methylisobutylketon/l (keine weiteren Angaben).

**Source:** Huels AG Marl (71)

**Type:** Neurotoxicity  
**Remark:** Electromyographic examination of male beagle dogs administered 300 mg/kg b.w. daily of methyl isobutyl ketone by subcutaneous injection for approximately eleven months did not demonstrate evidence of neurotoxicity. Subcutaneous injection of the test substance produced local tissue damage at the injection side.

**Source:** Huels AG Marl (125)

**Type:** Neurotoxicity  
**Remark:** The joint neurotoxic action of simultaneous exposure to vapors of n-hexane and methyl isobutyl ketone (MIBK) and dermally applied O-ethyl O-nitrophenyl phenylphosphonothioate (EPN) was studied in groups of five adult hens. Four groups of hens were concurrently exposed to a dermal 2.5 mg/kg of EPN, 1000 ppm of n-hexane and 100, 250, 500 or 1000 ppm of MIBK. Two groups were each exposed to binary mixtures of a dermal dose of 2.5 mg/kg of EPN and 250 ppm of MIBK or 1000 ppm of n-hexane. Another three groups were exposed to either 250 ppm of MIBK, 1000 ppm of n-hexane or a dermal dose of 2.5 mg/kg of EPN. One group of hens was kept untreated. Hens exposed to MIBK or n-hexane vapor did not exhibit any toxicity signs. In contrast, hens treated with EPN alone or in combination with n-hexane and/or MIBK developed acute cholinergic and delayed neurotoxicity signs. Hen brain acetylcholinesterase and neurotoxic esterase activities were inhibited in hens treated concurrently with EPN, n-hexane and MIBK. MIBK alone or in combination with EPN and n-hexane induced liver microsomal cytochrome P450 content and phenobarbital-inducible P450 enzyme activities. Microsomes of hens treated with EPN, n-hexane and MIBK, either alone or in mixtures, enhanced the biotransformation of EPN to the more neurotoxic oxidation metabolite O-ethyl O-4-nitrophenyl phosphonate.

**Source:** Huels AG Marl (126)

**Type:** Toxicokinetics  
**Remark:** Bei 8 anaesthesierten weiblichen Meerschweinchen, denen Methylisobutylketon in einer Dosierung von 0.680 - 0.928 umol/min x kg Kgw. (68 - 93 ug/min x kg Kgw.) ueber 30 min intravenoes verabreicht wurde, betrug die Steady-state-Konzentration im Blut nach 14 - 30minuetiger Infusion durchschnittlich 3.94 umol Methylisobutylketon/l (ca. 0.4 mg/l). Die Blut-Clearance betrug durchschnittlich 130 ml/min und die Eliminationshalbwertszeit ca. 3.29 min. Nach einer 150 - 190minuetigen applikationsfreien Zeit erhielten dieselben Tiere unverduenntes Methylisobutylketon in einem Applikationsvolumen von 1 ml dermal in einem Glaszylinder (Applikationsflaeche 3.14 cm<sup>2</sup>) fuer 2.5 h auf die geschorene Rueckenhaut appliziert. Maximale Blutkonzentrationswerte von durchschnittlich 26.7 (Bereich 7.1 - 54.7) umol Methylisobutylketon/l (ca. 2.7 mg/l) wurden nach 23.1 (Bereich 10 - 45) min erreicht. Die maximale Hautresorptionsrate betrug 1.1 (Bereich 0.15 - 2.2) umol/min x cm<sup>2</sup> (ca. 0.1 mg/min x cm<sup>2</sup>) und wurde nach 10 - 45 min erreicht. Die durchschnittliche Hautresorptionsrate nach 15 - 75 min betrug 0.86 (Bereich 0.11 - 2.2) umol/min x cm<sup>2</sup> (0.086 mg/min x cm<sup>2</sup>) und verringerte sich innerhalb einer 75 - 135minuetigen dermalen Exposition um durchschnittlich 34%. Nach einmaliger intravenoeser Verabreichung von 1.1, 5.1 bzw. 15.4 mg Methylisobutylketon/kg Kgw. an jeweils 1 weibliches Meerschweinchen betrug das scheinbare Verteilungsvolumen (Vss) 1.5 l/kg Kgw.

**Source:** Huels AG Marl

(127)

**Type:** Toxicokinetics  
**Remark:** Nach 2stuendiger Ganzkoerperexposition von 5 maennlichen Sprague-Dawley Ratten gegenueber 500 ppm Methylisobutylketon (ca. 2080 mg/m<sup>3</sup>) wurden durchschnittlich ca. 25.3 ug unveraenderte Testsubstanz/ml Blut nachgewiesen. Die Konzentration im Plasma bzw. in den Erythrozyten betrug durchschnittlich ca. 12.32 bzw. 12.98 ug Methylisobutylketon/ml Blut (keine weiteren Angaben). Nach Inkubation von 0.5 ml gesaettigter Methylisobutylketon-Loesung in isotonischem Puffer mit 10 ml Rattenblut (Sprague- Dawley) betrug die Konzentration im Plasma bzw. in den Erythrozyten durchschnittlich 368 bzw. 382 ug Methylisobutylketon/ml Blut (keine weiteren Angaben). Im menschlichen Blut betrug die Konzentration im Plasma bzw. in den Erythrozyten nach Inkubation von 800 ug Methylisobutylketon/ml Blut durchschnittlich 468 bzw. 396 ?g unveraenderte Testsubstanz/ml Blut (keine weiteren Angaben). Nach Inkubation von Humanplasma mit Methylisobutylketon wurden ca. 20 % der unveraenderten Testsubstanz im Plasmawasser und ca. 80 % im Plasmapraecipitat (Proteine) gefunden. Nach Inkubation von Methylisobutylketon mit Humanerythrozyten wurden ca. 6 % der unveraenderten Testsubstanz in den Zellmembranen, ca. 26 % im Zellwasser und ca. 68 % in der Haemoglobinfraktion gefunden.

**Source:** Huels AG Marl

(128)

### 5.11 Experience with Human Exposure

- Remark:** MIBK produces CNS depression and narcosis at high vapour concentrations (>1000ppm). Workers exposed to MIBK report headache, vertigo, loss of appetite, nausea and irritation of the eyes and respiratory tract. Volunteer studies in which 8 males were exposed to 10, 100 or 200 mg/m<sup>3</sup> for 2 hours on 4 occasions confirmed the CNS and irritant effects of MIBK. Degree of effect increased with exposure level. There were no significant effects on reaction time or a test of mental arithmetic.  
Epidemiological review of 231 workers exposed to chemically contaminated sewer wastes did not show any evidence of impairment of fertility.  
Investigation of liver function of workers exposed to solvents (including MIBK) showed an increased gamma-glutamyl transferase. Activation of platelets has also been reported in another study of 97 workers exposed to mixed solvents.
- Source:** Dutch Expert Committee for Occupational Standards Health based recommended occupational exposure limit for Methyl Isobutyl Ketone. Dutch Directorate General of Labour, The Hague, 1991.  
Shell Nederland Chemie B.V. Hoogvliet-Rotterdam  
(129) (130) (109) (131) (132) (133)
- Remark:** Bei 15minuetiger Ganzkoerperexposition von je ca. 12 Versuchspersonen gegenueber verschiedenen Methylisobutylketon-Konzentrationen wurde von der Mehrheit der Versuchspersonen eine Konzentration von 200 ppm Methylisobutylketon (832 mg/m<sup>3</sup>) als reizend fuer die Augenschleimhaeute und nicht-reizend fuer Nasen- und Rachenschleimhaeute empfunden.
- Source:** Huels AG Marl  
(134)
- Remark:** Bei jeweils 7minuetiger Exposition (Gesichtsmaske) von 5 - 6 Versuchspersonen gegenueber Methylisobutylketon in steigenden Konzentrationen von 402, 915, 1363, 1680, 2301 bzw. 2827 mg/m<sup>3</sup> betrug die Schwellenkonzentration fuer eine Reizung der Augen-, Nasen- bzw. Rachenschleimhaeute 402, 915 bzw. 1363 mg/m<sup>3</sup>. Bei einem 2. Experiment, welches unter den gleichen Versuchsbedingungen mit denselben Versuchspersonen 2 Wochen nach dem 1. Experiment durchgefuehrt wurde, wurde Methylisobutylketon in steigenden Konzentrationen von 845, 1493 bzw. 2066 mg/m<sup>3</sup> eingesetzt. Eine Konzentration von 845 mg/m<sup>3</sup> wurde von jeweils einer der 6 Versuchspersonen als reizend fuer Augen- und Nasenschleimhaeute empfunden. Keine der 6 Versuchspersonen empfand Konzentrationen von bis zu 2066 mg Methylisobutylketon/m<sup>3</sup> als reizend fuer die Rachenschleimhaut.
- Source:** Huels AG Marl  
(135)

**Remark:** Nach einer Expositionszeit von durchschnittlich 23.4 bzw. 27.5 Sekunden wurde eine Konzentration von 5 bzw. 20 ppm Methylisobutylketon (ca. 21 bzw. 83 mg/m<sup>3</sup>) von 8 - 11 Probanden in einem Augenreiztest (mittels Augenmaske) als reizend empfunden. Die maximale Expositionszeit, wenn keine Augenreizung auftrat, betrug 90 Sekunden. Die Exposition erfolgte nach einer 1stuendigen Bestrahlung der Testsubstanz mit Quecksilberlampen (400 W) bei einer NO<sub>2</sub>-Konzentration von 1 ppm. Nach einer 1stuendigen Bestrahlung der Testsubstanz mit Sonnenlicht (NO<sub>2</sub>-Konzentration: 1 ppm) empfanden weniger als die Haelfte der Probanden eine Konzentration von 5 ppm Methylisobutylketon (ca. 21 mg/m<sup>3</sup>) nach einer durchschnittlichen Expositionszeit von 83 Sekunden als reizend fuer die Augenschleimhaeute. Die Mehrheit der Probanden empfand diese Konzentration als nicht reizend fuer die Augenschleimhaeute innerhalb der maximalen Expositionszeit von 90 Sekunden.

**Source:** Huels AG Marl

(136)

**Remark:** In einem Inhalationskammerexperiment wurden 8 maennliche Probanden (18-35 Jahre alt) gegenueber 10, 100 und 200 mg Methylisobutylketon/m<sup>3</sup> fuer jeweils 2 h exponiert, bei gleichzeitiger koerperlicher Belastung (Fahrradergometer; 50 W). Konzentrations- unabhængig wurden ca. 60 % der eingeatmeten Testsubstanz ueber die Lunge resorbiert. Von der gesamten aufgenommenen Methylisobutylketonmenge wurden ca. 0.04 % als unveraenderte Testsubstanz innerhalb von 3 h nach der Exposition im Urin ausgeschieden. Die maximale Methylisobutylketonkonzentration im Blut wurde jeweils am Ende der Exposition (2 h) erreicht mit maximal ca. 12.5 umol/l (1.25 mg/l) in der hohen Konzentration. Die berechnete Eliminationshalbwertszeit im Blut fuer die schnelle Eliminationsphase (alpha-Phase; 0 - 30 min nach der Exposition) betrug 11 bzw. 13 min in der 100 bzw. 200 mg/m<sup>3</sup>-Gruppe und fuer die langsame Eliminationsphase (beta-Phase; 60 - 180 min nach der Exposition) 59 bzw. 74 min. Die durchschnittliche Blut-Clearance betrug konzentrationsunabhængig 1.6 l/h/kg. Die Metaboliten 4-Methyl-2-pentanol und 4-Hydroxy-4-methyl-2-pentanon konnten im Urin nicht nachgewiesen werden (Nachweisgrenze: 5 nmol/l). Folgende, waehrend der Exposition auftretende, akute Symptome wurden von den Probanden in allen Konzentrationen benannt: Reizung von Augen-, Nasen- und Rachenschleimhaeuten, Kopfschmerz und Schwindel. Keines der genannten Symptome trat bei mehr als 3 Probanden/Konzentration gleichzeitig auf. Das Verhalten der Probanden blieb unbeeinflusst. Die Leistungen in einem Reaktionszeittest sowie im Additionstest blieben gleichfalls unbeeinflusst.

**Source:** Huels AG Marl

(137)

- Remark:** Bei Arbeitern, die gegenueber 500 ppm Methylisobutylketon (2080 mg/m<sup>3</sup>) fuer 30 min/Tag exponiert waren (keine Angaben zur Studiendauer), traten Mattigkeit, Appetitlosigkeit, Kopfschmerz, Schmerzen im Magenbereich, Uebelkeit, Erbrechen sowie eine Reizung der Augen- und Rachenschleimhaeute auf. Einige der Arbeiter wiesen eine Vergroesserung der Leber sowie Kolitis auf (keine weiteren Angaben).
- Source:** Huels AG Marl (138)
- Remark:** Die ausgeatmete Luft von 8 nicht-exponierten Probanden wurde gas- chromatographisch-massenspektrometrisch untersucht; bei 3 Probanden wurde 3.9 - 24.0 ug Methylisobutylketon/h in der ausgeatmeten Luft nachgewiesen (Sammelperiode 1 h).
- Source:** Huels AG Marl (139)
- Remark:** Subjects were tested for neurobehavioral performance in an environmental chamber to detect the presence of subclinical central nervous system effects from 4-hr exposures to methyl isobutyl ketone (MIBK) at 100 ppm, methyl ethyl ketone (MEK) at 200 ppm, MIBK at 50 ppm with MEK at 100 ppm, or a placebo. Ethanol by ingestion was used as a positive control. Five psychomotor tests were used to measure neurobehavioral effects. Additionally, chemical measurements and reports of sensory and irritant effects were measured. The chemical exposures produced statistically significant performance effects on only 4 of 32 measures, however, these effects were not substantial and could not be attributed directly to the chemical exposures. Alcohol ingestion produced significant decrements on the performance tests. Significant odor sensations and irritant effects were reported by the subjects during the chemical exposures.
- Source:** Huels AG Marl (140)

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**7.1 Risk Assessment**

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