2,4,4-TRIMETHYLPENTENE

CAS No: 25167-70-8

EINECS No: 246-690-9

SUMMARY RISK ASSESSMENT REPORT

Final report, 2008

Germany

FINAL APPROVED VERSION

Rapporteur for the risk assessment of 2,4,4-trimethylpentene is Germany

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PREFACE

This report provides a summary, with conclusions, of the risk assessment report of the substance 2,4,4-trimethylpentene that has been prepared by Germany in the context of Council Regulation (EEC) No. 793/93 on the evaluation and control of existing substances.

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

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

CONTENTS

TABLES

1 GENERAL SUBSTANCE INFORMATION

1.1 IDENTIFICATION OF THE SUBSTANCE

CAS No.: 25167-70-8

EINECS No.: 246-690-9

IUPAC Name: 2,4,4-Trimethylpentene

Synonyms: Pentene, 2,4,4-trimethyl.

Diisobutylene

2,4,4-Trimethylpenten

Diisobutylen

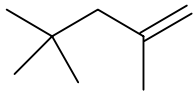
Diisobutene

Molecular weight: 112 g/mol

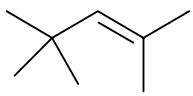
Empirical formula: C_8H_{16}

Structural formula:

2,4,4-Trimethylpent-1-ene



2,4,4-Trimethylpent-2-ene



1.2 PURITY/IMPURITIES, ADDITIVES

Purity:

2,4,4-Trimethylpentene is a mixture of two isomers

1. 2,4,4-Trimethylpent-1-ene (CAS-No.: 107-39-1) with a typical content of > 71.0 % (range 70 - 80%)

2. 2,4,4-Trimethylpent-2-ene (CAS-No.: 107-40-4) with a typical content of < 22.4 % (range 15 - 25%)

Impurities:

3,4,4-Trimethylpent-1-ene < 1.2 %

5,5-Diemethyl-trans-hex-2-ene < 5.2 %

5,5-Dimethyl-cis-hex-2-ene < 0.8 %

2,3,3-Trimethylpent-1-ene < 0.7 %

3,4,4-Trimethylpent-2-ene (CAS-No.:598-96-9) < 2.4 %

2,3,4-Trimethylpent-2-ene < 1.9 %

2,3,4-Trimethylpent-1-ene < 1.1 %

2,2-Dimethyl-trans-hex-3-ene < 1.6 %

3-Methyl-2-isopropylbut-1-ene < 0.8 %

other C-8-Alkyl-isomers < 4.5 %

1.3 PHYSICO-CHEMICAL PROPERTIES

Table 1.1 Summary of physico-chemical properties

Physical form	colourless liquid at 20 °C, 10.13 kPa
Melting point	< -50 °C (freezing point)
Boiling point	101.4 – 103.6 °C at 1 013 hPa (method according to Siwoloboff)
Relative Density	0.7166 at 20 °C (hydrometer method)

Vapour pressure	57.90 hPa at 25 °C (static method)
Henry´s law constant	2.127 * 10^5 Pa * m^3/mol
Surface tension	69.9 mN/m at 20 °C c: ca. 1.6 mg/l (ring method)
Partition coefficient (logPow)	5.0 at 25 °C (HPLC-method)
Water solubility	1.8 mg/l at 20 °C (flask method)
Flash point	-7 °C
Auto flammability	380 °C
Flammability	highly flammable
Explosive properties	not explosive
Oxidizing properties	not applicable for liquids

1.4 CLASSIFICATION

Classification:

F N	R 11 R 51/53	Classification according to Annex I of the substance 2,4,4-Trimethylpent-1-ene; CAS-No. 107-39-1
N	R 50/53	Proposal of the rapporteur (**related to Environment)**
Xi Xn	R 38 R 65	Should be additionally labelled (**related to Human Health)**

2 GENERAL INFORMATION ON EXPOSURE

There are two producers in the European Union (Prod.Site A and Prod.Site B). Depending iso-butenes used as feedstock and the process parameters, compositions of different grades are produced. The two main components are 2,4,4-trimethylpentene-1 and 2,4,4-trimethylpentene-2 . The complete process takes place in a closed system.

The production volume of both companies is listed within the range of 10,000 to 50,000 t/a (1992 – 1996) and in the range of 40,000 to 50,000 tonnes in 2002. An amount of 4,000 to 5,000 t/a were exported from the EU in the same year. The production volume used in the risk assessment report is based on the production volume reduced by the export volume.

2,4,4-trimethylpentene is processed at 25 sites in the EU (15[2]) in amounts between 25 t/a and 9,000 t/a. The total amount processed in the EU is within the range of 40,000 to 50,000 t/a. 2,4,4-trimethylpentene is mainly used as chemical intermediate (> 99%) for the production of 3,5,5-trimethylhexanal (Isononal), 3,5,5-trimethylhexanoic acid, 2,2,4-trimethylpentan and 3,5,5-trimethylhexanol.

< 1% of the total production volume is also used as solvent for paints, lacquers and varnishes.

[2] Work on this risk assessment began before enlargement of the EU in 2004. All tonnage data, and references to the 'EU' in this risk assessment report, therefore refer to the former EU of 15 Member States.

3 ENVIRONMENT

3.1 ENVIRONMENTAL EXPOSURE

Environmental releases

During production and use of 2,4,4-trimethylpentene as intermediate (processing) direct releases into the environment might occur to waste water and air. Due to the physicochemical properties of the substance, the main target compartment is the atmosphere (> 99%). In addition, minor indirect releases are expected to surface water via the sewage treatment plants of the processing sites, to sediment and to soil.

Environmental fate

Possibly emitted 2,4,4-trimethylpentene will be degraded rapidly in the air. According to both QSAR model packages PropertEst and EPI Suite, both including AOPWIN version 1.9, the half life is 7.24 h for indirect photo transformation by OH radicals (500 000 OH radicals/cm³). A half life of 22.92 h was calculated for photo transformation by ozone molecules ($7 * 10^{11}$ mol/cm³).
In the risk assessment the half life of 7.24 h is used.

Based on the available information a sound assessment of biodegradation in the aquatic environment is not possible, so as a worst-case 2,4,4-trimethylpentene has to be assessed as not biodegradable.

Based on the molecular structure hydrolysis of 2,4,4-trimethylpentene is not expected at environmental conditions. Tests concerning hydrolysis are not available.

No data about the degradation in soil are available.

Based on the fugacity model “Level I” and using a vapour pressure of 3040 Pa at 12 °C and a water solubility of 1.604 mg/l at 12 °C, the target compartment for the steady-state distribution is the atmosphere.

Apart from calculated Koc, an adsorption coefficient log Koc of 2,4,4-trimethylpentene was determined as 2.75 by the HPLC screening test method. Since this measured log Koc value of 2.75 is considered as most reliable it was chosen for the calculation in the risk assessment. Based on the measured log Koc the mobility of 2,4,4-trimethylpentene in soil can be classified as low.

Based on that figure and the default organic carbon contents as proposed in table 3 of chapter 3 of the TGD the partition coefficients for each compartment were calculated (Table 3.1).

Table 3.1 Partition coefficients

Parameters	Organic carbon content [%]	Partition coefficients [l/kg]
Kp (soil)	2	11.25

Kp (sediment)	5	28.12
Kp (suspended matter)	10	56.23
Kp (raw sewage)	30	168.70
Kp (activated sludge)	37	208.07

The Henry's law constant of 2.127 * 10^5 Pa * m^3/mol, calculated from the environmental physical and chemical properties, indicates that the volatility from water is very high.

Using the simulation model SimpleTreat 3.0 (debugged version February 1997) with the above estimated partition coefficients for raw sewage and activated sludge, the Henry's law constant as well as a biodegradation rate of 0 hr^{-1}, the elimination was estimated. The main portion of 2,4,4-trimethylpentene is directed into the atmosphere. The fractions directed to sludge and water are each < 5 %.

As all measured and calculated log Kow values are > 3, there is an indication of a bioaccumulation potential. Due to the higher reliability of the HPLC-measured value compared to the others, the log Kow value used in the further assessment is 5.0.

Only one study on bioaccumulation in aquatic organisms is available, which determined a BCF = 350 – 868. For a sound assessment of the bioaccumulation potential additional information like metabolism, incomplete elimination and organ-specific accumulation are necessary. Hence, besides these limitations the BCF of 868 is used for a preliminary assessment.

Environmental concentrations

Aquatic compartment (incl. sediment) calculation of PEClocal for production:

No site-specific information about the annual releases from production sites of 2,4,4-trimethylpentene are available. Therefore the releases were calculated using the default values of the TGD.

At Prod.Site B a certain amount of the produced 2,4,4-trimethylpentene is directly processed. Therefore the PEC-values for Prod.Site B are derived from the emissions from the production process and the emissions from the use as intermediate together.

Tab 3.2 Clocal $_{effluent}$, PEC_{local} (water)and PEC_{local} (sediment) for production

Company	Clocal effluent [µg • l^{-1}]	PEClocal (water) [µg • l^{-1}]	PEClocal (sediment) [µg • kg^{-1}]
Prod.Site A	1010	25.2	328
Prod.Site B	1691	42.3	550

Aquatic compartment (incl. sediment) Calculation of PEClocal for industrial/professional use:

2,4,4-trimethylpentene is used as intermediate by 25 sites. Since site-specific information was received only from three sites (A,B and C), releases from the other sites are calculated according to the default values of the TGD IC 3 (for releases to waste water: table A 3.3, f = 0.007; for releases to air: table A 3.3, MC = 1c, f = 0.001).

Table 3.3 Clocal $_{effluent}$, PEC local (water) and PEC local (sediment) for use as intermediate

Company	Clocal $_{effluent}$ [µg • l^{-1}]	PEC$_{local}$ (water) [µg • l^{-1}]	PEC$_{local}$ (sediment) [µg • kg^{-1}]
Proc.Site A	0.4	0.003	0.03
Proc.Site B	14.84	0.02	0.26
Proc.Site C	3380	560	7.280
Proc.Site D	134.4	3.4	43.7
Proc.Site E	551.0	14	179
Proc.Site F	2880.0	72	937
Proc.Site G	134.4	3.4	43.7
Proc.Site H	134.4	3.4	43.7
Proc.Site I	208.3	5.2	67.8
Proc.Site J	134.4	3.4	43.7
Proc.Site K	84.0	2.1	27.3
Proc.Site L	84.0	2.1	27.3
Proc.Site M	134.4	3.4	43.7
Proc.Site N	133.3	3.3	43.3
Proc.Site O	84.0	2.1	27.3
Proc.Site P	133.3	3.3	43.3
Proc.Site Q	84.0	2.1	27.3
Proc.Site R	526.4	13	171
Proc.Site S	134.4	3.4	43.7
Proc.Site T	84.0	2.1	27.3
Proc.Site U	134.4	3.4	43.7
Proc.Site V	134.4	3.4	43.7
Proc.Site W	399.8	10	130
Proc.Site X	134.4	3.4	43.7
Proc.Site Y	134.4	3.4	43.7
Others	84.0	2.1	26.8

Terrestrial compartment:

Due to the high volatility release to soil may occur by deposition from atmosphere. The main part of 2,4,4-trimethylpenten entering the waste water treatment plant is distributed into air (90,5%) and just a minor part of 4.7 % adsorbs to sludge. Spreading of contaminated sewage sludge is not considered as all sites are assumed to be connected to an industrial wwtp. Therefore it is assumed that sludge is incinerated.

For the calculation of the local PEC only deposition from air was considered. Site-specific information was not available for the calculation.

Terrestrial compartment calculation of PEClocal for production:

Table 3.4 PEC local (terrestrial) based on measured Koc

	DEP_{total_ann}	PEC local for					
	($mg/m^2.d^1$)	soil (mg/kg)	agric. Soil (mg/kg)	grassland (mg/kg)	soil porewater (mg/l)	agric. soil porewater (mg/l)	grassland porewater (mg/l)
Prod.Site A	0.219	$1.0 \cdot 10^{-4}$	$1.0 \cdot 10^{-4}$	$1.1 \cdot 10^{-4}$	$5.1 \cdot 10^{-6}$	$5.1 \cdot 10^{-6}$	$5.1 \cdot 10^{-6}$
Prod.Site B	0.329	0.0002	0.0002	0.0002	$7.7 \cdot 10^{-6}$	$7.7 \cdot 10^{-6}$	$7.7 \cdot 10^{-6}$

Terrestrial compartment, calculation of PEClocal for industrial/professional use:

Table 3.5 PEC local (terrestrial) based on measured Koc ,use as intermediate

	DEP_{total_ann}	PEC local for					
	($mg/m^2.d^1$)	soil (mg/kg)	agric. Soil (mg/kg)	grassland (mg/kg)	soil porewater (mg/l)	agric. soil porewater (mg/l)	grassland porewater (mg/l)
Proc.Site A	0.0009	$4.4 \cdot 10^{-7}$	$4.4 \cdot 10^{-7}$	$4.4 \cdot 10^{-7}$	$5.8 \cdot 10^{-7}$	$2.1 \cdot 10^{-8}$	$2.1 \cdot 10^{-8}$
Proc.Site B	0.011	$5.3 \cdot 10^{-6}$	$5.3 \cdot 10^{-6}$	$5.3 \cdot 10^{-6}$	$2.6 \cdot 10^{-7}$	$2.6 \cdot 10^{-7}$	$2.6 \cdot 10^{-7}$
Proc.Site C	0.054	$2.6 \cdot 10^{-5}$	$2.6 \cdot 10^{-5}$	$2.6 \cdot 10^{-5}$	$1.3 \cdot 10^{-6}$	$1.3 \cdot 10^{-6}$	$1.3 \cdot 10^{-6}$
Proc.Site D	0.0012	$5.8 \cdot 10^{-7}$	$5.8 \cdot 10^{-7}$	$5.8 \cdot 10^{-7}$	$2.8 \cdot 10^{-8}$	$2.8 \cdot 10^{-8}$	$2.8 \cdot 10^{-8}$
Proc.Site E	0.03	$1.4 \cdot 10^{-5}$	$1.4 \cdot 10^{-5}$	$1.4 \cdot 10^{-5}$	$6.9 \cdot 10^{-7}$	$6.9 \cdot 10^{-7}$	$6.9 \cdot 10^{-7}$
Proc.Site F	0.036	$1.7 \cdot 10^{-5}$	$1.7 \cdot 10^{-5}$	$1.7 \cdot 10^{-5}$	$8.4 \cdot 10^{-7}$	$8.4 \cdot 10^{-7}$	$8.4 \cdot 10^{-7}$
Proc.Site G	0.006	$2.9 \cdot 10^{-7}$	$2.9 \cdot 10^{-7}$	$2.9 \cdot 10^{-7}$	$1.4 \cdot 10^{-8}$	$1.4 \cdot 10^{-8}$	$1.4 \cdot 10^{-8}$
Proc.Site H	0.0012	$5.8 \cdot 10^{-7}$	$5.8 \cdot 10^{-7}$	$5.8 \cdot 10^{-7}$	$2.8 \cdot 10^{-8}$	$2.8 \cdot 10^{-8}$	$2.8 \cdot 10^{-8}$
Proc.Site I	0.011	$5.8 \cdot 10^{-7}$	$5.8 \cdot 10^{-7}$	$5.8 \cdot 10^{-7}$	$2.8 \cdot 10^{-8}$	$2.8 \cdot 10^{-8}$	$2.8 \cdot 10^{-8}$
Proc.Site J	0.0048	$2.3 \cdot 10^{-6}$	$2.3 \cdot 10^{-6}$	$2.3 \cdot 10^{-6}$	$1.1 \cdot 10^{-7}$	$1.1 \cdot 10^{-7}$	$1.1 \cdot 10^{-7}$
Proc.Site K	0.0003	$1.5 \cdot 10^{-7}$	$1.5 \cdot 10^{-7}$	$1.5 \cdot 10^{-7}$	$7.0 \cdot 10^{-9}$	$7.0 \cdot 10^{-9}$	$7.0 \cdot 10^{-9}$
Proc.Site L	0.0007	$3.5 \cdot 10^{-7}$	$3.5 \cdot 10^{-7}$	$3.5 \cdot 10^{-7}$	$1.7 \cdot 10^{-8}$	$1.7 \cdot 10^{-8}$	$1.7 \cdot 10^{-8}$
Proc.Site M	0.0012	$5.8 \cdot 10^{-7}$	$5.8 \cdot 10^{-7}$	$5.8 \cdot 10^{-7}$	$2.8 \cdot 10^{-8}$	$2.8 \cdot 10^{-8}$	$2.8 \cdot 10^{-8}$
Proc.Site N	0.0015	$7.2 \cdot 10^{-7}$	$7.2 \cdot 10^{-7}$	$7.2 \cdot 10^{-7}$	$3.5 \cdot 10^{-8}$	$3.5 \cdot 10^{-8}$	$3.5 \cdot 10^{-8}$
Proc.Site O	0.0003	$1.5 \cdot 10^{-7}$	$1.5 \cdot 10^{-7}$	$1.5 \cdot 10^{-7}$	$7.0 \cdot 10^{-9}$	$7.0 \cdot 10^{-9}$	$7.0 \cdot 10^{-9}$
Proc.Site P	0.002	$7.2 \cdot 10^{-7}$	$7.2 \cdot 10^{-7}$	$7.2 \cdot 10^{-7}$	$3.5 \cdot 10^{-8}$	$3.5 \cdot 10^{-8}$	$3.5 \cdot 10^{-8}$
Proc.Site Q	0.0003	$1.5 \cdot 10^{-7}$	$1.5 \cdot 10^{-7}$	$1.5 \cdot 10^{-7}$	$7.0 \cdot 10^{-9}$	$7.0 \cdot 10^{-9}$	$7.0 \cdot 10^{-9}$
Proc.Site R	0.028	$1.3 \cdot 10^{-5}$	$1.3 \cdot 10^{-5}$	$1.3 \cdot 10^{-5}$	$6.5 \cdot 10^{-7}$	$6.5 \cdot 10^{-7}$	$6.5 \cdot 10^{-7}$
Proc.Site S	0.0012	$5.8 \cdot 10^{-7}$	$5.8 \cdot 10^{-7}$	$5.8 \cdot 10^{-7}$	$2.8 \cdot 10^{-8}$	$2.8 \cdot 10^{-8}$	$2.8 \cdot 10^{-8}$
Proc.Site T	0.0024	$1.2 \cdot 10^{-6}$	$1.2 \cdot 10^{-6}$	$1.2 \cdot 10^{-6}$	$5.6 \cdot 10^{-8}$	$5.6 \cdot 10^{-8}$	$5.6 \cdot 10^{-8}$

Proc.Site U	0.006	$2.9 \cdot 10^{-6}$	$2.9 \cdot 10^{-6}$	$2.9 \cdot 10^{-6}$	$1.4 \cdot 10^{-7}$	$1.4 \cdot 10^{-7}$	$1.4 \cdot 10^{-7}$
Proc.Site V	0.0006	$2.9 \cdot 10^{-7}$	$2.9 \cdot 10^{-7}$	$2.9 \cdot 10^{-7}$	$1.4 \cdot 10^{-8}$	$1.4 \cdot 10^{-8}$	$1.4 \cdot 10^{-8}$
Proc.Site W	0.002	$1.1 \cdot 10^{-5}$	$1.1 \cdot 10^{-5}$	$1.1 \cdot 10^{-5}$	$5.1 \cdot 10^{-7}$	$5.1 \cdot 10^{-7}$	$5.1 \cdot 10^{-7}$
Proc.Site X	0.006	$2.9 \cdot 10^{-7}$	$2.9 \cdot 10^{-7}$	$2.9 \cdot 10^{-7}$	$1.4 \cdot 10^{-8}$	$1.4 \cdot 10^{-8}$	$1.4 \cdot 10^{-8}$
Proc.Site Y	0.005	$2.3 \cdot 10^{-6}$	$2.3 \cdot 10^{-6}$	$2.3 \cdot 10^{-6}$	$1.1 \cdot 10^{-7}$	$1.1 \cdot 10^{-7}$	$1.1 \cdot 10^{-7}$
Others	0.0005	$2.2 \cdot 10^{-7}$	$2.2 \cdot 10^{-7}$	$2.2 \cdot 10^{-7}$	$1.1 \cdot 10^{-8}$	$1.1 \cdot 10^{-8}$	$1.1 \cdot 10^{-8}$

Atmospheric compartment calculation of PEClocal for production:

Table 3.6 PEC_{local}(air) and deposition rates for production

Company	$PEClocal_{air\_ann}$ [mg • m^{-3}]
Prod.Site A	0.22
Prod.Site B	0.16

Atmospheric compartment, calculation of PEClocal for industrial/professional use:

Table 3.7 PEC_{local}(air) and deposition rates for industrial, use as intermediate

Company	$PEClocal_{air\_ann}$ [mg • m^{-3}]
Proc.Site A	$7.282 \cdot 10^{-4}$
Proc.Site B	$9.171 \cdot 10^{-3}$
Proc.Site C	0.043
Proc.Site D	$9.695 \cdot 10^{-4}$
Proc.Site E	0.024
Proc.Site F	0.029
Proc.Site G	$4.87 \cdot 10^{-4}$
Proc.Site H	$9.695 \cdot 10^{-4}$
Proc.Site I	$8.979 \cdot 10^{-3}$
Proc.Site J	$3.864 \cdot 10^{-3}$
Proc.Site K	$2.457 \cdot 10^{-4}$
Proc.Site L	$5.835 \cdot 10^{-4}$
Proc.Site M	$9.695 \cdot 10^{-4}$
Proc.Site N	$1.211 \cdot 10^{-3}$
Proc.Site O	$2.457 \cdot 10^{-4}$
Proc.Site P	$1.211 \cdot 10^{-3}$
Proc.Site Q	$2.457 \cdot 10^{-4}$

Proc.Site R	0.023
Proc.Site S	$9.695 \cdot 10^{-4}$
Proc.Site T	$1.934 \cdot 10^{-3}$
Proc.Site U	$4.829 \cdot 10^{-3}$
Proc.Site V	$4.87 \cdot 10^{-4}$
Proc.Site W	0.017
Proc.Site X	$4.829 \cdot 10^{-3}$
Proc.Site Y	$3.768 \cdot 10^{-3}$
Others	$3.663 \cdot 10^{-4}$

The calculations of PEC_{local} for the atmosphere were carried out according to the A- and B-tables of the TGD with the model OPS. Specific data for releases into the atmosphere are not available.

Non compartment specific exposure relevant to the food chain:

Due to log Kow and the bioconcentration factor of 868 for fish a bioaccumulation via the aquatic food chain can not be excluded. Based on the derived PEC-values for the terrestrial compartment releases into soil are considered as negligible. Hence, bioaccumulation via the terrestrial food chain is considered as not relevant

Table 3.8 PEC_{oral} for industrial use and processing

Company	modified PEC (water) [µg/l]	PEC oral, predator [$mg/kg_{wet\ fish}$]
Prod.Site A	10.4	9.0
Prod.Site B	36.1	31.4
Proc.Site A	0.001	0.001
Proc.Site B	0.01	0.009
Proc.Site C	94.3	81.9
Proc.Site D	0.2	0.2
Proc.Site E	5.7	4.9
Proc.Site F	6.9	6.0
Proc.Site G	0.1	0.1
Proc.Site H	0.2	0.2
Proc.Site I	2.1	1.9
Proc.Site J	0.9	0.8
Proc.Site K	0.1	0.1
Proc.Site L	0.1	0.1
Proc.Site M	0.2	0.2
Proc.Site N	0.3	0.3
Proc.Site O	0.1	0.1
Proc.Site P	0.3	0.3

Proc.Site Q	0.1	0.1
Proc.Site R	5.4	4.7
Proc.Site S	0.2	0.2
Proc.Site T	0.5	0.4
Proc.Site U	1.2	1.0
Proc.Site V	0.1	0.1
Proc.Site W	4.1	3.6
Proc.Site X	1.2	1.0
Proc.Site Y	0.9	0.8
Others	0.1	0.1

Calculation of PECregional and PECcontinental:

All releases are taken into account. A share of 90 per cent of the total releases was allocated to the continental scale, whilst 10 per cent are allocated to the regional sector. The software program EUSES 2.0 was used to calculate regional concentrations.

Table 3.9 PECregional and PECcontinental based on the measured Koc

continental PECs		**regional PECs**	
$PECcont_{surfacewater}$	$5.36 \cdot 10^{-12}$ mg/l	$PECreg_{surfacewater}$	$3.1 \cdot 10^{-10}$ mg/l
$PECcont_{air}$	3.65 • 10-^{07} mg/m^3	$PECreg_{air}$	$4.47 \cdot 10^{-06}$ mg/m^3
$PECcont_{agrsoil}$	$9.71 \cdot 10^{-11}$ mg/kg	$PECreg_{agrsoil}$	$1.19 \cdot 10^{-09}$ mg/kg
$PECcont_{agrsoilporew}$	$5.38 \cdot 10^{-12}$ mg/l	$PECreg_{agrsoilporew}$	$6.59 \cdot 10^{-11}$ mg/l
$PECcont_{natsoil}$	$9.68 \cdot 10^{-11}$ mg/kg	$PECreg_{natsoil}$	$1.19 \cdot 10^{-09}$ mg/kg

3.2 EFFECTS ASSESSMENT

Aquatic compartment

Due to the physicochemical properties of 2,4,4-trimethylpentene, volatility and low water solubility, only effect values based on analytically verified concentrations were used to calculate PNEC-values. Such results are available from three acute tests conducted under standardized conditions. The relevant LC_{50}-/EC_{50}- values are 0.58 mg/l (fish), 1.2 mg/l (daphnid) and 1.67 mg/l (algae, growth rate). The most sensitive species was *Oncorhynchus mykiss* with a 96 h-LC_{50} of 0.58 mg/l.

Since only short-term tests using species from three trophic levels are available; an assessment factor of 1000 is applied to this value.

$PNEC_{water}$ = 0.58 mg/l / 1000 = 0.58 µg/l

Additionally, a comparison between comparable experimental and predicted data (using equations for non-polar narcosis) for 2,4,4-trimethylpent-1-ene could be used to support the assumption that baseline toxicity is correct. A QSAR estimation of a minimum chronic toxicity for fish and Daphnia might be provided assuming – as a minimum - a chronic narcotic mode of action and indicate whether further testing might increase the PNEC and thus decrease the PEC/PNEC ratio.

Microorganisms

The derived PNEC is only used for a preliminary estimation. For a proper assessment of microbal inhibition an OECD 209 inhibition test is needed.

The nominal tested concentration of 3 mg/l is equal to an exposure concentration equal to the water solubility limit (i.e. 1.8 mg/l). For the derivation of the $PNEC_{STP}$ an assessment factor of 100 is applied to the water solubility limit, resulting in a preliminary PNEC

$PNEC_{micro\text{-}organism}$ = 0.018 mg/l.

Sediment

Provisionally calculated, using the equilibrium partitioning method the PNEC value is

$PNEC_{sed,\ calculated}$ = 0.00754 mg/kg (wwt) = 7.54 µg/kg (wwt)

Air

Experimental data for fate and behaviour of 2,4,4-trimethylpentene in the atmosphere are not available. Therefore, the data base is considered to be not sufficient for the derivation of a $PNEC_{air}$ for 2,4,4-trimethylpentene.

2,4,4-trimethylpentene contributes in the order of 0.004 % to the total NMVOC emission in the EU15. Thus the substance in general only contributes to a small extent to the total SMOG problem. Furthermore, the short half-life in air (t1/2 = approx. 7.24 h) presumably limits the

effect of 2,4,4-trimethylpentene on ozone formation. However, a significant contribution to ozone formation can not be excluded.

Terrestrial compartment

In an indicative risk assessment for the soil compartment the equilibrium partitioning method can be applied

$PNEC_{soil,\ calculated}$ = 0.00927 mg/kg (wwt) = 9.27 µg/kg (wwt)

Secondary poisoning

A biomagnification via food chain can not be excluded. Therefore a $PNEC_{oral}$ was derived from a 28-day rat toxicity study. The NOAEL for 2,4,4-trimethylpentene was considered to be 300 mg/kg bw/day. According to the TGD the NOAEL was converted into a $NOEC_{mammal,food\_chr}$ using a conversion factor (CONV). A conversion factor of 10 was considered as appropriate.

$PNEC_{oral}$ = 10 mg/kg_{food}

3.3 RISK CHARACTERISATION

Aquatic compartment

Waste water treatment plants

Table 3.10 $Clocal_{effl.}$/PNEC-ratios for waste water treatment plants

Company	PEC/PNEC
Prod.Site A	**56.1**
Prod.Site B	**93.9**
Proc.Site A	< 0.1
Proc.Site B	0.8
Proc.Site C	**187.8**
Proc.Site D	**7.5**
Proc.Site E	**30.6**
Proc.Site F	**160.0**
Proc.Site G	**7.5**
Proc.Site H	**7.5**
Proc.Site I	**11.6**
Proc.Site J	**7.5**
Proc.Site K	**4.7**
Proc.Site L	**4.7**
Proc.Site M	**7.5**
Proc.Site N	**7.4**
Proc.Site O	**4.7**
Proc.Site P	**7.4**
Proc.Site Q	**4.7**
Proc.Site R	**29.2**
Proc.Site S	**7.5**
Proc.Site T	**4.7**
Proc.Site U	**7.5**
Proc.Site V	**7.5**
Proc.Site W	**22.2**
Proc.Site X	**7.5**
Proc.Site Y	**7.5**
Others	**4.7**

For Proc.Site A and Proc.Site B a PEC/PNEC-ratio < 1 was calculated. Therefore **conclusion (ii)** applies to these sites.

Beside these sites **conclusion (i)** has to be drawn for the waste water treatment plants.

Due to the insufficient data base further exposure information should be required (for instance emission factor and effluent concentration). Furthermore, an OECD 209 respiration inhibition study is needed to derive a more reliable $PNEC_{micro\text{-}organism}$.

Aquatic environment

Table 3.11 PEC./PNEC-ratios for the aquatic compartment

Company	PEC/PNEC
Prod.Site A	**43.5**
Prod.Site B	**72.9**
Proc.Site A	< 0.1
Proc.Site B	< 0.1
Proc.Site C	**964.9**
Proc.Site D	**5.8**
Proc.Site E	**23.8**
Proc.Site F	**124.1**
Proc.Site G	**5.8**
Proc.Site H	**5.8**
Proc.Site I	**9.0**
Proc.Site J	**5.8**
Proc.Site K	**3.6**
Proc.Site L	**3.6**
Proc.Site M	**5.8**
Proc.Site N	**5.7**
Proc.Site O	**3.6**
Proc.Site P	**5.7**
Proc.Site Q	**3.6**
Proc.Site R	**22.7**
Proc.Site S	**5.8**
Proc.Site T	**3.6**
Proc.Site U	**5.8**
Proc.Site V	**5.8**
Proc.Site W	**17.2**
Proc.Site X	**5.8**
Proc.Site Y	**5.8**
Others	**3.6**

For Proc.Site A and Proc.Site B a PEC/PNEC-ratio < 1 was calculated. Therefore **conclusion (ii)** applies to these sites.

For Proc.Site C site specific data about the effluent flow and the receiving water flow were available. This site has to refine the exposure data. For all other sites PEC values were derived by using generic scenarios only. Therefore further exposure data are required. **Conclusion (i)**

Sediment

The equilibrium partitioning method was used to calculate PNEC and PEC for sediment from the freshwater data.. Therefore risk characterisation ratios for sediment are identical to the surface water risk characterisation ratios.

For Proc.Site A and Proc.Site B a PEC/PNEC-ratio < 1 was calculated. Therefore **conclusion (ii)** applies to these sites.

Beside these sites **conclusion (i)** has to be drawn.

Terrestrial compartment

Releases into the terrestrial compartment only occur from atmospherical deposition. Since no ecotoxicological data for suitable organisms are available the calculation is based on the $PNEC_{soil}$ of 9.27 µg/kg (wwt) estimated by using Equilibrium Partitioning method and the calculated soil concentrations.

All PEC/PNEC ratios are far below 1. Therefore **conclusion (ii)** has to be drawn.

Atmosphere

Since the problem of NMVOC is addressed by existing EU legislation and taking into consideration that 2,4,4-trimethylpentene from production and processing only contributes to 0.004% of total NMVOC-emissions there is at present no need for further information and/or testing and for risk reduction measures beyond those which are being applied already. **Conclusion (ii)**

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

Table 3.12 PEC/PNEC-ratios for secondary poisoning

Company	PEC oral/PNEC oral
Prod.Site A	0.9
Prod.Site B	**3.1**
Proc.Site A	< 0.1
Proc.Site B	< 0.1
Proc.Site C	**8.2**
Proc.Site D	< 0.1
Proc.Site E	0.5
Proc.Site F	0.6
Proc.Site G	< 0.1
Proc.Site H	< 0.1
Proc.Site I	0.2
Proc.Site J	< 0.1
Proc.Site K	< 0.1

Proc.Site L	< 0.1
Proc.Site M	< 0.1
Proc.Site N	< 0.1
Proc.Site O	< 0.1
Proc.Site P	< 0.1
Proc.Site Q	< 0.1
Proc.Site R	0.5
Proc.Site S	< 0.1
Proc.Site T	< 0.1
Proc.Site U	0.1
Proc.Site V	< 0.1
Proc.Site W	0.4
Proc.Site X	0.1
Proc.Site Y	< 0.1
Others	< 0.1

Beside two sites the PEC/PNEC ratio is < 1 indicating no risk for the food chain. Therefore **conclusion (ii)** has to be drawn for these sites.

For production site B and processing site C a PEC/PNEC ratio > 1 was calculated.. For Proc.Site C the underlying PEC_{local}(water) was calculated according to the TGD, table A 3.3 and site specific data about the effluent flow and the receiving water flow. For production site B the PEC was calculated according to the ESD IC 3. Due to the uncertainty of the underlying PEC values the assessment of secondary poisoning should be revised based on site-specific exposure data. **Conclusion (i)**

PBT assessment

2,4,4-trimethylpentene has to be considered as non biodegradable in the aquatic compartment. The highest measured BCF in fish is 868.

Based on the available BCF, it can be concluded that 2,4,4-trimethylpentene does not meet the PBT or vPvB criteria.

4 HUMAN HEALTH

4.1 HUMAN HEALTH (TOXICITY0

4.1.1 Exposure assessment

Occupational exposure

2,4,4-Trimethylpentene is primarily used as a chemical intermediate which is further processed to aldehydes, alkyl phenols or polymers. A small portion (according to the Danish Product Register, < 1 t/a) of 2,4,4-trimethylpentene is used in the metal industry in stabilising degreasing agents.

Detailed information on the production volumes is given in chapter 2.

Based on the available information, the exposure assessment reveals that handling of 2,4,4-trimethylpentene during production and further processing is the main source for occupational exposure.

On account of the low concentration of 2,4,4-trimethylpentene in degreasing agents (average concentration is 0.2 % w/w) and assuming a very low concentration of residual 2,4,4-trimethylpentene in polymers (< 0.1 %), exposure scenarios in the context of producing and handling these materials are regarded to be of minor relevance.

Occupational exposure limits have not been established.

The exposure assessment is based on measured data and literature data, expert judgement and estimations according to the EASE model (Estimation and Assessment of Substance Exposure). The exposure levels should be regarded as reasonable worst case estimates representing the highly exposed workers.

For the large-scale chemical industry, it is assumed that the production and further processing of 2,4,4-trimethylpentene is mainly performed in closed systems. Exposure occurs if the closed system is breached. Since 2,4,4-trimethylpentene is highly flammable it is to be expected that high exposure levels at the workplaces are avoided to a large extent.

Dermal exposure during the production and further processing of substances may occur during activities like drumming, sampling, cleaning, maintenance, coupling and uncoupling transfer lines and repair. With regard to dermal exposure, measured results are not available. Therefore, actual dermal exposure is assessed based on the EASE model. In general, dermal exposure is assessed as exposure to part of hands and forearms. For 2,4,4-trimethylpentene, importers and producers provide only limited information about personal protection equipment (here gloves and eye protection). Taking the lack of information into account for assessing dermal exposure the use of unsuitable gloves is presupposed. Since the extent of protection cannot be estimated the potential exposure assessed for the unprotected worker. On account of the high vapour pressure of 2,4,4-trimethylpentene (5.8 kPa), the resulting retention time of the substance on the gloves or the skin is shortened and lower levels of dermal exposure than the estimated ones are to be expected.

Summary of exposure data

Exposure scenario	Duration and frequency of activities relevant for exposure	Inhalation exposure Shift average [mg/m^3]	Dermal exposure Shift average [mg/p/day]
Production and further processing in the large scale chemical industry	shift length, daily	5.0 (1) (95th percentile)	210 (2)

1) Short term exposure is estimated to 90 mg/m^3 (duration: 45 min)
2) Dermal exposure is reduced due to the fast evaporation of the substance.

Consumer exposure

There is no evidence available on the use of 2,4,4-trimethylpentene in consumer products (GIFAS, Federal Institute for Risk Assessment (formerly BgVV), 1998), hence it is concluded that consumer exposure does not exist.

Humans exposed via the environment

The main route of indirect exposure in local scenario is the intake via ingestion of roots whilst main intake route in regional scenario is the inhalation by air

Combined exposure

[click here to insert text]

4.1.2 Effects assessment

Toxicokinetics, metabolism and distribution

No data are available on 2,4,4-trimethylpentene.

There are no studies available on oral, dermal or inhalative absorption. From the physico-chemical data (log Pow 5.0, water solubility 1.8 mg/l, molecular weight 112 g/mol, vapour pressure 57.9 hPa at 25°C) the substance shows a good oral and dermal bioavailability. It is proposed to take forward for the risk characterisation values of 100% for oral, dermal and inhalative absorption.

Results from studies on structurally similar compounds

In vitro studies on short chain olefins (n-1-octene, n-4-octene, and 3-ethyl-2-pentene) with rat liver microsomes demonstrated the conversion of olefins to diols via epoxide intermediates (Maynert et al., 1970). Similar reactions can be assumed for 2,4,4-trimethylpentene although the quantitative extent remains to be determined.

Acute toxicity

Human data on acute toxicity of 2,4,4-trimethylpentene are not available. In animal studies the acute toxicity of this olefin has proven to be low for the oral, dermal and inhalation routes of exposure with oral LD50 values > 2 000 mg/kg for rats, an inhalation LC50 value for rats of 30 000 mg/m^3/4 hours and dermal LD50 values for rats and for rabbits > 2 000 mg/kg. Thus, R phrases according to EU regulations labelling for acute oral, dermal or inhalation toxicity are not appropriate. In compilation of all toxicological information on C6-C28 olefins it is stated that aspiration may be a hazard with C6-C14 olefins.

Irritation / Corrosivity

Human data on local irritation of 2,4,4-trimethylpentene showed effects on the mucosa of nose and throat at a concentration of 465 mg/m^3. In Draize tests with rabbits according to EU test guidelines 2,4,4-trimethylpentene demonstrated mild skin irritation after a 4-hours semi-occluded application and mild eye irritation after instillation into the conjunctival sac. The lesions caused after 4 h contact with skin were increasing irritation, eschar formation and exfoliation. A compilation of unpublished toxicological test data carried out by the Shell Oil Company, linear alpha olefins containing 8 carbon atoms (CAS No. 111-66-0) are reported to cause skin irritation. However, since exposure time was 24 hours these results cannot be used to conclude R38. No conclusion could be drawn from the statement of the authors that “a proposal for classification is required” due to the lack of detailed data on skin irritation in the test data compilation. Overall, the data available does not warrant classification concerning skin and respiratory tract irritation.

Sensitisation

Human data on sensitization by skin contact or after inhalation as well as animal data on inhalation sensitization are not available. In a guinea pig maximization test a significant dermal response (a reaction more marked than the most severe among the control animals) were observed in 3/20 test animals following challenge application of the 75% substance formulation. A poorly reported Buehler test does not allow a sound assessment of the skin sensitizing properties of TMP. Overall, classification regarding sensitizing properties of TMP is not warranted.

This weak incidence, however, does not result in classification and labelling as sensitizing.

Repeated dose toxicity

In a well performed and reported study on 28-day toxicity study of 2,4,4-trimethylpentene the liver and kidneys were identified as target organs. Significantly increased liver weights (absolute and relative) associated with variations in plasma protein (males) and glucose (females) concentrations but without corroborating findings in histology were recorded in male and female rats of the 1 000 mg/kg bw/day groups. In addition, males receiving 1 000 mg/kg bw/day 2,4,4-trimethylpentene showed a clear increase in kidney weight when compared with the controls but this was also not associated with any histopathological change. The increased urea concentration may be related to a minor alteration in renal function. No relevant toxic effect was seen at 300 mg/kg bw/day (Huntingdon Life Science, 1997a).

In an oral reproductive developmental screening test of 2,4,4-trimethylpentene (OECD TG 421), renal lesions (increased kidney weight, and nephropathy induced by a dose-related increased accumulation of α_{2u}-Globulin) were seen in male Sprague Dawley CD-1 rats at doses of ≥100 mg/kg bw/day (LOAEL). This was confirmed by immunohistochemistry staining using mouse anti-α_{2u}-Globulin monoclonal antibodies. The severity of this alteration induced was moderate to severe which was identical to other chemicals such as d-limonene or the close structural analog, 2,2,4-trimethylpentane, which have also been shown to induce moderate to severe α_{2u}-Globulin nephropathy. Females receiving 1 000 mg/kg bw/day had slightly elevated kidney weights without such microscopic changes.

Kidney effects in male rats observed in the reproductive developmental screening test on 2,4,4-trimethylpentene are linked with the accumulation of α_{2u}-Globulin, a low molecular weight protein almost exclusively produced by the male rat, and are, therefore, not relevant to humans. (Huntingdon Life Sciences, 1997b; Swenberg and Schoonhoven, 2004, unpublished report).

There were no other valid data with other routes of exposure than oral to 2,4,4-trimethylpentene.

No observed adverse effect level (NOAEL):

Oral administration

For the purpose of quantitative risk assessment procedures the 28-day rat toxicity study and the reproductive developmental screening test of Huntingdon Life Science (1997a,b) were

considered to give the most reliable data on the effect levels of systemic toxicity of 2,4,4-trimethylpentene. Both studies were performed at the same dose levels in Sprague Dawley CD-1 rats.. The 28-day toxicity study was designed to the requirements of the OECD TG 407 (revised 1995). No adverse effect was observed at 100 and 300 mg/kg bw/day 2,4,4-trimethylpentene in both male and female rats in this study, therefore 300 mg/kg bw/day derived from the effect on the liver is considered to be the NOAEL for 2,4,4-trimethylpentene.

The oral reproductive developmental screening test according to OECD TG 421 showed that there is an appreciable difference between male and female rats because nephropathy observed in male rats at all 2,4,4-trimethylpentene treatment groups (LOAEL 100 mg/kg bw/day). Basophilic cortical tubules were seen in all male rats treated with 2,4,4-trimethylpentene whilst proteinaceous casts and interstitial inflammatory cells were detected only at dosages of 300 or 1 000 mg/kg bw/day. The severity of basophilic cortical tubular changes was more pronounced in males given 300 or 1 000 mg/kg bw/day than those given 100 mg/kg bw/day. α_{2u}-Globulin immunohistochemistry of male and female kidneys from this study demonstrated that the renal lesions seen in male rats in this study are a consequence of the formation of α_{2u}-Globulin (Huntingdon Life Sciences, 1997b; Swenberg and Schoonhoven, 2004, unpublished report).

In the described 4-week oral gavage toxicity study, there was no male nephrotoxicity demonstrated although 2,4,4-trimethylpentene was tested at the same dose levels. In contrast, α_{2u}-Globulin immunohistochemistry of the male kidneys in the reproductive developmental screening test exhibited that 2,4,4-trimethylpentene induces α_{2u}-globulin-associated nephropathy. A possible cause of this difference is that male rats in the reproductive developmental screening test with 2,4,4-trimethylpentene were sexually mature, compared to the pubescent males in the 4-week toxicity study. Because α_{2u}-globulin is not produced in the male rat until after puberty (Short et al., 1989 a,b; Swenberg et al., 1989), the nephrotoxicity would therefore not be expected to be present in the 4-week toxicity study.

In previous evaluations it was considered that humans are not at risk to develop this special type of nephropathy, since they seem to be unable to synthesize α_{2u}-Globulin and the urinary secretion of proteins is in general less than that of the rat. Furthermore, the proteins are either not structurally related to α_{2u}-Globulin or do not bind compounds that bind to α_{2u}-Globulin (Borghoff et al., 1991; Kohn and Melnick, 1999; Swenberg and Lehmann-McKeeman, 1999). Therefore, α_{2u}-Globulin mediated kidney effects in male rats proved in the reproductive developmental screening test with 2,4,4-trimethylpentene by immunohistochemistry staining cannot be regarded as a reliable indicator for the purpose of risk assessment for humans.

So, a NOAEL of 300 mg/kg bw/day based on the effect on the liver in male and female rats from the 28-day oral toxicity study is used as the starting point for risk characterization.

Male and female CD-1 rats (28-day oral (gavage) study) 300 mg/kg bw/day

Inhalation/Dermal application

There are no valid animal inhalation studies of 2,4,4-trimethylpentene available. At present, no studies with dermal administration of 2,4,4-trimethylpentene are available.

Human data:

No data available.

The data submitted are acceptable with respect to the basic requirements as specified in Annex VIIA of Directive 67/548/EEC. The effects seen in the repeated dose toxicity tests do not justify classification of 2,4,4-trimethylpentene with Xn and R 48 according to the criteria of Directive 93/21/EEC.

Mutagenicity

On the basis of negative results from a bacterial mutation test and a chromosomal aberration test with human lymphocytes in vitro there is no evidence of a genotoxic potential of 2,4,4-trimethylpentene. Furthermore there is no structural alert for genotoxic potential.

Carcinogenicity

There are no cancer studies on 2,4,4-trimethylpentene available. Data from mutagenicity testing give no concern on genotoxic properties of the substance.

In a reproductive developmental screening test accumulation of hyaline droplets in kidney tubules was observed in male rats known as a species and sex-specific phenomenon, which results from the excessive accumulation of α_{2u}-Globulin in renal proximal tubular epithelial cells. Results from α_{2u}-Globulin immunohistochemistry of kidneys of male and female rats from this study exhibited that oral administration of 2,4,4-trimethylpentene at daily dose of 100, 300 or 1 000 mg/kg bw/d induces α_{2u}-Globulin nephropathy identical in severity to other chemicals such is demonstrated in several studies with d-limonene or for the structurally analogous substance 2,2,4-trimethylpentane. Numerous studies with 2,2,4-trimethylpentane have been performed to examine the mechanism of inducing renal toxicity and renal cortical tumors in male rats through an α_{2u}-Globulin-associated response. 2,2,4-trimethylpentane is one of the known non-genotoxic chemicals causing α_{2u}-Globulin nephropathy. Biochemical and pathophysiological data from selected studies on 2,2,4-trimethylpentane have shown the major events linked between the α_{2u}-Globulin nephropathy and the carcinogenic outcome such as protein droplets, increased α_{2u}-Globulin, binding to α_{2u}-Globulin, cell proliferation, and initiation/promotion. These data provide convincing evidence to support a linkage between α_{2u}-Globulin nephropathy and renal tubule neoplasia, a mechanism that occurs exclusively in male rats.

Humans lack the α_{2u}-Globulin that is secreted by male rats and that is associated with this species specific form of nephropathy. Therefore, the male rat kidney response to 2,4,4-trimethylpentene is not relevant to human risk assessment. Taking into account the negative mutagenicity data it is concluded that carcinogenicity should not be an endpoint of concern for humans.

Toxicity for reproduction

Oral administration of 2,4,4-trimethylpentene to CD rats for 40 to 46 days (during premating, mating, gestation and up to lactation day 4) at dosages of up to 1 000 mg/kg bw/day did not reveal any indications for an impairment of reproductive performance and capability or peri/postnatal viability and performance of offspring up to postnatal day 4 at a screening level. (NOAEL for reprotoxic effects: 1 000 mg/kg bw/d).

4.1.3 Risk characterisation

Workers

Introduction to occupational risk assessment

There is one relevant exposure scenario for 2,4,4- trimethylpentene at the workplace which is described and discussed in section 4.1.1. Exposure routes to be considered are inhalation against 2,4,4-trimethylpentene vapours and skin contact with the liquid substance. The shift average values as reported in the summary table of the exposure assessment are taken forward to risk characterisation.

Quantitative human toxicity data are not available therefore risk considerations and estimations have to be based on animal data which have to be extrapolated accordingly. Default values concerning physiological parameters are taken according the proposal of the TGD. The toxicity profile of 2,4,4-trimethylpentene does not appear to be very marked, repeated dose toxicity reflecting the most sensitive endpoint.

There are no data from toxicokinetics to decide on absorption of 2,4,4-trimethylpentene via the dermal, oral and inhalation route. From the physico-chemical data of 2,4,4-trimethylpentene it is proposed to take forward for the risk characterisation a value of 100 % for all routes. In table 4.1.3.A the route specific exposure values are listed and the internal body burden of workers as result of combined exposure via inhalation and dermal exposure is identified. From this calculation skin contact appears to be the major source for the internal body burden of 2,4,4-trimethylpentene. It has to be kept in mind, however, that dermal absorption might be overestimated because of evaporation.

Table 4.1.3.A: 2,4,4-Trimethylpentene exposure levels which are relevant for occupational risk assessment and internal body burden

Exposure scenario	Inhalation shift average (mg/m^3)	Dermal contact shift average (mg/p/d)	Internal body burden of workers after repeated exposure (mg/p/d)		
			Inhalation[(1)]	Dermal[(2)]	Combined
1. Production and further processing	5	210[(3)]	50	210	260

[(1)] systemic availability after inhalation: default value 100%; internal body burden: shift average x 10 m^3

[(2)]systemic availability after dermal contact: default value 100%
[(3)]use of unsuitable gloves

Calculation of MOS values

MOS values are calculated as quotient of experimental NOAEL (or LOAEL) from animal studies and workplace exposure levels. Scientifically based adjustment factors are used for the stepwise extrapolation of animal data to the worker population (e.g. adaption of scenarios, route-to-route extrapolation, inter- and intraspecies extrapolation, duration adjustment and uncertainty considerations). The multiplicative combination of these different factors and an additional uncertainty factor yield the minimal MOS value as a decision mark for concern. Minimal MOS values may be different for each toxicological endpoint.

In a parallel procedure, which gives identical but more direct results, a "critical exposure level" (quotient of experimental NOAEL and the according minimal MOS) is identified for each endpoint, indicating concern if occupational exposure levels exceed this value.

In the following risks at the workplace are considered specifically for each toxicological endpoint. A summary table containing all endpoints is given at the end of this section.

Acute Toxicity

Local effects ***see irritation, no further information available***

systemic effects

conclusion (ii) There is at present no need for further information and/or testing

Acute toxicity by inhalation

From an acute inhalation test with twenty female Wistar rats per dose for 4 hours a LC50 value of 30 000 mg/m^3 is reported. The LC50 is chosen as starting point for MOS calculation.

Evaluation of the MOS values has to account for the following aspects: (i) study duration was 4 hours compared to occupational exposure of 8 hours, (ii) physiological differences between humans at rest and workers account for a factor of 1.5, (iii) for adaptation of the LC50 to an air concentration without acute toxicity a default factor of 3 is proposed, (vi) human intraspecies variation is accounted for by a factor of 5, (v) an uncertainty factor of 3 seems appropriate because the information used for the assessment is of low quality. Altogether the minimal MOS calculates to 135 (8/4 x 1.5 x 3 x 5 x 3). The critical exposure level is identified as 222 mg/m^3 (30 000 mg/m^3 / 135).

The shift average value for inhalation is reported as 5 mg/m^3. The resultant MOS value calculates to 6 000 (30 000 / 5), which is well above the minimal MOS, thus not leading to concern.

Acute toxicity by dermal and combined contact

In a rat limit test with occlusive exposure for 24 hours a dose of 2 000 mg/kg did not result in apparent signs of systemic toxicity. As starting point for MOS calculation the human dose corresponding to the dermal NOAEL in rats is calculated to 140 000 mg/person (2 000 mg/kg x 70 kg).

Evaluation of the MOS values has to account for the following aspects: (i) metabolic rate scaling from rats to humans reveals a factor of 4, (ii) human intraspecies variation is accounted for by a factor of 5, (iii) an uncertainty factor of 3 is proposed in analogy to a standard estimate, although it might assumed, on the background of the dermal NOAEL, that this factor errs on the side of caution. Altogether the minimal MOS calculates to 60 (4 x 5 x 3). The critical exposure level is identified as 2 300 mg/person (140 000 mg/person / 60).

The combined and dermal exposure level for production and further processing are reported to 215 resp. 210 mg/p/d. The corresponding MOS values calculate to 650 (140 000 / 215) resp. 666 (140 000 / 210) which give no reason for concern.

Irritation/Corrosivity

conclusion (ii) There is at present no need for further information and/or testing

Dermal and eye irritation

In studies with rabbits mild skin irritation after 4-hours semi-occluded application and slight eye irritation was observed for 2,4,4-trimethylpentene. Therefore 2,4,4-trimethylpentene is proposed to be classified as a skin irritant.

According to the exposure assessment skin contact with 2,4,4-trimethylpentene critically depends on the proper use of suitable gloves. Even though the use of PPE generally is highly accepted in the large scale chemical industry there is a possibility that unsuitable glove material is provided. On the grounds that control measures exist for 2,4,4-trimethylpentene which should be able to efficiently minimize exposure conclusion ii is proposed. However, these control measures must be implemented and complied with to reduce the risk of skin damage.

Acute respiratory irritation

No animal studies are available concerning the irritation potential of 2,4,4-trimethylpentene after inhalation. Three human volunteers were exposed for 5 minutes to a mixture of 8-Olefines (ca. 75% 2.4.4-Trimethylpentene-1 and ca. 15% 2.4.4-Trimethylpentene-2). A concentration of 465 mg/m^3 resulted in irritating effects on the mucosa of nose and throat. 279 mg/m^3 smelled distinctly but did not cause irritating effects.

The highest inhalation exposure level at the workplace is a short-term value up to 90 mg/m^3. This value is below the irritation level, although it is recognized that the duration of occupational exposure for this short term level can last up to 45 minutes. Taking into account that during all the years of use no notice of specific case reports has been given, a damage of the airways by acute irritation of TMP at the workplace is not anticipated. There is no reason for concern.

Sensitisation

conclusion (ii) There is at present no need for further information and/or testing

Skin sensitisation

From animal data no skin sensitising properties of 2,4,4-trimethylpentene can be derived. There is no concern with respect to skin sensitisation at the workplace.

Respiratory sensitisation

No information on the sensitising potential of the substance at the respiratory tract is available. For the time being a valid study to investigate respiratory sensitisation in experimental animals cannot be recommended. However, 2,4,4-trimethylpentene is not expected to be a potent respiratory sensitiser in humans according to the fact that during all the years of use no notice of specific case reports has been given. There is no concern from respiratory sensitisation at the workplace.

Repeated dose toxicity

conclusion (ii) There is at present no need for further information and/or testing

Local effects by inhalation

Extrapolation from the irritating concentration of 465 mg/m³ (5 minutes, volunteers, see chapter 4.1.2) to an irritation level for repeated exposure is considered too speculative. In the “german list of occupational exposure levels” (TRGS 900) the OELs for 32 substances which are solely classified as irritants spread over a range from 5 mg/m^3 until 1 200 mg/m^3. The

central 50% of the OELs lie between 70 and 450 mg/m^3. Looking at this distribution of OELs for irritating substances there seems to be no concern for local effects by repeated inhalation.

Local effects by dermal contact

2,4,4-Trimethylpentene has irritating properties and is proposed to be classified as a skin irritant (see chapter 4.1.2). No further information about local effects after repeated dermal contact is available.

According to the exposure assessment skin contact with 2,4,4-trimethylpentene critically depends on the proper use of suitable gloves. Even though the use of PPE generally is highly accepted in the large scale chemical industry there is no information on the suitability of used gloves. On the grounds that control measures exist for 2,4,4-trimethylpentene which should be able to minimize exposure conclusion ii is proposed. However, these control measures must be implemented and complied with to reduce the risk of skin damage.

Systemic effects by inhalation, dermal contact and combined exposure

Inhalation data concerning this endpoint are not available. From a valid 28-day oral study in rats a NOAEL of 300 mg/kg/day is reported for female animals. At higher doses (1 000 mg/kg/day) adaptive liver effects were observed (Huntigton Life Sciences 1997a). The NOAEL of 300 mg/kg/day, derived from this study is taken for the following calculations.

For systemic effects by inhalation, the NOAEL of 300 mg/kg/day is converted to an internal human dose of 21 000 mg/person/day (300 mg/kg/day x 70 kg). For this calculation 100% oral absorption is assumed. Against the background of a 100% absorption by inhalation the corresponding airborne concentration is calculated to be 2 100 mg/m^3 (21 000 mg/person/day / 10 m^3).

In evaluation of MOS values the following aspects have to be considered: (a) metabolic rate scaling from rats to humans yields a factor of 4, (b) duration adjustment from a subacute to a chronic study reveals a factor of 6, (c) human intraspecies variation is accounted for by a factor of 5. No additional uncertainty factor is applied, because the effects observed at high doses are considered to be an adaptive response with a low adverse character. Altogether the minimal MOS for systemic effects after repeated exposure calculates to 120 (4 x 6 x 5). The corresponding critical exposure level, is 17.5 mg/m^3 2 100 mg/m^3 /120) .

For the only occupational scenario (production and further processing) the distance between the inhalative exposure of 5 mg/m^3 and the critical exposure level of 17.5 mg/m^3 seems big enough to draw for conclusion ii.

Both for the dermal and oral routes of exposure a 100% absorption is assumed. For the dermal and combined exposure situation (which is predominated by skin contact) the critical exposure level of 175 mg/person/day reaches borderline. It has to be kept in mind that dermal exposure probably is lower than estimated because of significant evaporation and because of some protection by gloves (see chap. 4.1.1). For these reasons no concern will be expressed.

Mutagenicity

conclusion (ii) There is at present no need for further information and/or testing

From relevant in vitro studies there is no evidence for mutagenicity of 2,4,4-trimethylpentene. There is no reason for concern.

Carcinogenicity

conclusion (ii) There is at present no need for further information and/or testing

No cancer studies on 2,4,4-trimethylpentene are available. From the available data there is no indication for concern with respect to 2,4,4-trimethylpentene. (for further discussion see chap. 4.1.2.8)

Reproductive toxicity, fertility and developmental effects

Fertility and developmental effects by inhalation, dermal and combined exposure

conclusion (ii) There is at present no need for further information and/or testing

In an OECD screening test (OECD 421) in rats dosages up to 1 000 mg/kg/day did not reveal indication for reproductive toxicity. There is no concern with respect to this endpoint for workers.

Summary of occupational risk assessment

Table 4.1.3.D summarises the conclusions of the occupational risk assessment for 2,4,4-trimethylpentene. For all toxicological endpoints conclusion ii is expressed.

Table 4.1.3.D: Endpoint-specific overall conclusions

Toxicological endpoints		Overall conclusion
Acute toxicity	inhalation	ii
	dermal	ii
	combined	ii
Acute respiratory tract irritation		ii
Dermal and Eye irritation/ corrosivity		ii
Skin and respiratory sensitization		ii
Local effects by repeated exposure	inhalation	ii
	dermal	ii
Systemic effects by repeated exposure	inhalation	ii
	dermal	ii
	combined	ii
Mutagenicity		ii
Carcinogenicity		ii
Reproductive toxicity (fertility impairment, developmental toxicity)		ii

Risk estimation is mainly based on oral studies. Since workers are exposed either by inhalation or by skin contact, a route to route transformation is necessary. In the risk assessment a for inhalation, dermal and oral absorption a default value of 100% is assumed. On the background of the exposure assessment and the proposed critical exposure levels, endpoint-specific health risks seem to be comparably low, leading to no concern for the only scenario 1 (production and further processing).

Consumers

Since consumer exposure does not exist, a health risk of consumers regarding Acute toxicity, Irritation, Corrosivity, Sensitization, Repeated dose toxicity, Mutagenicity, Carcinogenicity, and Reproductive toxicity is not expected.

Humans exposed via the environment

When considering possible risks to human health arising from indirect exposure to 2,4,4-trimethylpentene via the environment the key areas of concerns are for repeated dose toxicity, mutagenicity, carcinogenicity, and reproductive toxicity. The performed MOS calculation showed no concern for the general population regarding the above endpoints

5 RESULTS

5.1 ENVIRONMENT

Environment

Conclusion (i) There is a need for further information and/or testing.

- Releases into the waste water treatment plant for both production sites and for 23 out of 25 processing sites.
- Releases into surface waters during production for both production sites and for 23 out of 25 processing sites.
- Releases into the sediment for both production sites and for 23 out of 25 processing sites.
- Site specific exposure information for 2 sites for refinement of the assessment of non compartment specific effects relevant for the food chain. (probably covered by previous information requests)
- Activated sludge respiration inhibition test (OECD 209)
- Prolonged daphnia magna reproduction test (OECD 211)

Test and exposure information requirements have been agreed at TC NES IV/07.

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

- Releases into the waste water treatment plant for processing sites A and B.
- Releases into surface waters during production for processing sites A and B.
- Releases into the sediment for processing sites A and B.
- Releases into the atmosphere.
- Releases into the terrestrial compartment.
- Non compartment specific effects relevant for the food chain for one production site and 24 out of 25 processing sites.
- 2,4,4-trimethylpentene does not meet the PBT criteria.

5.2 HUMAN HEALTH

5.2.1 Human health (toxicity)

Workers

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

The toxicity profile of 2,4,4-trimethylpentene does not appear to be very marked. In combination with the dermal and inhalation exposure levels at the workplace no occupational scenario of concern has been identified.

Consumers

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

Humans exposed via the environment

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