FOREWORD INTRODUCTION

DI-ISO-BUTYLKETONE

CAS No.: 108-83-8

SIDS Initial Assessment Report for 8th SIAM

(Paris, 28-30 June 1998)

Chemical Name: Di-iso-butyl ketone

CAS No.: 108-83-8

Sponsor Country: France

National SIDS Contact Point in Sponsor Country:

Mme Laurence Musset

HISTORY:

no testing	( )
testing	(X)

Acute toxicity (oral, dermal & inhalation), Sensitization, Dermal irritation, Reprotoxicity

COMMENTS:

Deadline for circulation: 31st of July 1998

Date of circulation: 31st of July 1998

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	108-83-8
Chemical Name	Diisobutylketone
Structural Formula	$(CH_3)_2$-CH-CH_2-CO-CH_2-CH-$(CH_3)_2$

CONCLUSIONS AND RECOMMENDATIONS

Environment

Based on structure activity relationship the chemical is not expected to exhibit ecotoxicity of concern. The derived PEC/PNEC ratio is less than 1. Based on the known use pattern and estimated exposure the chemical is currently considered of low potential risk and low priority for further work.

Human Health

The chemical is a respiratory irritant but otherwise considered as having low toxicity. Exposure is considered to be low in the Sponsor country. Therefore, it is currently considered of low potential risk and low priority for further work.

SHORT SUMMARY WHICH SUPPORTS THE REASONS FOR THE CONCLUSIONS AND RECOMMENDATIONS

The EU consumption volume of diisobutylketone (DIBK) is ca.5500-6500 t/a. It is mostly used as an solvent in leather finishing products and in paints and lacquerers.

DIBK is "readily biodegradable" and has a low potential for accumulation (logPow = 2.56). Aquatic PECs of up to 16.2 µg/l were estimated for the different uses. Only short-term test results are available with aquatic species from three trophic levels and the PNEC for the aquatic compartment is estimated to be 23 µg/l.

For the environment, based on the known properties and exposure pattern, it can be concluded that there presently is no risk for the environment.

The consumer exposure is considered to be low as only very few of the DIBK-containing products are accessible to the consumer. Mean occupational exposure during formulation and use of DIBK-containing products is estimated to be about 16-39 mg/m^3

DIBK is not corrosive or sensitizing. Respiratory irritation was observed in humans at concentrations above 50 ppm. The NOAEL for repeated dose following inhalation exposure is in the region of 534 ppm. For reproductive toxicity, no increased risks to offspring were observed in the absence of parental effects. The NOAEL for parental toxicity was determined as 300 mg/kg bw/d and for reproductive effects 1000 mg/kg bw/d. Bacterial mutagenicity tests are negative, as well as a *Saccharomyces cerevisiae* mitotic gene conversion assay. DIBK does not induce chromosome aberrations in rat liver cells *in vitro*.

Satisfactory margins of safety could be derived for the exposure of workers and therefore it can be concluded that there is currently no need for further information and/or testing of for risk reduction measures beyond those which are being applied.

NATURE OF FURTHER WORK RECOMMENDED

None.

FULL SIDS SUMMARY:

CAS no: 108-83-8		Species	Protocol	Results
Physical-chemical				
2.1	Melting- point		NA	-41/-46°C
2.2	Boiling-point		NA	163 - 175°C
2.3	Density		NA	0.806 - 0.812 g/cm^3
2.4	Vapour pressure		NA	100 - 220 Pa at 20 °C
2.5	Part.coef. (Log Pow)		NA	2.56
2.6 A	Water solubility		NA	430 mg/l at 20°C
B	pH			-
	pKa			-
2.12	Oxidoreduct. potential			-
Environmental fate/biodegradation				
3.1.1	Photodegradation			-
3.1.2	Stability in water		NA	no hydrolysis to be expected
3.2	Monitoring data			surface water: /l sediment: / biota: /
3.3	Transport / distribut.			
3.5	Biodegradation		APHA	readily biodegradable
Cas no :108-83-8		Species	Protocol	Results
Ecotoxicology				
4.1	Acute/prolonged toxicity to fish	Oncorhynchus mykiss	OECD 203	LC50 (96h) = 140 mg/l
4.2	Acute toxicity to aquatic invertebrates: daphnia	Daphnia magna	OECD 202	EC50 (48h) = 250 mg/l
4.3	Toxicity to aquatic plants e.g. algae	Selenastrum capricornutum	OECD 201	EC50 (96h) = 87 mg/l
4.5.1	Chronic toxicity to fish			
4.5.2	Chronic toxicity to aquatic invertebrates (daphnia)			
4.6.1	Toxicity to soil			

4.6.2	dwelling organisms Toxicity to terrestrial plants			
	Toxicology			
5.1.1	Acute oral toxicity	Rat	OECD	LD50 > 2000 mg/kg
5.1.2	Acute inhalation toxicity	Rat	OECD	LD50 (4h) > 5.0 mg/l
5.1.3	Acute dermal toxicity	Rat	OECD	LD50 > 2000 mg/kg
5.4	Repeated dose toxicity	Rat	OECD	Inh, 6w : NOAEL = 534 ppm
5.5	Genetic toxicity in vitro			
A	Bacterial test (gene mutation)	S. typhimurium E. coli		Negative +/- S9 mix Negative +/- S9 mix
B	Non bacterial in vitro test	Chromosome aberration		Negative
5.6	Genetic toxicity in vivo			
5.8	Toxicity to reproduction	Rat	OECD 421	NOAEL parental toxicity: 300 mg/kg/d NOAEL devel/repro: 1000 mg/kg/d
5.11	Experience with human exposure			

SIDS INITIAL ASSESSMENT REPORT

1. GENERAL SUBSTANCE INFORMATION

Identity

Chemical name:	2,6-dimethylheptan-4-one
CAS-Nr.:	108-83-8
EINECS Nr.:	203-620-1
Synonyms	Diisobutylketone DIBK
Empirical Formula:	$C_9H_{18}O$
Structural Formula:	$(CH_3)_2$-CH-CH_2-CO-CH_2-CH-$(CH_3)_2$
Purity:	65 - 94 %
Impurities	4,6-dimethylheptan-2-one 6 - 35 %

Note: Diisobutylketone is commercialized as a mixture of the two above isomers. The composition of the commercialized product varies with the producer.

Physico-chemical properties

Diisobutylketone is a stable, colourless liquid (melting point -41/-46 °C; boiling point 163-175 °C). Its water solubility was measured at 430 mg/l (an estimated value of 500 mg/l is also available and a value of 360 mg/l has been estimated for the analog di-n-butylketone). Its vapour pressure is approx. 100 - 220 Pa at 20°C. Its logPow is estimated at 2.56.
The main impurity 4,6-dimethylheptan-2-one will probably have similar physico-chemical properties. The same values for LogPow and Henry's law constant are estimated for both isomers.

2. GENERAL INFORMATION ON EXPOSURE

There are only 2 major producers/importers within the EU. The production/import volume in the EU is 5500 to 6500 t/a.
In Canada, 2 companies manufactured DIBK between 1984 and 1986 (personal communication, no recent data available). The total production for 1986 was between 1 000 and 10 000 tons. The total import quantites for 1986 was between 23 and 230 tons.

DIBK is used as a solvent in the leather processing industry during the coating of leather for shoes, furniture, cars etc. DIBK is also used as a solvent in formulations of paints, laquers and varnishes. Its use in the solvents for paints is relatively small at approximately 3500 t/a out of a total solvents use by the European paints sector of approximately $2x10^6$ t/a.

According to Baumann & Muth (1995), DIBK has a high solvent potential for cellulosenitrate, vinyl resins, waxes, natural and synthetic resins for leather lacquers and rubber lacquers.
In the Finnish product register, 9 paints, lacquers or leather finishing products containing DIBK are registered, with a DIBK-content of 1 - 50% (personal communication).

In the Swedish product register, 91 products were registered in 1997, containing a total of 7-9 tons. Seventy-nine of the products are registered as paints and varnishes. The content of DIBK in most of the products was < 10%

3. ENVIRONMENT

3.1 Exposure assessment

3.1.0 General discussion

Release into the environment

An environmental exposure assessment has to be performed for the following life-stages of DIBK:

- production
- formulation of paints & laquers
- industrial use of paints and laquers
- formulation of leather finishing products
- industrial use of leather finishing products

The exact quantitative distribution to the different uses is not known. The following worst case assumptions will therefore be used in this assessment:

quantity used in the EU: 6500 t/a
quantity used in leather finishing products: 3250 t/a
quantity used in paints, laquers and varnishes: 3250 t/a
content in the finished formulations: 10%

Degradation

Hydrolysis

No test result on hydrolysis is available. Based on the chemical structure of DIBK, it can be assumed that hydrolysis will not be an important fate process.

Biodegradation

Several test results on biodegradation are available, but only one with non-adapted inoculum, according to the APHA-method:

88 % degradation after 20 days (BOD/ThOD). The 10-day window criterion was fulfilled. Although this is not a standardized test on ready biodegradation, a high test substance / inoculum ratio was used (7 mg/l test substance / 10 ml/l filtered waste water). The test conditions can therefore be considered to be close to those in the standardized OECD tests on ready biodegradation.
With synthetic sea water, a negative result was nevertheless obtained. As the inoculum was not of marine origin though,the validity of the test result is questionable.

DIBK can be considered as **readily biodegradable** in the aquatic compartment (fresh water only).

Results from biodegradation simulation tests in WWTPs, in surface water and soil are not available and have to be estimated based on the above described screening test and the partition behaviour of DIBK (CEC, 1996):

compartment / medium	biodegradation rate
activated sludge (WWTP)	k_{WWTP} = 1 h^{-1}
surface water	k_{sw} = 0.047 d^{-1}
sediment	k_{sed} = 0.0023 d^{-1} *
soil	k_{soil} = 0.023 d^{-1} *

* Values taking into account the partitioning behaviour in these compartments (cf. below)

Photooxidation

In the atmosphere, DIBK will react with the photochemically produced hydroxyl radicals. Based upon atmospheric concentrations of 5. 10^5 ·OH/cm^3 the atmospheric half-life of DIBK has been estimated to be 14.2 - 22 hours.

Distribution and accumulation

The Henry's law constant of H = 27 - 45 Pa.m^3/mol at 25 °C suggests that DIBK is highly volatile from aqueous solutions.
No test on soil adsorption has been performed. The low logPow-value of 2.56 suggests that the compound is mobile in soil and that it has a low potential for accumulation in soil. Based on the recommended (Q)SAR equation for nonhydrophobics in the TGD (CEC, 1996), an organic carbon / water partition coefficient can be estimated:

LogKoc = 0.52 logPow + 1.02 = 2.35 => Koc = 225 l/kg

The estimated partition coefficients between the different compartments are presented in the following table:

Partition coefficients between different compartments

compartments	OC-content (%) of solid phase	solid-water partition coefficient	total compartment - water part. coefficient
soil-water	2	K_{p_soil} = 4.5 l/kg	K_{soil_water}= 6.95 m^3/m^3
sediment - water	5	K_{p_sed} = 11.3 l/kg	K_{sed_water} = 6.43 m^3/m^3
suspended matter - water	10	K_{p_susp}= 22.5 l/kg	K_{susp_water}= 6.53 m^3/m^3

There are no experimental results on bioaccumulation available. The measured logPow of 2.56 indicates a low potential for bioaccumulation.

Based on the physical chemical properties of DIBK, the atmosphere is the preferred target compartment.

Elimination in WWTPs

Based on the above cited physical chemical properties (log H = ca. 1.5; logPow = 2.56), as well as the biodegradation rate of 1 h^{-1} in STP, the elimination through biodegradation and distribution can be estimated with the model SIMPLETREAT:

% to air	10
% to water	10
% to sludge	2
% degraded	78
% removal	90

With the STP-model developed by the US-EPA, a removal rate of 93% was estimated, with biodegradation (91%) being the major removal mechanism.

3.1.1 Aquatic compartment (incl. sediment)

Production

In the Technical Guidance Document for New Chemicals (CEC, 1996), a generic (i.e. non site-specific) exposure scenario ("use category document",UCD) for the release into surface water of chemical substances during production is proposed. This scenario reflects a realistic worst case situation:

Production volume: 5 000 t/a (highest volume at one single site)
Release fraction during processing: 0.3% (default)
Yearly duration of operation: 300 days (default)
Removal in STP: 90% (SIMPLETREAT, see above)
Flow of receiving river: 60 m^3/s (default)

With these "worst case" default parameters, a daily release of **5 kg/d** and a **PEC_{local} of 1 µg/l** in surface water can be calculated.
The corresponding transfers in the STP to air and sludge would amount to 5 and 1 kg/d respectively.

Formulation of paints & lacquers

According to CEC (1996), the percentage of lost material to waste water during formulation of paints and varnishes is roughly 0.3%. Based on a worst case assumption, a content of DIBK in finished formulations of 10% (corresponding to a volume of coating material of 32500 t/a) will be used in the assessment.

The following scenario can be used (see also EUSES output in annex 1);

Volume of DIBK used on a regional level: 325 t/a (10% of total)
Release during formulation: 0.3% (default)
Fraction of main source: 1
Yearly duration of operation: 300 days
Removal in STP: 90%
Waste water flow in STP: 2000 m^3/d
Dilution factor: 10

With these "worst case" default parameters, a daily release of **0.325 kg/d** and a **PEC_{local} of 16.25 µg/l** in surface water can be calculated.
The corresponding transfers in the STP to air and sludge would amount to 0.325 and 0.065 kg/d respectively.

Use of paints and laquers

According to CEC (1996), the percentage of lost volatile material to waste water during localized industrial use of paints and varnishes is roughly 1%. Based on a worst case assumption, a content of DIBK in finished formulations of 10% (corresponding to a volume of coating material of 32500 t/a) will be used in the assessment.

The following scenario can be used (see also EUSES-output in annex 1);

Volume of DIBK used on a regional level: 325 t/a
Release during use: 1% (release category document)
Fraction of main source: 0.15
Yearly duration of operation: 300 days
Removal in STP: 90%
Waste water flow in STP: 2000 m^3/d
Dilution factor: 10

With these "worst case" default parameters, a daily release of **0.16 kg/d** and a **PEC_{local} of 8.12 µg/l** in surface water can be calculated.
The corresponding transfers in the STP to air and sludge would amount to 0.16 and 0.03 kg/d respectively.

Formulation of leather finishing products

The same scenario as for paints and varnishes can be used;

Volume of DIBK used on a regional level: 325 t/a (10% of total)
Release during formulation: 0.3% (default)
Fraction of main source: 1
Yearly duration of operation: 300 days
Removal in STP: 90%
Waste water flow in STP: 2000 m^3/d
Dilution factor: 10

With these "worst case" default parameters, a daily release of **0.325 kg/d** and a **PEC_{local} of 16.25 µg/l** in surface water can be calculated.
The corresponding transfers in the STP to air and sludge would amount to 0.325 and 0.065 kg/d respectively.

Use of leather finishing products

According to CEC (1996), the percentage of lost volatile material to waste water during localized industrial use of chemicals in the leather industry is roughly 99%. This could of course only apply for a solvent for dye stuff applied in baths, which is not the case here. The application mode is probably comparable to that of paints in other industrial branches and a release factor of 1% as for other paints is probably more realistic.

Furthermore, the releases reported for solvent-type chemicals from leather industry in the Toxic Release Inventory in the USA (US-EPA, 1996) can be used for further improvement

of the release estimation. Although DIBK is not subject to reporting to the TRI, the results for methyl ethyl ketone and methyl isobutyl ketone can be used instead. The highest release to a POTW reported for these two substances from a leather finishing facility is 940 lbs/a = 423 kg/y. Higher releases have only been reported for n-butyl alcohol (2600 lbs/a), phenol (1584 lbs/a) and glycol ethers (up to 81000 lbs/a).

Direct water releases are all reported to be negligible, except for glycol ethers (up to 250 lbs/a).

The highest single site release to a POTW for other ketone-based solvents is 940 lbs/a = 423 kg/a. This amount can be used in the following scenario:

Quantity of DIBK released to a POTW: 423 kg/a
Yearly duration of operation: 300 days
Removal in STP: 90%
Waste water flow in STP: 2000 m^3/d
Dilution factor: 10

With these "worst case" default parameters, a daily release of **0.14 kg/d** and a **PEC_{local} of 7 µg/l** in surface water can be calculated.
The corresponding transfers in the STP to air and sludge would amount to 0.14 and 0.03 kg/d respectively.

Monitoring data

There is no data on actual measurements of DIBK in surface waters available.

Sediment

DIBK has a low tendency to partition to the sediment. Furthermore, as no experimental results with benthic organisms are available, there is no need for performing a risk assessment for this compartment.

3.1.2 Atmosphere

In parallel to the estimations for surface water concentrations, the local air concentrations and wet and dry depositions onto soil can be estimated for the different life-stages of DIBK.

NOTE: the contribution of the amount stripped in the STP is taken into account. The highest amount between the release from the processing site and the STP is used to derive the local air concentration while the sum of both is used to derive the deposition onto agricultural soil. Only annual averages are derived.

Production

The highest single-plant production capacity for DIBK is 5000 t/a. The following exposure scenario, as proposed in CEC (1996), can be used for the PEC-estimation:

Production volume: 5000 t/a
Release fraction to air: 1 % (default)
= >Daily release rate: 167 kg/d

(Release from STP: 5 kg/d)

As proposed in CEC (1996), the model OPS can be used to estimate the air concentration at a distance of 100 m from the source. For a source strength of 1 kg/d, a concentration of 0.278 µg/m^3 was derived, so that with the above estimated release rate of 167 kg/d: **PEC_{local_air} = 46.3 µg/m^3**.

The average deposition over a radius of 1 km around the source can also be estimated. The deposition flux is dependent on the fraction of the chemical that is associated with the aerosols:

$$DEP_{total} = Emission \cdot [FR_{aerosol} \cdot Dstd_{aer} + (1 - FR_{aerosol}) \cdot Dstd_{gas}]$$

with:

DEP_{total} = total deposition flux [$kg.m^{-2}.d^{-1}$]

$FR_{aerosol}$ = fraction of the chemical bound to aerosol [-]

$Dstd_{aer}$ = standard deposition flux of aerosol bound compounds at source strength of 1 kg/d (= $1 \cdot 10^{-8}$ $kg.m^{-2}.d^{-1}$)

$Dstd_{gas}$ = standard deposition flux of gaseous compounds at a source strength of 1 kg/d as a function of the Henry's law constant:

$^{10}\log H < -2$	$5 \cdot 10^{-10}$ [$kg.m^{-2}.d^{-1}$]
$-2 < {}^{10}\log H < 2$	$4 \cdot 10^{-10}$ [$kg.m^{-2}.d^{-1}$]
$^{10}\log H > 2$	$3 \cdot 10^{-10}$ [$kg.m^{-2}.d^{-1}$]

The fraction of the chemical associated with aerosol particles can be estimated on the basis of the chemical's vapour pressure, according to Junge (described in CEC, 1996):

$$FR_{aerosol} = \frac{CON_{junge} \cdot SURF_{aer}}{VP + CON_{junge} \cdot SURF_{aer}}$$

with:

CON_{junge} constant of Junge-equation [Pa.m]

$SURF_{aer}$ surface area of aerosol particles [$m^2.m^{-3}$]

VP vapour pressure [Pa] (here 220 Pa)

As a default, the product of CON_{junge} and $SURF_{aer}$ is set to 10^{-4} Pa.

=> **$DEP_{total} = 6.9 \cdot 10^{-8}$ $kg.m^{-2}.d^{-1}$**

Formulation of paints & lacquers

According to CEC (1996), the percentage of lost material to air during formulation of paints and varnishes is roughly 1%. Based on a worst case assumption, a content of DIBK in finished formulations of 10% (corresponding to a volume of coating material of 32500 t/a) will be used in the assessment.

The following scenario can be used (see also EUSES output in annex 1);

Volume of DIBK used on a regional level: 325 t/a (10% of total)
Release during formulation: 1% (default)
Fraction of main source: 1
Number of days: 300
= >Daily release rate: 10.8 kg/d

(Release from STP: 0.325 kg/d)

=> **$PEC_{local\_air} = 3\ \mu g/m^3$**.

=> **$DEP_{total} = 4.5 \cdot 10^{-9}\ kg.m^{-2}.d^{-1}$**

Use of paints and laquers

According to CEC (1996), the percentage of lost volatile material to air during localized industrial use of paints and varnishes is roughly 80%. Based on a worst case assumption, a content of DIBK in finished formulations of 10% (corresponding to a volume of coating material of 32500 t/a) will be used in the assessment.

The following scenario can be used;

Volume of DIBK used on a regional level: 325 t/a (10% of total)
Release during use: 80% (default)
Fraction of main source: 0.15
Number of days: 300
= >Daily release rate: 130 kg/d

(Release from STP: 0.16 kg/d)

=> **$PEC_{local\_air} = 35\ \mu g/m^3$**.

=> **$DEP_{total} = 5.1 \cdot 10^{-8}\ kg.m^{-2}.d^{-1}$**

Formulation of leather finishing products

The same scenario as for paints can be used (see also EUSES output in annex 1);

Volume of DIBK used on a regional level: 325 t/a (10% of total)
Release during formulation: 1% (default)
Fraction of main source: 1
Number of days: 300
= >Daily release rate: 10.8 kg/d

(Release from STP: 0.325 kg/d)

=> **$PEC_{local\_air} = 3\ \mu g/m^3$**.

=> **$DEP_{total} = 4.5 \cdot 10^{-9}\ kg.m^{-2}.d^{-1}$**

Use of leather finishing products

The releases of DIBK to air during the use of leather finishing products should be comparable to those during the use of paints. The releases reported for solvent-type chemicals from the leather industry in the Toxic Release Inventory in the USA (US-EPA, 1996) can be used for further improvement of the release estimation. Although DIBK is not subject to reporting to the TRI, the results for methyl ethyl ketone and methyl isobutyl ketone can be used instead. The highest release to air (addition of point and non-point releases) reported for these two substances from a leather finishing facility is 112211 lbs/a = 50495 kg/y = 138 kg/d. Higher releases have not been reported for other solvent-type compounds. This amount can be used for the PEC-estimations:

=> **$PEC_{local\_air} = 38\ \mu g/m^3$**.

=> **$DEP_{total} = 5.5 \cdot 10^{-8}\ kg.m^{-2}.d^{-1}$**

3.1.3 Terrestrial compartment

Direct releases to soil are not to expected. Indirect releases occur through atmospheric deposition and sewage sludge application. The details of the estimation are listed in the EUSES output in annex 1:

Formulation of paints, laquers and leather finishing products

concentration in dry sewage sludge: Csludge = 83.7 mg/kg
deposition rate: $DEP_{total} = 4.5 \cdot 10^{-9}\ kg.m^{-2}.d^{-1}$

=> PEClocal_soil = 81 µg/kg (wet soil)
=> PEClocal_soil = 19.8 µg/l (soil pore water)

Use of paints

concentration in dry sewage sludge: Csludge = 41.3 mg/kg
deposition rate: $DEP_{total} = 5.1 \cdot 10^{-8}\ kg.m^{-2}.d^{-1}$

=> PEClocal_soil = 44 µg/kg (wet soil)
=> PEClocal_soil = 10.8 µg/l (soil pore water)

Use of leather finishing products

concentration in dry sewage sludge: Csludge = 36.3 mg/kg
deposition rate: $DEP_{total} = 5.5 \cdot 10^{-8}\ kg.m^{-2}.d^{-1}$

=> PEClocal_soil = 39.7 µg/kg (wet soil)
=> PEClocal_soil = 9.7 µg/l (soil pore water)

3.1.4 Non compartment specific exposure relevant to the food chain (secondary poisoning)

As DIBK has a low potential for bioaccumulation (logPow = 2.56), a risk characterisation for secondary poisoning is not necessary.

3.1.5 Regional concentrations

As DIBK is readily biodegradable and has a low half-life in the atmosphere (14.2 hours), the regional concentrations are probably negligible compared to the local concentrations.

3.2 Effects assessment: Hazard identification and Dose (concentration) - response (effect) assessment

3.2.1 Aquatic compartment (incl. sediment)

Available effect data

In the following, the results from acute toxicity tests with aquatic organisms are presented:

vertebrates:

Onchorynchus mykiss	96h-LC50	140 mg/l
(semi-static; nominal concentration; open system)		

invertebrates:

Daphnia magna	48h-EC50	250 mg/l
(effect: immobilization; static, open system, nominal concentration)		
Artemia salina	24h-LC50	65 mg/l
(effect: immobilization; static, nominal concentration)		

plants:

Selenastrum capricornutum	96h-EbC50	87 mg/l
(nominal concentrations; open system)	96h-EμC50	230 mg/l
	96h-EbC10	15 mg/l
	96h-EμC10	55 mg/l

Determination of $PNEC_{aqua}$

Due to the high volatility of DIBK, there is some doubt on the validity of the test results. The toxicity of DIBK might be underestimated. A verification by (Q)SARs might clarify the situation.

Ketones, unless they are α,β-unsaturated ketones, can be considered as narcosis or baseline toxicity compounds (CEC, 1995). Based on the (Q)SARs proposed in the EU-Technical Guidance

Document (CEC, 1996) for baseline-toxicity compounds, the aquatic toxicity of DIBK can be estimated as follows:

Pimephales promelas	96h-LC50 = 39 mg/l 32d-NOEC = 3.5 mg/l
Daphnia magna	48h-EC50 = 25 mg/l 16d-NOEC = 4.1 mg/l
Selenastrum capricornutum	72h-EC50 = 23 mg/l

Further estimates were proposed by the US-EPA:

Fish	96h-LC50 = 29 mg/l chronic value: 4.1 mg/l
daphnid	48h-EC50 = 32 mg/l chronic value: 2.1 mg/l
algae	96h-EC50 = 21 mg/l chronic value: 2.9 mg/l

The different estimations are in good agreement with each other.

A comparison can be made with methyl isobutyl ketone (MIBK: CAS-Nr: 108-10-1; cf respective SIDS for MIBK). In the following table, the most relevant validated experimental test results are compared with the (Q)SAR-values (logPow = 1.31):

MIBK (logPOW = 1.31)		
Species	**experimental results**	**(Q)SAR value**
Pimephales promelas	96h-LC50 = 505 mg/l 32d-NOEC = 57 mg/l	96h-LC50 = 307 mg/l 32d-NOEC = 28 mg/l
Daphnia magna	48h-EC50 = 170 mg/l 21d-NOEC = 7.8 - 39 mg/l	48h-EC50 = 267 16d-NOEC = 58 mg/l
Selenastrum capricornutum	96h-EC50 = 400 mg/l	96h-EC50 = 282 mg/l

Except for the long-term daphnia-test, all the (Q)SAR results are less than a factor of 2 different from the experimental test results. A high degree of confidence can therefore be attributed to the (Q)SAR-values.

The experimental results actually appear to underestimate the inherent toxicity of DIBK, especially for daphnids. The result on *Artemia salina* is more in line with the expected toxicity. For the PNEC derivation, it is therefore more appropriate to use the (Q)SAR values.

As DIBK is a narcosis or baseline toxicity compound, one could argue that an assessment factor of 100 would be sufficient to estimate a PNEC. But in order to account for the additionnal uncertainty due to the use of the (Q)SAR-value, especially the possible long-term effects on daphnids, an assessment factor of 1000 appears to be most appropriate. The estimated EC50 for Selenastrum capricornutum can be used for the PNEC derivation:

$$\mathbf{PNEC_{aqua} = 23\ 000 / 1000 = 23\ \mu g/l.}$$

Sediment

No experimental results with benthic organisms are available. As DIBK has a low tendency to partition to the sediment, there is no need for performing a risk assessment for this compartment.

3.2.2 Terrestrial compartment

No test results with terrestrial organisms are available. Therefore, for an indicative risk assessment for the soil compartment, the aquatic PNEC will be used and compared to the concentration in soil pore water:

$PNEC_{soil\_pore\ water}$ = 23 µg/l (soil pore water)

3.2.3 Atmosphere

No data are available.

3.2.4 Non compartment specific exposure relevant to the food chain (secondary poisoning)

As DIBK has a low potential for bioaccumulation (logPow = 2.56), a risk characterisation for secondary poisoning is not necessary.

3.3 Risk characterisation

3.3.1 Aquatic compartment (incl. sediment)

In the following table, the PEC/PNEC-ratios are summarised:

Use	PEC [µg/l]	PEC/PNEC
Production	1	0.043
Formulation of paints and lacquers	16.25	0.7
Industrial use of paints and laquers	8.12	0.35
Formulation of leather finishing products	16.25	0.7
Industrial use of leather finishing products	7	0.3

As all PEC/PNEC ratios are below 1, the substance does not present a risk to the aquatic environment.

Sediment

No risk assessment can be performed for the sediment. But, as DIBK has a low tendency to partition to the sediment, the risk characterisation for the aquatic compartment probably covers the possible risks for the sediment.

3.3.2 Terrestrial compartment

In the following table, the PEC/PNEC-ratios are summarised:

Use	PEC [µg/l]	PEC/PNEC
Formulation of paints and lacquers	19.8	0.86
Industrial use of paints and laquers	10.8	0.47

Formulation of leather finishing products	19.8	0.86
Industrial use of leather finishing products	9.7	0.42

As all PEC/PNEC ratios are below 1, the substance does not present a risk to the terrestrial environment.

4. HUMAN HEALTH

4.1. HUMAN HEALTH (TOXICITY)

4.1.1 Exposure assessment

4.1.1.0.General discussion

The following table describes the exposure potential to DIBK

DIBK Manufacturing	The DIBK manufacturing processes operate in closed systems. The systems are only breached to take small samples to check product quality. The potential for human exposure is very low.
Formulating product containing DIBK. Leather and paint industry	The procedures for formulating products containing DIBK are automated and mostly enclosed. Exposure is expected to be low.
Handling product containing DIBK. Leather and paint products.	Products containing DIBK are formulated for industrial and professional use. Typical concentration of DIBK in finished product is approximately 10%. Application may be manual or automated. Exposure to DIBK is possible, but likely to be controlled by using engineering controls or personal protective equipment.

4.1.1.1 Occupational exposure

There is very little data on DIBK exposure available. For the risk characterisation a selection of the data on MIBK, MEK and DEGBE was used. MEK and MIBK were selected because they are comparable to DIBK in effects and use. DEGBE was included, because a detailed EC risk assessment is almost completed on this chemical and many of the assumption in the report (DEGBE, 1998) can be applied generally.
The exposure data considered is presented in Annex 2 and 3. The data selected for use in the risk characterisation is presented in table 4.1.1.1.A.

Table 4.1.1.1.A: Exposure inhalation data selected for risk characterization (highlighted in annex 2):

Process	Exposure		
	Minimum	Worst case	Mean
Manufacturing	18 mg/m^3	59 mg/m^3	
Pure product handling	3 mg/m^3	18.9 mg/m^3 (3.2 ppm)	
Formulating products containing DIBK	16 mg/m^3	190 mg/m^3	39 mg/m^3
Use of product containing DIBK coating paint	1 mg/m^3	23 mg/m^3	
Use of product containing DIBK coating leather	1 mg/m^3	31 mg/m^3 *	16 mg/m^3
Use/Formulate product containing DIBK	3 mg/m^3	18 mg/m^3	

* Range and mean of 37 measurements.

4.1.1.2. Consumer exposure

Consumer exposure is probably negligible. Among the 9 products registered in the Finnish product register, all are for professional use only. Among the 91 products registered in the Swedish product register, 79 are paint and varnish products and of those only 1 is accessible to consumers. Moreover, the total marketed DIBK-volume in these 79 products is less than 2 t/a in Sweden. It can therefore concluded that the total volume marketed in the consumer product is very low and that the overall exposure to consumers is also very low.

4.1.1.3.Indirect exposure via the environment

DIBK releases to ambient air and water are expected to be very low, consequently human exposure resulting from these sources is very low.

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

4.1.2.1.Toxico-kinetics, metabolism and distribution

There is no specific data on the metabolism of diisobutyl ketone (DIBK) however it is expected to undergo the metabolic change typical of many ketones, that is reduction to the corresponding secondary alcohol and elimination as a glucuronic acid conjugate (Browning 1965). Data available for the related ketone methyl isobutyl ketone (MIBK) indicate that it is metabolised to the corresponding secondary alcohol 4-methyl-2-pentanol and 4-hydroxy-4-methyl-2pentanone (major metabolite). The structure of MIBK and DIBK precludes metabolism to the neurotoxic metabolite 2,5-hexanedione formed from both hexane and methyl n-butyl ketone.

4.1.2.2.Acute toxicity

Acute toxicity studies are summarised in table 4.1.2.2A.

Various studies were carried out on the acute inhalational toxicity of DIBK to rats between 1941 and 1953 (Union Carbide, 1941 & 1948, McOmie & Anderson, 1949, Smyth et al, 1949, Carpenter et al, 1953). Despite some difference in degree of toxicity between tests is clear that rats survive at least a 4 hour exposure to the saturated vapours of DIBK (Smyth et al, 1949). Behavioural changes were observed in mice at about 300 ppm (De Ceaurriz et al, 1983).

From the available data it is concluded that DIBK is of low acute toxicity following oral, dermal and inhalational exposure. Signs of intoxication include irritation of the eyes and nose, salivation, lethargy, instability, respiratory difficulty, unsteady gait and narcosis. Following dermal administration slight skin irritation has been observed. Gross pathological examination of animals exposed orally or dermally to 2000 mg/kg or inhalationally to 5 mg/l DIBK (non-lethal doses) showed no treatment related findings (Shell,1995a,b&c). Exposure to near saturated vapours (7.5 to 16 hours) induced only minor histopathological changes in the lung, kidney, liver, spleen and adrenals (McOmie & Anderson, 1949). Autopsies following administration of oral doses revealed congested and haemorrhagic lungs, mottled liver, pale kidneys and some damage to the intestinal tract (Union Carbide, 1948).

Conclusion

Information presented from a range of studies in rats, mice and rabbits including studies conducted to OECD standards, show that DIBK is of a low order of acute oral, dermal and inhalational toxicity.

Table 4.1.2.2A Summary of acute toxicity data

Route	Species	Vehicle	LD50/LC50	Observations	Reference
Oral	Rat	20% in corn oil	>2000 mg/kg	No mortalities. Non-specific clinical signs (eg. piloerection, urinary incontinence) in females only from day 1-4. No treatment related gross pathological changes at post mortem.	Shell 1995a
	Rat	Undiluted	male 8.57 ml/kg female 6.50 ml/kg	Deaths occurred within 1-4 days. Signs of intoxication were lethargy, unsteady gait, slow respiration, lacrymation, discharge, piloerection and prostration. Necropsy showed red lungs in the mortalities and no effects in the survivors.	Union Carbide Corp. 1983
	Rat	20% dispersion in 1% Tergitol	5750 mg/kg	Deaths occurred within 3 days of dosing. Lethargy, prostration and narcosis were observed following administration of the dose. Post mortem examination revealed congested and haemorrhagic lungs, mottled livers, pale kidneys and some damage to the intestinal tract.	Union Carbide Corp. 1948 Smyth et al, 1949
	Mouse	Not reported	1416 mg/kg	No details available.	Patty 1994 (reporting unpublished data)
Dermal	Rat	Undiluted	>2000 mg/kg	No mortalities. Slight skin irritation from days 2-8. No other clinical signs of intoxication. No treatment related gross pathological changes at post mortem.	Shell 1995b
	Rabbit	Undiluted	male 3.36 ml/kg male (retest) 8.57 female 13.50 ml/kg	Most deaths occurred within 3 days. Signs of intoxication were lethargy and unsteady gait. Skin irritation was observed with initial erythema and later desquamation in all animals. Post mortem examination revealed red lungs in mortalities and a few intestinaes with fluid or paste-like material.	Union Carbide Corp. 1983
	Rabbit	Undiluted	>20 ml/kg	3/10 died no other details available.	Union Carbide Corp. 1948 Smyth et al, 1949
Inhalation	Rat	Vapour exposure	>5.0 mg/l (>850 ppm)	No mortalities. Clinical signs in both sexes associated with solvent exposure (salivation, decreased activity, shaking and reduced stability) were observed during and immediately after exposure. Non specific signs of systemic toxicity (piloerection, hunched appearance) were observed from days 1-5. No gross pathological changes at post mortem.	Shell 1995c
	Rat	Near saturated 6 hour exposure	>near saturated vapour conc.	No mortalities. Clinical signs were hypoactivity, ataxia, impaired reflexes and laboured breathing. All animals recovered within 1 day. No gross pathological changes attributable to exposure.	Union Carbide Corp. 1983
	Rat	Saturated vapours 4 hour exposure	> saturated vapour concentration	No mortalities	Smyth et al, 1949
	Guinea pig	Vapour exposure 8 hours	2500 ppm	2/4 died	Unon Carbide 1941
	Rabbit	Vapour exposure 8 hours	>2246 ppm	1/8 died	Union Carbide 1948
Intraperitoneal	Rat	Not reported	>1.6 g/kg	No data available	Patty 1994 (reporting unpublished data)

4.1.2.3.Irritation

Skin (see table 4.1.2.3A)

A study (Union Carbide, 1983) using a 4 hour occluded exposure to 0.5 ml undiluted DIBK gave 24+48+72 hour mean scores for 6 rabbits of 1.9 and 0.4 for erythema and oedema respectively. At 7 days slight erythema (mean 0.2) and some desquamation were observed both resolving during the time course of the study. The results of a more recent skin irritation study using a 4 hour semi-occluded application, conducted according to OECD guidelines show that DIBK is only slightly irritating to the skin (Shell 1996a). Group mean 24+48+72 hour erythema and oedema scores from three rabbits following a 4 hour semi-occluded exposure were 0.6 and 0.3 respectively. No individual rabbit attained mean 24+48+72 hour scores ≥2 for either erythema or
oedema. Superficial eschar, fissuring and/or desquamation were observed which had totally resolved within two weeks of exposure.

Table 4.1.2.3.A: Skin Irritation Scores

Parameter	Group Mean Scores						
	24 hours	**48 hours**	**72 hours**	**7/8 days**	**10 days**	**14/15 days**	**24+48+72 hours**
Study 1: 4 hour semi-occluded exposure OECD 404 (Shell 1996a) [Scores recorded at the above times after patch removal]							
Erythema	0.3	0.3	1.0	0.3	-	0	0.6
Oedema	0.3	0.3	0.3	0	-	0	0.3
Other	-	-	-	d,e,f	-	-	-
Study 2: 4 hour occluded exposure (Union Carbide 1983) [Scores recorded at the above times after dosing]							
Erythema	2	2	1.7	0.2	0	0	1.9
Oedema	0.5	0.5	0.3	0	0	0	0.4
Other	d	d	d	d	d	d	-

e = localised and superficial eschar (1/3 rabbits)
f = localised fissuring (1/3 rabbits)
d = desquamation (2/3 in Study 1, 6/6 in study 2, diminishing in study 2 at days 10 & 14.)

A similar difference in degree of skin irritancy following occluded and semi-occluded exposure was reported by Potokar 1985. DIBK was tested using a method based on OECD 1981 and classified according to criteria given by the EEC 1983. 6 rabbits were used and local reactions determined after 1 or 4 hour exposure to 0.5 ml of undiluted material using semi-occlusive and occlusive dressings. Actual oedema and erythema scores were not reported. The classification given was of non-irritant following both 1 and 4 hour exposures using a semi-occlusive dressing and irritant at both exposure times using the occlusive dressing.

Eye (see table 4.1.2.3B)

A study was carried out using essentially the procedure and scoring regime to that required by the OECD (Union Carbide 1983). Two groups of 6 rabbits were used with instillation volumes of 0.1(as for OECD) and 0.01 ml. Scores were given for discharge and corneal area affected in addition to conjunctival redness and chemosis and corneal opacity but these parameters were all reported separately allowing calculation of OECD-type mean scores. Group mean 24+48+72 hour scores were as follows: cornea and iris 0, conjunctival redness 0.3, chemosis 0.4 following instillation of 0.1 ml and 0 for all parameters following instillation of 0.01 ml undiluted DIBK into the conjunctival sac of six rabbits. This study demonstrates that DIBK is not irritating to the eye.

Table 4.1.2.3B: Eye Irritation Scores

Parameter	Group Mean Scores following instillation of 0.1 ml undiluted DIBK						
	1 hour	4 hours	24 hours	48 hours	72 hours	7 days	24+48+72 hours
Cornea	0	0	0	0	0	0	0
Iris	0	0	0	0	0	0	0
Conjunctiva							
redness	1	1	0.5	0.3	0.2	0	0.3
chemosis	1.7	1	0.5	0.5	0.2	0	0.4

Respiratory tract

At dose levels of 184-351 ppm DIBK caused a significant decrease in respiratory rate in mice following head only vapour exposure for 15 minutes suggesting some sensory irritation of the respiratory tract (De Ceaurriz et al, 1984).

Observations in man

Silverman et al 1946 exposed a group of 12 volunteers for 15 minutes to the vapours of DIBK. Several individuals reported some degree of eye irritation and an unpleasant odour at 50 ppm. 25 ppm was the concentration which most subjects considered satisfactory for an 8 hour exposure. Carpenter et al 1953 exposed 2 subjects for 3 hours to 50 ppm DIBK. Despite slight transitory eye irritation and the persistent smell and taste these subjects felt the concentration was acceptable. Three subjects exposed to 100 ppm for 3 hours reported eye, nose and throat irritation and felt this concentration to be unacceptable. In these three subjects there was no evidence of reduced performance in a simple co-ordination test (drawing circles and squares) conducted before, during and after the exposure to 100 ppm (Carpenter et al, 1953).
In these older studies, it will not have been possible to discriminate between the detection of odour and irritation. Recent studies using latest methodology to detect sensory irritation and descriminate irritation from odour have been carried out with acetone (Dalton et al, 1997) and MIBK (Dalton et al, 1998). These studies showed that exposure levels that caused irritation were significantly higher then the levels that are detected by volunteers, because of the ketone's odour.

Conclusions
DIBK applied as a liquid to the skin and eyes is slightly irritating with all effects resolving over the duration of the studies. Human volunteers in experiment using old technology experience respiratory and eye irritation to the vapours at exposure levels of approximately 50 ppm. Based experience gained studying acetone and MIBK in experiments using latest methodology, the no-effect level for sensory irritation of DIBK is considered to be at least 50 ppm.
DIBK is not a primary skin irritant, but it is expected to cause defatting on repeated skin contact.

4.1.2.4.Corrosivity

The substance is not corrosive to the skin, eyes or respiratory tract (see 4.1.2.3).

4.1.2.5.Sensitisation

DIBK when tested in the skin sensitisation assay of Magnusson & Kligman in accordance with OECD guidelines was not a skin sensitiser (Shell 1995d). There were no positive responses at challenge in either control or treated guinea pigs.

Conclusions
DIBK is not a skin sensitiser.

4.1.2.6.Repeated dose toxicity

Results of repeated dose inhalation toxicity studies are summarised in table 4.1.2.6A

10M and 10F rats/dose level were exposed to 0, 98, 300 or 905 ppm DIBK by inhalation for 6 hours/day, 5 days/week for 9 days (Dodd et al, 1987; Union Carbide Corp, 1985). There were reductions in body weight gain in males and females at 905 ppm. Increases in liver and kidney weights at the high and mid dose were dose related. Following a recovery period of 2 weeks post dosing (top dose animals only) liver and kidney weights were no longer elevated in females. In males the difference although reduced remained statistically significantly. A slight decrease in platelet levels at 905 ppm was not considered of biological significance in the absence of any other change in haematological parameters. The only histopathological changes observed were the kidney changes (dose related) seen in male rats at 300 and 905 ppm. The kidneys of the 905 ppm DIBK recovery group males had lesions similar in appearance to recovery group control males indicating that the severity of the nephrosis was reversible. The kidney changes (hyalin droplet nephrosis) are typical of male rat specific α-2μ-globulin mediated nephropathy which is seen with other aliphatic ketones such as methyl isobutyl ketone and methyl isoamyl ketone (Phillips et al, 1987; Katz et al, 1986). In this study particular attention was paid to the kidney histology (including the use of Mallory-Heidenhain stain). The relevance of this type of male rat specific nephropathy to man has been reviewed by the EPA 1991 who concluded that such findings were of no practical significance to man. In the absence of any other histopathological changes the slight increases in liver and kidney weight seen at 300 ppm are considered adaptive. Such changes in the absence of histopathological change have also been seen with MIBK at dose levels of 250 ppm and were considered adaptive in the SIDS Risk Assessment in support of a NOAEL of 1000 ppm. The NOAEL for this study is therefore 300 ppm based on reductions in body weight at 905 ppm.

Groups of 15M and 15F rats were exposed to 0, 125, 252, 534, 925 or 1654 ppm DIBK vapour, 7 hours/day, 5 days/week for 6 weeks. A sex difference in susceptibility to DIBK vapours was seen in this study. At 1650 ppm all females died during the first exposure while 12/15 males survived 30 exposures at this concentration. Clinical signs of intoxication were not reported for any other dose level. The tissues of rats which died during the first exposure showed severe liver, lung and kidney pathology. Among surviving males at 1654 ppm there was no major histopathological change in the adrenal, kidney, liver, lung or spleen. Minor pathological change in the form of cloudy swelling of the liver, lung congestion and in the kidneys cloudy swelling of the convoluted tubules was observed in some surviving top dose males. At 925 ppm an increased incidence of minor pathological change was reported in the publication (Carpenter et al, 1953) without further description of the type of change. These 'minor' changes were possibly cloudy swelling of the kidney convoluted tubules although this is not explicit from the reported data. Increased liver and kidney weights at lower dose levels are considered adaptive. Taking a conservative view that the reported 'minor' pathological changes were a significant finding, the NOAEL for this study is 534 ppm.

The only oral toxicity study available was reported in summary by Patty, 1994. Rats received up to 2000 mg/kg/day by gavage for 90 days. No neurotoxicity was reported but liver, adrenal (absolute and relative) and kidney (relative) weights were increased. Decreases were observed in absolute brain and heart weights. Histopathological changes included minor changes in the stomach, liver and kidneys. No further details are available.

Conclusion

The data submitted are acceptable with respect to the basic SIDS requirements. The NOAEL for rats following inhalational exposure is in excess of 534 ppm. The kidney changes (accumulation of hyalin droplets) seen in males at high dose levels (905 ppm) are considered to be indicative of male rat specific nephropathy and as such not of relevance to human risk assessment. Changes in liver and kidney weight in the absence of histopathological change are considered adaptive. The data support a NOAEL of 534 and LOAEL of 905 ppm.

Table 4.1.2.6.A: Summary of repeated dose inhalation toxicity studies with DIBK

Route/Species No./group	Exposure period	Dose levels Actual	NOAEL	LOAEL	Observations	Reference
Rat F344 10M+10F	**9 day**, 6 hours/day 5 days/week plus a recovery group at the top dose level observed for 2 weeks after cessation of exposure.	0, 98, 300 or 905 ppm	300 ppm	905 ppm	**905 ppm:** Eye irritation M+F Ataxia in females after the first exposure only. Body weight & food consumption reduced in females. Body weight gain reduced in males. Total serum protein increased M+F. **905 & 300 ppm:** Absolute & relative liver weights increased M+F. Absolute & relative kidney weights increased in males. Relative kidney weight increased in females. In males only total serum protein was increased as was urine volume and water intake while osmolality decreased. In males only microscopic examination revealed a reversible increase in the severity of hyaline droplet nephrosis in proximal tubules, typical of male rat specific nephropathy. Increased organ weights in the absence of histopathological change considered adaptive. **98 ppm:** No adverse effects in females, increase in urine volume and osmolality in males. **Reversibility:** Organ & body weights and histopathological changes showed reversal.	Dodd et al, 1987 Union Carbide, 1985
Rat/Sherman 15M+15F	**6 weeks** 7 hours/day, 5 days/week	0, 125, 252, 534, 925 & 1654 ppm	534 ppm	925 ppm	**1654 ppm:** Mortality in all females and 3/15 males. Surviving males showed reduced body weight gain and increased liver and kidney weights. No irreversible pathology in survivors only cloudy swelling of the liver in 5 & cloudy swelling of convoluted tubules of kidney in 3 rats. Lung congestion in 7 survivors. **925 ppm:** Liver and kidney wts increased M+F, slight pathological changes (possibly cloudy swelling of convoluted tubules M+F) in 5/15 males, 4/15 females (controls 2/15 M, 1/15 F) **534 ppm:** Liver and kidney weights increased M+F. considered adaptive. **252 ppm:** Liver and kidney weights increased in females only considered adaptive. **125 ppm:** No adverse effects.	Carpenter et al, 1953 Union Carbide, 1951
Guinea pig 10M/group	**6 weeks** 7 hours/day, 5 days/week	0, 125, 250 & ppm	125 ppm	250 ppm	The only statistically significant effect was reduced liver weight at 250 ppm.	Carpenter et al, 1953; Union Carbide 1951

4.1.2.7.Mutagenicity

The bacterial mutagenicity of DIBK has been assessed in Salmonella typhimurium (strains TA 98, 100, 1535, 1537 and 1538) and Escherichia coli (strain WP2 uvr A pkm) (Brooks et al, 1985 & 1988). At test concentrations ranging from 31.25 to 4000 µg/ml in the presence or absence of rat liver S9 there was no increase in the rate of reverse mutation. Cytotoxicity was observed in all strains at either 500 or 1000 µg/ml. Mortelmans et al, 1986 also reported negative results in S. typhimurium strains in the presence or absence of rat or hamster liver S9 at dose levels ranging from 1-333 µg/plate. Cytotoxicity was not observed in this study. Negative results were obtained in the Saccharomyces cerevisiae mitotic gene conversion assay. in the presence and absence of rat liver S9 at dose levels of 0.01-5.0 mg/ml. Cytotoxicity was observed at 0.5 mg/ml in the absence of S9 and at 5.0 mg/ml in the presence of S9.

In a rat liver cell (RL4) *in vitro* cytogenetic assay there was no increased incidence of chromosome aberrations at test concentrations of 62.5-500 µg/ml. Rat liver cells are metabolically competent. Cytotoxicity was observed at the highest dose level tested (Brooks et al, 1985 & 1988).

Additionally the related ketone, MIBK which has been tested more extensively, was considered non-genotoxic from an overall assessment of the in vitro and in vivo assays carried out (IPCS, 1990). Negative results for bacterial mutagenicity, in vitro UDS and an in vivo micronucleus test support this conclusion. The in vitro mammalian assays (mouse lymphoma and cell transformation assay) are at best equivocal.

Conclusions
DIBK does not exhibit gene mutation or chromosome effects when tested in *in vitro* assays.

4.1.2.8.Carcinogenicity

There are no carcinogenicity studies available.

4.1.2.9.Toxicity for reproduction

DIBK has been assessed in a Reproduction/Developmental toxicity screen (OECD 421). Groups of 10M+10F Alpk:APfsSD rats were given 0, 100, 300 or 1000 mg/kg/day DIBK in corn oil by gavage from two weeks prior to mating throughout pregnancy until weaning day 5 post partum when the dams and offspring were sacrificed. The death of two dams at the top dose level during lactation was considered attributable to DIBK. Male body weight gains were suppressed at the top dose level. There were no changes in organ weight and no toxicologically significant histopathological changes in the male or female reproductive organs. Other organs were not examined microscopically. There was no evidence of an effect on any of the reproductive parameters investigated or on any of the surviving litters. There was no effect on the number of pregnancies or positive smears, litters born, number of implantations or proportion of pups born live in any dose group. The NOAEL for developmental/reproductive effects is > 1000 mg/kg/day by gavage, with a parental NOAEL of 300 mg/kg/day.

A developmental/teratology study with the related ketone MIBK showed no evidence of treatment-related malformations and concluded a NOEL for maternal animals and off spring of 1000ppm (Tyl et al, 1987).

Observations in man

DIBK was reported as just one of a number of chemicals detected in at a tannery where a cluster of 3 men developed testicular cancer. The authors of the Health Hazard Evaluation Report concluded that it was impossible to determine if any specific agent was responsible due to a lack
of records and numerous changes in engineering controls and chemical processing (NIOSH, 1991).

Conclusion

There is no evidence that DIBK has an adverse effect on fertility or development following oral administration even at dose levels where there is evidence of parental toxicity. The NOAEL for parental toxicity is 300 mg/kg/day by gavage and for reproductive effects > 1000 mg/kg/day.

The conclusion is supported by the lack of treatment-related malformations a developmental/teratology study with the DIBK analogue MIBK.

4.1.3. Risk characterisation

4.1.3.0.General aspects

The data for the risk characterisation is presented in the sections 4.1.1 and 4.1.2.
Conversion factor: 1 ppm = 5.92 mg/m^3, 1 mg/m^3 = 0.17 ppm

4.1.3.1 Workers

Acute toxicity.

Only in the event of accidental releases or exposure a risk from DIBK exposure can occur. This will not be further considered.

Skin and Eye irritation.

Based on the data presented DIBK will exert some irritation, but not create any risk that needs further consideration.

Respiratory irritation.

The following table shows the margins of safety for respiratory irritation.

Population	NOAEL	Exposure	Margin of Safety
Workers	296 mg/m^3 (50ppm)	31.2 mg/m^3 (worst case DIBK measured data)	9.5
Workers	296 mg/m^3	16 mg/m^3 (mean DIBK measured data)	18.5
Workers	296 mg/m^3	190 mg/m^3 (worst case all industries)	1.6
Workers	296 mg/m^3	39 mg/m^3 (mean paint manufacture)	7.6

The data is based on human experience. Extrapolation was not required for the risk characterisation, therefore the MOS, (although small) is sufficient.

Repeat dose

Inhalation

The following table gives the margins of safety for workers exposed to DIBK.

Population	NOAEL - LOAEL	Exposure	Margin of Safety
Workers	3161 – 5358 mg/m^3 (534-905 ppm)	31.2 mg/m^3 (worst case DIBK measured data)	101-172
Workers	3161 – 5358 mg/m^3	16 mg/m^3 (mean DIBK measured data).	198-335
Workers	3161 – 5358 mg/m^3	190 mg/m^3 (worst case all industries)	17-28
Workers	3161 – 5358 mg/m^3	39 mg/m^3 (mean paint manufacture)	81-137

Specific DIBK exposure measurements (mean of 37 measurements) give a satisfactory MOS.

Dermal

The following table gives the margins of safety for workers exposed dermally to DIBK.

Population	Maximum internal dose absorbed	Exposure (external)	Margin of Safety
Workers	17000 mg/day	130-1300 mg/day (EASE prediction)	>>13-131

A NOAEL of 21.000 mg/day could be derived by route to route extrapolation from the oral OECD 421 study (based on 300 mg/kg/day for parental effects and 70 kg body weight). However, modelling of dermal absorption using Dermwin v.1.33 (Syracuse Research Corporation) shows that the internal dose is limited by physical-chemical properties. The maximum level to be absorbed is approximately 17000 mg/day, which is below the estimated NOAEL.

Exposure to pure DIBK was modelled as worst case scenario using EASE (EASE v.2.0). The input values for the EASE model are reported in Annex 4.1. Exposed skin area used was 1300 cm^2 (worst case)
EASE predicted an external exposure range of 130-1300 mg/day for DIBK.
The margin of safety is calculated from the maximum attainable internal dose resulting from absorption through the skin and the external exposure without considering what fraction of this dose will be absorbed across the skin. This provides a margin of >>13-131.
It is concluded that the risk from dermal exposure is negligible.

Toxicity to Reproduction

The following table gives the margin of safety for workers exposed to DIBK.

Population	NOAEL	Exposure	Margin of Safety
Workers worst case all industries	>1000 mg/kg/day	27 mg/kg/day* (= 190 mg/m^3, worst case all industries)	>37

* Route to route extrapolation from worst case all industries (table 1). Based on inhalation volume of 10m3/day and 70kg body weight.

The NOAEL is the highest tested dose level in a study were no effects were seen. The MOS could therefore not exactly be established but is greater than 37. Although this is a moderate MOS these considerations make that the conclusion is drawn that there is negligible risk.

4.1.3.2. Consumers

As shown above the exposure to consumers is probably negligible and therefore the potential risk can be considered to be negligible.

4.1.3.3. Man exposed indirectly via the environment

The following table shows the margins of safety for man exposed to DIBK indirectly via the environment.

NOAEL	Exposure	MOS
296 mg/m^3 (50ppm)	0.038 mg/m^3 (highest local PECair)	7790
296 mg/m^3	negligible (regional PEC)	>>

The MOS is sufficiently great considering the fact that the NOAEL is based on human irritation data.

5. RESULTS

Environment

Based on structure activity relationship the chemical is not expected to exhibit ecotoxicity of concern. The derived PEC/PNEC ratio is less than 1. Based on the known use pattern and estimated exposure the chemical is currently considered of low potential risk and low priority for further work.

Human health

The chemical is a respiratory irritant but otherwise considered as having low toxicity. Exposure is considered to be low in the Sponsor country. Therefore it is currently considered of low potential risk and low priority for further work.

6. REFERENCES

Baumann W., Muth A., 1995, Untersuchung zur erfassung der Umweltexposition von Chemikalien der Farben- und Lackindustrie, Endbericht zum Forschungsvorhaben (Umweltbundesamt) 106 04 124.

Brooks, T.M.; Clare, M.G.; Wiggins, D.E. 1985. Genotoxicity studies with diisobutyl ketone. Sittingbourne, Shell Research Ltd, SBGR.84.314, 1985.

Brooks, T.M; Meyers, A.L.; Hutson, D.H. 1988. The genetic toxicology of some hydrocarbon and oxygenated solvents. Mutagenesis 3(3): 227-232, 1988.

Browning, E. 1965. Toxicity and metabolism of industrial solvents. New York, American Elsevier, 1965.

Carpenter, C.P.; Pozzani, U.C.; Weil, C.S. 1953. Toxicity and hazard of diisobutyl ketone vapours. Arch. Ind. Hyg. Occ. Med., 8:377-381, 1953

CEC (Commission of the European Communities), 1996, Technical Guidance Document in support of Directive 93/67/EEC on risk assessment of notified new substances and Regulation (EC) N° 1488/94 on risk assessment of existing substances (Parts I, II, III and IV)

CEC (Commission of the European Communities), 1995, Overview of Structure-Activity Relationships for Environmental Endpoints, DG XII, Contract # EV5V-CT92-0211

Dalton, P.H., Wysocki, C.J., Brody, M.J., Lawley, H.J. 1997. Perceived odor, irritation and health symptoms following short-term exposure to acetone. Am. J. Ind. Med. 31, 558-569.

Dalton, P.H., Dilks, D.D., Banton, M.I. 1998. Evaluation of odor and sensory irritation thresholds for methyl iso-butyl ketone (MIBK) in humans. Monell Chemicals Senses Center, Philadelphia, Pensylvania, USA.

De Ceaurriz, J.; Desiles, J.P.; Bonnet, P.; Marignac, B.; Muller, J.; Guenier, J.P. 1983 Concentration dependent behavioural changes in mice following short-term inhalation exposure to various industrial solvents. Tox. Appl. Pharm. 67: 383-389, 1983.

De Ceaurriz, J.; Micillino, J.C.; Marignac, B.; Bonnet, P.; Muller, J.; Guenier, J.P. 1984 Quantitative evaluation of sensory irritating and neurobehavioural properties of aliphatic ketones in mice. Fd. Chem. Toxicol. 22(7): 545-549, 1984.

DEGBE. 2-(2-butoxyethoxy)ethanol. Risk Assessment for EC793/93. Draft report 7 May 1998.

Dodd, D.E.; Losco, P.E.; Troup, C.M.; Pritts, I.M.; Tyler, T.R. Hyalin droplet nephrosis in male Fischer-344 rats following inhalation of diisobutyl ketone. Tox. Ind. Hlth 3(4):443-457, 1987

ECETOC technical report No. 70. Chronic neurotoxicity of solvents. ECETOC 1996.

EASE exposure model v 2.0. UK Health and Safety Executive.

EPA 1991. Baetchke, K.P.; Rodgers, I.S.; Hard, G.C.; McGaughty, R. E.; Tahan, L.M. Alpha$_{2\mu}$-globulin: Association with chemically induced renal toxicity and neoplasia in the male rat. USEPA Risk Assessment Forum, publication number PB92-143668, 1991

IPCS 1990. Environmental Health Criteria 117 Methyl Isobutyl Ketone. WHO Geneva, 1990

Katz, G.V., Renner, E.R. Jnr, Terhaar, C.J. 1986. Subchronic inhalation toxicity of methyl isoamyl ketone in rats. Fund. Appl. Tox. 6:498-505, 1986

McOmie, W.A., Anderson, H.H. 1949. Comparative toxicologic effects of some isobutyl carbinols and ketones. Univ. California Publ. Pharmacol. 2:217, 1949

Mortelmans, K.; Haworth, S.; Lawlor, T.; Speck, W.; Tainer, B.; Zeiger, E. 1986. Salmonella mutagenicity tests: II. Results from the testing of 270 chemicals. Env. Mut. 8 (Supplement 7): 1-119, 1986.

NIOSH Health Hazard Evaluation Report HETA 89-125-2021, Pan American Tannery, Gloversville, New York. NTIS/PB91-108217, 1991

Patty 1994. Topping, D.C.; Morgott, D.A.; David, R.M.; O'Donaghue, J.L. Chapter 26 Ketones in Patty's Industrial Hygiene and Toxicology, 4th Edition Vol IIC, pp 1816-1818. Editors Clayton, G.D. & F.E., Wiley Interscience, 1994

Phillips, R.D., Moran, E.J., Dodd, D.E., Fowler, E.H., Kary, C.D. 1987. A 14 week vapour inhalation toxicity study of methyl isobutyl ketone. Fund. Appl. Tox. 9:380-388, 1987

Potokar, M.; Grundler, O.J.; Heusener, A.; Jung, R.; Murmann, P.; Schobel, C.; Suberg, H.; Zechel, H.J. Studies on the design of animal tests for the corrosiveness of industrial chemicals. Fd. Chem. Toxic. 23(6): 615-617, 1985.

Shell HSE 1995a. Diisobutyl Ketone (DIBK): Acute oral toxicity in the rat. Report from Zeneca Central Toxicology Laboratory No. CTL/E/101, July 1995 to SIPM Report No. HSE 95.1069, 1995.

Shell HSE 1995b. Diisobutyl Ketone (DIBK): Acute dermal toxicity in the rat. Report from Zeneca Central Toxicology Laboratory No. CTL/E/102, July 1995 to SIPM Report No. HSE 95.1070, 1995.

Shell HSE 1995c. Diisobutyl Ketone (DIBK): 4 hour acute inhalation toxicity in the rat. Report from Zeneca Central Toxicology Laboratory No. CTL/E/107, July 1995 to SIPM Report No. HSE 95.1072, 1995.

Shell HSE 1995d. Diisobutyl ketone (DIBK): Skin sensitisation study in the guinea pig (Magnusson and Kligman method). Report from Zeneca Central Toxicology Laboratory No. CTL/E/105, September 1995 to SIPM Report No. HSE 95.1071, 1995.

Shell HSE 1996a. Diisobutyl ketone: Skin irritation in the rabbit. Report from Corning Hazelton No. 1439/19-1032 October 1996 to SICC. Toxicology Report No. 96.1247, 1996

Shell HSE 1996b. Diisobutyl ketone (DIBK): Reproduction/developmental toxicity screening test in rats. Report from Zeneca Central Toxicology Laboratory No. CTL/P/4592 to Shell Chemicals Europe Ltd Report No. HSE 96.1068, 1996

Silverman, L.; Schulte, H.F.; First, M.W. 1946. Further studies on sensory response to certain industrial solvent vapors. J. Ind. Hyg. Toxicol. 28(6): 262-266, 1946.

Smyth, H.F.; Carpenter, C.P.; Weil, C.S. 1949. Range-finding toxicity data, list III. J. Ind. Hyg. Toxicol. 31: 60-62, 1949.

Tyl, R.W., France, K.A. 1987. Developmental toxicity evaluation of inhaled methyl isobutyl ketone in Fischer 344 rats and CD-1 mice. Fundam. Appl. Tox. 8 (3): 310-327.

Union Carbide Corp. 1941. Acute response of guinea pigs and rats to inhalation of the vapours of diisobutyl ketone. Report to Carbide & Carbon Chemicals Corp. from the Mellon Institute of Industrial Research, Report No. 4-54, July 3, 1941

Union Carbide Corporation 1948. The acute toxicity of diisobutyl ketone. Report from the Mellon Institute of Industrial Research, University of Pittsburgh. Report No. 11-91 to Carbide and Carbon Chemicals Corp. July 1948

Union Carbide Corporation 1951. Repeated exposures of rats and guinea pigs to vapours of diisobutyl ketone. Report from the Mellon Institute of Industrial Research, University of Pittsburgh. Report No. 14-34 to Carbide and Carbon Chemicals Division of UCC, April 1951

Union Carbide Corporation 1983. Diisobutyl Ketone: Acute toxicity and primary irritancy studies. Report from Bushy Run Research Centre Report No. 46-31 for Union Carbide Corporation, July 1983.

Union Carbide Corporation 1985. Diisobutyl ketone (DIBK) - Nine-day vapour inhalation study in rats. Report from Bushy Run Research Centre project report 47-85 for Union Carbide Corporation, May 1985

US-EPA, 1996, Toxic Release Inventory 1987-1994, EPA 749-C-96-003, August 1996

Annex 1: EUSES output

EUSES Compact report	Single substance			
Printed on	09/07/98 09:06:38			
Study	DIBK			
Substance	DIBK			
Defaults	Standard			
Assessment types	1A, 1B, 2, 3A, 3B			
Base set complete	No			
Name	Reference	Value	Units	Status
SUBSTANCE				
SUBSTANCE IDENTIFICATION				
General name	DIBK	DIBK		S
Description				D
CAS-No	108-83-8	108-83-8		S
EC-notification no.				D
EINECS no.	203-620-1	203-620-1		S
PHYSICO-CHEMICAL PROPERTIES				
Molecular weight	142	142	[g.mol-1]	S
Melting point	-41	-41	[oC]	S
Boiling point	163	163	[oC]	S
Vapour pressure at 25 [oC]	220	220	[Pa]	S
Octanol-water partition coefficient.	2.56	2.56	[log10]	S
Water solubility	500	500	[mg.l-1]	S
RELEASE ESTIMATION				
CHARACTERIZATION AND TONNAGE				
High Production Volume Chemical	Yes	Yes		S
Production volume of chemical in EU	6.5E+03	6.5E+03	[tonnes.yr-1]	S
Volume of chemical imported to EU	0	0	[tonnes.yr-1]	D
Volume of chemical exported from EU	0	0	[tonnes.yr-1]	D
Intermittent release	No	No		D
USE PATTERNS				
EMISSION INPUT DATA[USE PATTERN 1]				
Industry category	14 Paints, lacquers and varnishes industry	14 Paints, lacquers and varnishes industry		S
Use category	48 Solvents	48 Solvents		S
Emission scenario document available	Yes	Yes		O
Extra details on use category	Solvent based	Solvent based		S
Extra details on use category	Constructions, maintenance, etc.	Constructions, maintenance, etc.		S
Fraction of tonnage for application	0.5	0.5	[-]	O
Fraction of chemical in formulation	0.1	0.1	[-]	S
Production	No	No		S
Formulation	Yes	Yes		D
Processing	Yes	Yes		D
Private use	No	No		S
Recovery	No	No		S
Main category production	III Multi-purpose equipment	III Multi-purpose equipment		D
Main category formulation	III Multi-purpose equipment	III Multi-purpose equipment		D
Main category processing	III Non-dispersive use	III Non-dispersive use		D

Name	Reference	Value	Units	Status
EMISSION INPUT DATA[USE PATTERN 2]				
Industry category	7 Leather processing industry	7 Leather processing industry		S
Use category	48 Solvents	48 Solvents		S
Emission scenario document available	Yes	Yes		O
Extra details on use category	No extra details necessary	No extra details necessary		D
Extra details on use category	No extra details necessary	No extra details necessary		D
Fraction of tonnage for application	0.5	0.5	[-]	S
Fraction of chemical in formulation	0.1	0.1	[-]	S
Production	No	No		S
Formulation	Yes	Yes		D
Processing	Yes	Yes		D
Private use	No	No		S
Recovery	No	No		S
Main category production	III Multi-purpose equipment	III Multi-purpose equipment		D
Main category formulation	III Multi-purpose equipment	III Multi-purpose equipment		D
Main category processing	III Non-dispersive use	III Non-dispersive use		D
[USE PATTERN 1] [FORMULATION]				
Fraction of tonnage released to waste water	0.02	3E-03	[-]	S
[USE PATTERN 1] [PROCESSING]				
Fraction of tonnage released to waste water	0.02	0.01	[-]	S
[USE PATTERN 2] [FORMULATION]				
Fraction of tonnage released to waste water	0.02	3E-03	[-]	S
[USE PATTERN 2] [PROCESSING]				
Fraction of tonnage released to air	0	0.8	[-]	S
Fraction of tonnage released to waste water	0.99	1.56E-04	[-]	S
[USE PATTERN 2] [PROCESSING]				
Local emission to air during episode	0	138	[kg.d-1]	S
Local emission to wastewater during episode	364.077	1.41	[kg.d-1]	S
DISTRIBUTION				
PARTITION COEFFICIENTS				
SOLIDS WATER PARTITIONING				
Organic carbon-water partition coefficient	149.269	225	[l.kg-1]	S
AIR-WATER PARTITIONING AND ADSORPTION TO AEROSOL PARTICLES				
Henry's law constant	62.48	45	[Pa.m3.mol-1]	S
DEGRADATION AND TRANSFORMATION RATES				
CHARACTERIZATION AND STP				
Characterization of biodegradability	Readily biodegradable	Readily biodegradable		S
Degradation calculation method in STP	First order, standard OECD/EU tests	First order, standard OECD/EU tests		D
Rate constant for biodegradation in STP	24	24	[d-1]	O
Total rate constant for degradation in STP	24	24	[d-1]	O
Maximum growth rate of specific microorganisms	2	2	[d-1]	D
Half saturation concentration	0.5	0.5	[g.m-3]	D

Name	Reference	Value	Units	Status
ENVIRONMENTAL				
Specific degradation rate constant with OH-radicals	0	0	[cm3.molec-1.s-1]	D
Rate constant for degradation in air	+INF	14.2	[hr] (Dt50)	S
Rate constant for hydrolysis in surface water	6.93E-07	6.93E-07	[d-1]	O
Rate constant for photolysis in surface water	6.93E-07	6.93E-07	[d-1]	O
Rate constant for biodegradation in surface water	0.0462	0.0462	[d-1]	O
Total rate constant for degradation in bulk surface water	0.0462	0.0462	[d-1]	O
Rate constant for biodegradation in bulk soil	0.0231	0.0231	[d-1]	O
Total rate constant for degradation in bulk soil	0.0231	0.0231	[d-1]	O
Rate constant for biodegradation in aerated sediment	0.0231	0.0231	[d-1]	O
Total rate constant for degradation in bulk sediment	2.31E-03	2.31E-03	[d-1]	O
[USE PATTERN 2] [PROCESSING]				
INPUT AND CONFIGURATION[USE PATTERN 2] [PROCESSING]				
Local emission to wastewater during episode	364.077	1.41	[kg.d-1]	S
EFFECTS				
INPUT OF EFFECTS DATA				
MICRO-ORGANISMS				
EC50 for micro-organisms in a STP	??	??	[mg.l-1]	D
Specific bacterial population?	No	No		D
EC10 for micro-organisms in a STP	??	??	[mg.l-1]	D
Specific bacterial population?	No	No		D
NOEC for micro-organisms in a STP	??	??	[mg.l-1]	D
Specific bacterial population?	No	No		D
AQUATIC ORGANISMS				
LC50 for fish	39	39	[mg.l-1]	S
L(E)C50 for Daphnia	25	25	[mg.l-1]	S
EC50 for algae	23	23	[mg.l-1]	S
LC50 for other aquatic species	??	??	[mg.l-1]	D
Species	other	other		D
NOEC for fish	??	??	[mg.l-1]	D
NOEC for Daphnia	??	??	[mg.l-1]	D
NOEC for algae	??	??	[mg.l-1]	D
NOEC for other aquatic species	??	??	[mg.l-1]	D
Additional aquatic NOEC	??	??	[mg.l-1]	D
Additional aquatic NOEC	??	??	[mg.l-1]	D
Additional aquatic NOEC	??	??	[mg.l-1]	D
Additional aquatic NOEC	??	??	[mg.l-1]	D
Additional aquatic NOEC	??	??	[mg.l-1]	D
Additional aquatic NOEC	??	??	[mg.l-1]	D
TERRESTRIAL ORGANISMS				
LC50 for plants	??	??	[mg.kgwwt-1]	D
LC50 for earthworms	??	??	[mg.kgwwt-1]	D
EC50 for microorganisms	??	??	[mg.kgwwt-1]	D
LC50 for other terrestrial species	??	??	[mg.kgwwt-1]	D
Species	other	other		D
NOEC for plants	??	??	[mg.kgwwt-1]	D
NOEC for earthworms	??	??	[mg.kgwwt-1]	D
NOEC for microorganisms	??	??	[mg.kgwwt-1]	D
NOEC for other terrestrial species	??	??	[mg.kgwwt-1]	D
NOEC for other terrestrial species	??	??	[mg.kgwwt-1]	D
Additional terrestrial NOEC	??	??	[mg.kgwwt-1]	D
Additional terrestrial NOEC	??	??	[mg.kgwwt-1]	D
Additional terrestrial NOEC	??	??	[mg.kgwwt-1]	D
Additional terrestrial NOEC	??	??	[mg.kgwwt-1]	D
Additional terrestrial NOEC	??	??	[mg.kgwwt-1]	D
Additional terrestrial NOEC	??	??	[mg.kgwwt-1]	D
BIRDS				
LC50 in avian dietary study (5 days)	??	??	[mg.kg-1]	D
NOAEL	??	??	[mg.kg-1.d-1]	D
NOEC via food	??	??	[mg.kg-1]	O
Duration of (sub-)chronic oral test	Chronic	Chronic		D
Conversion factor NOAEL to NOEC	8	8	[kg.d.kg-1]	D

Name	Reference	Value	Units	Status
ENVIRONMENTAL EFFECTS ASSESSMENT				
INTERMEDIATE RESULTS AQUATIC ORGANISMS, MICRO-ORGANISMS AND PREDATORS				
Toxicological data used for extrapolation to PNEC Aqua	23	23	[mg.l-1]	O
Assessment factor applied in extrapolation to PNEC Aqua	1000	1000	[-]	O
Toxicological data used for extrapolation to PNEC Aqua	23	23	[mg.l-1]	O
Assessment factor applied in extrapolation to PNEC Aqua	100	100	[-]	O
Toxicological data used for extrapolation to PNEC micro	??	??	[mg.l-1]	O
Assessment factor applied in extrapolation to PNEC micro	??	??	[-]	O
Toxicological data used for extrapolation to PNEC oral	??	??	[mg.kg-1]	O
Assessment factor applied in extrapolation to PNEC oral	??	??	[-]	O
INTERMEDIATE RESULTS TERRESTRIAL AND SEDIMENT ORGANISMS				
Toxicological data used for extrapolation to PNEC Terr	0.0634	0.0941	[mg.kgwwt-1]	O
Assessment factor applied in extrapolation to PNEC Terr	1	1	[-]	O
Equilibrium partitioning used for PNEC in soil?	Yes	Yes		O
Equilibrium partitioning used for PNEC in sediment?	Yes	Yes		O
PNECS FOR AQUATIC ORGANISMS, MICRO-ORGANISMS AND PREDATORS				
PNEC for aquatic organisms	0.023	0.023	[mg.l-1]	O
PNEC for aquatic organisms, intermittent releases	0.23	0.23	[mg.l-1]	O
PNEC for micro-organisms in a STP	??	??	[mg.l-1]	O
PNEC for secondary poisoning of birds and mammals	??	??	[mg.kg-1]	O
PNEC for aquatic organisms with statistical method	??	??	[mg.l-1]	O
PNECS FOR TERRESTRIAL AND SEDIMENT ORGANISMS				
PNEC for terrestrial organisms	0.0634	0.0941	[mg.kgwwt-1]	O
PNEC for terrestrial organisms with statistical method	??	??	[mg.kgwwt-1]	O
PNEC for sediment-dwelling organisms	0.0802	0.114	[mg.kgwwt-1]	O
RISK CHARACTERIZATION				
ENVIRONMENTAL EXPOSURE				
LOCAL				
RISK CHARACTERIZATION OF [USE PATTERN 1] [FORMULATION]				
ENVIRONMENTAL				
RCR for the local water compartment	4.54	0.706	[-]	O
Intermittent release	No	No		D
RCR for the local soil compartment	5.23	0.867	[-]	O
Extra factor 10 applied to PEC	No	No		O
RCR for the local sediment compartment	5.25	0.811	[-]	O
Extra factor 10 applied to PEC	No	No		O
RCR for the sewage treatment plant	??	??	[-]	O
PREDATORS				
RCR for fish-eating birds and mammals	??	??	[-]	O
RCR for worm-eating birds and mammals	??	??	[-]	O
HUMANS				
MOS local, total exposure via all media	??	??	[-]	O
MOS local, exposure via air	??	??	[-]	O

Name	Reference	Value	Units	Status
RISK CHARACTERIZATION OF [USE PATTERN 1] [PROCESSING]				
ENVIRONMENTAL				
RCR for the local water compartment	0.67	0.349	[-]	O
Intermittent release	No	No		D
RCR for the local soil compartment	0.818	0.475	[-]	O
Extra factor 10 applied to PEC	No	No		O
RCR for the local sediment compartment	0.774	0.4	[-]	O
Extra factor 10 applied to PEC	No	No		O
RCR for the sewage treatment plant	??	??	[-]	O
PREDATORS				
RCR for fish-eating birds and mammals	??	??	[-]	O
RCR for worm-eating birds and mammals	??	??	[-]	O
HUMANS				
MOS local, total exposure via all media	??	??	[-]	O
MOS local, exposure via air	??	??	[-]	O
RISK CHARACTERIZATION OF [USE PATTERN 2] [FORMULATION]				
ENVIRONMENTAL				
RCR for the local water compartment	4.54	0.706	[-]	O
Intermittent release	No	No		D
RCR for the local soil compartment	5.23	0.867	[-]	O
Extra factor 10 applied to PEC	No	No		O
RCR for the local sediment compartment	5.25	0.811	[-]	O
Extra factor 10 applied to PEC	No	No		O
RCR for the sewage treatment plant	??	??	[-]	O
PREDATORS				
RCR for fish-eating birds and mammals	??	??	[-]	O
RCR for worm-eating birds and mammals	??	??	[-]	O
HUMANS				
MOS local, total exposure via all media	??	??	[-]	O
MOS local, exposure via air	??	??	[-]	O
RISK CHARACTERIZATION OF [USE PATTERN 2] [PROCESSING]				
ENVIRONMENTAL				
RCR for the local water compartment	76.1	0.307	[-]	O
Intermittent release	No	No		D
RCR for the local soil compartment	87.8	0.422	[-]	O
Extra factor 10 applied to PEC	No	No		O
RCR for the local sediment compartment	87.9	0.352	[-]	O
Extra factor 10 applied to PEC	No	No		O
RCR for the sewage treatment plant	??	??	[-]	O
PREDATORS				
RCR for fish-eating birds and mammals	??	??	[-]	O
RCR for worm-eating birds and mammals	??	??	[-]	O
HUMANS				
MOS local, total exposure via all media	??	??	[-]	O
MOS local, exposure via air	??	??	[-]	O
REGIONAL				
ENVIRONMENT				
RCR for the regional water compartment	0.0113	2.32E-04	[-]	O
RCR for the regional soil compartment	1.01E-03	2.91E-05	[-]	O
Extra factor 10 applied to PEC	No	No		O
RCR for the regional sediment compartment	0.0109	2.26E-04	[-]	O
Extra factor 10 applied to PEC	No	No		O
HUMANS				
MOS regional, total exposure via all media	??	??	[-]	O
MOS regional, exposure via air	??	??	[-]	O

Annex 2: DIBK exposure - inhalation

	MIBK	MEK	DEGBE	DIBK	Source
Vapour pressure (kPa)	1.9	9.5	0.0055	0.16	
Process/Use					
Manufacturing	1.03ppm and 3.35ppm				MIBK OECD-SIDS, 1996
Drumming warm product	**3.2 ppm**				**MIBK OECD-SIDS 1996**
Manufacturing				**18-59mg/m3 (3-10ppm)**	**EASE prediction**
Handling pure product				**3-18mg/m3 (0.5-3ppm)**	**EASE prediction. Annex 4.2.**
Bulk unloading	<2ppm				MIBK OECD-SIDS 1996
Manufacturing	<1ppm				MIBK OECD-SIDS 1996
Various use (Automotive refinish/spray painting)	Mean TWA 1.7ppm. Range 1-39ppm				MIBK OECD-SIDS 1996
Manufacturing, maintenance staff		<0.3ppm			MEK OECD-SIDS, 1997
Manufacturing, operations staff		0.3-1.4ppm			MEK OECD-SIDS, 1997
Manufacturing, loaders		1.7-2.0ppm			MEK OECD-SIDS, 1997
Consumer		"extremely small"			MEK OECD-SIDS, 1997
Manufacturing			<<0.6mg/m3		DEGBE RA
Production products containing DEGBE			1.3-2.5mg/m3		DEGBE RA
Automated application products containing DEGBE (includes leather finishing)			<1 - 3.4 mg/m3		DEGBE RA
Manual application of products containing DEGBE			5-10mg/m3		DEGBE RA
Consumer Latex paint (0.6%)			0.03 0.05ppm		DEGBE RA,
Paint refinish, vehicle refinish (spray booth)	39 ppm(1hr) 1.7 ppm (mean)				ECETOC nr 70
Paint Aircraft maintainance-primer		77 mg/m3 (max) 39 mg/m3 (mean)			ECETOC nr 70
Paint Aircraft maintainance - top coat	117 mg/m3 (max) 44 mg/m3 (mean)	219 mg/m3 (max) 69 mg/m3 (mean)			ECETOC nr 70
Paint Aircraft painting (short term)		3250mg/m3 (max) 1436 (mean)			ECETOC nr 70
Paint air craft painting (long term)		440 mg/m3 (max) 197 mg/m3 (mean)			ECETOC nr 70
Paint Paint manufacture	**16-192mg/m3**	3-170 mg/m3			**ECETOC nr 70**
Paint Paint manufacture		8-124 **39 (mean) mg/m3**			**ECETOC nr 70**
Paint, roller/brush application	11 ppm (max)				ECETOC nr 70
Paint, heavy equipment spray painting; metal furniture spray painting (solvents and waterborne)				**<1-23mg/m3**	**ECETOC nr 70**
Printing light metal packaging				5-13mg/m3. Mean 12.7mg/m3 *	INRS. Via B. Diderich fax18/12/96
Leather tanning and dressing				**1-31.2mg/m3. Mean 16mg/m3** **	**INRS Via B.Diderich fax18/12/96**
Use of product containing DIBK				**3-18mg/m3 (0.5-3ppm)**	**EASE prediction**

*Range and mean of 59 measurements
** Range and mean of 37 measurements.

Annex 3: DIBK exposure dermal (mg/day).

Process	DEGBE	DIBK	Source
Production of DIBK		very low	EASE
Production of DEGBE	200mg/day		DEGBE RA
Production of products containing DEGBE	40mg/day		DEGBE RA
Automated application of products containing DEGBE	100mg/day		DEGBE RA
Manual application of products containing DIBK		**130-1300mg/day**	**EASE**
Manual application of products containing DEGBE	1950mg/day		DEGBE RA

Annex 4.1 EASE input and output dermal exposure - log file

Fri Jul 24 10:48:33 1998
The name of the substance is DIBK
The temperature of the process is 50
The physical-state is liquid
The exposure-type is dermal
The use-pattern is Non-dispersive use
The pattern-of-control is Direct handling
The contact-level is Intermittent
CONCLUSION: The predicted dermal exposure to DIBK is 0.1-1 mg/square cm/day

Dermal exposure to a substance which is directly handled is determined by the
use pattern (Non-dispersive use) and the contact level (Intermittent), resulting in an exposure range of 0.1-1 mg/square cm/day

Annex 4.2 EASE input and output inhalation exposure handling pure product- log file

Mon Jul 27 09:50:31 1998
The name of the substance is DIBK
The temperature of the process is 50
The physical-state is liquid
The exposure-type is gas/vapour/liquid aerosol
aerosol-formed is false
The use-pattern is Non-dispersive use
The pattern-of-control is LEV
The status-vp-value is Value measured at process temperature
The vp-value of the substance is 1.1
The volatility of the substance is Low
The ability-airborne-vapour of the substance is Low
CONCLUSION: The predicted gas/vapour/liquid aerosol exposure to DIBK is 0.5-3 ppm

Inhalation exposure to a gas, vapour or liquid aerosol which is not
directly handled is determined by the pattern of use (Non-dispersive use), the pattern of control (LEV), and the ability of the substance to become airborne (Low) resulting in an exposure range of 0.5-3 ppm

I U C L I D D a t a S e t

Existing Chemical	Substance ID: 108-83-8
CAS No.	108-83-8
EINECS Name	2,6-dimethylheptan-4-one
EINECS No.	203-620-1
Molecular Weight	142.24
Structural Formula	(CH3)2-CH-CH2-CO-CH2-CH-(CH3)2
Molecular Formula	C9H18O
Producer Related Part	
Company:	Ministere de l'Environment
Creation date:	29-NOV-96
Substance Related Part	
Company:	Ministere de l'Environment
Creation date:	29-NOV-96
Memo:	OECD-SIDS
Printing date:	02-FEB-99
Revision date:	
Date of last Update:	29-DEC-98
Number of Pages:	21
Chapter (profile):	Chapter: 1, 2, 3, 4, 5, 7
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

1.0.1 OECD and Company Information

Type: lead organisation
Name: SHELL CHIMIE
Street: 89 Bd Franklin Roosevelt
Town: 92564 Rueil Malmaison
Country: France
Phone: 33 1 47 14 71 00
Telefax: 33 1 47 14 74 67
Telex: SHELL 615013F

Flag: confidential
06-DEC-96

Type: lead organisation
Name: Shell Nederland Chemie B.V.
Partner: Ir. H. Jolie Date:
Street: Vondelingenweg 601
Town: 3196 KK Rotterdam (Pernis)
Country: Netherlands
Phone: +31.(0)10.2317005
Telefax: 30502 NL
Telex: +31.(0)10.2317125

Flag: confidential
06-DEC-96

Type: cooperating company
Name: Union Carbide Benelux
Street: Noorderlaan 147
Town: B-2030 Antwerp
Country: Belgium

Flag: confidential
06-DEC-96

1.0.2 Location of Production Site

1.0.3 Identity of Recipients

1.1 General Substance Information

Substance type: organic
Physical status: liquid
Purity: ca. 65 - 94 % w/w
Flag: confidential
06-DEC-96 (12) (14)

Substance type:
Physical status:

Remark: Diisobutyl ketone is commercialised as a mixture of 2 isomers:
2,6-Dimethyl-4-heptanone 70 - 85%
4,6-Dimethyl-2-haptanone 15 - 30%
The composition of the commercialised product varies with the producer.
Flag: confidential
06-DEC-96

1.1.1 Spectra

1.2 Synonyms

DIBK
29-NOV-96

Diisobutyl ketone
29-NOV-96

Isovalerone
29-NOV-96

1.3 Impurities

CAS-No: 19549-80-5
EINECS-No: 243-148-3
EINECS-Name: 4,6-dimethylheptan-2-one
Contents: ca. 6 - 35 % w/w
Flag: confidential
06-DEC-96 (12) (14)

CAS-No: 108-82-7
EINECS-No: 203-619-6
EINECS-Name: 2,6-dimethylheptan-4-ol
Contents: < 2 % w/w
Flag: confidential
06-DEC-96

CAS-No: 7732-18-5
EINECS-No: 231-791-2
EINECS-Name: water, distilled, conductivity or of similar purity
Contents: < .15 % w/w
Flag: confidential
06-DEC-96

1.4 Additives

CAS-No:
EINECS-No:
EINECS-Name:

Remark: no additives used
Flag: confidential
29-NOV-96

1.5 Quantity

1.6.1 Labelling

Labelling: as in Directive 67/548/EEC
Symbols: Xi
R-Phrases: (10) Flammable
(37) Irritating to respiratory system
S-Phrases: (24) Avoid contact with skin
Flag: confidential
29-NOV-96

1.6.2 Classification

Classification: as in Directive 67/548/EEC
Class of danger: flammable
R-Phrases: (10) Flammable
Flag: confidential
29-NOV-96

Classification: as in Directive 67/548/EEC
Class of danger: irritating
R-Phrases: (37) Irritating to respiratory system
Flag: confidential
29-NOV-96

1.7 Use Pattern

Type: type
Category: Non dispersive use
Flag: confidential
29-NOV-96

Type: type
Category: Wide dispersive use
Flag: confidential
29-NOV-96

Type: industrial
Category: Leather processing industry
Remark: leather coatings used in shoes, furniture, automotive coatings
Flag: confidential
29-NOV-96

Type: industrial
Category: Paints, lacquers and varnishes industry
Flag: confidential
29-NOV-96

Type: use
Category: Solvents
Flag: confidential
29-NOV-96

1.7.1 Technology Production/Use

1.8 Occupational Exposure Limit Values

Type of limit: MAC (NL)
Limit value: 150 mg/m3
29-NOV-96 (5)

Type of limit: TLV (US)
Limit value: 145 mg/m3
29-NOV-96 (1)

Type of limit: other: VME (FR)
Limit value: 25 other: ppm
Short term expos.
Limit value: 145 mg/m3
Remark: Use only in well ventilated areas.
Hand protection : neoprene or nitrile gloves.
Eye protection : safety monogoggles.
Body protection : safety issue work clothes.
chemicals resistant safety shoes or boots.
29-NOV-96

1.9 Source of Exposure

1.10.1 Recommendations/Precautionary Measures

1.10.2 Emergency Measures

1.11 Packaging

1.12 Possib. of Rendering Subst. Harmless

1.13 Statements Concerning Waste

1.14.1 Water Pollution

1.14.2 Major Accident Hazards

1.14.3 Air Pollution

1.15 Additional Remarks

Remark: TRANSPORT INFORMATION

UN Number 1157
Class: 3
Packing Group: III
Proper Shipping Name: Diisobutyl ketone

Sea (IMO)
Class: 3.3
Packing Group: III
Symbol: Flammable liquid
Marine Pollutant (Y/N): No

Rail/Road (RID/ADR)
Class: 3
Item: 31(c)
Symbol: Flammable liquid
Kemler Plate: 30/1157

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

29-NOV-96

Remark: Recover or recycle if possible. Otherwise : incineration.
Avoid electrostatic discharge generation.
Earth all equipment.
Keep in a well ventilated place.
Do not smoke. Avoid naked flames. Remove ignition sources.

29-NOV-96

1.16 Last Literature Search

1.17 Reviews

1.18 Listings e.g. Chemical Inventories

2.1 Melting Point

Value: -46 degree C
Method: other: no further data available
Test substance: DIBK purity ca. 94%
06-DEC-96 (14)

Value: -46 degree C
Method: other: no further indication
Test substance: DIBK, no indication about purity
06-DEC-96 (7)

Value: = -41.5 degree C
Method: other: no further information available
GLP: no
Test substance: DIBK, purity ca. 65%
06-DEC-96 (12)

2.2 Boiling Point

Value: ca. 163 - 175 degree C at 1012 hPa
Decomposition: no
Method: other: ASTM D1078, Standard method for boiling range
GLP: no
Test substance: DIBK, purity ca. 65%
06-DEC-96 (12)

Value: 168.2 degree C at 1013 hPa
Method: other: no further data available
Test substance: DIBK, no indication about purity
06-DEC-96 (7)

Value: 169.4 degree C at 1013 hPa
Method: other: no other indications
Test substance: DIBK purity ca. 94%
06-DEC-96 (14)

2.3 Density

Type: density
Value: ca. .806 - .812 g/cm3 at 20 degree C
Method: other
GLP: no
Test condition: ASTM D4052, Standard method for density
06-DEC-96 (12)

2.3.1 Granulometry

2.4 Vapour Pressure

Value: 1 hPa at 20 degree C
Method: other (measured): no further data available
Test substance: DIBK purity ca. 94%
06-DEC-96 (14)

Value: = 2.2 hPa at 20 degree C
Method: other (measured): no further data available
Test substance: DIBK, purity ca. 65%
06-DEC-96 (12)

Value: 2.26 hPa at 20 degree C
Method: other (measured): no further data available
Remark: for 30°C, a value of 3.1 hPa is reported
Test substance: DIBK, no indication about purity
06-DEC-96 (16)

2.5 Partition Coefficient

log Pow: 2.56
Method: other (calculated): LOGKOW program
Year:
Remark: The same value is estimated for 2,6-dimethyl-4-heptanone and 4,6-dimethyl-2-heptanone
06-DEC-96 (13)

2.6.1 Water Solubility

Value: = 500 mg/l at 20 degree C
Method: other: no further data available
Test substance: DIBK, no indication about purity
06-DEC-96 (16)

Value: 360 mg/l at 25 degree C
Method: other: no further data available
Test substance: di-n-butyl ketone
29-DEC-98 (4)

Value: 430 mg/l at 25 degree C
Method: other: no further data available
29-DEC-98 (4)

Value: 460 mg/l at 25 degree C
Method: other: no further data available
Test substance: DIBK, no indication about purity
06-DEC-96 (7)

2.6.2 Surface Tension

2.7 Flash Point

Value: = 47 degree C
Type: closed cup
Method:
Year:
GLP: no
Test condition: IP 170, Standard method for flash point
Test substance: DIBK, purity ca. 65%
06-DEC-96 (12)

Value: 49 degree C
Type: other: same value for open and closed cup
Method:
Year:
Test substance: DIBK purity ca. 94%
06-DEC-96 (14)

2.8 Auto Flammability

Value: = 345 degree C
GLP: no
Test condition: ASTM D2155, Standard method for autoignition
Test substance: DIBK, purity ca. 65%
06-DEC-96 (12)

2.9 Flammability

Result: flammable
06-DEC-96

2.10 Explosive Properties

2.11 Oxidizing Properties

2.12 Additional Remarks

3.1.1 Photodegradation

```
Type:              air
Light source:      Sun light
Conc. of subst.:   at 26 degree C
INDIRECT PHOTOLYSIS
  Sensitizer:      OH
  Conc. of sens.:  500000 molecule/cm3
  Rate constant:   = .0000000000271 cm3/(molecule * sec)
  Degradation:     = 50 % after 14.2 hour(s)
Method:            other (measured)
  Year:            1985                          GLP: no data
Test substance:    other TS: DIBK, no inducation about purity
06-DEC-96                                                                  (2)
```

```
Type:              air
Light source:      Sun light
INDIRECT PHOTOLYSIS
  Sensitizer:      OH
  Conc. of sens.:  500000 molecule/cm3
  Degradation:     50 % after 22 day
Method:            other (calculated): US-EPA method
  Year:                                          GLP:
Test substance:
29-DEC-98                                                                 (10)
```

3.1.2 Stability in Water

3.1.3 Stability in Soil

3.2 Monitoring Data (Environment)

```
Type of
   measurement:    concentration at contaminated site
Medium:            ground water
Remark:            Measurements at pumping stations in the Neatherlands in 1976
                   - 1978
Result:            highest concentration measured: 0.3 µg/l
06-DEC-96                                                                 (17)
```

3.3.1 Transport between Environmental Compartments

```
Type:              volatility
Media:             water - air
Method:            other: estimation method
  Year:            1982
Remark:            The Henry's law constant can be estimated by a bond or group
                   contribution method.
                   Result: H = 27 - 45 Pa*m3/mol
                   The same value is estimated for 2,6-dimethyl-4-heptanone and
                   4,6-dimethyl-2-heptanone
06-DEC-96                                                                  (6)
```

```
Type:              volatility
Media:             water - air
Method:            other: estimation method
```

Year:
Remark: based upon the vapour pressure and the water solubility, a Henry's law constant of 28 - 62 Pa*m3/mol can be estimated
06-DEC-96

3.3.2 Distribution

Media: air - biota - sediment(s) - soil - water
Method: Calculation according Mackay, Level I
Year: 1981
Result: Air : 94.2 %
Water : 5.0 %
Soil : 0.4 %
Sediments: 0.4 %
Biota : 0.0 %.
06-DEC-96 (8)

3.4 Mode of Degradation in Actual Use

3.5 Biodegradation

Type: aerobic
Inoculum: domestic sewage, non-adapted
Concentration: 7 mg/l related to Test substance
Degradation: 18 % after 20 day
Kinetic: 5 day 0 %
10 day 4 %
15 day 9 %
20 day 18 %
Method: other: Standard Methods for the Examination of Water and Wastewater, APHA, 1971
Year: 1974 GLP: no
Test substance: other TS: DIBK, no indication about purity
Test condition: - test in artificial seawater
- inoculum concentration: 3 ml of filtered wastewater per bottle
- DO-measurement
09-DEC-96 (11)

Type: aerobic
Inoculum: domestic sewage, non-adapted
Concentration: 7 mg/l related to Test substance
Degradation: = 88 % after 20 day

Kinetic: 5 day = 4 %
10 day = 39 %
15 day = 57 %
20 day = 88 %
Method: other: Standard Methods for the Examination of Water and Wastewater, APHA, 1971
Year: 1974 GLP: no
Test substance: other TS: DIBK, no indication about purity
Test condition: - inoculum concentration: 3 ml of filtered wastewater per bottle
- DO-measurement

- 10-day window criterion reached
09-DEC-96 (11)

Type: aerobic
Inoculum: other: mixed microbial cultures, adapted
Concentration: 3.2 mg/l related to Test substance
Degradation: 37.4 % after 5 day
Method: other: Standard Methods for the Examination of Water and Wastewater, APHA, 1980
Year: 1987 GLP: no data
Test substance: other TS: DIBK, analytical grade
Test condition: - inoculum concentration: 1 ml/300 ml
- DO-measurement
- temp.: 21+-3 degree C
- mean of ten replicates
09-DEC-96 (15)

Type: aerobic
Inoculum: other: mixed microbial cultures, adapted
Concentration: 3.2 mg/l related to Test substance
Degradation: 46.8 % after 5 day
Method: other: Standard Methods for the Examination of Water and Wastewater, APHA, 1980
Year: 1987 GLP: no data
Test substance: other TS: DIBK, analytical grade
Test condition: - inoculum concentration: 1 ml/300 ml
- DO-measurement
- temp.: 21+-3 degree C
09-DEC-96 (3)

3.6 BOD5, COD or BOD5/COD Ratio

3.7 Bioaccumulation

3.8 Additional Remarks

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: semistatic
Species: Oncorhynchus mykiss (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC0: = 100
LC50: = 140
LC100: = 200
Method: other: in accordance with OECD 203
Year: 1984 GLP: yes
Test substance: other TS: DIBK, purity ca. 70%
Remark: It is noted that in the toxicity tests, the test substance was not wholly soluble at concentrations > 100 mg/l. The test results are expressed in terms of nominal concentrations. Therefore, losses of the test substance during testing which are caused by evaporation is not accounted for. This means the results obtained in these tests may have underestimated toxicity.
Test condition: - daily renewal of test medium
- aeration
- DO 9-10 mg/l
- pH 7.7-8.3
- hardness ca. 250 mg/l as CaCO3

09-DEC-96 (9)

4.2 Acute Toxicity to Aquatic Invertebrates

Species: Artemia salina (Crustacea)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring: no
LC50 : = 65
Method:
Year: 1974 GLP: no
Test substance: other TS: DIBK, no indication about purity
Test condition: - static system
- effect: immobilisation of phylopodia
- age: < 48 hours
- temp.: 24.5 degree C
- 5 concentrations between 10 and 100 mg/l tested
- bottles loosely capped
- 30-50 shrimp per test concentration

09-DEC-96 (11)

Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no

NOEC: = 100
EC50: = 250
Method: other: in accordance with OECD 202
Year: 1984 GLP: yes

Test substance: other TS: DIBK, purity ca. 70%
Remark: It is noted that in the toxicity tests, the test substance was not wholly soluble at concentrations > 100 mg/l. The test results are expressed in terms of nominal concentrations. Therefore, losses of the test substance during testing which are caused by evaporation is not accounted for. This means the results obtained in these tests may have underestimated toxicity.
Test condition: - static open test
- 3 replicats of 10 animals per test concentration
- DO 8.8 mg/l
- pH 8.2 - 8.4
- temp.: 18 - 22 degree C
- hardness: 180 mg/l as CaCO3

09-DEC-96 (9)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Selenastrum capricornutum (Algae)
Endpoint: biomass
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
EC10: 15
EC50: 87
Method: other: in accordance with OECD 201
Year: 1984 GLP: yes
Test substance: other TS: DIBK, purity ca. 70%
Remark: For the endpoint specific growth rate, the results are:
96h - EC10 = 55 mg/l
96h - EC50 = 230 mg/l
It is noted that in the toxicity tests, the test substance was not wholly soluble at concentrations > 100 mg/l. The test results are expressed in terms of nominal concentrations. Therefore, losses of the test substance during testing which are caused by evaporation is not accounted for. This means the results obtained in these tests may have underestimated toxicity.
Test condition: - initial cell concentration: 500 cells/ml
- temp.: 22-26 degree C
- pH 7.3 - 7.7

09-DEC-96 (9)

4.4 Toxicity to Microorganisms e.g. Bacteria

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

4.5.2 Chronic Toxicity to Aquatic Invertebrates

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

4.6.2 Toxicity to Terrestrial Plants

4.6.3 Toxicity to other Non-Mamm. Terrestrial Species

4.7 Biological Effects Monitoring

4.8 Biotransformation and Kinetics

4.9 Additional Remarks

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

```
Type:             LD50
Species:          rat
Value:            = 5750 mg/kg bw

Method:           other
  Year:           1949
   GLP:           no
Test substance:   as prescribed by 1.1 - 1.4

02-FEB-99                                                        (21) (40)

Type:             LD50
Species:          rat
Value:            > 2000 mg/kg bw

Method:           Directive 84/449/EEC, B.1  "Acute toxicity (oral)"
  Year:           1984
   GLP:           yes
Test substance:   as prescribed by 1.1 - 1.4

Remark:           There were no mortalities at the single dose level
                  administered. All animals gained weight over the 14 day
                  observation period. Females exhibited slight non-specific
                  signs of systemic toxicity (piloerection, urinary
                  incontinence and pinched sides). There were no treatment
                  related findings at necropsy.
02-FEB-99                                                           (29)

Type:             LD50
Species:          rat
Value:            > 3200 mg/kg bw

Method:           other
  Year:           1994
   GLP:           no
Test substance:   as prescribed by 1.1 - 1.4

02-FEB-99                                                           (41)

Type:             LD50
Species:          rat
Value:            = 5258 - 6933 mg/kg bw

Method:           other: no data
  Year:           1983
   GLP:           no data
Test substance:   as prescribed by 1.1 - 1.4

Remark:           LD50 was reported separately for males and females.
                  Female LD50 : 6.50 ml/kg (5285 mg/kg)
                  Male LD50   : 8.57 ml/kg (6933 mg/kg)
```

02-FEB-99 (34)

Type: LD50
Species: mouse
Value: = 1416 mg/kg bw

Method: other
Year: 1994
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

02-FEB-99 (41)

Type: LD50
Species: mouse
Value: = 2830 mg/kg bw

Method: other
Year: 1949
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: Histopathological examination revealed hyperaemia of the stomach wall and duodenum in mice which died.
02-FEB-99 (31)

5.1.2 Acute Inhalation Toxicity

Type: LC50
Species: rat
Sex: male
Exposure time: 4 hour(s)
Value: > 2300 ppm

Method: other
Year: 1949
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: The saturated vapour concentration was administered.
02-FEB-99 (40)

Type: LC50
Species: rat
Sex: male/female
Exposure time: 4 hour(s)
Value: > 5 mg/l

Method: OECD Guide-line 403 "Acute Inhalation Toxicity"
Year: 1981
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Result: In this limit test, a maximum concentration of 5 mg/l was used. Animals were exposed nose only and the achieved concentration was 4.7 mg/l. There were no mortalities or compound related effects on body weight or macroscopic post-mortem findings. Clinical signs (salivation, lethargy, shaking and reduced stability) were typical of CNC depression and occurred during and immediately after exposure.
02-FEB-99 (35)

Type: LC50
Species: rat
Sex: male/female
Exposure time: 6 hour(s)

Year: 1983
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Remark: The 5M+5F rats were exposed to substantially saturated vapours of DIBK for 6 hours in a static chamber. None of the animals died. Signs of intoxication were hypoactivity, ataxia, impaired reflexes and laboured breathing. LC50 is > saturated vapour concentration. All animals recovered within one day and there were no treatment related findings at necropsy.
02-FEB-99 (34)

Type: LC50
Species: rat
Sex: no data

Method: other
Year: 1949
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: Rats were exposed to the saturated vapours for periods from 7.5 to 16 hours without deaths. There was no reference made to other signs of toxicity.
02-FEB-99 (31)

Type: LC50
Species: mouse
Sex: no data
Exposure time: 7.5 hour(s)

Method: other
Year: 1949
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: Groups of 10 mice were exposed to the saturated vapours of DIBK for 6-11.5 hours. The LC50 was greater than the saturated vapour concentration following a 7.5 hour exposure. All mice exposed to the saturated vapours for 9.5 hours and above died.

Other signs of intoxiciation were irritation of the nose and eyes, somnolence and anaesthesia.
02-FEB-99 (31)

Type: LC50
Species: rabbit
Sex: no data
Exposure time: 8 hour(s)
Value: > 2246 ppm

Method: other
Year: 1948
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: 1/8 rabbits died.
02-FEB-99 (21)

Type: LC50
Species: guinea pig
Sex: no data

Method: other
Year: 1949
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: Guinea pigs were exposed to the saturated vapours for periods from 7.5 to 16 hours without deaths. There was no reference made to other signs of toxicity.
02-FEB-99 (31)

Type: LC50
Species: guinea pig
Sex: no data
Exposure time: 8 hour(s)
Value: ca. 2500 ppm

Method: other
Year: 1941
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: The vapours were irritant to the nose and eyes. Death was due to narcosis or respiratory paralysis. histopathological changes were minimal.
02-FEB-99 (39)

5.1.3 Acute Dermal Toxicity

Type: LD50
Species: rat
Value: > 2000 mg/kg bw

Method: OECD Guide-line 402 "Acute dermal Toxicity"
Year: 1981
GLP: yes

Test substance: as prescribed by 1.1 - 1.4

Result: A single dose of 2000 mg/kg was applied to the skin for 24 hours using an occluded dressing. There were no mortalities or other evidence of systemic toxicity. All animals gained in weight over the 14 day observation period. Slight skin irritation was observed at the application site.

02-FEB-99 (28)

Type: LD50
Species: rabbit
Value: > 16200 mg/kg bw

Method: other
Year: 1949
GLP: no
Test substance: as prescribed by 1.1 - 1.4

02-FEB-99 (21) (40)

Type: LD50
Species: rabbit

Method: other
Year: 1983
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Remark: Groups of 5M+5F rabbits were tested. A significant difference in toxicity between male and female was observed the LD50 values being Male 3.57 ml/kg (2888 mg/kg); Female 13.5 ml/kg (10922 mg/kg). As this value for male toxicity did not correspond to the percutaneous toxicity previously reported for DIBK in rabbits by the same laboratory and was also lower than the oral toxicity the test was repeated in males. The repeat test gave a male LD50 of 8.57 ml/kg (6933 mg/kg). Using both sets of mortality data for the males the LD50 was 5.66 ml/kg (4579 mg/kg).

Signs of intoxication were discomfort, sluggishness and unsteady gait. There was also evidence of skin irritation with erythema, oedema and desquamation. At necropsy red lungs were observed occasionally and a fluid or paste-like material was observed in the intestines of a few animals.

02-FEB-99 (34)

5.1.4 Acute Toxicity, other Routes

Type: LD50
Species: rat
Route of admin.: i.p.
Value: > 1600 mg/kg bw

Method: other
Year: 1994
GLP: no

Test substance: as prescribed by 1.1 - 1.4

02-FEB-99 (41)

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Result: slightly irritating
EC classificat.: not irritating

Method: other
Year: 1949
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: Marked capillary injection was reported but no oedema.
02-FEB-99 (21) (40)

Species: rabbit
Result: not irritating
EC classificat.: not irritating

Method: OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year: 1981
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Remark: This study was performed using both occluded and semi-occluded procedures and a 1 or 4 hour exosure period. Actual erythema and oedema scores were not reported, the overall classification for all types and lengths of exposure was non-irritant.
02-FEB-99 (36)

Species: rabbit
Result: slightly irritating
EC classificat.: not irritating

Method: OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year: 1981
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Result: Erythema, oedema and other dermal changes (superficial eschar, fissuring and desquamation) were observed which resolved within 2 weeks of exposure. Group mean 24+48+72 hour scores for erythema and oedema were 0.6 and 0.3 respectively, No individual rabbit attained mean 24+48+72 erythema or oedema hours scores of > or = to 2.
02-FEB-99 (27)

Species: rabbit
Result: slightly irritating
EC classificat.: not irritating

Method: other:
Year: 1983
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Remark: Group mean 24+48+72 hour scores for erythema and oedema were 1.9 and 0.4 respectively. At 7 days slight erythema (mean 0.2) and some desquamation were observed. Diminishing desquamation persisted in some animals until 14 days.
02-FEB-99 (34)

5.2.2 Eye Irritation

Species: rabbit
Result: slightly irritating
EC classificat.: not irritating

Method: other
Year: 1949
GLP: no
Test substance: as prescribed by 1.1 - 1.4

02-FEB-99 (40)

Species: rabbit
Result: slightly irritating
EC classificat.: not irritating

Method: other: similar to OECD 405
Year: 1981
GLP: no data
Test substance: as prescribed by 1.1 - 1.4

Remark: 0.01 or 0.01 ml was instilled into the conjunctival sac for 1 second. Scores were reported individually and allowed calculation of OECD type mean scores. Following instillation of 0.1 ml, group mean 24+48+72 hour scores for corneal opacity and iritis were 0, the score for conjunctival redness was 0.3 and for chemosis 0.4. All eyes were normal by 7 days. Following instillation of 0.01 ml there was slight redness up to 6 hours after administration in some rabbits but no evidence of irritation at 24 hours.
26-MAR-2002 (17)

5.3 Sensitization

Type: Guinea pig maximization test
Species: guinea pig
Result: not sensitizing
Classification: not sensitizing

Method: OECD Guide-line 406 "Skin Sensitization"
Year: 1981
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Remark: No reaction was seen in any test or negative control animal. The positive control group treated with undiluted hexylcinnamaldehyde gave a 50% positive response.
02-FEB-99 (30)

5.4 Repeated Dose Toxicity

Species: rat Sex: male/female
Strain: Fischer 344
Route of administration: inhalation
Exposure period: 6 hours per day
Frequency of treatment: 5 days/week for 9 days.
Post exposure period: 2-week recovery.
Doses: 98, 300 and 905 ppm
Control Group: yes
NOAEL: = 300 ppm
LOAEL: = 905 ppm

Method: other
Year: 1985
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Remark: Groups of 10M+10F rats were used. Body weight gains were decreased in top dose males and females. Increases in liver and kidney weights at the high and mid dose levels were dose related. Following a two week recovery period (top dose animals only) female organ weights were no longer increased.

In males the difference remained statistically significant. There were few treatment related changes. A slight decrease in platelet levels at 905 ppm was not considered of biological significance in the absence of any other change in haematological parameters. The only histopathological changes were the dose related kidney changes seen in male rats at 300 and 905 ppm. The kidney changes (hyalin droplet nephrosis) were typical of male rat specific alpha-2-microglobulin mediated nephropathy. Particular attention was paid to kidney histology in this study with the use of Mallory-Heidenhain stain. This male rat specific nephropathy was reversible over the two-week recovery period. The NOAEL of 300 ppm is based on decreased body weights in both sexes at 905 ppm. The effects on the male kidney are not considered of relevance to man (EPA, 1991). The minor changes in liver and kidney weight in the absence of other histopathology are considered adaptive.
02-FEB-99 (24) (25) (26)

Species: rat Sex: male/female
Strain: Sherman
Route of administration: inhalation
Exposure period: 7 hours per day
Frequency of treatment:5 days/week for 6 weeks.
Post exposure period: none
Doses: 125, 252, 534, 925 and 1654 ppm
Control Group: yes

NOAEL: = 534 ppm
LOAEL: = 925 ppm

Method: other
Year: 1953
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: A sex difference in susceptibility was seen in this study. At 1650 ppm all females died during exposure while 12/15 males survived 30 exposures. The tissues of rats which died during the first exposure showed severe liver, lung and kidney pathology. Among survivors at 1650 ppm there was no major histopathological change in the adrenal, liver, kidney, lung or spleen. Minor histopathological change in the form of cloudy swelling of the liver, lung congestion and in the kidneys cloudy swelling of the convoluted tubules was seen in the 5 surviving top dose males. At 925 ppm an increased incidence of minor pathological change was reported by Carpenter et al, 1953. These minor changes were possibly cloudy swelling of the convoluted tubules of the kidney although this is not explicit from the reported data. Effects at lower levels were confined to slightly increased liver and kidney weights which in the absence of histopathological change were considered adaptive. The NOEL of 534 ppm was based on the conservative premise that the 'minor' pathological changes at 925 ppm were significant.
02-FEB-99 (20) (37)

Species: rat Sex: no data
Strain: no data
Route of administration: gavage
Exposure period: 90 days
Frequency of treatment:daily
Post exposure period:none
Doses: 2000 mg/kg/day
Control Group: yes
NOAEL: < 2000 mg/kg bw

Method: other
Year: 1982
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: While never formally reported, this study represents the only available oral study with DIBK and is therefore summarised here.
No neurotoxicity was noted, but weight increases were noted in liver, kidneys and adrenals. Decreased heart and brain weights were also reported. Histopathological changes included minor changes in the stomach, liver and kidneys.
02-FEB-99 (41)

Species: mouse Sex: no data
Strain: no data
Route of administration: inhalation
Exposure period: 3 hours

Frequency of treatment:12 exposures
Post exposure period: no data
Doses: 14.4-22.2 mg/l
Control Group: no data specified

Method: other
Year: 1949
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: There were no mortalities at an dose level. There did not appear to be a cumulative effect.
02-FEB-99 (31)

Species: guinea pig Sex: male
Strain: other
Route of administration: inhalation
Exposure period: 7 hours per day
Frequency of treatment: 5 days/week for 6 weeks.
Post exposure period: none

Doses: 125 and 250 ppm
Control Group: yes
NOAEL: = 250 ppm

Method: other
Year: 1951
GLP: no
Test substance: as prescribed by 1.1 - 1.4

Remark: The only statistically significant effect was reduced liver weight at 250 ppm. It is unlikely that this has any biological significance.
02-FEB-99 (20) (37)

5.5 Genetic Toxicity 'in Vitro'

Type: Gene mutation in Saccharomyces cerevisiae
System of testing:jd1
Concentration: 0.01 - 5.0 mg/ml
Metabolic activation: with and without
Result: negative

Method: other
Year: 1985
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

02-FEB-99 (18) (19)

Type: Salmonella typhimurium reverse mutation assay
System of testing: TA 98, 100, 1535, 1537 and 1538
Concentration: 31.25 - 4000 ug/ml
Metabolic activation: with and without
Result: negative

Method: other
Year: 1985
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

02-FEB-99 (18) (19)

Type: Salmonella typhimurium reverse mutation assay
System of testing: TA 97, 98, 1535 and 1537.
Concentration: 1 - 333 ug/plate
Metabolic activation: with and without
Result: negative

Method: other
Year: 1986
GLP: no data

Test substance: as prescribed by 1.1 - 1.4

02-FEB-99 (33)

Type: Mammalian cell gene mutation assay
System of testing: Rat liver cell (RL4)
Concentration: 62.5 - 500 ug/ml
Metabolic activation:no data
Result: negative

Method: other
Year: 1985
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

02-FEB-99 (18) (19)

5.6 Genetic Toxicity 'in Vivo'

5.7 Carcinogenicity

5.8.1 Toxicity to Fertility

Type: Fertility
Species: rat
Sex: male/female
Strain: Sprague-Dawley
Route of administration: gavage
Exposure Period: males 28 days, females 41 days minimum, 14 days premating and throughout pregnancy and lactation
Frequency of treatment:daily
Premating Exposure Period
male: 14 days
female: 14 days
Duration of test: ca 41 days
Doses: 100, 300, 1000 mg/kg/day
Control Group: yes, concurrent no treatment

NOAEL Parental: = 300 mg/kg bw
NOAEL F1 Offspring:= 1000 mg/kg bw

Method: OECD preliminary reproduction toxicity screening test

Year: 1995
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: OECD 421
Result: DIBK was administered in corn oil. The death of 2 dams at the top dose level during lactation was considered attributable to treatment.

Male bodyweights were suppressed at the top dose level. There were no changes in organ weights and no toxicologically significant histopathological changes in the male or female reproductive organs. Other organs were not examined.
There was no evidence of an effect on any of the reproductive parameters investigated or on any of the surviving litters. There was no effect on the number of pregnancies or positive smears, litters born, number of implantations or proportion of pups born live in any dose group.
02-FEB-99 (32)

5.8.2 Developmental Toxicity/Teratogenicity

Remark: A preliminary reproduction toxicity screening test has been udertaken with DIBK to OECD protocol 421. This study is detailed in chapter 5.8. There was no evidence of an adverse effect on development. The NOEL for parental toxicity in this gavage stduy was 300 mg/kg/day and for the offspring 1000 mg/kg/day, the highest dose level tested.
02-FEB-99 (32)

5.8.3 Toxicity to Reproduction, Other Studies

5.9 Specific Investigations

5.10 Exposure Experience

Remark: A group of 12 volunteers was exposed for 15 minutes to DIBK vapour. Most individuals reported eye irritation at 50 ppm. 25 ppm was the concentration that most individuals reported as acceptable for 8 hour exposure.
02-FEB-99 (38)

Remark: Two subjects were exposed for 3 hours to 50 ppm DIBK. Other than slight transitory eye irritation and the persistant smell and taste, these subjects reported that the concentration was 'acceptable'. Three subjects exposed to 100 ppm reported eye, nose and throat irritation. This concentration was considered 'unacceptable'. There was no evidence of a reduced performance in the completion of a simple co-ordination test conducted before, during and

after
exposure to 100 ppm.

12-FEB-98 (20)

Remark: A 60 year old man was exposed to DIBK in his job as a senior laboratory technician while involved in hydraulic stripping experiments on iron ore. After about a months exposure he developed a severe headache and a 20-minute loss of vision.

Neurological examination revealed a back problem, headache and peripheral neuropathy. A CT scan was normal. MRI showed multiple small foci in the white matter and pons. Neuropsychological testing indicated affective changes, deficits in manual motor speed, verbal fluency, visuospatial organisation and short-term memory. MRI findings and neurobehavioural assessment indicate a localisation of pathology in the subcortical regions.

There was no report of exposure levels or details of exposure to other chemicals. In the absence of details of exposure this single cse report cannot be considered conclusive evidence of toxic encephalopathy due attributable to DIBK.

12-FEB-98 (42)

5.11 Additional Remarks

Type: Behaviour

Remark: Groups of 10 male Swiss mice were exposed to DIBK for 4 hours at concentrations ranging from 243-415 ppm. At the end of the exposure the mice were subjected to the behavioural despair swimming test. The animals were immersed in water and the time of immobility before they began to try to escape was measured. There was a dose related decrease in the period of immobility observed in the first 3 minutes following immersion in DIBK treated animals compared to controls. This effect was also seen with the 12 other solvents tested. A system of ranking of neurological effect using the ID50 (dose causing 50% reduction in immobilisation time) was proposed

10-FEB-98 (23)

Type: other: Sensory irritation

Remark: At dose levels of 184 - 351 ppm, DIBK caused a significant decrease in the respiratory rate of mice following head only exposure for 15 minutes. This is an indication of sensory irritation of the respiratory tract.

10-FEB-98 (22)

(1) ACGIH list 1993-1994

(2) Atkinson, R.,Kinetics and Mechanisms of the Gas-Phase Reactions of the Hydroxyl Radical with Organic Compounds under Atmospheric Conditions. Chem. Rev. 1985. 85. 69 -201

(3) Babeu L., Vaishnav D.D., Journal of Industrial Microbiology, 2 (1987) 107-115

(4) Beilstein

(5) Dutch MAC list 1994

(6) Hine J. & Mookerjee P.K. (1975) The intrinsic hydrophilic character of organic compounds. Correlations in terms of structural contributions. J. Org. Chem., Vol. 40, (3), 292-298

(7) Howard P.H., 1993, Handbook of Environmental Fate and Exposure Data for Organic Chemicals, Volume IV, Lewis Publishers

(8) Mackay, D. & S. Paterson, Calculation Fugacity, Environ. Sci. Technol. 15(9), 1981, 1006 - 1014.

(9) Pearson, N.,
Di-isobutylketone : Acute toxicity to Salmo gairdneri, Daphnia magna and Selenastrum capricornutum,
Group Research Report: SBGR 84.313
Shell Research Limited, Sittingbourne Research Centre, Sittingbourne UK, 1984

(10) personal communication; US-EPA exposure assessment branch; october 1998

(11) Price, K.S., G.T. Waggy & R.A. Conway, Brine Shrimp Bioassay and Seawater BOD of Petrochemicals, J. Water Pollut. Contr. Fed. 46, 1974, 63 - 77.

(12) Shell Chemicals MSDS dated November 1993

(13) Syracuse Research Corporation

(14) Union Carbide MSDS dated October 1990

(15) Vaishnav D.D., Boethling R.S., Babeu L., Chemosphere, Vol. 16, No. 4, pp 695-703, 1987

(16) Verschueren K., 1983, Handbook of environmental data on organic chemicals, Van Nostrand Reinhold Company

(17) Zoeteman B.C.J., de Greef E., Brinkmann F.J.J., The Science of the Total Environment, 21 (1981) 187-202

(18) Brooks, T.M. et al, Genotoxicity studies with di-isobutyl ketone (DIBK). Shell Research Ltd, Report No. SBGR.84.314, 1985

(19) Brooks, T.M., et al., The genetic toxicology of some hydrocarbon and oxygenated solvents. Mutagenesis, 3(3): 227 - 232, 1988.

(20) Carpenter, C.P. et al., Toxicity and hazard of diisobutyl ketone vapours. Arch. Ind. Hyg. Occ. Med., 8: 377 - 381, 1953.

(21) Carpenter, C.P. The acute toxicity of diisobutyl ketone Mellon Institute Special Report 11-91, 1st July 1948

(22) De Ceaurriz et al., Quantitative evaluation of sensory irritation and neurobehavioural properties of aliphatic ketones in mice. Fd. Chem. Toxicol. 22 (7): 545 - 549, 1984.

(23) De Ceaurriz, J et al, Concentration-dependent behavioural changes in mice following short-term inhalation exposure to various industrial solvents. Tox. Appl. Pharm. 67:383-389, 1983

(24) Dodd, D.E. et al., Hyalin droplet nephrosis in male Fischer-344 rats following inhalation of diisobutyl ketone. Tox. Ind. Hlth. 3(4): 443 - 457, 1987.

(25) Dodd, D.E., Diisobutyl ketone (DIBK) - Nine-day vapour inhalation study in rats. Report no. 47-85 from Bushy Run Research Centre to Union Carbide Corporation, May 2, 1985

(26) EPA, Baetchke, K.P. et al. Alpha 2-microglobulin: Association with chemically induced renal toxicity and neoplasia in the male rat. USEPA Risk Assessment Forum, publication number PB92-143668, 1991

(27) Gardner, J.R. Diisobutyl ketone: Skin irritation study in the rabbit. Report to Shell Chemicals Europe Ltd from Corning Hazleton, Shell Toxicology Report No. 96.1247, 1996

(28) Lees, D. Diisobutyl ketone, (DIBK): Acute dermal toxicity to the rat. Report to SIPM from Zeneca CTL, Shell HSE Report No. HSE 95.1070, 1995

(29) Lees, D., Diisobutyl ketone (DIBK): Acute oral toxicity to the rat. Report to SIPM from Zeneca CTL, Shell Report No. HSE 95.1069, 1995.

(30) Lees, D., Diisobutyl ketone: Skin sensitisation study in the guinea pig (Magnusson and Kligman method). Report to SIPM from Zeneca CTL, Shell Report No. HSE 95.1071, 1995

(31) McOmie, W.A. & Anderson, H.H., Comparative toxicologic efects of some isobutyl carbinols and ketones. Univ. California. Publ. in Pharmacol. 2:217-230, 1949

(32) Milburn, G.M. DIBK: Reproduction/developmental toxicity screening test in rats. Report from Zeneca CTL to SIPM, Shell report No. HSE 96.1068, 1996

(33) Mortelmans, K. et al., Salmonella mutagenicity tests: II. Results from the testing of 270 chemicals. Env. Mut. (Supplement 7): 1 - 119, 1986.

(34) Myers, R.C. Diisobutyl ketone: Acute toxicity and primary irritancy studies. Report no. 46-31 from Bushy Run Research Centre to Union Carbide Corporation, July 12, 1983

(35) Parr-Dobrzanski, R.J. Diisobutyl ketone (DIBK): 4 hour acute inhalation toxicity study in the rat. Report to SIPM from Zeneca CTL, Shell HSE Report No. HSE 95.1072, 1995

(36) Potokar, M, et al., Studies on the design of animal tests for the corrosiveness of industrial chemicals. Fd. Chem. Toxic. 23 (6): 615-617, 1985.

(37) Pozzani, U.C. Repeated exposures of rats and guinea pigs to vapours of diisobutyl ketone. Report no. 14-34 from the Mellon Institute to Carbide and Carbon Chemicals division of UCC, April 18, 1951.

(38) Silverman, L. et al, Further studies on sensory response to certain industrial solvent vapours. J. Ind. Hyg. Tox. 28(6): 262-266, 1946

(39) Smyth, H.F. & Carpenter, C.P. Acute response of guinea pigs and rats to inhalation of the vapours of diisobutyl ketone. Report no. 4-54 from the Mellon Institute to Carbide & Carbon Chemicals Corp. July 3, 1941

(40) Smyth, H.F., Carpenter, C.P., Weil, C.S., Range-finding toxicity data, list III. J. Ind. Hyg. Toxicol. 31: 60-62, 1949.

(41) Topping, D.C. et al, Chapter 26: Ketones in Patty's Industrial Hygiene and Toxicology, Vol II part C pp1816-1818, 4th edition, 1994 Eds Clayton G.D. and F.C.

(42) White, R.F. et al, Magnetic resonance imaging (MRI), neurobehavioural testing and toxic encephalopathy. Env. Res. 61: 117-123, 1993