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TOLUENE

CAS No: 108-88-3

EINECS No: 203-625-9

Summary Risk Assessment Report

2003 **Special Publication I.02.156**

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SUMMARY RISK ASSESSMENT REPORT

Final report, 2003

Denmark

Rapporteur for the risk assessment report on toluene is the Danish Environmental Protection Agency.

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PREFACE

This report provides a summary, with conclusions, of the risk assessment report of the substance toluene that has been prepared by Denmark 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

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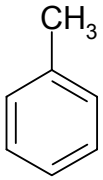
1 GENERAL SUBSTANCE INFORMATION

1.1 IDENTIFICATION OF THE SUBSTANCE

CAS-No.:	108-88-3
EINECS-No.:	203-625-9
IUPAC name:	Toluene
Synonyms:	Methylbenzene, phenyl methane, toluol, methyl benzol, methacide
Molecular formula:	$C_7 H_8$
Molecular weight	92.15 g/mole
Structure:	



1.2 PURITY/IMPURITIES, ADDITIVES

Purity:	≥ 99%	
Impurity:	benzene (CAS: 71-43-2)	≤0.02% w/w
	xylene, mixed isomers (CAS: 1330-20-7)	≤0.02% w/w
Additives:	No information	

1.3 PHYSICO-CHEMICAL PROPERTIES

Physical state:	liquid
Melting point:	-95°C
Boiling point:	110.6°C at 1,013 hPa
Relative density:	0.871 g/cm^3 at 15°C
	0.8669 g/cm^3 at 20°C
Vapour pressure:	3,000 Pa at 20°C
	3,800 Pa at 25°C
Surface tension:	27.93 mN/m at 25°C
Water solubility:	515 mg/l at 20°C
	534.8 mg/l at 25°C
Octanol/water (Kow):	log Kow = 2.65
Flash point	4°C (closed cup)
Auto flammability	535°C
Air conversion factor	1 ppmv ≅ 3.83 mg/m^3 at 20°C and 1013 hPa
	1 ppmv = 3.75 mg/m^3 at 25°C and 1 atm
	1 mg/m^3 = 0.266 ppm at 25°C and 1 atm
Viscosity	>0.56 mPa s (>0.64 x 10^{-6} m^2/sec) at 25°C
	0.424 mPa s (0.49 x 10^{-6} m^2/sec) at 50°C

1.4 CLASSIFICATION

The classification and labelling of toluene has been agreed at technical levels to be listed in Annex I to Directive 67/548/EEC following the adoption of the 29th Adaptation to Technical Progress, as follows:

Classification

F, R11	Highly flammable.
Repr.Cat.3; R63	Possible risk of harm to the unborn child.
Xn; R48/20-65	Harmful: danger of serious damage to health by prolonged exposure through inhalation. May cause lung damage if swallowed.
Xi; R38	Irritating to skin.
R67	Vapours may cause drosinessa and dizziness.

Labelling

F; Xn
R: 11-38-48/20-63-65-67
S: (2-)36/37-46/62

Environment: No classification.

R38 is justified because significant, persisting skin inflammation (score for erythema >2 at 72 hours and 7 days) has been observed in a skin irritation study in animals (Annex V B4 study), and because toluene has a degreasing effect on human skin (see Section 4.1.2.3.1).

R48/20 is justified because toluene causes several types of serious toxic effects after inhalation. Toluene-induced chronic impairment of auditory function has been demonstrated in a number of animal studies. This has been substantiated by morphological evidence of cell loss in the rat cochlea. Existing data suggest that humans are sensitive to this effect at exposure levels, which may be encountered in the working environment.

Toluene causes irreversible changes, including neuron loss, in the central nervous system of animals. In humans severe central nervous system effects including brain atrophy have been found at very high exposure levels. Neuropsychological effects at working environment exposure levels have been demonstrated.

Toluene causes an increase in the occurrence of non-malignant pituitary tumours in mice.

R65 is justified on the basis of viscosity and surface tension. A viscosity value at 40ºC has not been found.

However, as a 25°C value of >0.56 mPa·s (>$0.64 \cdot 10^{-6}$ m^2/sec), and a 50°C value of 0.424 mPa·s ($0.49 \cdot 10^{-6}$ m^2/sec) have been found (Lide, 1996), it can be assumed that toluene would fulfil the criteria for R65 of viscosity below $7 \cdot 10^{-6}$ m^2/sec at 40°C. The criteria for R65 state that substances with surface tension above 33 mN/m at 25ºC not necessarily should be classified, but since toluene has been reported to have a surface tension of 27.93 mN/m at 25ºC (Lide, 1996) no exemption is warranted.

R67 is justified since data from experimental exposure of human volunteers show that dizziness and sleepiness are experienced at air levels substantially below the level of 20 mg/l/4h mentioned in the criteria for R67 (for toluene this equals 5,300 ppm). In rats exposed to 20 mg/l/4h in the BASF (1980) study rocking gait and narcosis were observed.

Toluene was classified as Reproductive Category 3 (**R63**) for fertility at the Commission Working Group Meeting on Classification and Labelling of Dangerous Substances. It will be listed in Annex I to Directive 67/548/EEC following the adoption of the 29th Adaptation to Technical Progress.

2 GENERAL INFORMATION ON EXPOSURE

Toluene occurs naturally and is a component of crude oil. Most of the refinery streams containing toluene are used as a base or blending feedstock to produce motor gasoline. The commercial toluene is isolated from the refinery streams and is used as an intermediate in closed systems to manufacture other chemicals and as a solvent carrier in paints, thinners, adhesives, inks and pharmaceutical products and as an additive in cosmetic preparations. Thus, toluene is used in a large number of industrial branches and consumer products.

As an intermediate in the chemical industry, toluene is used as a raw material in the organic synthesis of other chemicals e.g. benzaldehyde, benzene, benzoic acid, benzyl chloride, phenol, toluene diisocyanate, xylene and other derivatives used as dye intermediates, resin modifiers and germicides. Toluene is also used in the synthesis of explosives (TNT), vinyl toluene, cresols and flavouring agents.

Toluene is used as a solvent for paints, lacquers, gums, resins in the extraction of various substances from plants. According to the main manufacturers approximately 20% of isolated toluene sold as solvent is used in paints, inks, thinners, coatings, adhesives, degreasers and other formulated products requiring a solvent carrier. Because of the vast amount of products in which toluene is used either as intermediate or as solvent (the main uses), toluene could be allocated to most industrial categories.

Toluene is a high production volume substance. In 1995, the production volume of toluene in the EU was 2,600 kTonnes. Import and export volumes were imprecise but the EU consumption is estimated to be approximately 2,750 kTonnes (1995 values).

Toluene may be released to the environment when substances containing toluene or preparations thereof are produced, distributed and handled. Besides the releases from use, distribution and handling of commercial toluene are the releases from natural sources (volcanoes, forest fires, etc.).

An important exposure of toluene in the environment is from the release of toluene from the combustion of fuels. As these latter sources may well be significantly higher than releases from manufactured toluene, they may be the main source for background concentrations and should be considered. The annual consumption of gasoline in the EU is approx. 120 million tonnes containing approximately 13,7 million tonnes of toluene. However, the production and use of gasoline is not included in the risk assessment of toluene although mentioned for illustrative purposes.

3 ENVIRONMENT

3.1 ENVIRONMENTAL EXPOSURE

3.1.1 Environmental releases

Toluene may be released into the environment during its production, processing (i.e. manufacturing of other chemical substances), formulation (i.e. mixing into other substances) and use. The atmospheric compartment is estimated to be the primary recipient based on the high vapour pressure. However, also release to surface waters and soil may occur.

Toluene is used and emitted in large quantities. Because toluene is a volatile organic compound, the emissions mainly take place into the air and the emissions to soil and water partly leads to re-emission to the air. As a result, most of the toluene is found in the air compartment.

Site-specific information from toluene production and processing sites has been gathered by the main manufacturers who have collected responses by means of a questionnaire from the involved industrial sites. The environmental exposure assessment was based on site-specific data when available, and Technical Guidance Document (TGD) default values when such data were unavailable. The site-specific data on production, and combined production and processing sites cover an acceptable number of sites to be used as an alternative to generic scenarios according to the TGD covering "upstream" release and exposure.

Production sites

For production sites, 19 sites were identified covering the production of 2,080 Ktonnes of toluene. The emissions to air vary from 0 to almost 7,000 kg/day and the emission to water varies from 0 to 5,700 kg/day. It is noted that the highest values were based on the use of TGD default values.

Production and processing sites

For sites where production and processing take place on the same site, 6 sites were identified covering 509 kTonnes of toluene production and processing of 494 kTonnes of toluene.

The emissions to air vary from 0.08 to almost 1,000 kg/day and the emission to water varies from 3 to 1,600 kg/day. It is noted that the highest values were based on the use of TGD default values.

Processing sites

Of processing sites, 6 sites are included in the main manufacturer study. The 6 sites cover the processing of approximately 21 kTonnes of toluene. It is noted that the highest values were based on the use of TGD default values.

Thus, the site-specific information covers the production of 2,080 + 509 = 2,589 kTonnes toluene and processing of 494 + 55 = 549 kTonnes toluene.

Downstream uses

For "downstream" uses site-specific information obtained by the main manufacturers was too scarce to be used as an alternative to default environmental release and exposure assessments according to the TGD. Therefore, downstream uses have been separated into industrial

categories and use categories according to information from main manufacturers and releases estimated according to the TGD by EUSES ver.1.0. The total continental and regional emissions were estimated to be:

	Continental	Regional
Total emission to air	1,090 t/d	122 t/d
Total emission to wastewater	180 t/d	20 t/d
Total emission to surface water	77 t/d	8.6 t/d
Total emission to industrial soil	2.4 t/d	0.3 t/d

3.1.2 Environmental fate

Toluene is estimated to be stable to hydrolysis and photo-degradation in surface water. In air, toluene is exposed to indirect photolysis by photochemical oxidative degradation with a half-life of 2 days.

Toluene is readily biodegradable, but simulation types of data suggest a decreased biodegradation at environmentally realistic low concentration in surface water: the half-life in sewage treatment plants (STP) is estimated to be 0.0289 days (rate constant of 1 $hour^{-1}$) and in surface water around 30 days. Only scarce data are available for degradation in soil, and the half-life is estimated to be 90 days under aerobic conditions according to "the realistic worst-case" concept. Because no information was available regarding anaerobic degradation at environmental concentrations and conditions, degradation in anaerobic sediment has been set to a half-life of 900 days according to the TGD.

Toluene has a low-adsorption capacity with an estimated Koc of 177 indicating a moderate to high-mobility potential. The log Kow 2.65 indicates a low bioaccumulation potential, which was confirmed in tests where BCF in two fish species were 13 and 90, respectively. The elimination half-life was <2 days in fish. Thus toluene is estimated to be unlikely to bioconcentrate in the aquatic food chain.

3.1.3 Predicted environmental concentrations

Aquatic compartment

Based on the site-specific emission information from the industry, the predicted environmental concentration (PEC) at production, production and processing and main processing sites are given in summary:

Table 3.1 Summary statistics for site-specific local surface water PECs (mg/l)

Site specific	Mean	Median	Max	N
Production	0.034	0.0000057	0.590	19
Production + processing	0.139	0.000253	0.830	6
Processing	0.312	0.00689	1.830	6

Note: The highest values are estimated at the sites where no site-specific data were provided. As a result the local PEC is conservatively biased in comparison to PEC estimates for other sites where some relevant site-specific data were provided. A similar concern applies to local air and soil PECs summarised below.

The dilution factor is essential when calculating the environmental concentration. The site-specific data from the industry (APA) demonstrates the variability in dilution. However, due to missing specified data, the TGD default dilution factor has been used for the generic scenarios not covered by APA, i.e. a dilution factor of 10 is used in the remaining scenarios.

Table 3.2 Generic scenarios for downstream uses: Estimated concentrations in local STP effluent, surface water, sediment, air and soil during emission episodes according to the TGD

Scenario	Life stage	C_{effl} (mg/l)	PEC_{water} (mg/l)	PEC_{sed} (mg/kg ww)	$PEClocal_{air,ann}$ (µg/m³)	$PEClocal_{soil}$ (mg/kg)
1: Intermediates	Processing	13.2	1.320	6.11	56.7	3.64
2: Basic chemicals	Formulation	5.43	0.549	2.54	384	1.51
	Processing	110	9.040	50.80	2410	30.5
3: Mineral oil and fuel	Formulation (10%)	3.51	0.357	1.65	250	0.977
	Private use	0.0013	0.004	0.030	13.8	0.0007
4: Polymers	Formulation (10%)	1.23	0.129	0.597	37.3	0.341
	Processing	0.05	0.011	0.0522	24.1	0.0145
5: Paint, etc.	Formulation (50%)	1.74	0.180	0.832	51.6	0.482
	Private use	0.0007	0.006	0.029	2.8	0.0002
6: Basic chemical	Formulation	1.63	0.169	0.780	117	0.452
	Processing	49.4	4.940	22.8	1090	13.7
7: Personal / domestic	Formulation	0.22	0.028	0.131	18.3	0.061
	Private use	0.047	0.011	0.0505	3.0	0.013
8: Pulp, paper and board	Formulation	0.596	0.066	0.304	44.7	0.166
	Processing	0.161	0.022	0.103	883	0.067
9: Textile	Processing	4.06	0.413	1.91	4.9	1.120
10: Other	Processing	0.27	0.033	0.154	202	0.080

$PEC_{regional}$ and $PEC_{continental}$ for water and sediment

The continental and regional concentrations of toluene were calculated with the EUSES v.1.0 programme. The regional and continental dimensions and properties as set out in the TGD are used.

	Continental	**Regional**
PEC surface water:	0.68 µg/l	6.26 µg/l
PEC sediment	3 µg/kg ww	26 µg/kg ww

It should be noted that the estimated concentrations are based on isolated toluene whereas the measured values include other sources of toluene as well, e.g. non-isolated toluene from combustion processes, etc. The estimated concentrations should therefore be expected to be in the lower end of the measured range, which seems to be the case for sediments but not for surface waters. However, including continental emissions of non-isolated toluene from the use of gasoline resulted in small insignificant increases in the continental and regional PECs.

Atmosphere

The atmosphere was considered the primary area for toluene releases based on its volatile character. This was confirmed by measurements in air. The measured and estimated PECs in air based on site-specific information are presented below. The PECs from downstream processing and use were given in **Table 3.2**.

Table 3.3 Summary statistics for site-specific PECs in air (mg/m^3) at production, production + processing and processing sites

Site specific	Mean	Median	Max	N
Production	0.333	0.0478	1.870	19
Production + processing	0.102	0.0497	0.267	6
Processing	0.116	0.0117	0.628	6

The estimated PECcontinental in air was 0.91 µg/m^3 and the PECregional in air 2.79 µg/m^3.

Because the continental and regional PECs are based on the commercial product toluene, the values are expected to underestimate the actual PEC including the contribution from combustion processes, gasoline, etc. The EUSES estimations are as expected in the lower end of the measured range. Including continental emissions of non-isolated toluene from the use of gasoline would result in an estimated PEC continental in air to be 2.35 µg/m^3 and the PEC regional in air to be 6.92 µg/m^3.

The inclusion of the continental emission of non-isolated toluene from the use of gasoline increases the continental and regional PECs with a factor 2-3 for the air environment. It should be noted that other major sources of toluene are not included in this evaluation e.g. emissions from power plants.

Terrestrial compartment

Toluene is not applied directly to the soil or crops, but it does occur in sewage sludge and thus may be applied to soil. The main manufacturers have informed that most sludges from production and processing are incinerated or landfilled, however, in a few instances it does end up on agricultural soil. The fate of the downstream users are unknown but the measured values of toluene in municipal sludge indicate that toluene finds its way to sludge, which may be applied to agricultural soil. Toluene is also released to air and may undergo deposition to soil. The PEC$local_{soil}$ is a summation of the concentration due to these two separate processes.

The values of PEC local soil presented in **Table 3.2** are referring to the generic downstream users.

The site-specific local concentration in soil for production sites and for production + on-site processing is based on air deposition alone since sludge is incinerated or landfilled. For site-specific processing sludge may be applied to soil at three sites and the sludge concentration and the resulting estimated soil concentration are presented (**Table 3.4**).

Table 3.4 Summary statistics for site-specific local PEC in soil (mg/kg dry) at production, production + processing and processing sites

Site specific		Mean	Median	Max	N
Production	Air deposition only	$7.12 \cdot 10.3$	$1.04 \cdot 10^{-3}$	$4.49 \cdot 10^{-2}$	19
Production + processing	Air deposition only	$1.77 \cdot 10.3$	$6.67 \cdot 10^{-4}$	$5.19 \cdot 10^{-3}$	6
Processing	Air deposition only	$2.10 \cdot 10.3$	$5.83 \cdot 10^{-5}$	$1.21 \cdot 10^{-2}$	6
	Air+sludge deposition	$2.50 \cdot 10^{-1}$	$2.45 \cdot 10^{-1}$	$4.67 \cdot 10^{-1}$	3

The continental and regional concentrations in soil were estimated with and without the contribution from gasoline:

PEC soil	**Continental**	**Regional**
PEC in agricultural soil	0.079 µg/kg ww	0.703 µg/kg ww
PEC in natural soil	0.011 µg/kg ww	0.033 µg/kg ww
Including continental emissions of non-isolated toluene from the use of gasoline		
PEC in agricultural soil	0.095 µg/kg ww	0.749 µg/kg ww
PEC in natural soil	0.028 µg/kg ww	0.081 µg/kg ww

The inclusion of the continental emission of non-isolated toluene from the use of gasoline has only little effect on continental and regional PECs for the soil compartment except for natural soils where PECs are increased with a factor 2-3.

Measured and estimated environmental concentrations

It is noted that the measured environmental concentrations also reflect other sources than the sources from current industrial production and processing of isolated toluene which are alone covered by this risk assessment report. The other sources of toluene are e.g. toluene emitted in exhaust gasses and natural sources such as forest fires and volcanos. Emissions from other sources to air may later be re-deposited to the aquatic and terrestrial environment. Therefore, besides the general uncertainty regarding the proximity of the sites of the measurements to the emission sources and other uncertainties and variability in the monitoring data, the lack of a general discrepancy between the measured and estimated environmental concentrations presented in the previous sections may be surprising. However, the lack of general disagreements in most of the previous sections may illustrate that the employed PEC estimations, which only takes the toluene emissions from industrial production and processing but not toluene emissions from other sources (such as toluene in exhaust gases) into account, actually are performed according to a realistic worst-case concept.

3.2 EFFECTS ASSESSMENT

3.2.1 Aquatic compartment (incl. sediment)

Aquatic organisms

Toluene has been tested in a wide variety of aquatic species. Due to the nature of the substance (high volatility) only a few of the studies were considered valid. The acute toxicity

to fish ranges from an LC50 of 5.4 for Pink salmon to 26 mg/l for Fathead minnow. The lowest valid acute toxicity for *Daphnia magna* was 11.5 mg/l. Other crustaceans ranged from 3.5 mg/l for *Crangon franciscorum* to 33 mg/l for *Artemia salina*. For algae, the acute toxic EC50 was not available in valid tests but in two species (*Selenastrum capricornutum* and *Skeletonema costatum*), the NOECs were 10 mg/l. The long-term toxicity NOEC for fish ranged from 1.4 mg/l for *Oncorhynchus kisutch* to 4 mg/l for *Pimephales promelas*. The chronic NOEC for *Daphnia magna* ranged from 0.53 mg/l to 1.0 mg/l and for *Ceriodaphnia dubia* 0.74 mg/l.

An assessment factor of 10 was used to calculate a predicted no effect concentration (PNEC) for toluene in the aqueous environment since long-term data were present for fish, crustacea and algae.

$PNEC_{aquatic\ organisms}$ = 0.074 mg/l.

Microorganisms

The EC50 for respiration of microorganisms in STPs was 110 mg/l and the EC50 for *Nitrosomonas* (nitrification) was observed to be 84 mg/l. However, inhibition of microbial nitrification is the preferred endpoint for STPs, because this process is more sensitive than inhibition of microbial respiration. Using the inhibition of nitrification and the assessment factor of 10 results in a:

$PNEC_{microorganisms}$ = 8.4 mg/l.

3.2.2 Atmosphere

Direct effects on plants

Toluene seems not to be of concern with regard to plant toxicity exposed via air except at very high concentrations. No formal PNEC will be established because of lack of appropriate long-term studies, however, the NOEC of 60 mg/m^3 based after an exposure period of 14 days can be used to evaluate the risk for terrestrial plants exposed via air.

Indirect effects

Toluene contributes to ozone formation in the near surface atmosphere. The relation between the ozone precursors in terms of VOC and thus toluene and ozone formation is complicated and depends on the speciation and concentrations of VOC, NOx, solar radiation and OH-radicals. Within Europe very different environmental conditions prevail i.e. NOx / VOC ratio and solar radiation but also different meteorological conditions (wind speed etc.) meaning that a concentration of a VOC may lead to very different ozone concentrations.

For example, a change in the VOC concentration may affect the ozone formation to a small extent in some parts of Europe (NO_x limited region), while in other parts of Europe a change in the VOC concentration will lead to a considerable change in the ozone formation (high NO_x regions). Thus there is no simple relationship between the VOC and NO_x concentrations and the resulting tropospheric ozone creation. Nevertheless, the Member countries in UNECE have agreed to use a Photochemical Ozone Creation Potential (POCP) factor system where the individual VOC's potential to create ozone is given as a relative equivalence factor expressed as g ethylene / g VOC (gas). Two sets of factors exist corresponding to a low and high NO_x situation.

The POCP of toluene is 0.47 g C_2H_4/g toluene gas (4 days) according to one reference and another gives POCP equivalence factors of 0.5 g C_2H_4/g toluene gas in a low NO_x situation and 0.6 g C_2H_4/g toluene gas in a high NO_x situation based on the same study.

Green plants, animals and humans seem to be equally sensitive to the toxic effects of ozone. Therefore, a more in-depth evaluation of the contribution of toluene to the complex issue of air quality should more appropriately be dealt with by authorities regulating air quality rather than as a part of this substance specific risk assessment.

3.2.3 Terrestrial compartment

For the terrestrial compartment, the earthworm acute EC50 was >150 but <280 mg/kg soil, NOEC values for mortality and cocoon production were ≤150 and <280 mg/kg, respectively, whereas a NOEC based on visual inspection was between 15 and 50 mg/kg soil. For plants, a yield decrease was observed in *Lactuca sativa* at 1,000 mg/kg. For soil microorganisms, NOEC for nitrification was <26 mg/kg soil dw.

For the terrestrial environment, an assessment factor of 50 was used because two long-term tests on soil organisms were available.

$PNEC_{soil}$ = 15/50 = 0.3 mg/kg.

For comparison this value is in close agreement with the estimation of $PNEC_{soil}$ employing the equilibrium partitioning method: $PNEC_{soil\ eql}$ = 0.26 mg/kg w/w.

3.2.4 Secondary poisoning

Not relevant because the worst-case BCF for fish is < 100. Furthermore, the substance has not a high lipophilicity and seems to be readily degradable.

3.3 RISK CHARACTERISATION

3.3.1 Aquatic compartment (incl. sediment)

The potential local risk for aquatic organisms from site-specific production, production + processing and processing is presented below. A potential risk is assumed when the PEC/PNEC ratio is above 1.

Site-specific scenarios

Table 3.5 Summary site-specific PEC/PNEC ratios for surface water at production, production + processing and processing sites

Site specific	Mean	Median	Max	N
Production sites	0.5	<0.01	8.0	19
Production+ processing	1.9	<0.01	11.2	6
Processing	4.2	0.1	24.7	6

Conclusion (iii) applies for two production sites, one combined production and processing site, and one site-specific processing site.

Conclusion (ii) applies for all but two production sites, all but one combined production and processing site, and all but one processing site.

Downstream scenarios

The downstream scenarios are mostly generic based on the use categories agreed on by industry and the rapporteur.

Table 3.6 PEC/PNEC ratios for local surface water at downstream use categories

Scenario	Life stage	$PEC/PNEC_{water}$	Conclusion	$PEC/PNEC_{microorg.}$	Conclusion
1: Intermediates	Processing	17.8	**iii**	1.57	**iii**
2: Basic chemicals	Formulation	7.4	**iii**	0.65	ii
	Processing	122.2	**iii**	13.10	**iii**
3: Mineral oil and fuel	Formulation (10%)	4.8	**iii**	0.42	ii
	Private use	0.1	ii	<0.01	ii
4: Polymers	Formulation (10%)	1.7	**iii**	0.15	ii
	Processing	0.2	ii	0.01	ii
5: Paint, etc.	Formulation (50%)	2.4	**iii**	0.21	ii
	Private use	0.1	ii	<0.01	ii
6: Basic chemical	Formulation	2.3	**iii**	0.19	ii
	Processing	66.8	**iii**	5.88	**iii**
7: Personal / domestic	Formulation	0.4	ii	0.03	ii
	Private use	0.2	ii	0.01	ii
8: Pulp, Paper and board	Formulation	0.9	ii	0.07	ii
	Processing	0.3	ii	0.02	ii
9: Textile	Processing	5.6	**iii**	0.48	ii
10: Other	Processing	0.5	ii	0.03	ii

For downstream uses the scenarios in **Table 3.60** indicate that locally there may be risks for aquatic organisms for:

- intermediates, processing (scenario 1),
- basic chemicals (including processing aid, “extraction” agent or solvent), processing and formulation (scenarios 2 and 6),
- mineral oil and fuel formulation (scenario 3),
- formulation of polymers (scenario 4),
- formulation of paints (scenario 5),
- textile processing (scenario 9).

For these scenarios, there is a **conclusion (iii).**

This conclusion applies for the generic scenarios of most large identified processors that presumably cover the major part of the total tonnage processed in the EU. The conclusion is

based on the recognition that it is unlikely that sufficient information can be gathered and be considered representative for the numerous downstream uses to exclude a risk.

Microorganisms

The results in **Table 3.6** indicate that locally there may be risks for microorganisms in STPs from one site-specific processing site and some downstream uses of toluene (**conclusion (iii)**):

- industry use as an intermediate, processing (scenario 1),
- industry use as basic chemicals (scenarios 2 and 6).

3.3.2 Atmosphere

Due to the high vapour pressure of toluene the atmosphere is a major recipient of toluene. Atmospheric concentrations on a regional scale are in the $\mu g/m^3$ level, while on a local scale at the perimeter of production/processing plants average levels are estimated to be at $\mu g/m^3$ level up to more than 1 mg/m^3. Local atmospheric concentrations due to emission of toluene in exhaust gases expelled from motor vehicles are expected to be less than the atmospheric concentrations in close proximity of larger industrial plants.

Some information regarding short-term effects of toluene on plants has been obtained indicating little concern at concentrations below 60 mg/m^3. No information on possible effects caused by long-term exposure (more than 14 days) is at present available. The TGD (1996) does not give guidance on how to assess the risk for plants exposed via air e.g. how to apply assessment factors. However, taking the available information into account it seems reasonable to conclude that there is no risk for plants at the present exposure levels.

It is known that toluene contributes to tropospheric VOC and contributes to the tropospheric formation of ozone and volatile air pollutants. The photochemical formation of ozone and other compounds depends on the emission of all VOCs and other compounds in a complex interaction with other factors. Thus the effects on the ozone creation of emissions arising from the production and use of the isolated commercial product toluene may differ substantially between different regions in the EU.

The industrial use of the commercial product toluene contributes significantly to the overall emission of toluene, however, emission of toluene in exhaust gases expelled from motor vehicles seems to be the largest single source. The current risk assessment does not cover non-isolated toluene. Thus the evaluation of the possible effects of emission of toluene from motor vehicles is outside the scope of this risk assessment.

Effects of ozone exposure are documented on plants, animals and humans. The vegetation and wildlife may be severely affected by ozone incidences and toluene is likely to contribute to these effects. However, no simple relationship has been established between the proportion of toluene to total NMVOC emitted - and thus also between emissions arising from the use of the commercial product toluene - and the creation of tropospheric ozone.

Results for the atmosphere

Conclusion (iii) applies in the context of the Regulation of Existing Substances to the contribution of the commercial product toluene to the formation of ozone and other harmful substances i.e. smog formation.

Conclusion (ii) applies to plants exposed via air.

3.3.3 Terrestrial compartment

The potential risk to the local soil compartment is summarised below. Sites where sludge is incinerated, only toluene contribution from air deposition is included.

Table 3.7 Site-specific risk characterisation for soil (PEC/PNEC ratio)

Site specific		Mean	Median	Max	N
Production	Air only	0.02	<0.01	0.15	19
Production + processing	Air only	<0.01	<0.01	0.02	6
Processing	Air only	<0.01	<0.01	0.04	3
	Air + sludge	0.8	0.85	1.6	3

Downstream uses

Table 3.8 PEC/PNEC local soil for downstream uses

Scenario	Life stage	$PEC/PNEC_{terrestrial}$	Conclusion
1: Intermediates	Processing	12	**iii**
2: Basic chemicals	Formulation	5	**iii**
	Processing	102	**iii**
3: Mineral oil and fuel	Formulation (10%)	3.3	**iii**
	Private use	0.002	ii
4: Polymers	Formulation (10%)	1.1	**iii**
	Processing	0.1	ii
5: Paint, etc.	Formulation (50%)	1.6	**iii**
	Private use	<0.01	ii
6: Basic chemical	Formulation	1.5	**iii**
	Processing	30.5	**iii**
7: Personal / domestic	Formulation	0.2	ii
	Private use	0.04	ii
8: Pulp, Paper and board	Formulation	0.6	ii
	Processing	0.2	ii
9: Textile	Processing	3.7	**iii**
10: Other	Processing	0.3	ii

Results for the terrestrial compartment

Conclusion (iii) applies to one processing site with sludge application to soil. This conclusion applies to industrial use as intermediate (scenario 1) and basic chemicals (scenario 2 and 6), mineral oil and fuel formulation (scenario 3), formulation of polymers (scenario 4), formulation of paints (scenario 5), and textile processing (scenario 9).

Conclusion (ii) applies to site-specific production, production+processing and processing sites and some downstream uses.

3.3.4 Secondary poisoning

Not considered relevant.

3.3.5 Humans exposed via the environment

The human intake from indirect exposure in local and regional scenarios is presented in the table below. The estimations were performed according to EUSES. In the local assessment, all food products are derived from the vicinity of one point source, in the regional assessment, all food products are taken from the regional model environment. The local and regional environments are not actual sites or regions but standardised environments as defined in the TGD.

Table 3.9 Estimated human intake of toluene in mg/kg bw/d by route and downstream scenarios

Scenario	Drinking water	Fish	Leaf crops	Root crops	Meat	Milk	Air	Total intake mg/kg/d
Local								
1: Processing	0.0155	0.161	$2.02 \cdot 10^{-5}$	$1.68 \cdot 10^{-5}$	$1.78 \cdot 10^{-6}$	$2.35 \cdot 10^{-6}$	0.0121	0.189
2: Formulation	0.0065	0.0669	$1.37 \cdot 10^{-4}$	0.0025	$2.89 \cdot 10^{-6}$	$3.81 \cdot 10^{-6}$	0.0824	0.158
2: Processing	0.129	1.34	$8.62 \cdot 10^{-4}$	0.0497	$2.64 \cdot 10^{-5}$	$3.48 \cdot 10^{-5}$	0.517	2.03
3: Formulation	0.0042	0.0436	$8.91 \cdot 10^{-5}$	0.00163	$1.88 \cdot 10^{-6}$	$2.48 \cdot 10^{-6}$	0.053	0.103
3: Private use	0.0001	0.0009	$4.91 \cdot 10^{-6}$	$3.49 \cdot 10^{-6}$	$9.04 \cdot 10^{-8}$	$1.19 \cdot 10^{-7}$	0.0030	0.004
4: Formulation	0.0015	0.0159	$1.33 \cdot 10^{-5}$	$5.57 \cdot 10^{-4}$	$3.65 \cdot 10^{-7}$	$4.81 \cdot 10^{-7}$	0.008	0.026
4: Processing	0.0001	0.0015	$8.60 \cdot 10^{-6}$	$2.79 \cdot 10^{-5}$	$1.57 \cdot 10^{-7}$	$2.08 \cdot 10^{-7}$	0.0052	0.007
5: Formulation	0.0021	0.022	$1.84 \cdot 10^{-5}$	$7.88 \cdot 10^{-4}$	$5.06 \cdot 10^{-7}$	$6.67 \cdot 10^{-7}$	0.0111	0.036
5: Private use	0.0001	0.0009	$9.96 \cdot 10^{-7}$	$6.01 \cdot 10^{-7}$	$2.50 \cdot 10^{-8}$	$3.30 \cdot 10^{-8}$	0.0006	0.0016
6: Formulation	0.0020	0.0207	$4.18 \cdot 10^{-5}$	$7.53 \cdot 10^{-4}$	$8.83 \cdot 10^{-7}$	$1.16 \cdot 10^{-6}$	0.0251	0.0486
6: Processing	0.0581	0.601	$3.88 \cdot 10^{-4}$	0.0223	$1.19 \cdot 10^{-5}$	$1.57 \cdot 10^{-5}$	0.233	0.914
7: Formulation	0.00018	0.0188	$6.53 \cdot 10^{-6}$	$6.6 \cdot 10^{-4}$	$2.78 \cdot 10^{-7}$	$3.66 \cdot 10^{-7}$	0.0039	0.025
7: Private use	0.00016	0.0016	$1.08 \cdot 10^{-6}$	$2.13 \cdot 10^{-5}$	$3.25 \cdot 10^{-8}$	$4.29 \cdot 10^{-8}$	0.0006	0.0024
8: Formulation	0.00079	0.0082	$1.59 \cdot 10^{-5}$	$2.76 \cdot 10^{-4}$	$3.39 \cdot 10^{-7}$	$4.48 \cdot 10^{-7}$	0.010	0.0188
8: Processing	0.00028	0.0029	$3.15 \cdot 10^{-4}$	$2.80 \cdot 10^{-4}$	$5.29 \cdot 10^{-6}$	$6.98 \cdot 10^{-6}$	0.189	0.193
9: Processing	0.0017	0.0072	$1.78 \cdot 10^{-6}$	$1.81 \cdot 10^{-3}$	$1.86 \cdot 10^{-7}$	$2.45 \cdot 10^{-7}$	0.0011	0.0117
10: Processing	0.0004	0.0038	$7.22 \cdot 10^{-5}$	$1.68 \cdot 10^{-4}$	$1.24 \cdot 10^{-6}$	$1.63 \cdot 10^{-6}$	0.0433	0.0477
Regional								
	$8.92 \cdot 10^{-5}$	0.0009	$9.96 \cdot 10^{-7}$	$6.65 \cdot 10^{-6}$	$2.49 \cdot 10^{-8}$	$3.29 \cdot 10^{-8}$	0.0006	0.0016
Incl. gasoline	$8.95 \cdot 10^{-5}$	0.0009	$2.47 \cdot 10^{-6}$	$7.09 \cdot 10^{-6}$	$4.96 \cdot 10^{-8}$	$6.54 \cdot 10^{-8}$	0.0015	0.0025

The calculated margin of safety for total exposure of humans via the environment is in the range of 430 to 600,000 based on the subchronic NOAEL 625 mg/kg bw/d.

Table 3.10 Estimated human intake of toluene in mg/kg bw/d by route, downstream scenarios and MOS

Scenario	Total intake mg/kg/d	MOS	Total intake incl. gasoline mg/kg/d	MOS incl. gasoline
Local				
1: Processing	0.189	3,307	0.189	3,307
2: Formulation	0.158	3,956	0.159	3,931
2: Processing	2.03	308	2.03	308
3: Formulation	0.103	6,068	0.104	6,010
3: Private use	0.004	156,250	0.005	125,000
4: Formulation	0.026	24,038	0.027	23,148
4: Processing	0.007	89,286	0.008	78,125
5: Formulation	0.036	17,361	0.037	16,892
5: Private use	0.0016	390,625	0.0025	250,000
6: Formulation	0.0486	12,860	0.0494	12,652
6: Processing	0.914	684	0.915	683
7: Formulation	0.0025	250,000	0.026	24,039
7: Private use	0.0024	260,417	0.0033	189,394
8: Formulation	0.0188	33,245	0.0197	31,726
8: Processing	0.193	3,238	0.194	3,222
9: Processing	0.0117	53,419	0.0126	49,603
10: Processing	0.0477	13,103	0.0486	12,860
Regional				
	0.0016	390,625	0.0025	250,000

Note: the contribution from toluene in gasoline was included in the last two columns

Results for humans exposed via the environment

The calculated margin of safety (MOS) for total exposure of humans via the environment is above 300 for all local and regional scenarios. This is considered to be sufficiently high to provide reassurance that adverse health will not occur, and thus there is no concern for effects of toluene in humans exposed indirectly to toluene itself via the food chain: conclusion (ii).

However, **conclusion (iii)** applies because there is concern for effects on humans due to the contribution of commercial product toluene to the formation of ozone and other harmful substances.

4 HUMAN HEALTH

4.1 HUMAN HEALTH (TOXICITY)

4.1.1 Exposure assessment

Humans may be exposed to toluene 1) at the workplace, 2) from the use of consumer products, and 3) via the environment.

4.1.1.1 Occupational exposure

Exposure to toluene can be by inhalation of vapours and liquid aerosols, dermal exposure to vapours and liquids and via the gastrointestinal tract. Dermal exposure to vapours is considered insignificant and ingestion is disregarded.

For the occupational exposure assessment the exposure situations can be clustered into four scenarios based on the type of use of toluene. In the first scenario production of toluene and use of toluene as an intermediate in the chemical industry (scenario Q) is considered. Although the production and use of gasoline is not formally a part of this risk assessment, exposure is assessed in the second scenario (R) for illustrative purposes in order to be able to compare the exposure to toluene in this scenario with other scenarios. The third scenario (S) considers the formulation of toluene containing products such as paints and the fourth scenario (T) considers the use of products containing toluene.

The exposure is assessed using the available information on the substance, processes, and work tasks. Information on the process and measured data have been provided for the production of toluene, and gasoline, on use of toluene in the chemical industry, and products containing toluene in the printing industry, in paint, coatings, and cleaning agents.

No account will be taken of personal protection equipment in this exposure section, since the actual degree of protection depends on the type of PPE, the way the equipment is used and maintained, and therefore cannot be known.

Table 4.1 shows the results of the occupational exposure assessment which is used in the risk characterisation.

Table 4.1 Results of the occupational exposure assessment

Scenario / subscenario	Exposure		Estimated inhalation exposure level (mg/m³)						Estimated skin exposure level
	Duration (hr/day)	Frequency (day/year)	Full shift (8 hour time weighted average)				Short term		(mg/kg bw/day) [1, 2]
			Typical	Method	RWC	Method	RWC	Method	RWC
1. Production and use as an intermediate									
a) production and use as an intermediate	6-8	200	3	measured	45	measured	100	expert judg.	6
b) use as an intermediate	6-8	200		measured	15	measured			6
c) maintenance	6-8	200		measured	45	measured			9
2. Production of gasoline									
a) maintenance and tank cleaning	2-4	200	1	measured	70	measured	140	expert judg.	1.9
b) operators at production sites	6-8	200	1	measured	20	measured	30	expert judg.	1.2
c) transfer of gasoline	6-8	200	2.5	measured	50	measured	100	expert judg.	1.2
d) attendants at service stations	4-6	200	0.5	measured	3	measured	6	expert judg.	0.6
3. Production of products (transfer, filling and drumming)	6-8	200	4	measured	98	measured	200	expert judg.	6
4. Use of toluene containing products									
a) manual cleaning	4-6	200	3	measured	120	measured	240	expert judg.	90
mechanical cleaning	4-6	200	7	measured	44	measured	90	expert judg.	0.6
b) use of adhesives	4-6	200	75	measured	400	measured	500	measured	279
c) printing	4-6	200	80	measured	300	measured	700	expert judg.	6
d) painting: manual	4-6	200	8	measured	50	measured	100	expert judg.	29
spraying	4-6	200	8	measured	50	measured	100	expert judg.	279
mechanical coating	4-6	200	10	measured	170	measured	340	expert judg.	6

RWC: Reasonable worst case

1) Evaporation from the skin due to the high volatility of toluene has not been taken into account in the dermal exposure assessment.

2) According to the US EPA, the estimated amount of substance deposited on the skin is approximately in line with results which could be obtained using the proposed revised CEB method for screening-level assessments of dermal exposure for similar working situations (US EPA, 2001)

4.1.1.2 Consumer exposure

According to the Danish Product Register, toluene is present in various consumer products, including paints, adhesives, varnishes, and inks for pens. The only measured data on toluene in consumer products were from glue products. No other references were found on consumer products containing toluene.

Five scenarios are considered for consumer exposure:

U1 Gluing,
U2 Spray painting,
U3 Car maintenance,
U4 Carpet laying, and
U5 Filling gasoline at self-service gas stations.

Although the production and use of gasoline is not formally a part of this risk assessment, exposure during filling gasoline at self-service gas stations (scenario U5) is assessed. This is done for illustrative purposes in order to be able to compare the exposure to toluene in this scenario with other scenarios.

The frequency of exposure scenarios U1 to U4 is expected to be low. Uptake via inhalation and potential dermal exposure is therefore expressed as mg/kg bw/event. For scenario U5 the frequency of exposure is considered to be sufficiently high to be regarded as chronic exposure. For this particular scenario, uptake via inhalation and potential dermal exposure is therefore expressed as mg/kg bw/day.

Table 4.2 shows the results of the consumer exposure assessment, which is used in the risk characterisation.

Table 4.2 Consumer exposure model scenarios

Exposure	Scenarios					
	U1 acute	U2 acute	U3A acute	U3A acute	U4 acute	U5 [1] chronic
Air concentration (mg/m^3)	7.1	1,000	10	Negligible	195	63
Uptake via inhalation (mg /kg bw/event)	0.3	41.7	0.42	Negligible	18.6	0.13 [3]
Potential dermal exposure (mg/kg bw/event) [2]	0.01	1.43	0.014	9.3	30	Negligible

1) Included for illustrative purposes
2) Dermal exposure modelled using the EASE, because of the similarity to workers exposure
3) mg/kg bw/day

4.1.2 Effects assessment

Toxicokinetics, metabolism and distribution

Toluene is absorbed rapidly via inhalation and the amount absorbed depends on pulmonary ventilation. Absorption from the gastrointestinal tract seems to be high. Dermal uptake occurs. Toluene distributes widely throughout the body with the highest concentrations in fat. Toluene readily passes the placenta and is excreted in human breast milk. Toluene biotransformation occurs by oxidation in the liver. The major metabolite is benzoic acid, which is linked to glycine, resulting in the formation of hippuric acid. Toluene is mainly

eliminated as hippuric acid in the urine, while a proportion is exhaled unchanged via the lungs.

Acute toxicity

Toluene has low acute toxicity. In humans experimentally exposed to toluene, concentrations of 75 ppm (281 mg/m^3) and above caused headache, dizziness, and feeling of intoxication, irritation and sleepiness. A NOAEC of 40 ppm (150 mg/m^3) for these effects has been identified and is used in the risk characterisation.

Furthermore, toluene causes impaired neuropsychological function. This acute effect of toluene has been demonstrated in performance tests. For impaired function in performance tests a LOAEC of 75 ppm (281 mg/m^3) is used in the risk characterisation.

Irritation

In rats, an inhalation LC50 of 28,100 mg/m^3/4h has been reported. However, for inhalation the risk characterisation will be based on the human NOAEC and LOAEC mentioned above.

A dermal LD50 of 12,400 mg/kg has been determined in the rabbit. This value is used in the risk characterisation for acute toxicity by dermal exposure, as no human studies are available.

Sensitisation

Toluene is irritating to the skin in rabbits, mice, and guinea pigs. According to textbooks, it is well known that toluene has a degreasing effect on the skin of humans. One study in rabbits has been performed according to a method of one EU guideline standard, however, the non-irritating concentration is not known, as the data are on the undiluted substance.

Liquid toluene is irritating to eyes in animals, while toluene vapours in concentrations at and above 75 ppm causes complaints of eye irritation in humans. A NOAEC of 40 ppm (150 mg/m^3) for eye irritation has been identified and is used in the risk characterisation.

The results of a guinea pig maximisation test indicate that toluene is not a skin sensitiser. It is unlikely that toluene is a respiratory allergen.

Repeated dose toxicity

General systemic toxicity

Oral exposure: in the rat a NOAEL for general systemic toxicity of 625 mg/kg/day for repeated oral exposure was identified in a 90-day study. At higher levels (1,250 mg/kg and above) neurone necrosis and organ weight increases were found. In a similar 90-day mouse study non-specific effects (liver enlargement and one death) were found at 1,250 mg/kg.

Inhalation: also in the rat, a NOAEC for general systemic toxicity of 625 ppm (2,344 mg/m^3) for repeated exposure via inhalation was identified in a 15-week study. At the higher exposure level (1,250 ppm (4,688 mg/m^3)) a decrease in leukocyte count in females, and relative organ weight increases were found. In a two-year rat study a NOAEC of 300 ppm (1,125 mg/m^3) was found, this was the highest dose level tested. In another two-year rat study, the lowest dose tested, 600 ppm (2,250 mg/m^3) was a LOAEC for increased occurrence of nasal toxicity and forestomach ulcers in males.

Dermal exposure: for the dermal route, no data on repeated dose toxicity have been found.

Conclusion: for general systemic toxicity after repeated dosing, the 90-day rat oral NOAEL of 625 mg/kg/day, and the 2-year rat inhalatory NOAEC of 300 ppm (1,125 mg/m^3) is used in the risk characterisation.

Specific organ toxicity

Repeated exposure to toluene via inhalation has been shown to affect the central nervous system and the inner ear. These endpoints were not part of the studies investigating general toxicity, but are toxicologically important, and are therefore treated as separate endpoints in the risk characterisation.

Long-term high-level exposure to toluene (abuse) via inhalation has caused serious damage to the brain including severe neurological abnormalities and brain atrophy. This effect is not considered in the risk characterisation, as it is not an effect associated with normal use of toluene.

Many scientists believe that long-term exposure to volatile solvents at exposure levels possible in occupational settings may lead to organic brain syndrome. Two studies show an increased prevalence in toluene-exposed workers compared with the control group. In both studies the length of employment was high, while only recent exposure data were well documented. Exposure during the years preceding the investigation was not well described. LOAECs and NOAECs cannot be determined for organic brain syndrome, since well-documented exposure information covering a considerable proportion of the entire period of employment would be necessary, but is not available. Consequently this endpoint cannot be evaluated quantitatively in the risk characterisation.

No evidence suggesting that the levels of toluene found in the working environment can cause damage to the peripheral nervous system has been found.

In animals several effects on the central nervous system have been found. These effects will not be evaluated as separate endpoints in the risk characterisation, but form part of the database on the neurotoxic effects of toluene.

Neuronal cell necrosis in the dentate gyrus and Ammons horn of the hippocampus was seen in both male and female rats that received 1,250 or 2,500 mg/kg in a 90-day study. Also necrosis and/or mineralisation was present in the granular layer of the cerebellar cortex.

A reduced number of neurones in the hippocampus and a reduced hippocampal weight in rats exposed to 1,500 ppm (5,625 mg/m^3) of toluene via inhalation for 6 months have been found.

In very young rats exposed to toluene via inhalation on postnatal day 1-28 reduced volume of certain hippocampal structures was found at 100 and 500 ppm (375 and 1,875 mg/m^3).

Changes in brain neurochemistry in rats have been described. Effects were found at an exposure level of 80 ppm (300 mg/m^3) after only 3 days of exposure. Long-term exposure has been shown to cause effects on brain neurochemistry at 500 ppm (1,875 mg/m^3) still present six months after the last exposure indicating possibly irreversible changes.

Occupational exposure to toluene at high concentrations may increase the risk of developing mild high-frequency hearing loss. However, the studies showing this effect are not appropriate for determining a LOAEC or NOAEC.

The ototoxicity of toluene in the rat is well documented by behavioural, electrophysiological, and morphological techniques. It is therefore possible to carry out a separate risk

characterisation for this endpoint by use of the animal data. Impaired hearing function in the rat has been demonstrated at exposure concentration levels of 1,000 ppm (3,750 mg/m^3) for as little as 2 weeks. A 16-week NOAEC of 700 ppm (2,625 mg/m^3) has been reported and is used in the risk characterisation.

Mutagenicity

Toluene is considered to be non-genotoxic.

Carcinogenicity

Toluene was not carcinogenic to rats or mice in inhalation studies.

In the mouse study, adenomas of the pars intermedia in the pituitary gland, a very rare tumour type, were found in all toluene-exposed groups of females, and in the highest dose group of males. A single adenoma was found in each of these groups. In a skin-painting study, toluene was found to cause skin irritation and tumour development. The difference in tumour incidence was just below statistical significance (p=0.055).

Toxicity for reproduction

In male rats exposed to 2,000 ppm (7,500 mg/m^3), reduced sperm count was found with a NOAEC of 600 ppm (2,250 mg/m^3).

Toluene abuse has been related to a syndrome in human foetuses characterised by physical and neurological abnormalities, resembling the foetal alcohol syndrome. In rats, lower foetal and birth weight has been found in offspring of dams exposed to inhalatory concentrations around 1,000 ppm (3,750 mg/m^3). Long-lasting developmental neurotoxicity (impairment of learning ability) has been demonstrated in offspring exposed prenatally or pre- and postnatally to 1,200 ppm (4,560 mg/m^3). The NOAECs for lower birth weight were around 600 ppm (2,250 mg/m^3).

Limited data in humans indicate an increased risk for spontaneous abortions at dose levels around 88 ppm (330 mg/m^3).

A rat NOAEC of 600 ppm (2,250 mg/m^3) and a human LOAEC of 88 ppm (330 mg/m^3) for reproductive toxicity is used in the risk characterisation.

Conclusion

Overall, the hazardous properties of toluene have been evaluated in animals to the extent that the minimum data requirements according to Article 9(2) of Regulation 793/93 have been met. The key health effects with respect to acute toxicity, skin and eye irritation, sensitisation, repeated dose toxicity, mutagenicity, carcinogenicity, and reproductive toxicity have been identified.

In the risk characterisation the human exposure levels are compared directly with NOAELs/LOAELs and NOAECs/LOAECs; and LD50 (LC50) values from animal or human studies when available.

4.1.3 Risk characterisation

Workers

The exposure conditions that are considered in this risk characterisation, have all been summarised in Section 4.1.1.1. The exposure routes considered are inhalation and dermal exposure, and each route has been considered separately.

Table 4.3 provides an overview of the conclusions reached in the risk characterisation for workers for different exposure scenarios and different toxicological endpoints.

Table 4.3 Results of the risk characterisation for workers

X. Scenario x) sub-scenario	Toxicological endpoint										
	Acute toxicity (inhalation)	Acute toxicity (dermal)	Skin irritation	Eye irritation	Corrosivity	Repeated dose toxicity (inhalation)	Repeated dose toxicity (dermal)	Repeated dose toxicity (total systemic dose)	Mutagenicity	Carcinogenicity	Toxicity for reproduction
Q. Production and use as an intermediate											
a) production and use as an intermediate	**iii**	ii	ii	ii	ii	ii	Ii	ii	ii	ii	ii
b) use as an intermediate	**iii**	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii
c) maintenance (regularly)	**iii**	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii
R. Production of gasoline											
a) drumming, maintenance and tank cleaning											
b) operators at production sites											
c) transfer of gasoline											
d) attendants at service stations											
S. Production of products (transfer, filling & drumming)	**iii**	ii	ii	**iii**	ii	**iii**	ii	**iii**	ii	ii	**iii**
T. Use of toluene containing products											
a) manual cleaning	**iii**	ii	ii	**iii**	ii	**iii**	**iii** *	**iii**	ii	ii	**iii**
mechanical cleaning	**iii**	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii
b) use of adhesives	**iii**	**iii**	ii	**iii**	ii	**iii**	**iii** *	**iii**	ii	ii	**iii**
c) printing	**iii**	ii	ii	**iii**	ii	**iii**	ii	**iii**	ii	ii	**iii**
d) painting: manual	**iii**	ii	ii	ii	ii	ii	ii	**iii** *	ii	ii	ii
spraying	**iii**	**iii**	ii	ii	ii	ii	**iii** *	**iii** *	ii	ii	ii
mechanical coating	**iii**	ii	ii	**iii**	ii	**iii**	ii	**iii**	ii	ii	**iii**

* Conclusion (iii) arising from or (mainly from) dermal exposure.

For the production of gasoline (scenario R) no formal risk characterisation has been performed, since toluene exposures arising from the production and handling of gasoline are not formally a part of this risk assessment.

As a NOAEC or a LOAEC cannot be determined for the organic brain syndrome this endpoint has not been evaluated quantitatively.

Consumers

The exposure conditions that are considered in this risk characterisation, have all been summarised in Section 4.1.1.2. The exposure routes considered are inhalation and dermal exposure, and each route has been considered separately.

Table 4.4 provides an overview of the conclusions reached in the risk characterisation for consumers for different exposure scenarios and different toxicological endpoints.

Table 4.4 Results of the risk characterisation for consumers

X. Scenario x) sub-scenario	Toxicological endpoint									
	Acute toxicity (inhalation)	Acute toxicity (dermal)	Skin irritation	Eye irritation	Corrosivity	Repeated dose toxicity (inhalation)	Repeated dose toxicity (dermal)	Mutagenicity	Carcinogenicity	Toxicity for reproduction
U1: Gluing	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii
U2: Spray painting	**iii**	ii	ii	**iii**	ii	ii	ii	ii	ii	i
U3A Car maintenance (car polishing)	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii
U3B: Car maintenance (cleaning hands)	ii	ii	ii	ii	ii	ii	ii	ii	ii	ii
U4: Carpet laying	**iii**	ii	ii	**iii**	ii	ii	ii	ii	ii	**i**
U5: Filling gasoline at self- service stations	-		-	-	-	-	-	-	-	-

Humans exposed via the environment

Conclusion (iii). Cf. Section 3.3.5.

Combined exposure

Combining local environmental exposure and occupational exposure will not influence the characterisation of the risks associated with environmental exposure alone.

4.2 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

Flammability is the only property of concern for toluene since it is a volatile liquid which is highly flammable.

In production and in occupational use, the flammability risk is not of concern provided adequate safety measures are taken. Information on flammability is provided on the label and in the safety data sheet.

Concerning use by consumers, information about the flammability risk and precautionary measures must be given by a label on the containers. In the EU, symbol, risk phrases and safety phrases are used for the labelling of highly flammable substances and preparations (mixtures), cf. Section 1 - classification.

There is at present no need for further information or testing or for risk reduction beyond those which are being applied already: **conclusion (ii)**.

5 RESULTS

5.1 ENVIRONMENT

Aquatic environment

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

This conclusion applies in relation to site-specific releases from two production sites, one combined production and processing site and one off site production site. A risk is also identified for a number of downstream processing sites according to generic assessments for the following use categories:

- industry use as an intermediate and as basic chemical,
- mineral oil and fuel formulation,
- formulation of polymers,
- formulation of paints,
- textile processing.

Sewage treatment plants

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

This conclusion applies to one site-specific releases from one off-site processing site and some downstream uses of toluene: industry use as basic chemicals.

Atmosphere

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

This conclusion applies in the context of the Council Regulation (EEC) 793/93 of Existing Substances to the contribution of the commercial product toluene to the formation of ozone and other harmful substances i.e. smog formation. In the context of the consideration of which risk reduction measures that would be the most appropriate, it is recommended that under the relevant air quality Directives a specific in-depth evaluation is performed. Such an evaluation should focus on the contribution of isolated as well as non-isolated toluene to the complex issue of ozone and smog formation and the resulting impact on air quality.

Terrestrial compartment

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

This conclusion applies to release via sludge application to soil from one processing site and to a range of downstream processing sites according to generic assessments for the following use categories:

- industry use as an intermediate and as basic chemical,
- mineral oil and fuel formulation,
- formulation of polymers,
- formulation of paints,
- textile processing.

5.2 HUMAN HEALTH

5.2.1 Human health (toxicity)

Workers

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

This conclusion is reached because of:

- concerns for acute toxicity as a consequence of dermal exposure arising from spraying painting or the use of adhesives,
- concerns for acute toxicity (headache, dizziness, feeling of intoxication, sleepiness and impaired functional performance) as a consequence of inhalation exposure arising from production and use as an intermediate, production of products containing the substance and use of products containing the substance,
- concerns for eye irritation as a consequence of exposure arising from production of products containing the substance and use of products containing the substance in the sectors of manual cleaning, use of adhesives, printing and painting (mechanical coating),
- concerns for general systemic toxicity as a consequence of inhalation exposure arising from production of products containing the substance and use of products containing the substance in the sectors of manual cleaning, use of adhesives, printing and painting (mechanical coating),
- concerns for general systemic toxicity as a consequence of dermal exposure arising from use of products containing the substance in the sectors of manual cleaning, use of adhesives and spray painting,
- concerns for general systemic toxicity as a consequence of the combined dermal and inhalation exposure arising the use of products containing the substance in the sectors of manual painting,
- concerns for specific organ toxicity (auditory system toxicity) as a consequence of inhalation exposure arising from production of products containing the substance and use of products containing the substance in the sectors of manual cleaning, use of adhesives, printing and painting (mechanical coating),
- concerns for fertility and developmental effects and spontaneous abortions as a consequence of inhalation exposure arising from production of products and use of toluene containing products in the sectors of manual cleaning, use of adhesives, printing and painting (mechanical coating).

Risk reduction measures should therefore be considered that will ensure a reduction in the levels of toluene found in the workplace during the production and use of toluene and during the production and use of toluene containing products**.**

Consumers

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

This conclusion is reached because of:

- concerns for acute toxicity (headache, dizziness, feeling of intoxication, sleepiness and impaired functional performance) and eye irritation as a consequence of inhalation exposure or eye exposure to vapours arising from spray painting and carpet laying.

The conclusion is based on the estimated exposure during use of toluene containing glues and paints. Risk reduction measures should therefore be considered that will ensure a reduction in the levels of toluene found when using consumer products containing toluene.

and

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

This conclusion is reached because of:

- concerns for effects on reproduction as a consequence of inhalation exposure.

The information and/or test requirement is:

- information on the relationship between the observed effects on reproduction and the duration of the exposure leading to these effects.

The need to actually obtain the information allowing the performance of the risk characterisation for this endpoint, will be considered when the recommended risk reduction strategy is published in the Official Journal.

Hence, any formal request for further information should be seen in the light of other possible risk reduction measures for the consumer scenarios based on the concerns for acute toxicity by inhalation and eye irritation identified for the Scenarios U2 (spray painting) and U4 (carpet laying).

Humans exposed via the environment

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

The conclusion applies in the context of the Council Regulation (EEC) 793/93 of Existing Substances to the contribution of the commercial product toluene to the formation of ozone and other harmful substances i.e. smog formation. Regarding which risk reduction measures would most appropriate, it is recommended that under the relevant air quality Directives a specific in-depth evaluation be performed. Such an evaluation should focus on the contribution of isolated as well as non-isolated toluene to the complex issue of ozone and smog formation and the resulting impact on air quality.

5.2.2 Human health (risks from physico-chemical properties)

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