

201-15001B

# I U C L I D

## Data Set

04 JAN -6 PM 2:02

RECEIVED  
00011810

**Existing Chemical** : ID: 60-29-7  
**CAS No.** : 60-29-7  
**EINECS Name** : diethyl ether  
**EC No.** : 200-467-2  
**TSCA Name** : Ethane, 1,1'-oxybis-  
**Molecular Formula** : C4H10O

**Producer related part**  
**Company** : Diethyl Ether Producers Association  
**Creation date** : 12.09.2003

**Substance related part**  
**Company** : Diethyl Ether Producers Association  
**Creation date** : 12.09.2003

**Status** :  
**Memo** :

**Printing date** : 29.12.2003  
**Revision date** :  
**Date of last update** : 29.12.2003

**Number of pages** : 79

**Chapter (profile)** : Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10  
**Reliability (profile)** : Reliability: without reliability, 1, 2, 3, 4  
**Flags (profile)** : Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE),  
Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

# 1. General Information

Id 60-29-7  
Date 29.12.2003

## 1.0.1 APPLICANT AND COMPANY INFORMATION

Type :  
Name : B.V. CONSOLCO  
Contact person :  
Date :  
Street : De Ruyterkade 44  
Town : 1012 AA Amsterdam  
Country : Netherlands  
Phone : 020-6221444  
Telefax : 020-6254449  
Telex : 12458  
Cedex :  
Email :  
Homepage :  
  
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

Type :  
Name : BASF AG  
Contact person :  
Date :  
Street : Karl-Bosch-Str  
Town : 67056 Ludwigshafen  
Country : Germany  
Phone :  
Telefax :  
Telex :  
Cedex :  
Email :  
Homepage :  
  
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

Type :  
Name : BP Chemicals Ltd.  
Contact person :  
Date :  
Street : 76, Buckingham Palace Road  
Town : SW1 WOSU London  
Country : United Kingdom  
Phone :  
Telefax :  
Telex :  
Cedex :  
Email :  
Homepage :  
  
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

Type :  
Name : Huels AG  
Contact person :  
Date :  
Street : Postfach  
Town : D-45764 Marl

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Country : Germany  
Phone :  
Telefax :  
Telex :  
Cedex :  
Email :  
Homepage :

Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

Type :  
Name : Petrasol B.V.  
Contact person :  
Date :  
Street : P.O.Box 222  
Town : 4200 AE Gorinchem  
Country : Netherlands  
Phone : +31 183 630555  
Telefax : +31 183 632272  
Telex : 23602 petr nl  
Cedex :  
Email :  
Homepage :

Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

Type :  
Name : Sodes  
Contact person :  
Date :  
Street : 44 rue Jean-Goujon  
Town : 75008 Paris  
Country : France  
Phone : 142561287  
Telefax : 142257346  
Telex : 651646  
Cedex :  
Email :  
Homepage :

Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

## 1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

## 1.0.3 IDENTITY OF RECIPIENTS

## 1.0.4 DETAILS ON CATEGORY/TEMPLATE

## 1.1.0 SUBSTANCE IDENTIFICATION

## 1.1.1 GENERAL SUBSTANCE INFORMATION

**Purity type** :  
**Substance type** : organic  
**Physical status** : liquid  
**Purity** : -  
**Colour** :  
**Odour** :  
  
**Source** : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

## 1.1.2 SPECTRA

## 1.2 SYNONYMS AND TRADENAMES

### 1,1'-Oxybisethane

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
29.08.1996

### 3-Oxapentane

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
29.08.1996

### Anaesthetic ether

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
29.08.1996

### Anesthesia ether

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
29.08.1996

### Anesthetic ether

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
29.08.1996

### Diethyl ether

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
29.08.1996

### Diethyl oxide

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
29.08.1996

## Diethylether

**Source** : Sodes Paris  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
30.05.1994

## Diethylether, Ethoxyethaan, Ether, Ethyloxyde, Diethyloxyde

**Source** : B.V. CONSOLCO Amsterdam  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
28.02.1997

## Diethylether; ethoxyethane

**Source** : ISIS/RISKLINE release VI, 1997, Haskoning  
Petrasol B.V. Gorinchem  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
04.05.1998

## Diethyloxyd

**Source** : Sodes Paris  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
25.05.1994

## Ethane, 1,1'-oxybis-

**Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
14.09.1993

## Ethane, 1,1'-oxybis- (9CI)

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
29.08.1996

## Ethane,1,1'-oxybis-

**Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
30.05.1994

## Ether

**Source** : Sodes Paris  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
25.05.1994

## Ether (6CI)

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
29.08.1996

## Ethoxyethan

**Source** : Sodes Paris

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25.05.1994  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

## Ethoxyethane

Source : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
29.08.1996

## Ethyl ether (8CI)

Source : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
29.08.1996

## Ethylether

Source : Sodes Paris  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
25.05.1994

## Ethyloxid

Source : Sodes Paris  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
30.05.1994

## Pronarcol

Source : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
29.08.1996

## Sulfuric ether

Source : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
30.05.1994

## 1.3 IMPURITIES

## 1.4 ADDITIVES

## 1.5 TOTAL QUANTITY

Quantity : 10000 - 50000 tonnes in

Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

## 1.6.1 LABELLING

# 1. General Information

Id 60-29-7  
Date 29.12.2003

**Labelling** : as in Directive 67/548/EEC  
**Specific limits** : no data  
**Symbols** : F+, Xn, ,  
**Nota** : , C,  
**R-Phrases** : (12) Extremely flammable  
(19) May form explosive peroxides  
(22) Harmful if swallowed  
(66) Repeated exposure may cause skin dryness or cracking  
(67) Vapours may cause drowsiness and dizziness  
**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  
(33) Take precautionary measures against static discharges  
**Source** : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

## 1.6.2 CLASSIFICATION

**Classified** : as in Directive 67/548/EEC  
**Class of danger** : corrosive  
**R-Phrases** : (22) Harmful if swallowed  
**Specific limits** :

**Source** : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

**Classified** : as in Directive 67/548/EEC  
**Class of danger** : extremely flammable  
**R-Phrases** : (12) Extremely flammable  
**Specific limits** :

**Source** : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

**Classified** : as in Directive 67/548/EEC  
**Class of danger** :  
**R-Phrases** : (67) Vapours may cause drowsiness and dizziness  
**Specific limits** :

**Source** : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

**Classified** : as in Directive 67/548/EEC  
**Class of danger** :  
**R-Phrases** : (19) May form explosive peroxides  
**Specific limits** :

**Source** : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

**Classified** : as in Directive 67/548/EEC  
**Class of danger** :  
**R-Phrases** : (66) Repeated exposure may cause skin dryness or cracking  
**Specific limits** :

**Source** : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

## 1.6.3 PACKAGING

## 1.7 USE PATTERN

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

**Source** : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

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

**Source** : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

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

**Source** : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

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

**Source** : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

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

**Source** : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

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

**Source** : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

**Type of use** : industrial  
**Category** : Fuel industry

**Source** : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

**Type of use** : industrial  
**Category** : Personal and domestic use

**Source** : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

**Type of use** : industrial

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**Category** : Photographic industry

**Source** : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

**Type of use** : use  
**Category** : Cleaning/washing agents and disinfectants

**Source** : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

**Type of use** : use  
**Category** : Explosives

**Source** : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

**Type of use** : use  
**Category** : Fuel

**Source** : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

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

**Source** : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

**Type of use** : use  
**Category** : Laboratory chemicals

**Source** : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

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

**Source** : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

**Type of use** : use  
**Category** : Photochemicals

**Source** : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

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

**Source** : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
11.02.2000

## 1.7.1 DETAILED USE PATTERN

## 1.7.2 METHODS OF MANUFACTURE

## 1.8 REGULATORY MEASURES

## 1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

Type of limit : MAK (DE)  
 Limit value : 400 ml/m<sup>3</sup>  
**Short term exposure limit value**  
 Limit value : 1600 ml/m<sup>3</sup>  
 Time schedule : 15 minute(s)  
 Frequency : 4 times

Country : Germany  
 Source : Huels AG Marl  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

18.02.1997

Type of limit : MAK (DE)  
 Limit value : 1200 mg/m<sup>3</sup>  
**Short term exposure limit value**  
 Limit value : 4800 mg/m<sup>3</sup>  
 Time schedule : 15 minute(s)  
 Frequency : 4 times

Country : Germany  
 Source : Huels AG Marl  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

18.02.1997

Type of limit : OES (UK)  
 Limit value : 400 ml/m<sup>3</sup>  
**Short term exposure limit value**  
 Limit value : 500 ml/m<sup>3</sup>  
 Time schedule :  
 Frequency : times

Source : BP Chemicals Ltd. London  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

02.06.1994

Type of limit : other  
 Limit value : 1200 mg/m<sup>3</sup>  
**Short term exposure limit value**  
 Limit value : 1500 mg/m<sup>3</sup>  
 Time schedule : 15 minute(s)  
 Frequency : times

Remark : Mean Exposure Limit Value (VME)  
 Source : Sodes Paris  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

30.05.1994

Type of limit : other  
 Limit value : 400 ml/m<sup>3</sup>  
**Short term exposure limit value**  
 Limit value : 500 ml/m<sup>3</sup>  
 Time schedule : 15 minute(s)  
 Frequency : times

Remark : Mean Exposure Limit Value (VME)

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**Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
30.05.1994

**Type of limit** :  
**Limit value** : 400 other

**Remark** : Opmerking: andere = ppm  
**Source** : B.V. CONSOLCO Amsterdam  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
18.11.2003

## 1.8.2 ACCEPTABLE RESIDUES LEVELS

## 1.8.3 WATER POLLUTION

**Classified by** : KBwS (DE)  
**Labelled by** : KBwS (DE)  
**Class of danger** : 1 (weakly water polluting)

**Country** : Germany  
**Remark** : Katalog-Nr. 80  
**Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
18.02.1997 (54)

## 1.8.4 MAJOR ACCIDENT HAZARDS

**Legislation** : Stoerfallverordnung (DE)  
**Substance listed** : yes  
**No. in Seveso directive** :

**Country** : Germany  
**Remark** : im Anhang IV genannt (Kat. 6; leichtentzuendliche  
Fluessigkeiten)  
**Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
18.02.1997 (54)

## 1.8.5 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** : Anhang E  
**Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
18.02.1997 (54)

## 1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

## 1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

## 1.9.2 COMPONENTS

## 1.10 SOURCE OF EXPOSURE

**Remark** : Diethylether is released into the atmosphere. Because of its high vapor pressure and volatility, diethylether emissions are expected to occur chiefly by means of exhaust resulting during production and use.  
In troposphere, the half life time of diethylether is estimated at 43 hours (see RE:1).

**Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

30.05.1994 (43)

**Remark** : Initial partitioning  
Release into the Atmosphere  
Because of its high vapor pressure and volatility, diethyl ether emissions are expected to occur chiefly by means of exhaust resulting during production and use.

**Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

17.02.1997 (16)

**Remark** : Huels: Emissionserklaerung 1992  
Release into the atmosphere on production site in 1992: 5000 kg/a

**Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

17.02.1997 (53)

## 1.11 ADDITIONAL REMARKS

## 1.12 LAST LITERATURE SEARCH

## 1.13 REVIEWS

## 2. Physico-Chemical Data

Id 60-29-7  
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### 2.1 MELTING POINT

<b>Value</b>	:	= -116.2- °C	
<b>Reliability</b>	:	(2) valid with restrictions	
<b>Flag</b>	:	Critical study for SIDS endpoint	
14.11.2003			(45)
<b>Value</b>	:	= -116.3- °C	
<b>Decomposition</b>	:	no, at - °C	
<b>Sublimation</b>	:	no	
<b>Method</b>	:		
<b>Year</b>	:		
<b>GLP</b>	:		
<b>Test substance</b>	:		
<b>Source</b>	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
17.02.1997			(47)
<b>Value</b>	:	-116- °C	
<b>Source</b>	:	Sodes Paris EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
13.12.1993			(82)

### 2.2 BOILING POINT

<b>Value</b>	:	= 34.5- °C at 1013 hPa	
<b>Reliability</b>	:	(2) valid with restrictions	
<b>Flag</b>	:	Critical study for SIDS endpoint	
14.11.2003			(45)
<b>Value</b>	:	34 - °C at 1013 hPa	
<b>Source</b>	:	Sodes Paris EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
13.12.1993			(82)
<b>Value</b>	:	= 34.5- °C at 1013 hPa	
<b>Decomposition</b>	:	no	
<b>Method</b>	:		
<b>Year</b>	:		
<b>GLP</b>	:		
<b>Test substance</b>	:		
<b>Source</b>	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
17.02.1997			(47)

### 2.3 DENSITY

<b>Type</b>	:	density	
<b>Value</b>	:	= .7138 - g/cm <sup>3</sup> at 20 °C	

## 2. Physico-Chemical Data

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<b>Reliability</b>	:	(2) valid with restrictions	
<b>Flag</b>	:	Critical study for SIDS endpoint	
14.11.2003			(45)
<b>Type</b>	:	density	
<b>Value</b>	:	.71 - g/cm <sup>3</sup> at 20 °C	
<b>Method</b>	:		
<b>Year</b>	:		
<b>GLP</b>	:	no	
<b>Test substance</b>	:		
<b>Source</b>	:	Sodes Paris EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
13.12.1993			(82)
<b>Type</b>	:	density	
<b>Value</b>	:	= .714 - g/cm <sup>3</sup> at 20 °C	
<b>Method</b>	:		
<b>Year</b>	:		
<b>GLP</b>	:	no	
<b>Test substance</b>	:		
<b>Source</b>	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
17.02.1997			(47)

### 2.3.1 GRANULOMETRY

### 2.4 VAPOUR PRESSURE

<b>Value</b>	:	= 589 - hPa at 20 °C	
<b>Reliability</b>	:	(2) valid with restrictions	
<b>Flag</b>	:	Critical study for SIDS endpoint	
14.11.2003			(90)
<b>Value</b>	:	= 563 - hPa at 20 °C	
<b>Result</b>	:	Values at other temperatures: 0 degree C: 189 hPa 10 degree C: 389 hPa 30 degree C: 863 hPa 40 degree C: 1228 hPa 60 degree C: 2311 hPa 80 degree C: 3964 hPa 100 degree C: 6472 hPa	
<b>Source</b>	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
17.02.1997			(47)
<b>Value</b>	:	587 - hPa at 20 °C	
<b>Source</b>	:	Sodes Paris EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
13.12.1993			(82)
<b>Value</b>	:	= 587 - hPa at 20 °C	

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**Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.02.1997 (54)

### 2.5 PARTITION COEFFICIENT

**Partition coefficient** :  
**Log pow** : = .82 - at 23 °C  
**pH value** : -  
**Method** : OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"  
**Year** : 1981  
**GLP** : no  
**Test substance** :  
**Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
**Reliability** : (2) valid with restrictions  
**Flag** : Critical study for SIDS endpoint  
29.12.2003 (55)

**Partition coefficient** : octanol-water  
**Log pow** : = .89 - at °C  
**pH value** : -  
**Method** : other (calculated): EPIWIN (v 3.11) KOWWIN Submodel (v 1.67)  
**Year** : 2003  
**GLP** :  
**Test substance** :  
**Remark** : The cited value is from the Experimental Database match in the model.  
The calculated value was 1.05.  
The EPIWIN model was run using the following measured physical chemical properties:  
Water solubility (mg/L): 65000;  
Vapor pressure (mm Hg): 442;  
Log Kow (octanol-water): 0.82;  
Boiling point (deg C): 34.50; and  
Melting point (deg C): -116.20.  
**Reliability** : (2) valid with restrictions  
20.11.2003 (95)

**Partition coefficient** :  
**Log pow** : .82 - at 23 °C  
**pH value** : -  
**Method** : OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"  
**Year** :  
**GLP** : no  
**Test substance** :  
**Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
13.12.1993 (56)

**Partition coefficient** :  
**Log pow** : .87 - at °C  
**pH value** : -  
**Method** : other (calculated): Leo, Hansch: Berechnung mit dem MedChem-Programm, Version 1989(POMONA89).  
**Year** :

## 2. Physico-Chemical Data

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**GLP** :  
**Test substance** :  
**Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
14.09.1993  
**Partition coefficient** :  
**Log pow** : = .87 - at °C  
**pH value** : -  
**Method** : other (calculated): CLOGP3 Computer program according to Leo & Hansch  
(MedChem, Version 1989)  
**Year** :  
**GLP** :  
**Test substance** :  
**Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.02.1997

### 2.6.1 SOLUBILITY IN DIFFERENT MEDIA

**Solubility in** : Water  
**Value** : = 65 - g/l at 20 °C  
**pH value** : -  
**concentration** : at °C  
**Temperature effects** :  
**Examine different pol.** :  
**pKa** : at 25 °C  
**Description** :  
**Stable** :  
**Result** : Slightly water soluble at room temperature.  
**Reliability** : (2) valid with restrictions  
**Flag** : Critical study for SIDS endpoint  
18.11.2003

(45)

**Solubility in** : Water  
**Value** : 60 - g/l at 25 °C  
**pH value** : -  
**concentration** : at °C  
**Temperature effects** :  
**Examine different pol.** :  
**pKa** : at 25 °C  
**Description** :  
**Stable** :  
**Deg. product** :  
**Method** : other: EPIWIN (v 3.11) WSKOWWIN Submodel (v 1.41)  
**Year** : 2003  
**GLP** :  
**Test substance** :

**Remark** : The EPIWIN model was run using the following measured physical  
chemical properties:  
Water solubility (mg/L): 65000;  
Vapor pressure (mm Hg): 442;  
Log Kow (octanol-water): 0.82;  
Boiling point (deg C): 34.50; and  
Melting point (deg C): -116.20.  
**Result** : Value represents experimental database value from model.

## 2. Physico-Chemical Data

Id 60-29-7  
Date 29.12.2003

<b>Reliability</b> 21.11.2003	:	The model estimated value was 30 g/l (2) valid with restrictions	(97)
<b>Solubility in Value</b>	:	70 - g/l at 20 °C	
<b>pH value concentration</b>	:	7 - at 20 °C	
<b>Temperature effects</b>	:		
<b>Examine different pol.</b>	:		
<b>pKa</b>	:	at 25 °C	
<b>Description</b>	:	of high solubility	
<b>Stable</b>	:		
<b>Deg. product</b>	:		
<b>Method</b>	:		
<b>Year</b>	:		
<b>GLP</b>	:	no	
<b>Test substance</b>	:		
<b>Source</b> 13.12.1993	:	Sodes Paris EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	(56)
<b>Solubility in Value</b>	:	= 70 - g/l at 20 °C	
<b>pH value concentration</b>	:	7 - at 20 °C	
<b>Temperature effects</b>	:		
<b>Examine different pol.</b>	:		
<b>pKa</b>	:	at 25 °C	
<b>Description</b>	:	of high solubility	
<b>Stable</b>	:		
<b>Deg. product</b>	:		
<b>Method</b>	:		
<b>Year</b>	:		
<b>GLP</b>	:	no	
<b>Test substance</b>	:		
<b>Source</b> 17.02.1997	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	(54)
<b>Solubility in Value</b>	:	= 65 - g/l at 20 °C	
<b>pH value concentration</b>	:	- at °C	
<b>Temperature effects</b>	:		
<b>Examine different pol.</b>	:		
<b>pKa</b>	:	at 25 °C	
<b>Description</b>	:		
<b>Stable</b>	:		
<b>Deg. product</b>	:		
<b>Method</b>	:	other: no data	
<b>Year</b>	:		
<b>GLP</b>	:		
<b>Test substance</b>	:		
<b>Result</b>	:	Values at other temperatures: 0 degree C: 117 g/l 10 degree C: 87 g/l 30 degree C: 52 g/l	

## 2. Physico-Chemical Data

Id 60-29-7  
Date 29.12.2003

**Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.02.1997 (47)

### 2.6.2 SURFACE TENSION

### 2.7 FLASH POINT

**Value** : = -45 °C  
**Type** :  
10.10.2003 (90)

**Value** : -40 °C  
**Type** : closed cup  
**Method** : other: DIN 51755  
**Year** :  
**GLP** : no  
**Test substance** :

**Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
13.12.1993 (56)

**Value** : = -40 °C  
**Type** : closed cup  
**Method** : other: DIN 51755  
**Year** :  
**GLP** : no  
**Test substance** :

**Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.02.1997 (47) (54)

### 2.8 AUTO FLAMMABILITY

**Value** : = 180 - °C at  
**Method** : other: DIN 51794  
**Year** :  
**GLP** :  
**Test substance** :

**Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.02.1997 (47) (54)

### 2.9 FLAMMABILITY

### 2.10 EXPLOSIVE PROPERTIES

## 2. Physico-Chemical Data

Id 60-29-7  
Date 29.12.2003

### 2.11 OXIDIZING PROPERTIES

### 2.12 DISSOCIATION CONSTANT

### 2.13 VISCOSITY

### 2.14 ADDITIONAL REMARKS

**Memo** : Explosive limits, peroxide formation

**Remark** : Explosive limits: lower limit 1.7 % v/v  
upper limit 48 % v/v  
Peroxides, which easily form in the presence of atmospheric oxygen, in particular under the influence of light, tend to explode when diethyl ether is distilled. Therefore, the presence of peroxide should always be tested before diethyl ether is utilized. Usually inhibitors are added.

**Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

17.02.1997

(54)

### 3. Environmental Fate and Pathways

Id 60-29-7  
Date 29.12.2003

#### 3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	
Light spectrum	:	- nm
Relative intensity	:	- based on intensity of sunlight
<b>DIRECT PHOTOLYSIS</b>		
Half-life t1/2	:	= 9.8 - hour(s)
Degradation	:	- % after
Quantum yield	:	
<b>INDIRECT PHOTOLYSIS</b>		
Sensitizer	:	OH
Conc. of sensitizer	:	500000 molecule/cm <sup>3</sup>
Rate constant	:	= .0000000000133 cm <sup>3</sup> /(molecule*sec)
Degradation	:	- % after
Deg. product	:	
Method	:	other (measured): method not specified
Year	:	1987
GLP	:	no data
Test substance	:	no data
Remark	:	Half-life refers to 24-hour days. Photodegradation value was reported in this manuscript to compare to calculated data. The measured value (13.3E-12 cm <sup>3</sup> /molecule*sec) compared well with the calculated value (10.6E-12) that was reported in the manuscript.
Source	:	Huels AG Marl
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint
29.12.2003		(5)
Type	:	other: EPIWIN (v 3.11) AOPWIN Submodel (v 1.91)
Light source	:	
Light spectrum	:	- nm
Relative intensity	:	- based on intensity of sunlight
<b>DIRECT PHOTOLYSIS</b>		
Half-life t1/2	:	= 10.4 - hour(s)
Degradation	:	- % after
Quantum yield	:	
Deg. product	:	
Method	:	other (calculated): EPIWIN (v 3.11) AOPWIN Submodel (v 1.91)
Year	:	2003
GLP	:	
Test substance	:	
Remark	:	Overall OH rate constant = 12.3468 E-12 cm <sup>3</sup> /molecule-sec The EPIWIN model was run using the following measured physical chemical properties: Water solubility (mg/L): 65000; Vapor pressure (mm Hg): 442; Log Kow (octanol-water): 0.82; Boiling point (deg C): 34.50; and Melting point (deg C): -116.20.
Reliability	:	(2) valid with restrictions
29.12.2003		(93)

### 3. Environmental Fate and Pathways

Id 60-29-7  
Date 29.12.2003

#### 3.1.2 STABILITY IN WATER

**Remark** : Expert statement: Does not react with water; the only functionality other than carbon-carbon and carbon-hydrogen bonds is the ether linkage (C-O-C) which does not hydrolyze.

**Reliability** : (2) valid with restrictions

**Flag** : Critical study for SIDS endpoint

18.11.2003

#### 3.1.3 STABILITY IN SOIL

#### 3.2.1 MONITORING DATA

**Type of measurement** : background concentration

**Media** : surface water

**Concentration** : -

**Method** :

**Remark** : Diethyl ether was found in 9 of 204 water samples from a nationwide study in the USA. Measurable concentrations in surface waters ranged from 0.003 mg/l (canal system on Lake Michigan) to 0.005 mg/l (Lake Michigan shore zone). Concentrations in sewage plant effluents varied from 0.001 to 0.01 mg/l.

**Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

17.02.1997

(100)

**Type of measurement** : concentration at contaminated site

**Media** : air

**Concentration** : -

**Method** :

**Remark** : Young and Parker examined several different types of landfills during their research of gaseous components of various refuse landfills in Great Britain. Gaseous diethyl ether could only be detected in the ventilation gases of only one of the municipal refuse landfills at a concentration of < 20 mg/m3.

**Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

17.02.1997

(109)

**Type of measurement** : concentration at contaminated site

**Media** : air

**Concentration** : -

**Method** :

**Remark** : In studies of landfill gases of two landfills in southern Germany, diethyl ether was detected but not quantified in the gas from a hazardous waste landfill but not in the gas from a municipal waste landfill.

**Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

17.02.1997

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### 3. Environmental Fate and Pathways

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<b>Type of measurement</b>	:	concentration at contaminated site	
<b>Media</b>	:	ground water	
<b>Concentration</b>	:	-	
<b>Method</b>	:		
<b>Remark</b>	:	Diethyl ether concentrations ranging from 0.002 to 1.5 mg/l were determined in the groundwater of a chemical landfill in the Netherlands which was openly operated without any groundwater protection measures during the period of 1960-1980, and where the disposed chemicals were regularly incinerated. Accumulation of diethyl ether was observed in the deeper clay layer of the southeast sampling site, whereby a concentration of 150 mg/l was measured in the groundwater samples taken there. Individual measurements of lower layers, in which diethyl ether was mostly undetected, indicated that this substance was adsorbed stronger to clay than to the soil of the surrounding layers and that it was leached out much slower from the clay layer than the other ground layers; the flow of leachate was apparently obstructed in the clay layer.	
<b>Source</b>	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
17.02.1997			(46)
<b>Type of measurement</b>	:	concentration at contaminated site	
<b>Media</b>	:	ground water	
<b>Concentration</b>	:	-	
<b>Method</b>	:		
<b>Remark</b>	:	Diethyl ether at concentrations near 0.0025 mg/l was found in 2 of 9 examined drinking water and groundwater samples from wells in the vicinity of a municipal and industrial landfill operated for 8 years in Delaware (USA). No diethyl ether could be detected in water samples from artesian wells which pump water for public use and which are located very close to this landfill (detection limit not reported).	
<b>Source</b>	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
17.02.1997			(29)
<b>Type of measurement</b>	:	concentration at contaminated site	
<b>Media</b>	:	ground water	
<b>Concentration</b>	:	-	
<b>Method</b>	:		
<b>Remark</b>	:	In Gloucester, Canada, diethyl ether was found in groundwater below a landfill (municipal, partially with hazardous wastes) at concentrations of $\geq 5$ mg/l (central area) and $\leq 0.1$ mg/l (about 50 m away; Devlin & Gorman). Other authors (Patterson et al., Chaput et al.) reported $> 10$ mg/l in groundwater of the central area of this landfill and "undetectable" (detection limit not reported) 50-70 m away.	
<b>Source</b>	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
17.02.1997			(19) (28) (75)
<b>Type of measurement</b>	:	other: city and national forest; potentially natural source	
<b>Media</b>	:	air	
<b>Concentration</b>	:	-	
<b>Method</b>	:		

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**Remark** : By a comparison of gaseous components of city air (Tuscaloosa, USA) and air from an unpopulated area (Talladega National Forest, USA), diethyl ether was detected but not quantified in both regions.

**Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

17.02.1997 (52)

**Type of measurement** : other: natural source  
**Media** : biota  
**Concentration** : -  
**Method** :

**Remark** : Diethyl ether was found in gases transpired from the moss Polytrichum commune. The mechanism of formation and the quantity formed are not reported.

**Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

17.02.1997 (57)

#### 3.2.2 FIELD STUDIES

##### 3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

**Type** : volatility  
**Media** : water - air  
**Air** : % (Fugacity Model Level I)  
**Water** : % (Fugacity Model Level I)  
**Soil** : % (Fugacity Model Level I)  
**Biota** : % (Fugacity Model Level II/III)  
**Soil** : % (Fugacity Model Level II/III)  
**Method** : other: calculation from vapour pressure and water solubility  
**Year** :

**Remark** : Henry's Law Constant was calculated from the data reported in the reference.

**Result** : Henry's Law Constant  
- at 20 degree C: 64.20 Pa m<sup>3</sup>/mol  
- at 0 degree C: 11.97 Pa m<sup>3</sup>/mol

**Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

17.02.1997 (47)

##### 3.3.2 DISTRIBUTION

**Media** : other: air (emissions to compartment = 1000 kg/hr)  
**Method** : Calculation according Mackay, Level III  
**Year** : 2003

**Method** : Equilibrium Concentration Model (EQC) Level III  
**Remark** : The EPIWIN model was run using the following measured physical chemical properties:  
Water solubility (mg/L): 65000;  
Vapor pressure (mm Hg): 442;  
Log Kow (octanol-water): 0.82;  
Boiling point (deg C): 34.50; and

### 3. Environmental Fate and Pathways

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**Result** : Melting point (deg C): -116.20.  
: Concentration (%):  
Air = 97.4  
Water = 2.5  
Soil < 1.0  
Sediment < 0.1

Level III Fugacity Model (Full-Output):

=====  
Chem Name : Ethane, 1,1'-oxybis-  
Molecular Wt: 74.12  
Henry's LC : 0.00123 atm-m<sup>3</sup>/mole (Henry database)  
Vapor Press : 442 mm Hg (user-entered)  
Log Kow : 0.82 (user-entered)  
Soil Koc : 2.71 (calc by model)

	Mass Amount (percent)	HalfLife (hr)	Emissions (kg/hr)
Air	97.4	9.8	1000
Water	2.49	3.6e+003	0
Soil	0.135	3.6e+003	0
Sediment	0.00518	1.44e+004	0

	Fugacity (atm)	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)
Air	4.08e-011	876	124	87.6	12.4
Water	2.63e-011	0.0611	0.317	0.00611	0.0317
Soil	4.22e-011	0.0033	0	0.00033	0
Sediment	2.57e-011	3.17e-005	1.32e-005	3.17e-006	1.32e-006

Persistence Time: 12.7 hr  
Reaction Time: 14.5 hr  
Advection Time: 102 hr  
Percent Reacted: 87.6  
Percent Advected: 12.4

Half-Lives (hr), (based upon user-entry):

Air: 9.8  
Water: 3600  
Soil: 3600  
Sediment: 1.44e+004

Advection Times (hr):

Air: 100  
Water: 1000  
Sediment: 5e+004

**Reliability Flag** : (2) valid with restrictions  
: Critical study for SIDS endpoint  
19.12.2003

(96)

**Media Method Year** : other: water (emissions to compartment = 1000 kg/hr)  
: Calculation according Mackay, Level III  
: 2003

**Method Remark** : Equilibrium Concentration Model (EQC) Level III  
: The EPIWIN model was run using the following measured physical chemical properties:  
Water solubility (mg/L): 65000;  
Vapor pressure (mm Hg): 442;  
Log Kow (octanol-water): 0.82;  
Boiling point (deg C): 34.50; and  
Melting point (deg C): -116.20.

### 3. Environmental Fate and Pathways

Id 60-29-7  
Date 29.12.2003

**Result** : Concentration (%)  
Air = 2.5  
Water = 97.3  
Soil < 0.1  
Sediment < 1.0

Level III Fugacity Model (Full-Output):

=====  
Chem Name : Ethane, 1,1'-oxybis-  
Molecular Wt: 74.12  
Henry's LC : 0.00123 atm-m<sup>3</sup>/mole (Henry database)  
Vapor Press : 442 mm Hg (user-entered)  
Log Kow : 0.82 (user-entered)  
Soil Koc : 2.71 (calc by model)

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	2.51	9.8	0
Water	97.3	3.6e+003	1000
Soil	0.00348	3.6e+003	0
Sediment	0.202	1.44e+004	0

	Fugacity (atm)	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)
Air	2.6e-011	557	78.8	55.7	7.88
Water	2.53e-008	58.8	305	5.88	30.5
Soil	2.68e-011	0.0021	0	0.00021	0
Sediment	2.47e-008	0.0305	0.0127	0.00305	0.00127

Persistence Time: 314 hr  
Reaction Time: 509 hr  
Advection Time: 817 hr  
Percent Reacted: 61.6  
Percent Adverted: 38.4

Half-Lives (hr), (based upon user-entry):

Air: 9.8  
Water: 3600  
Soil: 3600  
Sediment: 1.44e+004

Advection Times (hr):

Air: 100  
Water: 1000  
Sediment: 5e+004

**Reliability Flag** : (2) valid with restrictions  
19.12.2003 : Critical study for SIDS endpoint

(96)

**Media Method Year** : air - biota - sediment(s) - soil - water  
: Calculation according Mackay, Level I  
:

**Result** : Air: 95.621 %  
Soil: 0.002 %  
Water: 4.375 %  
Sediment: 0.002 %  
Biota: 0.000 %

**Source** : Huels AG, Marl  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

**Test condition** : Data used:

### 3. Environmental Fate and Pathways

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Date 29.12.2003

Molar mass: 74.12 g/mol  
Log Pow: 0.82  
Vapour pressure: 58700 Pa  
Water solubility: 70.0 g/l

-----  
Equations used for additional data:  
log Koc = 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

14.11.2003

#### 3.4 MODE OF DEGRADATION IN ACTUAL USE

#### 3.5 BIODEGRADATION

**Type** : aerobic  
**Inoculum** : activated sludge, non-adapted  
**Concentration** : 100 mg/l related to related to  
**Contact time** : 14 day(s)  
**Degradation** : 0 - (±) % after 240 hour(s)  
**Result** : under test conditions no biodegradation observed  
**Deg. product** :  
**Method** : other: similar to OECD 301C  
**Year** : 1986  
**GLP** : no data  
**Test substance** : no data

**Method** : This study investigated the biological degradation of the test substance in a static electrolytic respirometer test for 14 days. Each culture flask containing 100 mg/L of diethyl ether in 300 ml of test solution and 1 ml JIS inorganic medium was inoculated with 30 mg/l non-acclimatized, activated sewage sludge and incubated at 20±1°C. The ThOD of diethyl ether was 2.59 g/g and the DOC was 0.65 g/g. The pH of the test solution was 7±1. The temperature was 20 +- 1 degrees C and the exposure period was 14 days. Measurements of biochemical oxygen demand (BOD) and removal of DOC were repeated 2-3 times.

**Remark** : In this test system, diethyl ether was not biodegradable after 240 h.  
**Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

**Reliability** : (2) valid with restrictions  
**Flag** : Critical study for SIDS endpoint

18.11.2003

(99)

**Remark** : For their studies concerning the microbic degradation of diethyl ether, Imai et al. (1986) used the thermophilic, obligate methane-oxidizing bacteria strain, "H-2", which was isolated from a gas field. This organism was taken from a continuously growing culture and employed without first being adapted. The measurable catabolite of diethyl ether degradation was acetic acid which was formed to 5,3 umol/h/mg protein. The authors attributed the fact that



## 4.1 ACUTE/PROLONGED TOXICITY TO FISH

**Type** : flow through  
**Species** : Pimephales promelas (Fish, fresh water)  
**Exposure period** : 96 hour(s)  
**Unit** : mg/l  
**LC50** : = 2560 - measured/nominal  
**EC50** : = 2260 - measured/nominal  
**Method** : other  
**Year** : 1986  
**GLP** : no data  
**Test substance** : other TS

**Method** : [According to ASTM (1980), Standard practice for conducting acute toxicity tests with fishes, macroinvertebrates and amphibians. American Society for Testing and Methods Committee E-35.]

Flow-through exposures were made with a continuous flow modified mini-diluter. One chemical stock solution was prepared and used for the entire test.

Gas-liquid chromatography (flame-ionisation detector) was used to analyze test substance concentrations in water samples from the exposure chambers. All test exposure chambers were sampled at approximately mid-depth at 0, 24, 48, 72 and 96 hours. All samples were analyzed immediately or adequately preserved for later analysis.

The fish were not fed 24 hours before or during the test. The tests were initiated by adding 20 fish per treatment and control groups. The number of dead fish was noted every 24 hours after the beginning of the test at which time they were also removed from the chambers. Observations of fish behavior and toxic signs were made at 2-8, 24, 48, 72 and 96 hours. Upon test termination, individual control fish were weighed (wet weight) and measured (standard length). Four surviving fish each from the control, the lowest concentration and the concentration nearest the LC50 were preserved for possible future histopathologic evaluation.

**Result** : The LC50 and EC50 values were calculated using the corrected averages of the analyzed tank concentrations and the Trimmed Spearman-Kärber Method. EC50's were based upon loss of equilibrium.

Analytical Results (in mg/l):

Nominal		Hours					Corrected
Conc.		0	24	48	72	96	Averages*
(mg/l)							
Control	<0.02	<0.02	<0.02	<0.02	<0.02	<0.02	<0.02
	1.96	0.487	0.382	0.428	0.350	0.429	0.40
	3.02	0.577	0.624	0.681	0.750	0.769	0.66
	4.65	0.861	1.14	1.26	1.27	1.27	1.12
	7.15	1.58	1.58	2.02	2.05	1.91	1.76
	11.0	2.72	2.57	3.33	3.18	3.06	2.87

\*Corrected for analytical recoveries of spiked water samples.

Fish exposed to DEE lost schooling behavior and swam in a cork-screw/spiral pattern near the tank surface. They were underreactive to external stimuli, had increased respiration, were darkly colored and lost equilibrium prior to death. Differences in the measured and nominal tank values were due to volatilization of the chemical. Calculations were based on measured values.

Cumulative Mortality (total number of animals in each group = 20):

Concentration (g/L)	Number of deaths			
	Time (hours) 24	48	72	96
0	0	0	0	0
1.96	0	0	0	0
3.02	0	0	0	0
4.65	0	0	0	0
7.15	0	0	15	0
11.0	10	13	13	13

Number of animals with effects (total number of animals in each group = 20):

Concentration (g/L)	Time (hours)			
	24	48	72	96
0	0	0	0	0
1.96	0	0	0	0
3.02	0	0	0	0
4.65	0	0	0	0
7.15	0	0	0	0
11.0	20	20	20	20

<b>Test condition</b>	: Species: P. promelas, Age: 29 days, Weight: 0.069 +/- 0.0264 g, Length: 17.0 +/- 1.959 mm, Loading: 0.69 g/L Test medium: filtered Lake Superior water, Water quality parameters as measured during the test: Temperature = 24.8 degrees C; Dissolved oxygen = 7.1 mg/L; pH = 7.76; Total hardness = 45.1 mg/L CaCO <sub>3</sub> ; and Total alkalinity = 41.5 mg/L CaCO <sub>3</sub> .	
<b>Test substance</b>	: Diethyl Ether (CAS RN 60-29-7); Purity not specified.	
<b>Reliability</b>	: (1) valid without restriction Similar to OECD 203	
<b>Flag</b> 29.12.2003	: Critical study for SIDS endpoint	(39)
<b>Type</b>	: semistatic	
<b>Species</b>	: Poecilia reticulata (Fish, fresh water)	
<b>Exposure period</b>	: 14 day(s)	
<b>Unit</b>	: mg/l	
<b>LC50</b>	: = 2134 -	
<b>Limit test</b>	:	
<b>Analytical monitoring</b>	: no data	
<b>Method</b>	: other: see text	
<b>Year</b>	:	
<b>GLP</b>	: no data	
<b>Test substance</b>	: no data	
<b>Method</b>	: The study measured the acute toxicity of the test substance to 2-3 month old guppies under static-renewal conditions for 14 days. The test substance was tested at several concentrations in a series with a 1.8-factor geometric progression. Stock solutions were prepared using a solvent (acetone or propanol-2) and diluted with standard water (hardness of 25	

mg/l as CaCO<sub>3</sub>). Each test vessel contained approximately 1 L of test solution and eight guppies. Test solutions were renewed daily. Guppies were fed a commercial fish food 0.5 h before each renewal. The temperature and dissolved oxygen concentration during the test were maintained at 22±1°C and 5 mg/l, respectively. The guppies were considered to be dead when gill movements ceased and no reaction occurred when fish were touched with a glass bar.

<b>Source</b>	:	Sodes Paris Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
<b>Test condition</b>	:	Testgefäesse abgedeckt, taeglicher Wasserwechsel, 22 Grad Celsius	
<b>Reliability</b> 19.12.2003	:	(2) valid with restrictions	(64)
<b>Type</b>	:	static	
<b>Species</b>	:	Lepomis macrochirus (Fish, fresh water)	
<b>Exposure period</b>	:	96 hour(s)	
<b>Unit</b>	:	mg/l	
<b>LC0</b>	:	>= 10000 -	
<b>Limit test</b>	:		
<b>Analytical monitoring</b>	:	no	
<b>Method</b>	:		
<b>Year</b>	:		
<b>GLP</b>	:	no data	
<b>Test substance</b>	:	no data	
<b>Source</b>	:	Sodes Paris Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
<b>Test condition</b> 19.12.2003	:	Open test system, 23 degree C	(26)
<b>Type</b>	:	static	
<b>Species</b>	:	Leuciscus idus (Fish, fresh water)	
<b>Exposure period</b>	:	48 hour(s)	
<b>Unit</b>	:	mg/l	
<b>LC0</b>	:	= 2130 -	
<b>LC50</b>	:	= 2840 -	
<b>LC100</b>	:	= 3600 -	
<b>Limit test</b>	:		
<b>Analytical monitoring</b>	:	no	
<b>Method</b>	:	other: Bestimmung der Wirkung von Wasserinhaltsstoffen auf Fische, DIN38412 Teil 15	
<b>Year</b>	:		
<b>GLP</b>	:	no data	
<b>Test substance</b>	:	no data	
<b>Source</b> 19.12.2003	:	Sodes Paris EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	(60)

## 4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

<b>Type</b>	:	static
<b>Species</b>	:	Daphnia magna (Crustacea)
<b>Exposure period</b>	:	24 hour(s)
<b>Unit</b>	:	mg/l
<b>EC50</b>	:	= 165 -
<b>Analytical monitoring</b>	:	no

**Method** : other: Daphnien-Kurzzeitest, DIN 38412 Teil 11, Bestimmung der Wirkung von Wasserinhaltsstoffen auf Kleinkrebse.  
Gefaesse leicht abgedeckt

**Year** : 1982

**GLP** : no

**Test substance** : no data

**Remark** : Following is a summary of the test conditions:  
 Test type: Static  
 Test duration: 24 hours  
 Temperature: 20 degrees C  
 Light quality: Artificial light, OSRAM Neon light, Leuchtfarbe 25  
 Light intensity:  $E_{0sy} = 2.5 \text{ W/m}^2$   
 Photoperiod: 9 hours  
 Feeding prior to test: Standardized dry algae  
 Feeding regime: None  
 Test chamber: 50 ml beakers filled with 20 ml liquid  
 Loading rate: 2 mL/daphnid  
 Test volume: Minimum 20 mL  
 Source: Standardized test strain IRCHA  
 Age of test organisms: 24 hours max.  
 Test concentrations: Not provided  
 Number of replicate test vessels per concentration in definitive test: 2 replicates per test and control concentration  
 Number of animals per replicate: 10  
 Aeration: None  
 Dilution water: Dilution water for culturing was tap water. Dilution water for testing was a chemically and physically defined standardized culture medium ("artificial fresh water").  
 Measured water chemistry parameters: Parameters determined at the end of the test:  
 pH (target: pH: 8.0 +/- 0.2); dissolved oxygen (target: 2 mg/l); conductivity (not measured); temperature (constant 20 °C in incubator); visual observations at 24 hours; Dilution water hardness at 0 hours (not measured).  
 Measured endpoint: Immobility

Test concentrations were not provided; only the dilution ratios are indicated; 1st step: dilution ratio 1:2. 2nd step further dilution steps (1:1.4 or 1:1.1) in case no 3 grading between EC0 and EC100. The definitive test was based on a total of 20 daphnids per concentration tested (i.e., 10 daphnids per replicate, in each of 2 replicates) exposed to each test concentration, as well as a control (100% dilution water). Immobility and abnormal behavior (e.g., erratic swimming) were recorded at 24 hours. An EC50 (concentration causing immobility in 50% of the organisms) was estimated based on the 24-hour immobility data. The test was considered valid if immobility did not exceed 10% in the control. No reference that the control was also checked for this parameter.

Test conditions: Dilution water for testing was a chemically and physically defined standardized culture medium ("artificial fresh water" according to above DIN). Dilution water used for culturing was tap water. Test solutions were prepared as follows: The substances tested were poured in closed bottles containing the artificial fresh water on a magnetic stirrer until solution was optically transparent. Then the dilutions were made with this stock solution.

The 24-hour EC50 was calculated as follows: EC0 and EC100 values were determined. The percentage of immobile specimens was plotted against the concentration of the substances tested in mg/l (on Schleicher Schüll logarithmic paper No. 440 ~~44~~; abscissa: the mg/l - concentration; ordinate: the percentage of immobilized daphnids). Ordinarily in the range of 16 - 84% immobilization the respective values

should be found on a straight line. If values were on a straight line, then the EC50 value could be extrapolated and the 95% confidence range calculated. The authors also referenced the statistical method "Chi-Quadrat-Test". In cases where the slope was too steep and further testing of the 1:1.1 dilution ratio did not provide sufficient data points, then the geometric middle of the EC0 and EC100 was taken as the EC50 value.

<b>Result</b>	:	24-hour EC50 = 165 mg/L	
<b>Source</b>	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
<b>Reliability</b>	:	(2) valid with restrictions	
<b>Flag</b>	:	Critical study for SIDS endpoint	
19.12.2003			(12)
<b>Type</b>	:		
<b>Species</b>	:	Daphnia magna (Crustacea)	
<b>Exposure period</b>	:	48 hour(s)	
<b>Unit</b>	:	mg/l	
<b>EC0</b>	:	= 1380 -	
<b>Analytical monitoring</b>	:	no data	
<b>Method</b>	:	other: see text	
<b>Year</b>	:		
<b>GLP</b>	:	no data	
<b>Test substance</b>	:	no data	
<b>Source</b>	:	Sodes Paris Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
<b>Test condition</b>	:	unklar, ob offene oder geschlossene Testsysteme verwendet wurden	
15.12.1993			(50)

**4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE**

<b>Species</b>	:	other algae: Green Algae	
<b>Endpoint</b>	:		
<b>Exposure period</b>	:	96 hour(s)	
<b>Unit</b>	:	mg/l	
<b>EC50</b>	:	= 407.622 - calculated	
<b>Method</b>	:	other: EPIWIN (v 3.11) ECOSAR Submodel (v 0.99g)	
<b>Year</b>	:	2003	
<b>GLP</b>	:		
<b>Test substance</b>	:		
<b>Remark</b>	:	The EPIWIN model was run using the following measured physical chemical properties: Water solubility (mg/L): 65000; Vapor pressure (mm Hg): 442; Log Kow (octanol-water): 0.82; Boiling point (deg C): 34.50; and Melting point (deg C): -116.20.	
20.11.2003			(94)

**4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA**

<b>Type</b>	:	aquatic
<b>Species</b>	:	Photobacterium phosphoreum (Bacteria)
<b>Exposure period</b>	:	15 minute(s)
<b>Unit</b>	:	mg/l

## 4. Ecotoxicity

Id 60-29-7  
Date 29.12.2003

**EC50** : = 5600 -  
**Analytical monitoring** : no data  
**Method** :  
**Year** :  
**GLP** : no data  
**Test substance** : no data

**Source** : Sodes Paris  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

15.12.1993 (50)

### 4.5.1 CHRONIC TOXICITY TO FISH

### 4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

### 4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

### 4.6.2 TOXICITY TO TERRESTRIAL PLANTS

**Species** : other terrestrial plant: Mimosa pudica, Oxalis stricta, Marsilia macropus  
**Endpoint** : other: inhibition opening / closing movements  
**Exposure period** :  
**Unit** : mg/l  
**EC100** : = 330 - 510  
**Method** :  
**Year** :  
**GLP** : no  
**Test substance** : no data

**Remark** : Effects were reversible after end of exposure within few hours.

**Source** : Sodes Paris  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

15.12.1993 (102)

### 4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

### 4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

### 4.7 BIOLOGICAL EFFECTS MONITORING

### 4.8 BIOTRANSFORMATION AND KINETICS

### 4.9 ADDITIONAL REMARKS

## 5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

## 5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	-
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	
Vehicle	:	other: none
Doses	:	
Method	:	
Year	:	1970
GLP	:	no
Test substance	:	no data
Remark	:	The test substance was administered undiluted to two groups of 6 nonfasted male Sprague-Dawley rats: Group 1 = young adults (80 - 160 g) and Group 2 = older adults (300 - 470 g). The test substance was also administered to groups of 6-12 nonfasted rats of both sexes at 14-days of age (16-50 g). The animals were observed for one week following dose administration. The LD50 and associated confidence limits were calculated both by the method of Litchfield and Wilcoxon (Litchfield, J.T. and F. Wilcoxon. 1949. A simplified method of evaluating dose-effect experiments. J. Pharmacol. Exp. Ther. 96:99-101) and by a probit analysis statistical program via an IBM-1800 calculator.
Result	:	The LD50 value listed above is the range of LD50 values for all age groups. Following are the LD50 values (95% confidence limits) for the individual age groups tested in this study: 14-day old rats: 1568 mg/kg (855 - 2352 mg/kg) young adults: 1710 mg/kg (1425 - 1924 mg/kg) older adults: 1211 mg/kg (1069 - 1354 mg/kg)
Source	:	Sodes Paris Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint
21.11.2003		

(62)

## 5.1.2 ACUTE INHALATION TOXICITY

Type	:	other: LT50
Value	:	-
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	150,000 and 200,000 ppm (450 and 605 mg/L, respectively)
Exposure time	:	
Method	:	
Year	:	1970
GLP	:	no
Test substance	:	no data

## 5. Toxicity

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Date 29.12.2003

- Remark** : Number of animals: 10 adult females and 40 neonatal rats  
The median time to death (LT50 values) were calculated for adult and neonatal rats exposed to concentrations of ether vapor of 150,000 or 200,000 ppm. Animals were exposed in a 10 L vapor exposure chamber that was arranged as a closed circuit anesthesia apparatus that included a soda lime canister for absorption of carbon dioxide. Specific quantities of the test substance were vaporized in a 2 L polyethylene container in the circuit. The ether vapor was evenly distributed throughout the exposure chamber via the continuous flow of room air through the circuit by a pump. One adult non-pregnant female (275 - 325 g) and 4 neonatal rats (5- 8 g) of either sex were exposed at a time, until a total of 10 adults and 40 neonatal rats were exposed. Animals were exposed to initial ether concentrations of 150,000 or 200,000 ppm (450 and 605 mg/L, respectively). The ether was not replenished throughout the exposure so the concentration of ether within the chamber gradually decreased as the exposure progressed. Ether concentrations were analyzed by use of a gas chromatograph and a flame ionization detector. Exposure chamber samples (100 µl) were obtained with a gas tight syringe through a rubber stoppered port in the chamber lid. Animals were observed, atmosphere samples were taken and blood ether concentrations were determined at 0.14 log time intervals. The blood ether concentration at the LT50 was determined from the blood ether-time plots constructed for neonates and adults.  
Calculations of the median time to death (LT50) values for adults and neonatal rats were determined by the method of Litchfield, J.T. (A method of rapid graphic solution of time-percent effect curves. 1949. J. Pharmacol. Exp. Ther. 97: 399-408).
- Result** : The LT50 values (95% confidence limits) for adult and neonatal rats are outlined below:
- |         | Number exposed | 150,000 ppm<br>LT50 (min.) | 200,000 ppm<br>LT50 (min.) |
|---------|----------------|----------------------------|----------------------------|
| Adult   | 10             | 20 (18-24)                 | 17 (14-20)                 |
| Neonate | 40             | 135 (123-148)              | 86 (80-92)                 |
- Source** : Sodes Paris  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
- Reliability Flag** : (2) valid with restrictions  
: Critical study for SIDS endpoint
- 20.11.2003 (80)
- Type** : LC50  
**Value** : -  
**Species** : mouse  
**Strain** : other: C57BL/6  
**Sex** : male/female  
**Number of animals** :  
**Vehicle** : other: none  
**Doses** : 32,000 to 96,000 ppm (97 to 291 mg/L, respectively)  
**Exposure time** : 90 minute(s)  
**Method** :  
**Year** : 1984  
**GLP** : no data  
**Test substance** : other TS: special grade diethyl ether from WAKO Pure Chemical Industries, Ltd., (Osaka)
- Remark** : In each trial, 5 or 6 mice were exposed for 120 min. to ether in a 14 L glass chamber connected to an anesthetic machine. Ether was vaporized and diluted with a fixed volume of air (6 L/min.) to result in several concentrations from 32,000 to 96,000 ppm (97 to 291 mg/L, respectively). Mortality was evaluated every 30 minutes during exposure and confirmed following exposure. The median lethal concentration (LC50) of ether was calculated using the data obtained after 90 minutes of exposure. This

exposure time was chosen for the LC50 calculation because it was considered to be the time point when the concentration of ether in the blood would be sufficiently in equilibrium with that of the vapor mixture. The LC50 values were determined using dose-mortality curves. Logarithm - probit transformation was employed for linearization of the dose-response curve. The LC50 values were estimated on the regression lines, and analysis of covariance was performed to examine the fitness of the lines and differences in susceptibility between the sexes.

Number of animals: 10 to 15/sex/group

**Result** : Mortality of 4 week old mice after 90 min. of exposure:

Concentration (ppm)	Male	Female
32,000	0/10	0/10
46,000	0/10	--
51,000	2/10	--
55,000	2/10	0/10
60,000	4/15	3/10
66,000	9/15	5/10
73,000	10/10	8/10
80,000	10/10	10/10
96,000	5/5	--

LC50 (95% confidence limit):  
Males: 60,000 ppm (54,500 - 66,100 ppm) or 182 mg/L (165 - 200 mg/L)  
Females: 65,800 ppm (60,800 - 71,300 ppm) or 199 mg/L (184 - 216 mg/L)

**Source** : Sodes Paris  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

**Reliability** : (2) valid with restrictions  
29.12.2003 (63)

**Type** : LC50  
**Value** : -  
**Species** : mouse  
**Strain** : other: C3H/He  
**Sex** : male/female  
**Number of animals** :  
**Vehicle** :  
**Doses** : 27,000 to 46,000 ppm (82 to 139 mg/L, respectively)  
**Exposure time** : 90 minute(s)  
**Method** :  
**Year** : 1984  
**GLP** : no data  
**Test substance** : other TS: special grade diethyl ether from WAKO Pure Chemical Industries, Ltd., (Osaka)

**Remark** : Number of animals: 10 to 15/sex/group  
In each trial, 5 or 6 mice were exposed for 120 min. to ether in a 14 L glass chamber connected to an anesthetic machine. Ether was vaporized and diluted with a fixed volume of air (6 L/min.) to result in several concentrations from 27,000 to 46,000 ppm (82 to 139 mg/L, respectively). Mortality was evaluated every 30 minutes during exposure and confirmed following exposure. The median lethal concentration (LC50) of ether was calculated using the data obtained after 90 minutes of exposure. This exposure time was chosen for the LC50 calculation because it was considered to be the time point when the concentration of ether in the blood would be sufficiently in equilibrium with that of the vapor mixture. The LC50 values were determined using dose-mortality curves. Logarithm - probit transformation was employed for linearization of the dose-response curve. The LC50 values were estimated on the regression lines, and analysis of covariance was performed to examine the fitness of the lines and differences in susceptibility between the sexes.

## 5. Toxicity

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<b>Result</b>	:	Mortality of 4 week old mice after 90 min. of exposure:	
		Concentration (ppm)	Male Female
		27,000	0/10 0/10
		29,000	4/15 3/10
		32,000	12/15 7/10
		35,000	13/15 9/10
		38,000	10/10 9/10
		42,000	-- 9/10
		46,000	10/10 10/10
		LC50 (95% confidence limit):	
		Males: 31,300 ppm (29,100 - 33,600 ppm) or 95 mg/L (88 - 102 mg/L)	
		Females: 32,400 ppm (28,900 - 36,200 ppm) or 98 mg/L (87 - 110 mg/L)	
<b>Source</b>	:	Sodes Paris Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
<b>Reliability</b> 29.12.2003	:	(2) valid with restrictions	(63)
<b>Type</b>	:	LC50	
<b>Value</b>	:	= 130 - mg/l	
<b>Species</b>	:	mouse	
<b>Strain</b>	:		
<b>Sex</b>	:		
<b>Number of animals</b>	:		
<b>Vehicle</b>	:		
<b>Doses</b>	:		
<b>Exposure time</b>	:	3 hour(s)	
<b>Method</b>	:	other: see reference	
<b>Year</b>	:		
<b>GLP</b>	:	no	
<b>Test substance</b>	:	no data	
<b>Remark</b>	:	Number of animals exposed: 300.	
<b>Source</b>	:	Sodes Paris Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
25.04.1994			(70)
<b>Type</b>	:	LCLo	
<b>Value</b>	:	= 397 - mg/l	
<b>Species</b>	:	mouse	
<b>Strain</b>	:		
<b>Sex</b>	:		
<b>Number of animals</b>	:		
<b>Vehicle</b>	:		
<b>Doses</b>	:		
<b>Exposure time</b>	:		
<b>Method</b>	:	other: see reference	
<b>Year</b>	:		
<b>GLP</b>	:	no	
<b>Test substance</b>	:	no data	
<b>Remark</b>	:	Number of animals exposed: 4. Result: 99.2 mg/l slight excitation, 198 mg/l deep anesthesia, 397 mg/l irregular respiration and respiratory arrest.	
<b>Source</b>	:	Sodes Paris Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
27.04.1994			(89)

## 5. Toxicity

Id 60-29-7  
Date 29.12.2003

Type : LCLo  
Value : = 90 - mg/l  
Species : mouse  
Strain :  
Sex :  
Number of animals :  
Vehicle :  
Doses :  
Exposure time : 100 minute(s)  
Method : other: see reference  
Year :  
GLP : no  
Test substance : no data

Remark : Time of exposure: ca. 100 min; LC100: 128,34 mg/l.  
Source : Sodes Paris  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

25.04.1994

(61)

Type : LCLo  
Value : = 329 - mg/l  
Species : rabbit  
Strain :  
Sex :  
Number of animals :  
Vehicle :  
Doses :  
Exposure time :  
Method :  
Year :  
GLP : no  
Test substance : no data

Remark : No data about time of exposure or number of animals provided.

Source : Sodes Paris  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

25.04.1994

(1)

Type : LCLo  
Value : = 208 - 247 mg/l  
Species : dog  
Strain :  
Sex :  
Number of animals :  
Vehicle :  
Doses :  
Exposure time : 71 minute(s)  
Method : other: see reference  
Year :  
GLP : no  
Test substance : no data

Remark : Number of animals exposed: 20. Time of exposure: 20 - 120 min, average exposure time: 71 min.

Source : Sodes Paris  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

25.04.1994

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## 5. Toxicity

Id 60-29-7  
Date 29.12.2003

Type : LCLo  
Value : = 235 - mg/l  
Species : dog  
Strain :  
Sex :  
Number of animals :  
Vehicle :  
Doses :  
Exposure time :  
Method : other: no data  
Year :  
GLP : no  
Test substance : no data

Remark : No data about time of exposure or number of animals provided.

Source : Sodes Paris  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

25.04.1994 (1)

### 5.1.3 ACUTE DERMAL TOXICITY

### 5.1.4 ACUTE TOXICITY, OTHER ROUTES

Type : LD50  
Value : 2420 - mg/kg bw  
Species : mouse  
Strain :  
Sex :  
Number of animals :  
Vehicle :  
Doses :  
Route of admin. : i.p.  
Exposure time :  
Method : other: see reference  
Year :  
GLP : no data  
Test substance : no data  
Remark : Number of animals exposed: 12.  
Source : Sodes Paris  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

25.04.1994 (32)

Type : LDLo  
Value : = 2000 - mg/kg bw  
Species : guinea pig  
Strain :  
Sex :  
Number of animals :  
Vehicle :  
Doses :  
Route of admin. : i.p.  
Exposure time :  
Method : other: see reference  
Year :  
GLP : no

## 5. Toxicity

Id 60-29-7  
Date 29.12.2003

**Test substance** : no data  
**Remark** : Number of animals exposed: 4.  
**Source** : Sodes Paris  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
25.04.1994 (31)

**Type** : LDLo  
**Value** : ca. 4290 - mg/kg bw  
**Species** : mouse  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Doses** :  
**Route of admin.** : s.c.  
**Exposure time** :  
**Method** :  
**Year** :  
**GLP** : no  
**Test substance** : no data  
**Remark** : Number of animals exposed not provided.  
**Source** : Sodes Paris  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
25.04.1994 (1)

**Type** : LD50  
**Value** : 996 - mg/kg bw  
**Species** : mouse  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Doses** :  
**Route of admin.** : i.v.  
**Exposure time** :  
**Method** : other: see reference  
**Year** :  
**GLP** : no  
**Test substance** : no data  
**Remark** : Ether was dissolved in an emulsion (vehicle not provided)  
and administered intravenously.  
**Source** : Sodes Paris  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
25.04.1994 (30)

### 5.2.1 SKIN IRRITATION

**Species** : rabbit  
**Concentration** :  
**Exposure** :  
**Exposure time** :  
**Number of animals** :  
**Vehicle** :  
**PDII** :  
**Result** :  
**Classification** :  
**Method** :

## 5. Toxicity

Id 60-29-7  
Date 29.12.2003

<b>Year</b>	:		
<b>GLP</b>	:	no	
<b>Test substance</b>	:	no data	
<b>Remark</b>	:	Dosage: 360 m g, open application, mild reaction. No further data provided.	
<b>Source</b>	:	Sodes Paris Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
27.04.1994			(98)
<b>Species</b>	:	guinea pig	
<b>Concentration</b>	:		
<b>Exposure</b>	:		
<b>Exposure time</b>	:		
<b>Number of animals</b>	:		
<b>Vehicle</b>	:		
<b>PDII</b>	:		
<b>Result</b>	:		
<b>Classification</b>	:		
<b>Method</b>	:		
<b>Year</b>	:		
<b>GLP</b>	:	no data	
<b>Test substance</b>	:	no data	
<b>Remark</b>	:	Dosage: 50 mg/24 h, severely irritating. No further data provided.	
<b>Source</b>	:	Sodes Paris Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
25.04.1994			(51)

### 5.2.2 EYE IRRITATION

<b>Species</b>	:	rabbit	
<b>Concentration</b>	:		
<b>Dose</b>	:		
<b>Exposure time</b>	:		
<b>Comment</b>	:		
<b>Number of animals</b>	:		
<b>Vehicle</b>	:		
<b>Result</b>	:		
<b>Classification</b>	:		
<b>Method</b>	:		
<b>Year</b>	:		
<b>GLP</b>	:	no	
<b>Test substance</b>	:	no data	
<b>Remark</b>	:	Dosage: 100 mg. Moderately irritating. No further data provided.	
<b>Source</b>	:	Sodes Paris EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
25.04.1994			(35)
<b>Species</b>	:	rabbit	
<b>Concentration</b>	:		
<b>Dose</b>	:		
<b>Exposure time</b>	:		
<b>Comment</b>	:		
<b>Number of animals</b>	:		

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**Vehicle** :  
**Result** :  
**Classification** :  
**Method** : other: see reference  
**Year** :  
**GLP** : no  
**Test substance** : no data

**Remark** : Open, undiluted application of test substance. Result: slight reversible injury, grade 2 on a scale of 10.

**Source** : Sodes Paris  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

25.04.1994 (84)

### 5.3 SENSITIZATION

**Remark** : A skin-sensitizing potential has not yet been detected.

**Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

25.04.1994 (17)

### 5.4 REPEATED DOSE TOXICITY

**Type** :  
**Species** : rat  
**Sex** : male/female  
**Strain** : Sprague-Dawley  
**Route of admin.** : inhalation  
**Exposure period** : 35 days  
**Frequency of treatm.** : 24 hours/day, occasional interruptions of no more than 2 hours once per day

**Post exposure period** : none  
**Doses** : 1000 ppm, 10,000 ppm (3.0 mg/L, 30 mg/L)  
**Control group** : yes  
**NOAEL** : = 30 - mg/l  
**Method** :  
**Year** : 1975  
**GLP** : no  
**Test substance** : no data

**Remark** : Groups of 16 rats (equal number of male and female) were exposed to the anesthetic concentrations of diethyl ether (1000 or 10,000 ppm) continuously for 35 days. A control group of 72 rats were treated in a similar manner except they were not exposed to ether. Animals were acclimated to the chambers for five days prior to initiation of exposures. The rats were 150 to 275 g at study initiation. Air was circulated in the chambers by two routes: through a carbon dioxide (soda lime) absorber, and through an air conditioner. Measured oxygen concentrations were 21 to 24% and carbon dioxide levels, which were measured periodically by gas chromatography (GC), never exceeded 0.37%. The concentrations of the test atmospheres were measured automatically at four-hour intervals by GC. Any traces of test substances that may have been found in the control chamber were always less than 1/100 of the concentration in the experimental chamber. Body weights were measured on day 7, 14 and 35 of exposure. Blood was obtained from rats exposed to 10,000 ppm ether at the end of the exposure period. Hematocrits and erythrocyte, leukocyte

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and differential counts were measured.  
After the 35-day exposure period, all animals were killed by CO<sub>2</sub> inhalation. The heart, lungs, liver, kidney and spleen were weighed and retained. Pieces of skeletal muscle, jejunum, proximal femur and brain were also retained. All liver specimens were examined microscopically for the presence or absence of degenerative lesions, which included granular, vacuolar degeneration, zonal centrilobular lipidosis, focal lipidosis and focal necrosis.

<b>Result</b>	: All rats survived 35 days of exposure. Ether treated animals revealed no significant deviation from the air-exposed controls in means of body weight, liver-to-bodyweight ratio, blood morphology, histology. NOAEL = 30 mg/L (10,000 ppm).
<b>Source</b>	: Sodes Paris Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
<b>Reliability</b> 14.11.2003	: (2) valid with restrictions
<b>Type</b>	:
<b>Species</b>	: mouse
<b>Sex</b>	: male/female
<b>Strain</b>	: ICR
<b>Route of admin.</b>	: inhalation
<b>Exposure period</b>	: 35 days
<b>Frequency of treatm.</b>	: 24 hour/day, occasional interruptions of no more than 2 hours, once per day
<b>Post exposure period</b>	: none
<b>Doses</b>	: 1000 ppm, 10000 ppm (3.0 mg/L, 30 mg/L)
<b>Control group</b>	: yes
<b>NOAEL</b>	: = 3 - mg/l
<b>LOAEL</b>	: = 30 - mg/l
<b>Method</b>	:
<b>Year</b>	: 1975
<b>GLP</b>	: no
<b>Test substance</b>	: no data
<b>Remark</b>	: Groups of 48 mice (equal number of male and female) were exposed to the anesthetic concentrations of diethyl ether (1000 or 10,000 ppm) continuously for 35 days. Two control groups of 32 animals each were also included. Animals were acclimated to the chambers for five days prior to initiation of exposures. The mice weighed 18 to 20 grams at study initiation. Air was circulated in the chambers by two routes: through a carbon dioxide (soda lime) absorber, and through an air conditioner. Measured oxygen concentrations were 21 to 24% and carbon dioxide levels, which were measured periodically by gas chromatography (GC), never exceeded 0.37%. The concentrations of the test atmospheres were measured automatically at four-hour intervals by GC. Any traces of test substances that may have been found in the control chamber were always less than 1/100 of the concentration in the experimental chamber. Body weights were measured on day 7, 14 and 35 of exposure. After the 35-day exposure period, all surviving animals were killed by CO <sub>2</sub> inhalation. The heart, lungs, liver, kidney and spleen were weighed and retained. Pieces of skeletal muscle, jejunum, proximal femur and brain were also retained. All liver specimens were examined microscopically for the presence or absence of degenerative lesions, which included granular, vacuolar degeneration, zonal centrilobular lipidosis, focal lipidosis and focal necrosis.
<b>Result</b>	: 10,000 ppm: By exposure day 20, 25% of the mice in the 10,000 ppm exposure group died; therefore, surviving animals in this group were killed on day 20. Animals showed statistically significant increases in liver weight and liver-to-body weight ratio, no other observed parameter was affected.

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		1,000 ppm: Treated animals revealed no significant deviation from the air - exposed controls in means of body weight, blood morphology or histology. Liver weight and liver-to-bodyweight ratios were significantly increased in the male mice compared to controls.	
<b>Source</b>	:	NOAEL = 3.0 mg/l (1,000 ppm); LOAEL = 30 mg/l (10,000 ppm). Sodes Paris Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
<b>Reliability</b> 20.11.2003	:	(2) valid with restrictions	(86)
<b>Type</b>	:		
<b>Species</b>	:	guinea pig	
<b>Sex</b>	:	male/female	
<b>Strain</b>	:	Hartley	
<b>Route of admin.</b>	:	inhalation	
<b>Exposure period</b>	:	35 days	
<b>Frequency of treatm.</b>	:	24 hour/day, occasional interruptions of no more than 2 hours, once per day	
<b>Post exposure period</b>	:	none	
<b>Doses</b>	:	1000 ppm, 10000 ppm (3.0 mg/L, 30 mg/L)	
<b>Control group</b>	:	yes	
<b>NOAEL</b>	:	= 3 - mg/l	
<b>LOAEL</b>	:	= 30 - mg/l	
<b>Method</b>	:		
<b>Year</b>	:	1975	
<b>GLP</b>	:	no	
<b>Test substance</b>	:	no data	
<b>Remark</b>	:	Groups of 16 guinea pigs (equal number of male and female) were exposed to the anesthetic concentrations of diethyl ether (1000 or 10,000 ppm) continuously for 35 days. Two control groups of 8 animals each were also included. Animals were acclimated to the chambers for five days prior to initiation of exposures. The guinea pigs weighed 250 to 350 grams at study initiation. Air was circulated in the chambers by two routes: through a carbon dioxide (soda lime) absorber, and through an air conditioner. Measured oxygen concentrations were 21 to 24% and carbon dioxide levels, which were measured periodically by gas chromatography (GC), never exceeded 0.37%. The concentrations of the test atmospheres were measured automatically at four-hour intervals by GC. Any traces of test substances that may have been found in the control chamber were always less than 1/100 of the concentration in the experimental chamber. Body weights were measured on day 7, 14 and 35 of exposure. After the 35-day exposure period, all surviving animals were killed by CO2 inhalation. The heart, lungs, liver, kidney and spleen were weighed and retained. Pieces of skeletal muscle, jejunum, proximal femur and brain were also retained. All liver specimens were examined microscopically for the presence or absence of degenerative lesions, which included granular, vacuolar degeneration, zonal centrilobular lipidosis, focal lipidosis and focal necrosis.	
<b>Result</b>	:	10,000 ppm: By exposure day 20, 25% of the guinea pigs in the 10,000 ppm exposure group died; therefore, surviving animals in this group were killed on day 20. Animals showed reduced body weight gain; no other observed parameter was affected. 1,000 ppm: treated animals revealed no significant deviation from the air-exposed controls in means of body weight, liver-to-bodyweight ratio, blood morphology, or histology.	
<b>Source</b>	:	NOAEL = 3.0 mg/l (1,000 ppm); LOAEL = 30 mg/l (10,000 ppm). Sodes Paris Huels AG Marl	

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<b>Reliability</b> 20.11.2003	:	EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA) (2) valid with restrictions	(86)
<b>Type</b>	:		
<b>Species</b>	:	rat	
<b>Sex</b>	:	male/female	
<b>Strain</b>	:	other: albino, not specified	
<b>Route of admin.</b>	:	gavage	
<b>Exposure period</b>	:	90 days	
<b>Frequency of treatm.</b>	:	no data	
<b>Post exposure period</b>	:	no data	
<b>Doses</b>	:	500, 2000, 3500 mg/kg bw d	
<b>Control group</b>	:	yes	
<b>NOAEL</b>	:	= 500 - mg/kg bw	
<b>LOAEL</b>	:	= 2000 - mg/kg bw	
<b>Method</b>	:	other: see reference	
<b>Year</b>	:		
<b>GLP</b>	:	no data	
<b>Test substance</b>	:	no data	
<b>Remark</b>	:	30 animals/dose/sex; four dose levels: 0, 500, 2000, and 3500 mg/kg bw d	
<b>Result</b>	:	At 3500 mg/kg bw d, 15/60 rats died, there were observed inhibition in body weight gain and decreased food consumption, decreases in hemoglobin and hematocrit values, and a slight increase in red blood cell count. SGPT (= SALT, Serum alanine amino transferase) and serum cholesterol levels were significantly increased. At 2000 mg/kg bw d, 4/60 rats died, and inhibitions in body weight gain, transient increases in serum cholesterol, retinal atrophy, elevated relative hepatic weights, and gross necropsy aberrations were observed. At 500 mg/kg bw d, one rat had retinal atrophy, but no other effects of histopathologic lesions were observed. Thus 500 mg/kg bw d might be considered as a NOEL.	
<b>Source</b>	:	Sodes Paris Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
<b>Reliability</b> 20.11.2003	:	(4) not assignable	(3)
<b>Type</b>	:		
<b>Species</b>	:	other: rat/guinea pig/rabbit	
<b>Sex</b>	:	male/female	
<b>Strain</b>	:	other: Wistar/-/-	
<b>Route of admin.</b>	:	inhalation	
<b>Exposure period</b>	:	7 weeks	
<b>Frequency of treatm.</b>	:	5 days/week, 7 hours/day	
<b>Post exposure period</b>	:	none	
<b>Doses</b>	:	2000 ppm (6.2 mg/l)	
<b>Control group</b>	:	yes	
<b>NOAEL</b>	:	= 6.2 - mg/l	
<b>Method</b>	:	other: see reference	
<b>Year</b>	:		
<b>GLP</b>	:	no	
<b>Test substance</b>	:	no data	
<b>Remark</b>	:	approximate group sizes: 20 rats, 10 guinea pigs, 4 rabbits, equally divided as to sex.	
<b>Result</b>	:	Ether treated animals revealed no deviation from the air-exposed controls in means of general toxicity, body	

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weight, organ-to-bodyweight ratio, hematological parameters, SGOT and SGPT (= SAST and SALT, serum aspartate amino transferase and serum alanine transferase), histology.

**Source** : Sodes Paris  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

**Reliability** : (4) not assignable  
18.11.2003 (21)

### 5.5 GENETIC TOXICITY 'IN VITRO'

**Type** : Ames test  
**System of testing** : Salmonella typhimurium TA 1535, TA 100, TA 1 538, TA 98, TA 1537  
**Test concentration** :  
**Cycotoxic concentr.** :  
**Metabolic activation** : with and without  
**Result** : negative  
**Method** : other: Ames (1975); Maron and Ames (1983)  
**Year** : 1984  
**GLP** : no data  
**Test substance** : other TS: ethyl ether

**Remark** : Ethyl ether was tested with each strain in duplicate or triplicate using the plate-incorporation method both with and without S9 activation. The test concentrations varied starting from the solubility or toxicity limit of the test substance. The S9 mix contained 10% liver S9 fractions from Aroclor-treated Sprague-Dawley rats, whose protein concentration had been adjusted to 30 mg/ml. The criteria for a positive response included rate of increase of induced versus spontaneous revertants, dose dependency, and reproducibility of results.

**Result** : The spontaneous reversions rates of the tester strains were within the expected ranges throughout the experiment.  
Ethyl ether did not increase the number of revertants in Salmonella typhimurium.

**Source** : Sodes Paris  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

**Reliability** : (2) valid with restrictions  
**Flag** : Critical study for SIDS endpoint  
14.11.2003 (27)

**Type** : DNA damage and repair assay  
**System of testing** : E. coli WP2, WP67, CM871  
**Test concentration** :  
**Cycotoxic concentr.** :  
**Metabolic activation** : with and without  
**Result** : negative  
**Method** : other: Liquid micromethod procedure  
**Year** :  
**GLP** : no data  
**Test substance** : other TS: ethyl ether

**Remark** : Disposable, sterile Microtiter plates containing 8 rows of 12 350 µl wells were utilized for this test. Fifty microliters of the test substance were distributed in each of the first wells of six 8-well rows. The test concentrations varied beginning with the solubility or toxicity limit of the test substance. With this as the starting concentration, the test substance was further diluted in nutrient broth for a total of eight, 2-fold dilutions (50 µl/well, 6 wells/dilution). Of these six 8-well rows, three were filled with 50 µl 0.2 M phosphate-buffered saline (PBS) and 3 with 50 µl S9 mix. The S9

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	<p>mix contained 10% liver S9 fractions from Aroclor-treated Sprague-Dawley rats, whose protein concentration had been adjusted to 30 mg/ml. Finally, each row of wells was filled with 100 µl of one of the three bacterial strains. The plates were sealed with self-adhesive acetate tape and then placed on a multiple microshaker apparatus for 5 minutes of mixing. Bacterial growth in each well was visually evaluated after 16 hours at 37 degrees C, by observing the increase in turbidity of the medium and/or formation of a pellet of settled cells on the bottom of the wells. Five separate experiments were performed in order to determine the reproducibility of results. The test was considered positive if the ratio between the minimal inhibitory concentrations (MICs) in repair-proficient (WP2) and repair-deficient (Wp67, CM871) tester strains were greater than 2.</p>	
<b>Result</b>	: Ethyl ether did not cause genotoxicity in E. coli strains deficient in tryptophan synthesis. The MIC of all tester strains both with and without S9 mix were identical (i.e >40,000 µg).	
<b>Source</b>	: Sodes Paris Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
<b>Reliability</b> 14.11.2003	: (2) valid with restrictions	(27)
<b>Type</b>	: Ames test	
<b>System of testing</b>	: Salmonella typhimurium TA 100, TA 98	
<b>Test concentration</b>	: 1, 5, or 10 %	
<b>Cycotoxic concentr.</b>	:	
<b>Metabolic activation</b>	: with and without	
<b>Result</b>	: negative	
<b>Method</b>	: other: see reference	
<b>Year</b>	:	
<b>GLP</b>	: no	
<b>Test substance</b>	: no data	
<b>Source</b>	: Sodes Paris Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
25.04.1994		(103)
<b>Type</b>	: Sister chromatid exchange assay	
<b>System of testing</b>	: Chinese hamster ovary (CHO) cells	
<b>Test concentration</b>	: 1,97%	
<b>Cycotoxic concentr.</b>	:	
<b>Metabolic activation</b>	: with and without	
<b>Result</b>	: negative	
<b>Method</b>	: other: see reference	
<b>Year</b>	:	
<b>GLP</b>	: no	
<b>Test substance</b>	: no data	
<b>Source</b>	: Sodes Paris Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
25.04.1994		(107)
<b>Type</b>	: Sister chromatid exchange assay	
<b>System of testing</b>	: Chinese hamster ovary (CHO) cells	
<b>Test concentration</b>	: no data	
<b>Cycotoxic concentr.</b>	:	
<b>Metabolic activation</b>	: no data	
<b>Result</b>	: negative	
<b>Method</b>	: other: no data	
<b>Year</b>	:	
<b>GLP</b>	: no data	

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**Test substance** : no data

**Remark** : Ethyl ether had no effect on the number of sister chromatid exchanges in cultured Chinese hamster ovary cells.

**Source** : Sodes Paris  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

26.04.1994 (2)

### 5.6 GENETIC TOXICITY 'IN VIVO'

### 5.7 CARCINOGENICITY

#### 5.8.1 TOXICITY TO FERTILITY

**Type** :  
**Species** : mouse  
**Sex** : male  
**Strain** : other: (C75BlxC3H)F1  
**Route of admin.** : inhalation  
**Exposure period** : 5 days  
**Frequency of treatm.** : 4 hours/day  
**Premating exposure period**  
    **Male** :  
    **Female** :  
**Duration of test** :  
**No. of generation studies** :  
**Doses** : 3,200 and 16,000 ppm (9.7 and 48 mg/L)  
**Control group** : yes  
**Method** : other: see remark  
**Year** :  
**GLP** : no data  
**Test substance** : no data

**Remark** : Five male mice per group, 11 weeks of age, were exposed to diethyl ether vapors four hours/day, for 5 consecutive days. Exposure chambers were constructed from 5-Liter glass desiccators with fenestrated porcelain floors. The test substance was delivered in air from calibrated vaporizers and entered the chamber below the floor and exhausted near the top of the chamber. The total flow of fresh gas to the chamber during exposure was 2.5 L/min. Three separate control groups of 5 mice each (15 total) were exposed to air under identical conditions as the test group. Each 4-hour exposure period was followed by a recovery period of one hour in air before animals were returned to their cages. The concentration of the vaporized test substance in the atmosphere and the CO<sub>2</sub> concentration of the exhausted chamber air were monitored periodically by gas chromatography. Chamber temperatures were also measured. The mice were killed 28 days after the first exposure day. Both cauda epididymides were removed, minced with scissors into 2 ml physiologic saline, pipetted and filtered through stainless gauze. The filtered suspension was stained overnight and duplicate slides were made for each animal. One thousand spermatozoa were examined on each slide for morphological abnormalities. All slides were read without knowledge of dose level. The number of morphologically abnormal cells was reported in percentages.

**Result** : The measured concentrations were within 5% of the target concentrations. The CO<sub>2</sub> concentration of the exhaust gas was maintained below 0.3%

throughout all exposures.

One mouse in the 3,200 ppm group did not survive the exposures. All surviving mice were evaluated for morphologically abnormal spermatozoa. No increase in the number of abnormal epididymal spermatozoa were found when compared to the control group as the following table indicates:

Group	Concentration (ppm)	Percent abnormal spermatozoa (+/- SEM)
Control	0	1.42 (+/- 0.08)
DEE	16,000	1.24 (+/- 0.11)
DEE	3,200	1.70 (+/- 0.23)

**Source** : Sodes Paris  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

**Reliability** : (2) valid with restrictions  
20.11.2003

(66)

### 5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

**Species** : Rat  
**Sex** : Female  
**Strain** : Sprague-Dawley  
**Route of admin.** : Inhalation  
**Exposure period** : 1 hour  
**Frequency of treatm.** : days 9, 10, 11, or days 13, 14, 15 of gestation  
**Duration of test** :  
**Doses** : 73,000 ppm (220 mg/L)  
**Control group** : no data specified  
**Method** : other: see remark  
**Year** :  
**GLP** : No  
**Test substance** : no data

**Remark** : Pregnant Sprague-Dawley rats were anesthetized with 7.3 vol% ether during early or late organogenesis. Animals were anesthetized for 1 hour in a 5.0 liter closed circuit anesthesia apparatus. Litters were delivered by cesarean section on day 19 of gestation, weighed, examined and measured.

**Result** : Ether anesthesia of pregnant rats caused early and late fetal resorptions and skeletal anomalies but did not alter the incidence of soft tissue anomalies. Thus ether did not show to be highly teratogenic, hypoxia might contribute to the embryotoxicity of ether.

**Source** : Sodes Paris  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

**Reliability** : (2) valid with restrictions  
20.11.2003

(78)

**Species** : rat  
**Sex** : female  
**Strain** : Sprague-Dawley  
**Route of admin.** : inhalation  
**Exposure period** : 60-360 min  
**Frequency of treatm.** : no data  
**Duration of test** : no data  
**Doses** : 73,000 ppm  
**Control group** : no data specified  
**Method** : other: see remark  
**Year** :

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<b>GLP</b>	:	no	
<b>Test substance</b>	:	no data	
<b>Remark</b>	:	<p>In a preliminary study, rats had been exposed to 7.3 vol% diethyl ether for various lengths of time (60-360 min). Twenty-four hours later, the number of dead per group was counted. Fifty percent of the rats died after 150 min anesthesia.</p> <p>Pregnant Sprague-Dawley rats (number of animals not provided) were then anesthetized for one hour in a 5 liter closed circuit vapor exposure chamber with 7.3 vol% diethyl ether during early or late embryogenesis. Fetuses were delivered by cesarean section one day before normal parturition.</p>	
<b>Result</b>	:	<p>Ether anesthesia (at 7.3 vol% for 60 min) of pregnant rats did not increase the incidence of resorptions, of soft tissue or skeletal anomalies. Anesthesia during early or late organogenesis did significantly decrease fetal bodyweight and length of long bones. Histologic examination of fetal brain, heart, kidney, liver, and skeletal muscle revealed no changes. Rats are more resistant than mice to the embryotoxic effects of ether anesthesia, however, ether is not highly embryotoxic to either mice or rats.</p>	
<b>Source</b>	:	<p>Sodes Paris Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)</p>	
<b>Reliability</b> 18.11.2003	:	(2) valid with restrictions	(79)
<b>Species</b>	:	mouse	
<b>Sex</b>	:	female	
<b>Strain</b>	:	Swiss Webster	
<b>Route of admin.</b>	:	inhalation	
<b>Exposure period</b>	:	1 hour	
<b>Frequency of treatm.</b>	:	days 8, 9, 10, or days 12, 13, 14 of gestation	
<b>Duration of test</b>	:		
<b>Doses</b>	:	65,000 ppm	
<b>Control group</b>	:	no data specified	
<b>Method</b>	:	other: see remark	
<b>Year</b>	:		
<b>GLP</b>	:	no	
<b>Test substance</b>	:	no data	
<b>Remark</b>	:	<p>Pregnant Swiss-webster mice were anesthetized with 6.5 vol% ether during early or late organogenesis. Animals were anesthetized for 1 hour in a 5.0 liter closed circuit anesthesia apparatus. Litters were delivered by cesarean section on day 19 of gestation, weighed, examined and measured.</p>	
<b>Result</b>	:	<p>Ether anesthesia of pregnant mice caused early and late fetal resorptions and skeletal anomalies but did not alter the incidence of soft tissue anomalies. Thus ether did not show to be highly teratogenic, hypoxia might contribute to the embryotoxicity of ether.</p>	
<b>Source</b>	:	<p>Sodes Paris Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)</p>	
26.04.1994			(78)
<b>Species</b>	:	mouse	
<b>Sex</b>	:	female	
<b>Strain</b>	:	Swiss Webster	

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<b>Route of admin.</b>	:	inhalation
<b>Exposure period</b>	:	60-360 min
<b>Frequency of treatm.</b>	:	no data
<b>Duration of test</b>	:	no data
<b>Doses</b>	:	65,000 ppm
<b>Control group</b>	:	no data specified
<b>Method</b>	:	other: see remark
<b>Year</b>	:	
<b>GLP</b>	:	no
<b>Test substance</b>	:	no data
<b>Remark</b>	:	<p>In a preliminary study, mice had been exposed to 6.5 vol% diethyl ether for various lengths of time (60-360 min). Twenty-four hours later, the number of dead per group was counted. Fifty percent of the mice died after 100 min anesthesia.</p> <p>Pregnant Swiss Webster mice (number of animals not provided) were then anesthetized for one hour in a 5 liter closed circuit vapor exposure chamber with 6.5 vol% diethyl ether during early or late embryogenesis. Fetuses were delivered by cesarean section one day before normal parturition.</p>
<b>Result</b>	:	<p>Ether anesthesia of pregnant mice during early organogenesis caused a significant incidence of fetal resorptions (14/56) and hydronephrosis (2/26). Anesthesia during early or late organogenesis caused a significant incidence of generalized edema (19/172), missing sternum (10/172), unossified phalanges (9/72), and missing cervical vertebrae (10/72). Anesthesia at either stage did not alter fetal bodyweight or crown-rump length. Length of fetal long bones was decreased by treatment during early organogenesis. Histologic examination of fetal brain, heart, kidney, liver, and skeletal muscle revealed no changes except hepatic parenchymal cell vacuolation.</p>
<b>Source</b>	:	<p>Sodes Paris Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)</p>
26.04.1994		(79)
<b>Species</b>	:	other: Chicken (embryo)
<b>Sex</b>	:	no data
<b>Strain</b>	:	other: White Leghorn
<b>Route of admin.</b>	:	other: Ambient gas phase
<b>Exposure period</b>	:	up to 4 days
<b>Frequency of treatm.</b>	:	5 - 6 hour/day
<b>Duration of test</b>	:	
<b>Doses</b>	:	10,000-20,000 ppm
<b>Control group</b>	:	yes
<b>Method</b>	:	other: see remark
<b>Year</b>	:	
<b>GLP</b>	:	no
<b>Test substance</b>	:	no data
<b>Remark</b>	:	<p>Fertile eggs were exposed to ether in glass chambers. Oxygen supply, ether concentration, temperature, humidity were monitored. One-fifth of embryos was opened on the 10th day. Blood concentration of ether in the embryo and yolk was determined. With the others, incubation was continued until the 18th day. The control group was air-exposed. A total of 1058 embryos was studied.</p>
<b>Result</b>	:	<p>Anomalies were observed in brain, eyes, extremities, beak. However, the peak of teratogenesis by ether in this study was at or near the embryo LD50 caused by the stress of this</p>

anesthetic concentration. Cellular death from toxicity of the agent is a relatively simple explanation for the teratogenic effect. Therefore, teratogenicity of ether is doubtful.

**Source** : Sodes Paris  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

26.04.1994 (83)

### 5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

### 5.9 SPECIFIC INVESTIGATIONS

### 5.10 EXPOSURE EXPERIENCE

**Remark** : Diethylether has an irritant action on the mucous membrane of the respiratory tract, it stimulates salivation and increases bronchial secretion; laryngeal spasm may occur. It causes vasodilation which may lead to a severe fall in blood pressure, it reduces blood flow to the kidneys and increases capillary bleeding. The bleeding time is unchanged but the prothrombin time may be prolonged. Leucocytosis occurs after ether anesthesia and convulsions occasionally occur in children or young adults under deep ether anesthesia. Recovery is slow from prolonged anesthesia and postoperative vomiting commonly occurs. Acute overdosage of ether is characterized by respiratory failure followed by cardiac arrest.

**Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

14.12.1993 (76)

**Remark** : Diethylether anesthesia caused detectable blood acetaldehyde levels in 15 patients. Ether dose given was not provided, but blood ether levels were within 1,2 and 1,7 g/l in every patient. The average acetaldehyde concentration was 21 uM which approximates the level found after ethanol intake (blood ethanol level was 1 g/l for two hours). No acetaldehyde could be found in patients anaesthetised without ether. The result supports the suggestion of acetaldehyde appearing as an intermediate during ether metabolism.

**Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

14.12.1993 (69)

**Remark** : The minimal alveolar concentration (MAC) to maintain anesthesia in man is 1,92 Vol-% (19200 ppm = 60 mg/l). At this concentration blood shows diethylether values of about 0,7 g/l.

**Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

14.12.1993 (18)

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- Remark** : Depending on dose, acute ether inhalation results, in the following clinical signs (no data provided about duration of exposure).  
10,000 ppm = 31 mg/l analgesia  
30,000 ppm = 93 mg/l consciousness  
30.000 - 50,000 ppm = 93-155 mg/l anesthesia  
60.000 - 83,000 ppm =186-257 mg/l cessation of breathing  
>103.000 ppm = 319 mg/l lethal damage  
Ether anesthesia can result in vomiting at the end of anesthesia, caused by a direct irritation of the gastric mucosa. Isolated cases of centrilobular liver necrosis and fatty degeneration of liver lobular are described, but a typical damage of liver or kidney tissue is not reported. Ether anesthesia can result in a metabolic acidosis followed by hyperglycemia.
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
- 26.04.1994 (36)
- Remark** : In 1904, 3 children were presented who developed tachycardia, pyrexia, and delirium, before dying on the second day after receiving diethylether for orthopedic procedures. Autopsy studies performed on the three patients revealed marked fatty hepatic infiltration. None of the children was noted to show signs of an icterus prior to death. The capability of ether to damage liver tissue is questionable.
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
- 15.12.1993 (34)
- Remark** : Henderson and Haggard estimated that a man of average weight would absorb a maximum of 1.25 g of ethyl ether, resulting in a blood concentration of 0.018 g/l, when exposed to an atmospheric concentration of 400 ppm (1,24 mg/l). Further details, such as the duration of exposure, were not provided in the ACGIH review of the study.
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
- 15.12.1993 (49)
- Remark** : Frozen abdominal cadaver skin samples were washed with ether for 30 minutes. Before and after treatment skin was analyzed by electron spectroscopy for chemical analyses (ESCA), which allows a valuable in vitro information about elemental and chemical composition of the skin surface to a depth of about 50 Angstroems. ESCA is used to evaluate the removal of skin lipid from epidermis by measuring changes in the skin's atomic percentage of nitrogen. Ether does not extract lipid from the surface of the skin. As a result, ether does not decrease the barrier properties of the skin.
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
- 15.12.1993 (8)
- Remark** : Repeated or prolonged contact to liquid diethyl ether

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- possibly causes dry scaly fissured dermatitis.
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (25)
- Remark** : Acute eye and mucosal irritation by ether was evaluated. Volunteers (N=10) were exposed to diethylether for 3 to 5 minutes. After exposure, each individual classified the effect of the vapor. Slight nasal irritation was observed at concentrations of 200 ppm (0,62 mg/l).
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (72)
- Remark** : Minimum lethal dose is given as 273 mg/kg per os for an adult human.
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
26.04.1994 (4)
- Remark** : Diethylether anesthesia caused detectable blood acetaldehyde levels in 15 patients. Ether dose given was not provided, but blood ether levels were within 1,2 and 1,7 g/l in every patient. The average acetaldehyde concentration was 21 uM which approximates the level found after ethanol intake (blood ethanol level was 1 g/l for two hours). No acetaldehyde could be found in patients anaesthetised without ether. The result supports the suggestion of acetaldehyde appearing as an intermediate during ether metabolism.
- Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
14.12.1993 (69)
- Remark** : The minimal alveolar concentration (MAC) to maintain anesthesia in man is 1,92 Vol-% (19200 ppm = 60 mg/l). At this concentration blood shows diethylether values of about 0,7 g/l.
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- Remark** : Depending on dose, acute ether inhalation results, in the following clinical signs (no data provided about duration of exposure).
- 10,000 ppm = 31 mg/l analgesia
  - 30,000 ppm = 93 mg/l consciousness
  - 30.000 - 50,000 ppm = 93-155 mg/l anesthesia
  - 60.000 - 83,000 ppm = 186-257 mg/l cessation of breathing
  - >103.000 ppm = 319 mg/l lethal damage
- Ether anesthesia can result in vomiting at the end of anesthesia, caused by a direct irritation of the gastric mucosa. Isolated cases of centrilobular liver necrosis and fatty degeneration of liver lobular are described, but a typical damage of liver or kidney tissue is not reported. Ether anesthesia can result in a metabolic acidosis followed

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- Source** : by hyperglycemia.  
: Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
26.04.1994 (36)
- Remark** : In 1904, 3 children were presented who developed tachycardia, pyrexia, and delirium, before dying on the second day after receiving diethylether for orthopedic procedures. Autopsy studies performed on the three patients revealed marked fatty hepatic infiltration. None of the children was noted to show signs of an icterus prior to death. The capability of ether to damage liver tissue is questionable.
- Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (34)
- Remark** : Ether inhalation leads to a rapid narcosis starting after signs of preliminary irritation; if ether is given for long enough and in sufficient concentration death takes place from respiratory paralysis. Recovery on removal from exposure to non-lethal concentrations is rapid and there are no apparent cumulative or after-effects. Ether anesthesia is accompanied by acidosis and hyperglycaemia. Lower concentrations result in drowsiness, confusion, excitement, dizziness and faintness. After-effects of acute intoxication include nausea, headache, lack of appetite, vomiting, perspiration, mental confusion and irritability. One fatal case is reported, where ether was used in perfumery manufacture as an extracting agent. The subject developed acute mania and died in uraemic convulsions.
- Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.02.1997 (15)
- Remark** : Henderson and Haggard estimated that a man of average weight would absorb a maximum of 1.25 g of ethyl ether, resulting in a blood concentration of 0.018 g/l, when exposed to an atmospheric concentration of 400 ppm (1,24 mg/l). Further details, such as the duration of exposure, were not provided in the ACGIH review of the study.
- Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (49)
- Remark** : A wide variation of symptoms is seen following chronic exposure, including occasional dizziness, faintness, loss of appetite and distaste for food, increased thirst (but vomiting when water was taken), nausea, constipation, lassitude, specks before the eyes, numbness in fingers and feet. Nephritis is not frequent but may occur. Some individuals show albuminuria. Ether abuse by drinking leads to "ether habit", chronic effects are inflammation of the respiratory passages, irritability, restlessness, sleeplessness, general debility, headache, and other nervous symptoms, cardiac irregularity and dilatation of blood vessels. Concentrations and/or dosages are not given in this reference.

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- Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.02.1997 (15)
- Remark** : Frozen abdominal cadaver skin samples were washed with ether for 30 minutes. Before and after treatment skin was analyzed by electron spectroscopy for chemical analyses (ESCA), which allows a valuable in vitro information about elemental and chemical composition of the skin surface to a depth of about 50 Angstroems. ESCA is used to evaluate the removal of skin lipid from epidermis by measuring changes in the skin's atomic percentage of nitrogen. Ether does not extract lipid from the surface of the skin. As a result, ether does not decrease the barrier properties of the skin.
- Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (8)
- Remark** : Repeated or prolonged contact to liquid diethyl ether possibly causes dry scaly fissured dermatitis.
- Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (25)
- Remark** : Acute eye and mucosal irritation by ether was evaluated. Volunteers (N=10) were exposed to diethylether for 3 to 5 minutes. After exposure, each individual classified the effect of the vapor. Slight nasal irritation was observed at concentrations of 200 ppm (0,62 mg/l).
- Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (72)
- Remark** : Minimum lethal dose is given as 273 mg/kg per os for an adult human.
- Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
26.04.1994 (4)

### 5.11 ADDITIONAL REMARKS

- Type** : Behaviour
- Remark** : NIH mice were exposed to a range of concentrations of ether (1,000-30,000 ppm) in an inhalation chamber and both behavioral and neuroendocrine responses were assessed. When responding was maintained under FI-60s schedules of milk presentation, 30 min exposure to 1,000 ppm ether resulted in minimal behavioral effects, 3,000 - 10,000 ppm increased rates of responding over two-fold and higher concentrations decreased responding almost completely. Five -min exposure to the same range of concentration resulted in concentration-related effects which were smaller than those produced by 30-min exposures. Exposure to a similar range of concentrations in naive mice increased adrenocorticotrophic hormone (ACTH) and corticosterone levels in a time- and

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	concentration-dependent manner. Five-min exposures to 10,000 ppm ether increased levels of ACTH from a baseline of 25.95 pg/ml to 310.5 pg/ml but did not effect corticosterone. Thirty-min exposures to the full range of concentrations of ether increased corticosterone from control levels of 70 ng/l to 418 ng/l at 30,000 ppm, in a concentration dependent manner.	
<b>Source</b>	: Sodes Paris EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
27.04.1994		(40)
<b>Type</b>	: Cytotoxicity	
<b>Remark</b>	: The effect of ether on the division of Chinese hamster fibroblasts in spinner cultures were studied. Ether caused dose dependent inhibition of cell multiplication. ED50 for ether (effective dose, where cell multiplication was reduced to 50% of that of controls, controls were exposed to carrier gas) was 5,97%. Carrier gas was 5% CO2 in air.	
<b>Source</b>	: Sodes Paris Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
27.04.1994		(88)
<b>Type</b>	: Neurotoxicity	
<b>Remark</b>	: Male mice, C57BL/6J and DBA/J2, were repeatedly exposed for 9 seconds (control: air). Method: Animals had to perform a daily learning trial (escape from shock, six times/day). After familiarization with the test apparatus and a first trial, animals were placed in a jar containing cotton saturated with diethyl ether. Result: The study revealed that an approximate 9-sec posttrial exposure to ether, not resulting in loss of the righting response, can enhance performances of DBA/2J mice. It has no significant effect upon performances of C57/6J mice.	
<b>Source</b>	: Sodes Paris Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
14.12.1993		(108)
<b>Type</b>	: other: Embryotoxicity	
<b>Remark</b>	: Pregnant rabbits were exposed to ether anesthesia. There was observed a significant decrease (>50 %) of the oxygen partial pressure (pO2) in the fetuses when compared to the pO2 of the dams. This reduction was probably caused by a decrease of blood pressure. No further data were reported concerning dose or time of exposure.	
<b>Source</b>	: Sodes Paris Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
15.12.1993		(73)
<b>Type</b>	: other: Mutation data	
<b>Remark</b>	: Species: Mouse Sex: male Application: 1000 mg/kg, Single dose, i.p.	

		Method: DNA synthesis inhibition test: By binding covalently to DNA chemical mutagens and carcinogens inhibit replication which can be measured as a decrease of thymidine incorporation into DNA. This DNA synthesis inhibition can be determined in testicular cells of mice. Mice received methyl- <sup>14</sup> C-thymidine, the following day they received the test substance and subsequently methyl- <sup>3</sup> H-thymidine. Testes were transferred and homogenized, DNA-content was measured.	
		----- Result: False positive, as cytotoxic effect of the anesthetic decreases thymidine incorporation too. When methyl- <sup>3</sup> H-thymidine was not administered to the animal but to the homogenized testes, no inhibition of DNA synthesis could be observed, the result then was negative.	
<b>Source</b>	:	Sodes Paris Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
15.12.1993			(81)
<b>Type</b>	:	other: Mutation data	
<b>Remark</b>	:	Method: P3478 E. coli technique, prescreen for chemical carcinogens: Differential growth inhibition was evaluated as a rapid screening technique for chemical carcinogens. Test system: E. coli, P3478 (DNA-polymerase-deficient mutant). Metabolic activation: with and without Result: negative	
<b>Source</b>	:	Sodes Paris EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
15.12.1993			(37)
<b>Type</b>	:	other: Mutation data	
<b>Remark</b>	:	Method: P3478 E. coli technique, prescreen for chemical carcinogens: Differential growth inhibition was evaluated as a rapid screening technique for chemical carcinogens. Test system: E. coli, P3478 (DNA-polymerase-deficient mutant). Metabolic activation: with and without Result: negative	
<b>Source</b>	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
15.12.1993			(37)
<b>Type</b>	:	other: Other relevant data for carcinogenicity	
<b>Remark</b>	:	Inhaled ether stimulated tumor growth in mice with subcutaneously or intravenously implanted tumor cells. In the same study, the mitotic index of implanted tumor cells in rats was not affected by administration of an unspecified concentration of diethyl ether.	
<b>Source</b>	:	Sodes Paris Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
15.12.1993			(38)
<b>Type</b>	:	other: Other relevant data for carcinogenicity	
<b>Remark</b>	:	Diethyl ether and disulfiram dissolved in diethyl ether was administered to 8 - and 9 -day embryos (inbred CH3 mice) in vitro in concentrations of 0.285 mg/ml and 2.85 mg/ml. Apart	

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- from a reduction in somite counts, ether in these concentrations caused no adverse effects on morphological development in 8- or 9-day embryos. DNA synthesis was inhibited at a concentration of 2.85 mg/ml in 9-day embryos.
- Source** : Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (91)
- Type** : other: Toxicokinetics/Metabolism
- Remark** : Exposure of 20 h fasted male Wistar albino rats, ca. 250 g, to ether anesthesia for 6 min (dose level of approx. 5 g/kg) resulted in increased exhalation of alkanes, and indication of lipid peroxidation in vivo. Total cytochromes P-450 of liver and kidney were decreased to 25-30 % of control values, but were restored to normal levels 2 h later. Cytochrome P450 I (EROD activity) was decreased to 35-44 % of control values and was restored to 80 % of normal levels 2 h later. Diethyl ether is known to be metabolized by cytochrome P450IIE1 which is induced by fasting and by diethyl ether, and is possibly involved in the observed radical production, lipid peroxidation, and loss of cytochromes P-450. The effect of ether seen in this study could readily explain the hepatic necrosis seen in fatalities following prolonged ether anesthesia.
- Source** : Sodes Paris  
Huels AG Marl  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (67)
- Type** : other: Toxicokinetics/Metabolism
- Remark** : The (acute) effect of diethyl ether anesthesia on in vivo hepatic protein synthesis was tested in male Wistar rats. Protein synthesis was measured by an isotope technique. It was shown that usual anesthetic levels of diethyl ether reduced the rate of synthesis of liver proteins to 80 % compared to a group receiving no anesthesia. The synthesis / secretion of plasma proteins was much more inhibited, to approximately 20-30 %, compared to animals either receiving no anesthesia or pentobarbital. No further data were given about number of animals or dosages.
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (10)
- Type** : other: Toxicokinetics/Metabolism
- Remark** : Eighteen male Sprague Dawley rats were instrumented with microspheres. Cardiac output and blood flow distribution were determined at five different periods: before ether anesthesia; at a surgical level of ether anesthesia; and 20 min, 1 hr, or 3 hr after cessation of anesthesia. Ether anesthesia initially decreased arterial pressure, increased cardiac index, and decreased total peripheral resistance. The residual effects of ether included progressive increases in arterial blood pressure and an increase in total peripheral resistance index. Cardiac index was returned to normal 1 hr after termination of anesthesia. Blood flow to the brain and heart increased during anesthesia and was significantly elevated 1 hr later. Other organs, including kidney, spleen, and intestine showed a decrease in blood

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- flow during anesthesia, which persisted for at least 20 min. Thus ether anesthesia produced acute and residual disturbances in hemodynamics and blood flow distribution. No further data were given about the ether dose administered.
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (85)
- Type** : other: Toxicokinetics/Metabolism
- Remark** : Dogs were exposed to an atmosphere of diethyl ether. About 87 % of the inspired ether was excreted unchanged in the expired air at the end of the experiment. Traces of ether were found in the urine (2 %, concentration approximately equal to that of blood passing through the kidneys). A slight accumulation of ether in fatty tissue was observed.
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (44)
- Type** : other: Toxicokinetics/Metabolism
- Remark** : Rats were exposed to an ether concentration of 10 % v/v (= 310 mg/l) for 5-60 min. Ether concentration was determined in omental and renal fat and given as mg ether per 1 g of tissue wet weight. A few minutes after administration the concentration of ether in fatty tissue was the same as in blood, after 15 minutes it was considerably higher in fat than in blood. The maximum concentration in fatty tissue (about 3 mg/g) was reached after 0.5-1 h. The elimination of ether from fatty tissues in rats did not begin immediately after the end of ether administration, but only when the concentration in the blood had become relatively low. It was practically finished after about 8 h.  
24 h after a 1 h exposure, ether concentration in fatty tissue was 0.12 mg/g and 0.03 in blood, respectively.
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (33)
- Type** : other: Toxicokinetics/Metabolism
- Remark** : Dogs were exposed to ether in a closed circuit system. Ether concentration was determined in arterial and venous blood by infrared spectrometry. In case of tissue determination of ether, infrared spectroscopy, mass spectroscopy and roentgenographic fluorescence spectroscopy were used. Concentration of ether in selected tissues after 2.5 h of ether anesthesia (Number of animals: 8; ether dose given not provided):
- |                |            |
|----------------|------------|
| arterial blood | 1.025 mg/g |
| brain          | 1.140 mg/g |
| adrenal        | 1.945 mg/g |
| fat            | 6.700 mg/g |
| skel. muscle   | 0.853 mg/g |
| liver          | 0.940 mg/g |
| kidney         | 2.420 mg/g |
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (23)
- Type** : other: Toxicokinetics/Metabolism

- Remark** : Dogs were exposed to ether anesthesia for a duration of 10 minutes or 2.5 hours. Ether concentration in anesthetic induction period was 10-20 % in oxygen (= concentration of 100,000-200,000 ppm or 308-616 mg/l). At the end of exposure, ether concentration was determined in various areas of the brain and in blood. Ranges of arterial blood concentration: from 0.74 to 1.31 mg/g for 10 minutes of anesthesia, and 0.966 - 1.464 mg/g for 2.5 h of anesthesia. The ratio of brain to blood concentration at 10 minutes was from 0.7 to 1.8.
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA) (22)
- 15.12.1993
- Type** : other: Toxicokinetics/Metabolism
- Remark** : Rats were dosed by intraperitoneal injection with isotopically labeled ether at a dose level of 357 mg/kg. Animals were placed in all-glass metabolism cage to allow the recovery of the expired gases and separate collection of urine and feces. The animals remained in these containers for periods up to 96 h. Rats were narcotized for periods up to 2 h.
- The total radioactivity in CO<sub>2</sub> and urine collected in a 24 hour period was 4 % and 2 %, respectively, of the amount injected. The authors summarized that ether is not inert but undergoes a biotransformation. They suggested that ether is cleaved by O-dealkylation, which occurs under catalysis of an enzyme found in microsomes.
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA) (101)
- 15.12.1993
- Type** : other: Toxicokinetics/Metabolism
- Remark** : Isotopically labeled ether was administered to NMRI mice by inhalation. Animals were exposed to a concentration of 80,000 ppm (246 mg/l), exposure duration of 15 minutes or 2 h, respectively. Uptake and metabolism of ether were studied with whole-body autoradiography. Increased relative concentration of radioactivity developed in liver and kidney, reflecting the accumulation of nonvolatile metabolites. At two hours the measured nonvolatile metabolites accounted for 3.6 % of the administered radioactivity. Further investigation of an extract of liver showed the presence of four nonvolatile metabolites. The authors suggest the following mechanism for ether metabolism:
- $$\text{CH}_3\text{-CH}_2\text{-O-CH}_2\text{-CH}_3 \rightarrow \text{CH}_3\text{-CH}_2\text{-O-CH(OH)-CH}_3$$
- $$\rightarrow \text{CH}_3\text{-CH}_2\text{OH} + \text{CH}_3\text{-CHO}$$
- diethyl ether → ethanol + acetaldehyde
- However, it was considered that there were additional pathways, as the investigation of liver extract indicated the presence of a glucuronide of ether.
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA) (24)
- 15.12.1993
- Type** : other: Toxicokinetics/Metabolism

- Remark** : Method: Isotopically labeled ether was administered to NMRI mice by inhalation. The animals were sacrificed 2 h after anesthesia. Livers were investigated for nonvolatile metabolites of ether by measuring the radioactivity of the liver extract. Approximately 1 % of the administered radioactivity was recovered in the extract. The extracted metabolites were then separated by thin layer chromatography.  
Result: A portion of diethyl ether administered by inhalation was rapidly transformed into fatty acids (palmitic, stearic and oleic acids), cholesterol, mono-, di- and triglycerides. The authors suggest that diethyl ether is transformed to acetate which enters the common metabolic pool and is subsequently degraded to CO<sub>2</sub>.
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (42)
- Type** : other: Toxicokinetics/Metabolism
- Remark** : Rats were treated with phenobarbital (80 mg/kg i.p.) for 3 days prior to sacrifice (24 h after final injection). Hepatic microsomes were prepared. The incubations consisted of NADP, MgCl<sub>2</sub>, glucose-6-phosphate, EDTA, glucose-6-phosphate dehydrogenase, microsomal protein, and diethyl ether in potassium phosphate buffer. Acetaldehyde formation was determined by photometry. The experiment indicated that diethyl ether was metabolized to acetaldehyde by microsomes and that this reaction was linear through 20 min. This reaction required NADPH and was inhibited by both carbon monoxide and antibody to rat liver cytochrome P-450. The authors suggest that microsomal metabolism of diethyl ether is catalysed by a cytochrome P-450-containing mono-oxygenase system.
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (20)
- Type** : other: Toxicokinetics/Metabolism
- Remark** : Isolated rat liver parenchymal cells incubated with anesthetic concentrations of diethyl ether were shown to produce acetaldehyde and ethanol in a dose dependent manner. The acetaldehyde and ethanol production from ether was stimulated in hepatocytes derived from phenobarbital treated rats and could be only partially inhibited by 4-methyl pyrazole. The study results support the suggestions that diethyl ether is metabolized by an inducible microsomal enzyme system which cleaves diethyl ether in a reaction analogous to the known O-dealkylation reactions.
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (87)
- Type** : other: Toxicokinetics/Metabolism
- Remark** : The ethanol disappearance rate was determined in fed rats given 20-40 mMol ethanol and anesthetized with pentobarbital (control group) and diethyl ether. Rats anesthetized with diethyl ether (blood levels of 9-13 mM) revealed a 52 % inhibition of ethanol disappearance when compared to

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- control. This observation indicated that the site of inhibition could be referred to the cytosolic enzyme alcohol dehydrogenase.
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (74)
- Type** : other: Toxicokinetics/Metabolism
- Remark** : The effect of diethyl ether on ethanol metabolism was studied in isolated rat hepatocytes and ether was found to inhibit ethanol oxidation in a dose-dependent manner. At ethanol concentrations of approximately 30 mM, diethyl ether inhibited ethanol oxidation by approximately 58 %, 40 %, and 20 % at ether concentrations of 30, 20, and 10 mM, respectively.
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (7)
- Type** : other: Toxicokinetics/Metabolism
- Remark** : Method: Diethyl ether was administered by inhalation to Sprague Dawley rats at a concentration of 16,000 ppm (49.6 mg/l). Exposure time was 7 h/day for five days. A control group was exposed to air. Animals were sacrificed and liver microsomes were prepared. Microsomal cytochrome P-450, NADPH cytochrome c reductase and cytochrome b5 were determined. Liver triglycerides were determined. A histologic evaluation of liver was performed.  
Result: The study showed that diethyl ether increases microsomal cytochrome P-450, NADPH cytochrome c reductase, cytochrome b5 and microsomal protein. No change in hepatic architecture was observed.
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (14)
- Type** : other: Toxicokinetics/Metabolism
- Remark** : Method: Mice were treated i.p. with sodium phenobarbital for 3 days and with beta-naphthoflavone on the 2nd day. Each day, immediately prior to treatment, the mice were exposed to an anesthetic ether atmosphere (about 1 min). Controls were treated the same way but without any ether anesthesia. Animals were killed by cervical dislocation, part of the ether dosed animals was killed by an over-dose of ether (inhalation about 3-5 min). Livers were homogenized. Aminopyrine demethylase, p-nitroanisole demethylase and protein were determined. The enzyme stability in the conditions of the liver microsomal assay was followed by determining the activities.
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (9)
- Type** : other: Toxicokinetics/Metabolism
- Remark** : Method: Male Sprague Dawley rats were pretreated with several agents to induce liver metabolism, i.e. phenobarbital, butylated hydroxytoluene, acetone, ethanol, and isofluorane. Animals were then exposed to an atmosphere

		<p>saturated with diethyl ether until loss of righting reflex. Ether treatment was repeated three times or five times daily for 3 days. In a second experiment, liver induction was performed by pretreatment with ether in the described way. Animals were sacrificed the fourth day. Liver microsomes were prepared. Demethylase activities, ether deethylase activity and O-dealkylation were estimated and immunoblot analysis was performed.</p> <p>Result: Microsomal oxidation of ether to acetaldehyde was elevated 1.5- to 2-fold by pretreatment with ether when compared to control. Ether also induced N-nitrosodimethylamine demethylase b up to 2-fold and O-dealkylation by up to 10-fold. These trends agreed with the result of the immunoblot experiment in which ether was an inducer of the P-450 isoenzyme IIE1, but a stronger inducer of IIB1. N-nitrosodimethylamine, as well as common inhibitors of IIE1 such as hexane strongly inhibited deethylation.</p>	
<b>Source</b>	:	Sodes Paris	
15.12.1993		EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	(11)
<b>Type</b>	:	other: Toxicokinetics/Metabolism	
<b>Remark</b>	:	Rats were pretreated with 1) microsomal enzyme inducers, 2) inhibitors of microsomal enzymes, 3) hepatotoxins, 4) commonly used anesthetics, e.g. diethyl ether. Ether was administered by inhalation to induce and maintain narcosis for 10 min before sacrifice. Animals were sacrificed and livers prepared. Hepatic UDPGA (UDP-glucuronosyltransferase) content was decreased to 5 % of the control after exposure to ether. This result indicated that ether was able to influence the rate of glucuronidation to a high extent.	
<b>Source</b>	:	Sodes Paris	
15.12.1993		EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	(104)
<b>Type</b>	:	other: Toxicokinetics/Metabolism	
<b>Remark</b>	:	Rats were fitted with bile duct and jugular vein catheters while anesthetized with diethyl ether. As anesthesia abated, bile was collected for the next 5 h and analyzed for flow rate, total bilirubin excretion, and bilirubin glucuronide composition. The HPLC method used allowed direct analysis of bile without derivation or extraction. Ether anesthesia was associated with a reversible suppression of diglucuronide formation and total bilirubin excretion, with reciprocal monoglucuronide changes. These results supported the hypothesis that alterations in UDP-glucuronic acid concentration were capable of influencing rates of hepatic glucuronide formation.	
<b>Source</b>	:	Sodes Paris	
15.12.1993		EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	(41)
<b>Type</b>	:	other: Toxicokinetics/Metabolism	
<b>Remark</b>	:	Acetaminophen (Paracetamol) is toxified by cytochromes P-450 to a hepatotoxic reactive metabolite. Brief general anesthesia with diethyl ether has been shown to inhibit both the toxifying cytochromes P-450 and enzymatic glucuronidation, the latter constituting up to 60 % of	

- acetaminophen elimination via a nontoxic pathway. Thus ether could potentially produce a temporally differentiated inhibition of bioactivating and detoxifying pathways, resulting in an enhancement of acetaminophen toxicity if the balance favored bioactivation. To evaluate this possibility, male NIH mice were treated with acetaminophen at different times after 5 min of anesthesia with ether. Ether produced a 40-fold enhancement in acetaminophen hepatotoxicity as determined by the increase of plasma GPT (= ALT, alanine amino transferase) concentrations. These results showed that glucuronidation was inhibited by ether anesthesia.
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (105)
- Type** : other: Toxicokinetics/Metabolism
- Remark** : Method: Ether was administered over 5 min to groups of 6 male CD-1 mice housed in an inhalation chamber till loss of righting reflex. Acetaminophen (= Paracetamol; 300 mg/kg) was injected i.p. at 2, 6, or 10 h after ether anesthesia. Hepatocellular damage was assessed by determining concentration of plasma GPT (= ALT, alanine amino transferase). Animals were sacrificed and livers prepared.
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- Result: Brief ether anesthesia resulted in 1) an increase of covalent binding of acetaminophen to hepatocellular protein, 2) a delayed decrease of hepatic activity of glucuronyl transferase, 3) a delayed decrease of hepatic activity of GSH (glutathione) sulfotransferase, 4) an initially reduced hepatic content but an unchanged activity of cytochrome P-450, 5) a delayed reduction of hepatic GSH contents, 6) an increase of plasma GPT indicating liver damage. This biochemical mechanism of this potentiation of hepatotoxicity was supposed to be due to delayed, complex effects of ether upon multiple enzymatic pathways of acetaminophen elimination and detoxification.
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (92)
- Type** : other: Toxicokinetics/Metabolism
- Remark** : Method: Ether was administered over 5 min to male CD-1 mice housed in an inhalation chamber till loss of righting reflex. Acetaminophen (APAP = Paracetamol; 300 mg/kg) was injected i.p. at various times after ether anesthesia. Hepatocellular damage was assessed by determining concentration of plasma GPT (= ALT, alanine amino transferase). Animals were sacrificed and livers prepared. The in vitro activities of enzymes responsible for 1) elimination (= glucuronyl transferase), 2) detoxification (= glutathione sulfotransferase) and 3) bioactivation / toxification (= cytochromes P-450) of APAP were estimated. The in vivo elimination of APAP and its metabolites was determined in plasma and urine. The covalent binding of APAP to hepatocellular protein in vivo was determined.
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- Result: Ether could initially inhibit both the elimination pathway and the toxifying pathway. It was shown that the toxifying pathway recovers first and causes by this way enhanced hepatotoxicity.

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- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (106)
- Type** : other: Toxicokinetics/Metabolism
- Remark** : The effects of two anesthetic procedures 1) continuous administration of ether throughout the periods of drug infusion (antipyrine and paracetamol) and blood sampling and 2) brief ether administration before drug infusion were examined. Ether was administered to rats till loss of righting reflex for 5 min or several hours. Continuous ether caused substantial reductions in the elimination rates of antipyrine and paracetamol. Brief ether anesthesia had no effect on antipyrine kinetics, but caused a decrease in total clearance of paracetamol. The rates of distribution and redistribution were unchanged by ether. This suggested that ether interfered with the hepatic conjugation of paracetamol and might interfere with the hepatic oxidation of antipyrine.
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (59)
- Type** : other: Toxicokinetics/Metabolism
- Remark** : The response of two different pathways of paracetamol metabolism to diethyl ether was examined. The elimination of paracetamol and the formation of paracetamol sulphate and glucuronide were measured in suspensions of isolated rat hepatocytes from fasted and fed animals over 1 h in the absence and presence of diethyl ether (30 mmol/l). Approximately 90 % of the paracetamol elimination was by sulphation and nearly 10 % by glucuronidation both in the controls and in the presence of ether. The overall disposition of paracetamol and the formation of sulphate were both reduced by about 50 % in the presence of ether compared to the controls while the formation of glucuronide was reduced by 70 %. The results were not influenced by the nutritional state of the animals before sacrifice. It is concluded that the inhibitory effect of ether on total paracetamol metabolism was mainly caused by reduced sulphation. Since microsomal glucuronidation was also inhibited by ether, both cytosolic and microsomal enzyme systems were sensitive to ether.
- Source** : Sodes Paris  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
15.12.1993 (6)
- Type** : other: Toxicokinetics/Metabolism
- Remark** : The effect of diethyl ether on rat-liver microsomal glucuronyltransferase activity was examined in vitro. Diethyl ether depressed this reaction in a dose-related, noncompetitive manner. Glucuronyltransferase activity was studied by measuring the rate of glucuronide conjugation of p-nitrophenol in the presence of various concentrations of ether in atmosphere (15, 20, 30 mM). Inhibition occurred when UDPGA (uridine diphosphoglucuronic acid) was used as a glucuronic acid donor and to a higher extent when the UDPGA-generating system (UDPG + NAD) was employed.
- Source** : Sodes Paris

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15.12.1993	EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	(13)
<b>Type</b>	: other: Toxicokinetics/Metabolism	
<b>Remark</b>	: In vitro experiments with rat liver microsomes (p-nitroanisol-demethylation) and in vivo experiments with rats (tritium release from 3H-mestranol due to demethylation) suggested an inhibition of the metabolism of certain drugs by competition for the binding site of cytochrome P-450 under anesthesia with diethyl ether.	
<b>Source</b>	: Sodes Paris EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
15.12.1993		(48)
<b>Type</b>	: other: Toxicokinetics/Metabolism	
<b>Remark</b>	: The effect of ether stress on mixed function oxidase activity in vivo was studied using the aminopyrine-14CO <sub>2</sub> exhalations rate method. Ether was administered to rats by inhalation for 6 h. Animals were transferred to a metabolism cage where a constant subanesthetic concentration of ether was maintained. Ether exposure did not produce any consistent effect on drug metabolizing status of the rat.	
<b>Source</b>	: Sodes Paris EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
15.12.1993		(68)
<b>Type</b>	: other: Toxicokinetics/Metabolism	
<b>Remark</b>	: The in vitro effect of diethyl ether on the Michaelis constant (Km) and maximal velocity (Vmax) of microsomal aniline hydroxylase and aminopyrine demethylase was determined. The microsomes were obtained from rats pretreated with phenobarbital or 3-methylcholanthrene as well as from untreated rats. Diethyl ether inhibited aniline hydroxylase lowering the Vmax and aminopyrine demethylase by increasing Km.	
<b>Source</b>	: Sodes Paris EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
15.12.1993		(65)
<b>Type</b>	: other: Toxicokinetics/Metabolism	
<b>Remark</b>	: The effect of ether as a possible antagonist of mediator-effected bronchoconstriction was tested in eight anesthetized, paralyzed and mechanically ventilated baboons. Ether administration was performed intravenously, a 13 minutes infusion to give approximately 1:3 MAC (minimum alveolar anesthetic concentration, baboons were assumed to have the same MAC as human patients). Ether had no effect on bronchoconstriction caused by acetylcholine, histamine, or phenylephrine administered by the same route.	
<b>Source</b>	: Sodes Paris EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
14.11.2003		(71)

**6.1 ANALYTICAL METHODS**

**6.2 DETECTION AND IDENTIFICATION**

## 7. Eff. Against Target Org. and Intended Uses

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7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

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**8.1 METHODS HANDLING AND STORING**

**8.2 FIRE GUIDANCE**

**8.3 EMERGENCY MEASURES**

**8.4 POSSIB. OF RENDERING SUBST. HARMLESS**

**8.5 WASTE MANAGEMENT**

**8.6 SIDE-EFFECTS DETECTION**

**8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER**

**8.8 REACTIVITY TOWARDS CONTAINER MATERIAL**

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# 10. Summary and Evaluation

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10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT