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# 1,2,4-TRICHLOROBENZENE

CAS No: 120-82-1

EINECS No: 204-428-0

**Summary Risk Assessment Report**

**2003** **Special Publication I.02.157**

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# SUMMARY RISK ASSESSMENT REPORT

*Final report, 2003*

Denmark

Rapporteur for the risk assessment report on 1,2,4-Trichlorobenzene is the Danish Environmental Protection Agency on behalf of the European Union, in consultation with The Danish Veterinary and Food Administration, The Danish Technological Institute, The Danish National Institute of Occupational Health and The Danish National Working Environment Authority.

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| | |
|---|---|
| **Date of Last Literature Search:** | **2000** |
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## PREFACE

This report provides a summary, with conclusions, of the risk assessment report of the substance 1,2,4-trichlorobenzene 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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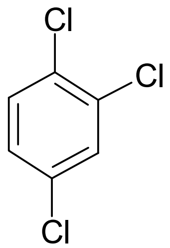
# 1 GENERAL SUBSTANCE INFORMATION

## 1.1 IDENTITY OF THE SUBSTANCE

| | |
|---|---|
| CAS-No.: | 120-82-1 |
| EINECS-No.: | 204-428-0 |
| IUPAC name: | 1,2,4-trichlorobenzene |
| Synonyms: | 1,2,4-TCB[2], 1,2,4-trichlorbenzol, 1,2,5-trichlorobenzene, 1,3,4-trichlorobenzene |
| Molecular weight: | 181.46 |
| Molecular formula: | $C_6 H_3 Cl_3$ |
| Structural formula: | |




## 1.2 PURITY/IMPURITIES, ADDITIVES

| | |
|---|---|
| Purity: | ≥ 99% |
| Impurity: | information from manufacturers (one or more of mentioned below):<br>total tetrachlorobenzenes, ≤0.2% w/w<br>1,2,3-trichlorobenzene <1% w/w (usually 0.1-0.4%)<br>1,3,5-trichlorobenzene < 2 % w/w<br>1,2-dichlorobenzene <0.25<br>1,4-dichlorobenzene < 0.25%<br>dichlorotoluenes <0.2%<br>2/4-bromo-chlorobenzenes <0.15% |
| Additives: | No information |

[2] The abbreviation 1,2,4-TCB is used for this substance throughout the report. The abbreviation TCB is used in cases where the substitution position is unspecified. Specific isomers, e.g. 1,2,3-trichlorobenzene are similarly abbreviated to 1,2,3-TCB.

## 1.3 PHYSICO-CHEMICAL PROPERTIES

**Table 1.1** Physico-chemical properties

| | |
|---|---|
| Physical state | liquid |
| Melting point | 17°C<br>16.05°C<br>16.95°C |
| Boiling point | 213.5°C at 1,013 hPa |
| Relative density | 1.456 g/cm³ at 20°C |
| Vapour pressure | 21.5 Pa at 20°C<br>36 Pa at 20°C<br>0.29 mm Hg at at 25°C (38.6 Pa)<br>46.8 Pa at 25°C<br>80 Pa at 30°C<br>270 Pa at at 50°C |
| Surface tension | 38.5 dyn/cm |
| Water solubility | 36 mg/l at 20°C<br>48.8 mg/l at 20°C |
| Octanol/water | log Kow: 4.2<br>log Kow: 4.05<br>log Kow: 4.02<br>log Kow: 3.93 |
| Flash point | 110°C |
| Auto Flammability | ≥500°C |
| Henry's Law constant | 101 Pa m³/mol (20ºC)<br>290 Pa m³/mol (25ºC)<br>181 Pa m³/mol (20ºC) |
| Air calculation factor | 1 ppm = 7.42 mg/m³ (25ºC, 1,013 hPa)<br>1 mg/m³ = 0.133 ppm |

## 1.4 CLASSIFICATION

Classification and labelling according to the 28th ATP of Directive 67/548/EEC[3]:

Classification

| | |
|---|---|
| Xn; R22 | Harmful if swallowed |
| Xi; R38 | Irritating to skin |
| N; R50-53 | Very toxic to aquatic organisms. May cause long-term adverse effects in the aquatic environment. |

[3] The classification of the substance is established by Commission Directive 2001/59/EC of 6 August 2001 adapting to technical progress for the 28th time Council Directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances (OJ L 225, 21.8.2001, p.1).

Specific concentration limits: None

Labelling

Xn; N
R: 22-38-50/53
S: (2-)23-37/39-60-61

# 2 GENERAL INFORMATION ON EXPOSURE

1,2,4-Trichlorobenzene (1,2,4-TCB) is a synthetic organic chemical which is not known to occur as a natural chemical. 1,2,4-TCB is manufactured and used in the chemical industry as an intermediate in closed systems in the manufacture of herbicides and higher chlorinated benzenes. Furthermore, 1,2,4-TCB is used as a process solvent, as a dye carrier, in metal working fluids, and sprays as a corrosion inhibitor. Significant quantities may still be used in existing electrical equipment as a dielectric fluid, solvent, and heat transfer medium. Unintentional release and leakage e.g. during use, recycling or disposal of existing electrical equipment may therefore occur.

Former uses include use of the substance in degreasing agents, septic tanks and drain cleaners, wood preservatives, and abrasive formulations. It has also been reported as being used as a termite exterminator. It has not been possible totally to exclude that such uses still occur.

Besides direct exposure from production and use of 1,2,4-TCB, indirect exposure may take place from the forming of trichlorobenzenes during the combustion of organic material when chlorine is also present (for example during incineration of waste, PVC, and other plastic materials). 1,2,4-TCB is also formed during industrial cracking or environmental degradation of hexachlorocyclohexanes (HCH) and other higher chlorinated benzenes.

# 3 ENVIRONMENT

## 3.1 ENVIRONMENTAL EXPOSURE

1,2,4-TCB may be released into the environment during its production, use and disposal. 1,2,4-TCB is released into and detected in most environmental compartments. The atmospheric compartment is estimated to be the primary recipient (based on the relatively high vapour pressure) in some of the use areas (e.g. solvent), in other use areas, the aquatic compartment is the primary recipient (e.g. intermediate in industrial processes, dye carrier).

The present exposure scenarios only include a very rough estimation of the release of 1,2,4-TCB from the accumulated volume of the substances in electrical equipment still in function or such equipment at the recycling/disposal place.

It is reported that trichlorobenzenes are formed, together with other chlorinated benzenes, during the combustion of PVC.

Exposure of the soil compartment via sludge application may, however, occur from municipal sewage treatment plants (STPs) receiving wastewater containing 1,2,4-TCB e.g. from processing of TCB. The sludge from the main manufacturers' production of 1,2,4-TCB is, however, incinerated at the production sites according to information from the main manufacturers.

It should be noted that when comparing estimated and measured concentrations it has neither been possible quantitatively to estimate the indirect release of 1,2,4-TCB from combustion processes generating 1,2,4-TCB nor from transformations to 1,2,4-TCB in the environment from higher chlorinated substances such as polychlorinated benzenes (PCB) and lindane (γ-HCH). Also the release of formerly produced 1,2,4-TCB from dielectric fluids in electrical equipment still in use has not been employed in the quantitative estimations of environmental concentrations. The measured data of environmental concentrations will however also reflect contributions from such sources.

A very rough estimation of the environmental release of 1,2,4-TCB from dielectric fluids in existing electrical equipment indicates that this may be of the same order of magnitude as the total release form the current production and processing of this substance. Because of present EU and national legislation regarding destruction of PCB and other chlorinated compounds in dielectrical fluids in electrical equipment it can be foreseen that the future level of environmental release of 1,2,4-TCB from this source will decrease significantly in EU.

On the basis of the available data it seems to be possible to estimate that dielectrical fluids, bio- and photodegradation of HCB, lindane and lindane isomers and emissions from landfills and contaminated sites should be the main sources for the environmental release of 1,2,4-TCB in Europe besides the release originating from the current production and processing of 1,2,4-TCB. In comparison to that combustion processes and effluent from paper mills and some other sources seem to be of only minor importance.

Atmospheric photodegradation occurs with a half-life of approximately 30 days which is used in the risk assessment. 1,2,4-TCB can be regarded as inherently biodegradable.

1,2,4-TCB has a high adsorption capacity and the mobility in soil is expected to be low. However, because the degradation is slow in soil, 1,2,4-TCB may leach through sandy soils low in organic carbon content and reach groundwater.

1,2,4-TCB has a log $K_{ow}$ of 4.05 indicating a bioaccumulation potential. This was confirmed by several tests on different fish species and other aquatic species. The bioconcentration factor BCF for fish/water (whole body) is according to the realistic worst-case concept approximately 2,000, which is used in the risk assessment. Based on experimental data, the BCF on earthworms (worm/sediment) is estimated to be 1, which is used in the risk assessment.

**Table 3.1** Estimated fate of 1,2,4-TCB in STP

| Estimation according to | % to air | % sludge | % degraded | % removal | % to water |
|---|---|---|---|---|---|
| EUSES ver.1 | 61.3 | 11.3 | 12.1 | 84.7 | 15.3 |

**Table 3.2** Estimations of concentration in local surface water and sediments during emission episodes

| Scenario | $E_{water}$ kg/d | $C_{infl}$ mg/l | $C_{effl}$ mg/l | $PEC_{water}$ ** mg/l | $PEC_{sed}$ mg/kg ww |
|---|---|---|---|---|---|
| **Production** | | | | | |
| A * | | | 0.028 | $9.6 \cdot 10^{-6}$ | 0.0003 |
| B * | 0.4 | 0.2 | 0.031 | $53.2 \cdot 10^{-6}$ | 0.0017 |
| **Processing** | | | | | |
| D1: intermediate | 25.7 | 12.8 | 1.96 | $17.7 \cdot 10^{-6}$ | 0.00055 |
| D2: process solvent | 13.3 | 6.6 | 1.02 | $1.46 \cdot 10^{-3}$ | 0.046 |
| D3: others | 4.95 | 2.47 | 0.378 | 0.038 | 1.18 |
| D4: dye carrier | 8.93 | 4.46 | 0.682 | 0.068 | 2.12 |

* Estimations based on information from the main manufacturer regarding dilution, further estimations based on the TGD

** The local $PEC_{water}$ is Clocal water + PECregional (PEC regional, c.f.below)

EUSES estimates the continental PEC in sediment to 0.86 ng/kg ww and the $PECregional_{sed}$ to 0.38 µg/kg ww sediment which is in the same level as the lower end of the measured concentrations.

**Table 3.3** Estimations of concentrations in local air during a STP emission episode

| Scenario | $PEClocal_{air,ann}$ ng/m³ |
|---|---|
| **Production** | |
| A * | 144 |
| B * | <19.5 |
| **Processing** | |
| D1: intermediate | 3.9 |
| D2: process solvent | 1,870 |
| D3: others | 76 |
| D4: dye carrier | 42 |

* Estimation based on the main manufacturer information

The regional $PEC_{air}$ is estimated to 0.5 ng/m$^3$ by employing EUSES. Thus, the estimated concentrations are considered to be in the relevant concentration range in comparison with measured concentrations.

**Table 3.4** Local concentration in soil

| Scenario | $PEClocal_{soil}$ (mg/kg) | $PEClocal_{agr. soil}$ (mg/kg) | $PEClocal_{grassland}$ (mg/kg) | $PEClocal_{natural soil}$ (mg/kg) * |
|---|---|---|---|---|
| **Production** | | | | |
| A ** | 0.079 | 0.047 | 0.013 | 1.4 · 10-4 |
| B ** | 0.079 | 0.047 | 0.013 | 1.7 · 10-5 |
| **Processing** | | | | |
| D1: intermediate *** | 5.09 | 3.03 | 0.810 | 3.6 · 10-6 |
| D2: process solvent *** | 2.64 | 1.57 | 0.421 | 1.9 · 10-3 |
| D3: other | 0.98 | 0.58 **** | 0.156 | 1.1 · 10-4 |
| D4: dye carrier | 1.77 | 1.05 | 0.281 | 4.3 · 10-5 |

* For natural soil, only deposition from air is included (no sludge application assumed)

** For the site-specific scenarios A and B only atmospheric deposition is included because sludge application does not take place

*** According to main manufacturers sludge application does not take place. However, the scenarios are retained as generic scenarios

**** Based on the monitored levels of 1,2,4-TCB in sludge it is possible to estimate the soil concentration resulting from the application of these actual sludges. The concentration in agricultural soil would be 0.33 µg/kg for a concentration in sludge of 400 µg/kg and 0.04 mg/kg for the highest measured value of 51.2 mg/kg. The activities which give rise to these levels are unknown. Therefore they could be taken as indicative of levels from the wider "other uses" as they are apparently not related to the major activities which use this substance. In conclusion: the local PEC for agricultural soil onto which sludge is applied is according to monitoring data and employment of the sludge application scenario of the TGD one to three orders of magnitude lower than the estimation in the table employing the TGD estimation method

The estimated 1,2,4-TCB concentrations from deposition alone according to the downstream uses (natural soils, D scenarios) range from 0.1 µg/kg to 0.3 µg/kg which is reasonably in agreement with the measured value. The estimated 1,2,4-TCB concentration in soil near the major production sites indicated 1,2,4-TCB concentrations three orders of magnitude higher.

According to monitoring data, the measured concentrations in marine fish were 3 to 300 µg/kg. The estimated concentration in fish based on the BCF(fish) and the estimated $PEC_{local, water}$ is between 20 µg/kg and 2 mg/kg, whereas the same estimated regional concentration is 20 µg/kg. Thus the reported range of concentrations in marine fish monitored in three different locations between one and two decades ago generally fit well with the estimated regional concentration in fish according to the TGD.

## 3.2 EFFECTS ASSESSMENT

Aquatic, sediment and soil compartment, STP and secondary poisoning.

Regarding the acute studies, a value from the lower end of tests with measured concentrations in fish studies gives $LC_{50}$ (96 h)= 1.0 mg/l,. The geometric mean of acceptable studies on *Daphnia magna* gives an $EC_{50}$ (48 h) of 2.1 mg/l and the results from a closed system test on algae gives an $EC_{50}$ (96 h) = 1.4 mg/l and a NOEC (96 h) = 0.37 mg/l.

The lowest NOEC in long-term aquatic ecotoxicity studies was 0.04 mg/l (mortality and behaviour, Zebra fish) and the lowest NOEC (21 d) on *Daphnia* is 0.06 mg/l. NOECs for chronic toxicity on aquatic organisms are within the same long-term toxicity range.

According to the TGD, an assessment factor of 10 applied to the lowest long term NOEC may therefore be used:

$PNEC_{aquatic\ organisms}$: 0.04 / 10 = 0.004 mg/l or 4 µg/l

$PNEC_{sediment}$ = 0.09 mg/kg ww based on equilibrium partitioning.

Based on the few data presented, an assessment factor of 1,000 may be applied to the lowest value of 50 mg/kg soil resulting in an indicative: $PNEC_{soil}$ = 0.05 mg/kg soil[4].

$PNEC_{STP}$ using activated sludge (inhibition on respiration): 35/100 = 0.35 mg/l
$PNEC_{STP}$ using Tetrahymena: 0.91/10 = 0.09 mg/l

Secondary poisoning: $PNEC_{oral}$ = 100/10 ppm = 10 ppm in diet (~0.6 mg/kg bw/d).

## 3.3 RISK CHARACTERISATION

### 3.3.1 Aquatic compartment

**Table 3.5** Estimations of PEC/PNEC in local surface water

| Scenario | $PEC_{water}$ µg/l | PEC/PNEC |
|---|---|---|
| **Production** | | |
| A | 0.010 | 0.002 |
| B | 0.053 | 0.013 |
| **Processing** | | |
| D1: intermediate | 0.018 | 0.005 |
| D2: process solvent | 1.47 | 0.37 |
| D3: others | 38 | 9.4 |
| D4: dye carrier | 68 | 17 |

It is concluded that the use of 1,2,4-TCBs may cause local problems for aquatic organisms.

Based on site-specific release information there were no indications of risks at the main manufacturer production and processing sites, but only for downstream industrial uses according to the TGD default scenarios for use scenarios D3 to D4.

[4] Another assessment report (DMU, 1998) has reached a soil quality objective (SQO) value of 0.001 mg/kg soil dw for chlorobenzenes. The SQO value is based on an evaluation of effect data on 1,2,3-TCB, i.e. an $EC_{50}$ value on plant of 1mg/kg and employment of an application factor of 1,000.

Microorganisms

PNEC microorganisms (based on sludge test): 0.35 mg/l
PNEC microorganisms (based on *Tetrahymena* test): 0.09 mg/l

**Table 3.6** Estimations of $PEC_{STP}$/PNEC in local STPs

| Scenario | $PEC_{STP}$ mg/l | PEC/PNEC (STP bacteria) | PEC/PNEC (STP ciliates) |
|---|---|---|---|
| **Production** | | | |
| A | 0.028 | 0.08 | 0.31 |
| B | 0.031 | 0.11 | 0.34 |
| **Processing** | | | |
| D1: intermediate | 1.96 | 5.6 | 21.5 |
| D2: process solvent | 1.02 | 2.9 | 11.2 |
| D3: others | 0.38 | 1.1 | 4.2 |
| D4: dye carrier | 0.68 | 2.0 | 7.5 |

The PEC/PNEC is >1 indicating risk for STP microorganisms. There were based on site-specific release information no indications of risks at main manufacturer production and processing sites, but only for down stream industrial uses according to TGD release defaults for use scenarios D1 to D4.

Sediments (equilibrium partition)

$PNEC_{sed}$: 0.1 mg/kg

**Table 3.7** Estimations of PEC/PNEC in local sediments

| Scenario | $PEC_{sed}$ mg/l | PEC/PNEC |
|---|---|---|
| **Production** | | |
| A | 0.0003 | 0.002 |
| B | 0.0017 | 0.015 |
| **Processing** | | |
| D1: intermediate | 0.00055 | 0.006 |
| D2: process solvent | 0.046 | 0.4 |
| D3: others | 1.18 | 12 |
| D4: dye carrier | 2.12 | 21 |

It is concluded that the use of 1,2,4-TCBs may cause local problems for sediment dwelling organisms. There were no indications of risks at main manufacturer production and processing sites based on site-specific release information, but only for downstream industrial uses according to TGD release defaults for use scenarios D3 to D4.

Results for the aquatic environment

For production and processing by the main manufacturers, for use as an intermediate and process solvent (cf. scenarios A, B, D1, D2) there is no concern **(conclusion (ii))**.

For the use of 1,2,4-TCB as a dye carrier and other downstream uses (cf. scenarios D3 and D4), there is concern **(conclusion (iii))**.

1,2,4-TCB is classified as N; R50-53. For classification, see Chapter 1.4.

Results for STP

For production and processing by the main manufacturers (cf. scenarios A, B) there is no concern **(conclusion (ii))**.

For all downstream uses of 1,2,4-TCB resulting in environmental release (cf. scenarios D1 to D4) there is concern **(conclusion (iii))**.

### 3.3.2 Atmosphere

The properties of 1,2,4-TCB compared with the guiding criteria on environmental fate related properties in the UNEP POP Convention and the EB Decision of the LRTAP POP protocol indicate that 1,2,4-TCB should be further considered in relation to POPs.

Results for the atmospheric environment

There is no concern for the atmospheric environment (**conclusion (ii)**). However, this risk assessment supports that it may be justified to consider 1,2,4-TCB further in relation to the POP issue in relation to other national and international regulations addressing POPs which may be transported long ranges via the atmospheric compartment.

### 3.3.3 Terrestrial compartment

The PEC/PNEC (soil) is estimated based on the few data on terrestrial organisms and the partition equilibrium method for comparison.

$PNEC_{soil} =$ 50/1,000 = 0.050 mg/kg.

**Table 3.8** Estimations of concentration in local soil

| Scenario | $PEC_{soil,agr,\ 30d}$ mg/kg | $PEC_{soil,agr,180d}$ mg/kg | PEC/PNEC (30 d) | PEC/PNEC (180 d) |
|---|---|---|---|---|
| **Production** | | | | |
| A | 0.079 | 0.047 | <<(1.6)* | <<(0.9) * |
| B | 0.079 | 0.047 | <<(1.6)* | <<(0.9) * |
| **Processing** | | | | |
| D1: intermediate | 5.09 | 3.03 | <<(102)* | <<(61) * |
| D2: process solvent | 2.64 | 1.57 | <<(53)* | <<(31) * |
| D3: others | 0.98 | 0.58 | 20 | 12 |
| D4: dye carrier | 1.77 | 1.05 | 35 | 21 |

* Based on sludge application to agricultural soil, which according to the main manufacturers is *not* relevant

$PEC/PNEC_{terrestrial}$ >1 in all downstream scenarios and thus, a risk is present for terrestrial organisms in these cases. The indicated risk results are based on sludge application. The relatively high concentrations measured in sludge from STPs from several countries in the EU and North America may, furthermore indicate release from unknown sources. The main manufacturers state that residues and sludge from their production and processing sites are incinerated, and thus this problem seems not to be related to the sites of the main manufacturers.

<u>Results for the terrestrial environment</u>

For the production and processing sites of the main manufacturers there is no concern **(conclusion (ii))**.

For all downstream uses resulting in environmental release (cf. scenarios D1 to D4) there is concern **(conclusion (iii))**.

### 3.3.4 Secondary poisoning

For fish eating mammals, the risk assessment is estimated as:

$PEC_{oral} = PEC_{water} \cdot BCF_{fish}$
PNEC oral = 10 ppm.

**Table 3.9** Estimations of $PEC_{oral, fish}/PNEC_{oral}$

| Scenario | $PEC_{oral, fish}$ (mg/kg) | $PEC_{oral, fish}/PNEC_{oral}$ |
|---|---|---|
| **Production** | | |
| A | 0.019 | 0.0019 |
| B | 0.055 | 0.0055 |
| **Processing** | | |
| D1: intermediate | 0.021 | 0.0021 |
| D2: process solvent | 1.22 | 0.122 |
| D3: other | 2.09 | 0.209 |
| D4: dye carrier | 1.88 | 0.188 |

Results for secondary poisoning

For the production and processing sites of the main manufacturers, use as an intermediate, as a process solvent, as a dye carrier and other uses (cf. scenarios A, B, D1 to D4) there is no concern **(conclusion (ii))**.

# 4 HUMAN HEALTH

## 4.1 HUMAN HEALTH (TOXICITY)

### 4.1.1 Exposure assessment

Humans may be exposed to 1,2,4-TCB at the workplace, from the use of consumer products and via the environment.

#### 4.1.1.1 Occupational exposure

Exposure to 1,2,4-TCB can occur by inhalation of vapours and liquid aerosols, by dermal contact to vapours and liquids and via the gastrointestinal tract. Dermal exposure to vapours is considered to be insignificant and ingestion is disregarded.

Information provided by Industry suggests that only few workers are exposed in Europe during production of 1,2,4-TCB, maybe as few as 50 persons.

Thus, for some scenarios the available measured data are scarce and, therefore, it has been decided also to include modelled exposure estimates for these scenarios if possible. No account will be taken of PPE in this exposure section because the actual degree of protection cannot be known.

**Table 4.1** provides an overview of the realistic worst-case exposure for each scenario, which is brought forward to the risk characterisation. Some sub-scenarios have been grouped together since they describe similar activities. Total systemic exposure has been calculated as the sum of the values chosen to represent the realistic worst case for full-shift inhalation and dermal exposures assuming 100% dermal absorption. This figure is therefore potentially an overestimate of the total systemic exposure.

**Table 4.1** Realistic worst-case exposure values for each sub-scenario

| | Type of work | Exposure, inhalation, full shift mg/m³ | Exposure, inhalation, short term mg/m³ | Exposure, dermal mg/kg/d | Exposure, dermal mg/cm² | Total systemic dose mg/kg/d |
|---|---|---|---|---|---|---|
| Q1-Q3 | Surveillance / no information | 0.7 | 2.9[1)] | Negligible | Negligible | 0.2 |
| Q4-Q5 | Collection of samples | 0.7 | 2.9[1)] | 0.6 | 0.1 | 0.8 |
| Q6-Q8 | Drumming | 7.4 | 15 | 0.6 | 0.1 | 2.6 |
| R1-R3 | Loading and collection of samples | 0.7 | 4.8[1)] | 0.6 | 0.1 | 0.8 |
| R4 | Dye carrier | No information | | | | |
| R5 | Process solvent | No information | | | | |
| S1 | Pre-dispersion on high speed dissolver | 14.8 | 30 | 0.6 | 0.1 | 4.7 |
| S2 | Dispersion on pearl mill | 0.7 | 1.4 | 0.1 | 0.01 | 0.3 |
| S3 | Canning of paint | 0.7 | 1.4 | 0.1 | 0.01 | 0.3 |
| S4 | Production of dielectric fluids | No information | | | | |
| T1 | Dismantling transformers | 0.68[1)] | 1.4 | 6 | 0.5 | 6.2 |
| T2 | Spray painting | 3.3 | 6.6 | 8 | 0.4 | 8.9 |
| T3 | Production of plastic pellets | 15.2[1)] | 30 | Negligible | Negligible | 4.2 |
| T4 | Production of wire and cabling | Lack of information | | | | |
| T5 | Polishing | 0.7 | 1.4 | 3.0 | 0.5 | 3.2 |

1) Measured values

#### 4.1.1.2 Consumer exposure

No data are available on consumer exposure, but according to the Nordic Product Registers, 1,2,4-TCB containing products have been available in the EU market recently. Consumer exposure can therefore not, be fully excluded. Hence, three scenarios for consumers have been modelled based partly on the Product Register information on former products and partly on assumptions of the exposure situation.

**Table 4.2** Calculated consumer exposure for the evaluation of risk for acute effects

| | Type of work | Air mg/m³ | Dermal mg/kg bw/event | Dermal mg/cm² | Total systemic dose mg/kg bw/event |
|---|---|---|---|---|---|
| U1 | Spray painting items | 83 | 0.5 | 0.03 | 1.2 |
| U2 | Polishing a bicycle | 5 | 1.4 | 0.1 | 1.4 |
| U3 | Polishing a car | 20 | 2.9 | 0.2 | 3.2 |

**Table 4.3** Calculated consumer exposure for the evaluation of risk for chronic effects

| | Type of work | Air mg/m³ | Inhalational mg/kg/d | Dermal mg/kg bw/day | Total systemic dose mg/kg bw/day |
|---|---|---|---|---|---|
| U1 | Spray painting items | 83 | 0.1 | 0.08 | 0.18 |
| U2 | Polishing a bicycle | 5 | 0.005 | 0.2 | 0.2 |
| U3 | Polishing a car | 20 | 0.02 | 0.2 | 0.2 |

#### 4.1.1.3 Humans exposed via the environment

Indirect human exposure to 1,2,4-TCB may occur. The presence of 1,2,4-TCB in the food chain may however in many cases be due to other sources of environmental release of 1,2,4-TCB rather than the result of a specific industrial use of this particular substance.

According to the EUSES estimations, the values for the total human intake of 1,2,4-TCB for the local scenario range from 0.00118 mg/kg bw/d to 0.0715 mg/kg bw/d depending on the release/use category etc. Regional values are estimated to be $3.3 \cdot 10^{-5}$ mg/kg bw/d.

#### 4.1.1.4 Combined exposure

No estimates of combined exposure have been made. Many of the examples of occupational or consumer exposure are limited either to relatively few exposed individuals or taken as examples of clearly “worst-case” situations. Combination of these examples is not considered to add any additional information to the risk assessment.

### 4.1.2 Effects assessment

1,2,4-TCB is absorbed well and rapidly after oral exposure. The relative amount absorbed after inhalational exposure has not been measured, but subchronic and chronic exposures show that the substance is well absorbed by this route. It is assumed that similar amounts are absorbed after inhalation as are after oral administration. There is also evidence that 1,2,4-TCB is absorbed through the skin, although both the acute and systemic effects seen after dermal administration appear at higher doses than those seen after oral or inhalation administration. This would suggest that absorption by the dermal route is lower.

The substance shows acute toxicity in the “Harmful” range after oral administration. An inhalational $LC_{50}$ of 20,000 mg/m$^3$ and a dermal $LD_{50}$ of 6,000 mg/kg bw/day is taken forward to the risk characterisation.

The substance has traditionally been regarded as irritating to the eyes, the skin and the respiratory tract. The substance shows some eye irritation, but this is not enough to fulfil the classification criteria. Whilst some skin irritation is seen after acute dermal application, irritation is mainly the result of repeated dosing. Evidence for respiratory tract irritation is largely anecdotal.

The substance appears to have weak sensitising properties, which are not considered significant for either classification or risk characterisation.

There are several assays to assess the repeated dose and chronic toxicity. For the purpose of the risk characterisation of total systemic dose, the oral NOAEL is taken as 6 mg/kg bw/d based on a 2-year carcinogenicity study in rats. This is consistent with the NOAEL of 8 mg/kg bw/d from the Côté et al. (1988) 13-week rat study. This figure is close to the level at which effects on liver enzymes and relative organ weights can be seen. At higher doses, elevated adrenal weights, elevated relative liver and kidney weights, histological changes in the liver and thyroid and porphyria are seen.

For chronic inhalational exposure, a NOAEC of 3 ppm (23 $mg/m^3$) has been used in the risk characterisation. The effects seen in this study are very similar to those seen in oral studies. The equivalent oral dose for the rat has been calculated as 3.2 mg/kg bw/d. Whilst slightly lower than the oral value, this is not considered to be unreasonable.

For dermal application the systemic LOAEL is 450 mg/kg bw/d and the NOAEL is 150 mg/kg bw/d based on a four-week rabbit study. These levels are higher than comparable figures for the oral or the inhalation route. The NOAEL will be taken forward to the risk characterisation.

For local effects on the skin, only a LOAEL of 0.9 $mg/cm^2$ could be determined.

The effects seen after long-term exposure to 1,2,4-TCB (e.g. increased liver weights and liver serum enzyme levels, increased adrenal and kidney weights and excretion of porphyrins) have been seen at dose levels below the limits for classification for chronic effects of 50 mg/kg bw/day after oral exposure and 0.25 mg/l, 6 hr/day after inhalational exposure. However, the effects seen at these dose levels are not sufficiently severe to warrant classification with R48/22 or R48/20 according to the EU classification criteria.

The database for genotoxicity is complicated and does not lead to a clear conclusion. There is some evidence of DNA-damage, and there are weakly positive results from two inadequately performed *in vivo* micronucleus assays. The negative Ames test results do not provide strong evidence of a lack of genotoxicity, and the negative clastogenicity studies suffer from a lack of metabolic activation. However, there are no effects on DNA repair in primary hepatocytes and a well-conducted *in vivo* micronucleus test was negative. On balance, 1,2,4-TCB is not considered to express systemic genotoxic effects *in vivo*.

1,2,4-TCB produced a significant increase in hepatocellular carcinomas in B6C3F1 mice, and an increase, however not statistically significant, in the tumours of the Zymbal's gland in F-344 rats after oral administration. No carcinogenic effect was seen in mice after dermal application. The use of the mouse strain B6C3F1 in the carcinogenicity study is complicated by the fact that this strain of mice is known to produce a high incidence of hepatocellular carcinomas when exposed to substances which have a toxic effect on the liver. The 1,2,4-TCB induced liver tumours in the B6C3F1 mice strain is not in itself considered to be relevant for humans. The Zymbal's gland tumours in the F344 rat are of some concern. Whilst the incidence reported here is not statistically significantly increased, in several groups the incidence of carcinomas is substantially higher than the levels normally seen.

In spite of the uncertainties associated with the evaluation of both the genotoxicity and the carcinogenicity of the substance, it is considered unlikely that additional guideline testing would provide further information that would lead to either a change in the conclusion for the mutagenicity or the carcinogenicity of the substance. An investigation of the capability of 1,2,4-TCB for covalent binding to DNA in the Zymbal's gland could be of interest.

Based upon the present data, classification for carcinogenicity or mutagenicity is not considered appropriate.

Since the concern for a carcinogenic effect in the mouse liver is associated with the potential of the substance to cause changes in this organ, a NOAEL that is based on the absence of effects in the liver, i.e. the NOAEL for repeated dose toxicity, is considered to be adequate for the purposes of this risk assessment.

The data on the effects of 1,2,4-TCB is inadequate to properly evaluate the possible effects on reproductive toxicity. The data on the effects of 1,2,4-TCB are inadequate to establish a LOAEL for reproductive effects. A NOAEL for effects on the foetus based on a 2-generation study can be established as greater or equal to 33 mg/kg bw/d for males and 53 mg/kg bw/day for females, which is at a level of 5 to 10 times the NOAEL chosen for repeated dose toxicity. It is considered unlikely that further testing will lead to a lower NOAEL/NOAEC for reproduction. The data presented here do not suggest that classification for reproductive toxicity is appropriate.

### 4.1.3 Risk characterisation

There is no reason for concern with respect to the physico-chemical properties of 1,2,4-TCB. With regard to toxicity see below.

#### 4.1.3.1 Workers

In **Table 4.4**, the conclusions of the risk characterisation for workers in relation to the critical effects, irritation and repeated dose toxicity, are presented.

**Table 4.4** Conclusions of the risk characterisation for workers in relation to critical toxic endpoints

| Scenario | Sub scenario | | Irritation (eye and respiratory tract) | Repeated dose toxicity (inhalation) | Repeated dose toxicity (dermal local effects) | Repeated dose toxicity (dermal systemic effects) |
|---|---|---|---|---|---|---|
| Production of 1,2,4-TCB | Q1-Q3 | Surveillance | ii | ii | ii | ii |
| | Q4-Q5 | Collection of samples | ii | ii | ii | ii |
| | Q6-Q8 | Drumming | ii | **iii** | ii | ii |
| Use of 1,2,4-TCB | R1-R3 | Loading and collection of samples | ii | ii | ii | ii |
| | R4 | As a dye carrier | **i** (insufficient information to evaluate exposure) | | | |
| | R5 | As a process solvent | **i** (insufficient information to evaluate exposure) | | | |
| Production of 1,2,4-TCB containing products | S1 | Pre-dispersion on high speed dissolver | **iii** | **iii** | ii | ii |
| | S2 | Dispersion on pearl mill | ii | ii | ii | ii |
| | S3 | Canning of paint | ii | ii | ii | ii |
| | S4 | Production of dielectric fluids | **i** (insufficient information to evaluate exposure) | | | |
| Use of 1,2,4-TCB containing products | T1 | Dismantling transformers | ii | ii | **iii** | **iii** |
| | T2 | Spray painting | ii | **iii** | **iii** | **iii** |
| | T3 | Production of plastic pellets | **iii** | **iii** | ii | ii |
| | T4 | Production of wire and cabling | **i** (insufficient information to evaluate exposure) | | | |
| | T5 | Polishing | ii | ii | **iii** | **iii** |

For the other toxic endpoints considered, there is no concern for the described workers exposure scenarios (**conclusion (ii)**).

#### 4.1.3.2 Consumers

In **Table 4.5**, the conclusions of the risk characterisation for consumers in relation to the critical effects, irritation and repeated dose toxicity, are presented.

**Table 4.5** Conclusions of the risk characterisation for consumers in relation to critical toxic endpoints

| Scenario | Irritation (eye and respiratory tract) | Repeated dose toxicity |
|---|---|---|
| Spray painting items (U1) | **iii** | **iii** |
| Polishing a bicycle (U2) | ii | **iii** |
| Polishing a car (U3) | **iii** | **iii** |

The acceptability of these consumer applications of 1,2,4-TCB containing products depends on the assumptions made about the frequency of use. The basis for the choice of these scenarios is an assumption that 1,2,4-TCB containing products of this type are in the market, and that they are used by consumers as well as by professionals. The conclusion for the professional use of these products is conclusion (iii). The same conclusion is therefore drawn for consumers (**conclusion (iii)**).

For the other toxic endpoints considered, there is no concern for the described consumer exposure scenarios (**conclusion (ii)**).

#### 4.1.3.3 Humans exposed via the environment

According to the EUSES estimations the values for the total human intake of 1,2,4-TCB for the local scenario range from 0.00118 mg/kg bw/d to 0.0715 mg/kg bw/d depending on the release/use category etc.

The calculated margin of safety (MOS) for total exposure of man via the environment for local production scenarios is approximately 5,000 based on the NOAEL for repeated dose toxicity of 6 mg/kg bw/d. For local use scenarios, the MOS ranges from 84 to 291 for the different scenarios.

The UK-MAFF has calculated the estimated dietary intake of 1,2,4-TCB based on the average concentrations measured in the 1995 survey (UK-MAFF, 1998)[5]. The average dietary intake has an upper bound of 0.48 µg/person/day and a lower bound of 0.04 µg/person/day. For a high-level dietary intake, the comparable figures are 1.3 and 0.09 µg/person/day. The UK report compares these figures directly with the WHO (WHO, 1991) TDI of 1,200 µg/person/day.

The calculated exposures in the local use scenarios range from 1 to 70 µg/kg bw/d. These figures should be compared with the TDI recommended by WHO (1991)[5] of 20 µg/kg bw/d or 7.7 µg/kg bw/d (WHO, 1993).

The drinking-water concentrations calculated for all local processing scenarios using EUSES range from 25 to 122 µg/l. These concentrations exceed both the odour threshold of 5–30 µg/l, the taste threshold of 30 µg/l and the recommended WHO guideline value of 20 µg/l.

In drawing the conclusion shown below it is recognised that

- the TDI set by WHO (1993)[5] may be over conservative, in that an extra uncertainty factor of 10 has been included to reflect the short-term nature of the study; this extra factor would not be required on the basis of the database reviewed here;
- the food sources of concern identified by the EUSES calculations are mainly root crops; the available measured data suggest that these are not likely to be a major source of 1,2,4-TCB intake;
- odour and taste thresholds can vary considerably from individual to individual and that the calculated drinking water concentrations are worst case assumptions.

However daily exposures that exceed WHO recommended TDI values for dietary intake or drinking water concentrations are not considered acceptable (**conclusion (iii)**).

There is concern that the TDI set by WHO (1991, 1993) may be exceeded for indirect exposure via the environment for local use scenarios. In particular, there is concern for the concentrations of 1,2,4-TCB in drinking water for these local use scenarios (scenarios D1 to D4).

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5 For references, see the comprehensive Final Risk Assessment Report that can be obtained from the European Chemicals Bureau: http://ecb.jrc.it

## 4.2 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

1,2,4-TCB has no explosive properties. Its flash point is 110°C, and the auto flammability temperature is >500°C, therefore it is not considered flammable. 1,2,4-TCB has no oxidising properties. **Conclusion (ii)**.

# 5 RESULTS

## 5.1 ENVIRONMENT

**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.

This conclusion applies to production by the main manufacturers and for 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 is reached because of:

- concerns for effects on the aquatic ecosystem and terrestrial ecosystem as a consequence of exposure arising from the use of the substance as a dye carrier and other uses;
- concerns for sewage treatment plants as a consequence of exposure arising from use as an intermediate, as well as from the use sectors of basic chemicals as a solvent, textile industry as dye carrier and other downstream uses.

Risk reduction measures should be considered that will ensure a reduction in the levels of 1,2,4-trichlorobenzene (1,2,4-TCB) found in the environment. Risk reduction measures in relation to downstream open use resulting in environmental exposure is indicated because of risks identified for STP and soil receiving sludge from STPs. This conclusion is supported by the identified risks to the aquatic environment (including the sediment compartment) in relation to use of the substance as a dye carrier and for “other” downstream uses.

The risk indicated above were identified by employing generic release and exposure scenarios because of lack of specific information of the possible open use and subsequent environmental release of the substance. Recent environmental monitoring data however indicate that such uses and environmental releases may still occur in the EU.

## 5.2 HUMAN HEALTH

### 5.2.1 Human health (toxicity)

#### 5.2.1.1 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 general systemic toxicity as a consequence of repeated inhalation exposure arising from drumming activities in the production of the substance, from the production of products containing the substance in the sector of pigment production and from the use of products containing the substance in the sector of spray painting;

- concerns for eye and respiratory tract irritation as a consequence of repeated exposure to the vapour of the substance arising from the production of products containing the substance in the sector of pigment production and from the use of products containing the substance in the sector of production of plastic pellets;
- concerns for general systemic toxicity and local dermal effects as a consequence of repeated dermal exposure arising from the use of the products containing the substance in the sectors of spray painting, dismantling transformers and polishing.

Adverse effects due to eye/respiratory tract irritation and due to repeated dose toxicity after inhalation and dermal exposure cannot be excluded for workers. Risk reduction measures should therefore be considered that will ensure a reduction in the levels of 1,2,4-TCB found in the workplace during the production of 1,2,4-TCB, the production of 1,2,4-TCB containing products, and the use of products containing 1,2,4-TCB.

Irritating effects on skin after repeated dermal exposure cannot be excluded for workers using 1,2,4-TCB containing products. Proper use of personal protective equipment (PPE) should be recommended.

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

This conclusion is reached because of:

- concerns for effects as a consequence of exposure.

The information and/or test requirements are

- information on occupational exposure during the use of the substance as a dye carrier and as a process solvent, during production of products containing the substance in the sector of production of dielectric fluids and during the use of products containing the substance in the sector of production of wire and cabling.

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

In order to make a formal risk characterisation for the scenarios R4 (Use of 1,2,4-TCB as a dye carrier), R5 (Use of 1,2,4-TCB as a process solvent), S4 (Production of dielectric fluids) and T4 (Production of wire and cabling) further information on occupational exposure is necessary.

The actual need to obtain this information allowing the performance of the risk characterisation for these scenarios (R4, R5, S4, and T4) will be considered when the risk reduction strategy is addressed. Hence, any formal request for further information on these processes should be seen in the light of other possible risk reduction measures for these scenarios based on concerns identified elsewhere in this report.

#### 5.2.1.2 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 eye and respiratory tract irritation as a consequence of repeated exposure to vapours and general systemic toxicity as a consequence of repeated inhalation and dermal exposure arising from spray painting and car polishing.

For consumers, adverse effects due to inhalation and dermal exposure cannot be excluded. Risk reduction measures should therefore be considered that will ensure a reduction in the levels of 1,2,4-TCB found during use of products containing 1,2,4-TCB (anti-corrosive paint and maintenance products). However, this conclusion should be seen in the light of a) the products concerned are almost certainly identical to those used by workers, b) for some consumers the use of these products may be highly infrequent, while for others, the use pattern may more closely resemble that of a professional user, and c) it is uncertain whether these products are in fact used at all by consumers.

#### 5.2.1.3 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.

This conclusion is reached because:

- concerns for indirect exposure as calculated exposures can exceed WHO TDIs, and WHO guideline values in drinking water for local use scenarios.

### 5.2.2 Human health (risks from physico-chemical properties)

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

This conclusion is reached because:

- the risk assessment shows that risks are not expected. Risk reduction measures already being applied are considered sufficient.