SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

1,2-dichlorobenzene

EC No 202-425-9

CAS No 95-50-1

Evaluating Member State(s): Hungary

Dated: 16 January 2020

Template Version 2.1
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Evaluating Member State Competent Authority

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Year of evaluation in CoRAP: 2013

Before concluding the substance evaluation a Decision to request further information was issued on: 30 March 2016

Further information on registered substances here:

http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances

DISCLAIMER

This document has been prepared by the evaluating Member State as a part of the substance evaluation process under the REACH Regulation (EC) No 1907/2006. The information and views set out in this document are those of the author and do not necessarily reflect the position or opinion of the European Chemicals Agency or other Member States. The Agency does not guarantee the accuracy of the information included in the document. Neither the Agency nor the evaluating Member State nor any person acting on either of their behalves may be held liable for the use which may be made of the information contained therein. Statements made or information contained in the document are without prejudice to any further regulatory work that the Agency or Member States may initiate at a later stage.

Foreword

Substance evaluation is an evaluation process under REACH Regulation (EC) No. 1907/2006. Under this process the Member States perform the evaluation and ECHA secretariat coordinates the work. The Community rolling action plan (CoRAP) of substances subject to evaluation, is updated and published annually on the ECHA web site[1].

Substance evaluation is a concern driven process, which aims to clarify whether a substance constitutes a risk to human health or the environment. Member States evaluate assigned substances in the CoRAP with the objective to clarify the potential concern and, if necessary, to request further information from the registrant(s) concerning the substance. If the evaluating Member State concludes that no further information needs to be requested, the substance evaluation is completed. If additional information is required, this is sought by the evaluating Member State. The evaluating Member State then draws conclusions on how to use the existing and obtained information for the safe use of the substance.

This Conclusion document, as required by Article 48 of the REACH Regulation, provides the final outcome of the Substance Evaluation carried out by the evaluating Member State. The document consists of two parts i.e. A) the conclusion and B) the evaluation report. In the conclusion part A, the evaluating Member State considers how the information on the substance can be used for the purposes of regulatory risk management such as identification of substances of very high concern (SVHC), restriction and/or classification and labelling. In the evaluation report part B the document provides explanation how the evaluating Member State assessed and drew the conclusions from the information available.

With this Conclusion document the substance evaluation process is finished and the Commission, the Registrant(s) of the substance and the Competent Authorities of the other Member States are informed of the considerations of the evaluating Member State. In case the evaluating Member State proposes further regulatory risk management measures, this document shall not be considered initiating those other measures or processes. Further analyses may need to be performed which may change the proposed regulatory measures in this document. Since this document only reflects the views of the evaluating Member State, it does not preclude other Member States or the European Commission from initiating regulatory risk management measures which they deem appropriate.

[1] http://echa.europa.eu/regulations/reach/evaluation/substance-evaluation/community-rolling-action-plan

Contents

Part A. Conclusion

1. CONCERN(S) SUBJECT TO EVALUATION

1,2-dichlorobenzene was originally selected for substance evaluation in order to clarify the initial concerns on the following grounds:

- Suspected CMR (mutagenic property)
- High (aggregated) tonnage
- Wide dispersive use
- Other (acute toxicity for human health and bioaccumulation)

During the evaluation also other concerns were identified. The additional concerns were:

- Reproductive toxicity
- Skin sensitisation.

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

Compliance check decision was issued for the substance.

3. CONCLUSION OF SUBSTANCE EVALUATION

The evaluation of the available information on the substance has led the evaluating Member State to the following conclusions, as summarised in the table below.

Table 1

CONCLUSION OF SUBSTANCE EVALUATION	
Conclusions	**Tick box**
Need for follow-up regulatory action at EU level	X
Harmonised Classification and Labelling	X
Identification as SVHC (authorisation)	
Restrictions	
Other EU-wide measures	
No need for regulatory follow-up action at EU level	

4. FOLLOW-UP AT EU LEVEL

4.1. Need for follow-up regulatory action at EU level

The initial and additional concerns, except acute toxicity, were removed based on the data in the updated registration dossier and the tests conducted by the Registrant.

During the substance evaluation the Registrant updated the registration dossier with data on the use of the substance. The single professional use (professional use as laboratory reagent) was deleted. Moreover, several industrial uses were withdrawn, and the remaining industrial uses are claimed to be performed in closed systems. Based on this information there is no exposure to 1,2-dichlorobenzene regarding professional workers and consumers.

The evaluating Member State was able to conclude on most concerned endpoints, and found no potential, inadequately controlled risks. Regarding toxicity the evaluating Member State concluded, however, that the concern is confirmed, and harmonised classification and labelling is the most appropriate risk management measure at EU-level.

4.1.1. Harmonised Classification and Labelling

Based upon the substance evaluation the evaluating Member State concludes that several well-conducted acute toxicity studies have shown hepatotoxicity, characterised by elevated plasma alanine aminotransferase and aspartate aminotransferase levels, the major systemic effect occurring at doses of 172 mg/kg bw (oral) or 147 mg/kg bw (intraperitoneal) or greater. An increase in hepatic cell proliferation was observed following a single dose (300 mg/kg bw) along with hepatocyte swelling and necrosis.

As liver effects were seen below the dose levels causing mortality in acute toxicity studies after a single exposure, and also the literature data proved acute hepatotoxic effect, the application of STOT SE Category 2 for hepatotoxicity may be warranted.

Skin sensitising potential of the substance is assumed from the increases in cell proliferation in draining lymph nodes. Differentiation indices being above 1 for the high dose group and the EC 1.4 value calculated to be 32.09% for the test item indicated a specific activation of the cells of the immune system via dermal route after application of 50% 1,2-dichlorobenzene.

In addition, 1,2-dichlorobenzene showed a weak sensitising potential in mice after dermal application in 50% concentration.

Based upon the above data, the Registrant's self-classification of 1,2-dichlorobenzene for skin sensitisation category 1B is appropriate.

Considering the high (aggregated) tonnage of 1,2-dichlorobenzene, harmonised classification for both hepatotoxicity and skin sensitisation is the most appropriate risk management option at EU level.

4.1.2. Identification as a substance of very high concern, SVHC (first step towards authorisation)

Not applicable.

4.1.3. Restriction

Not applicable.

4.1.4. Other EU-wide regulatory risk management measures

Not applicable.

5. CURRENTLY NO FOLLOW-UP FORESEEN AT EU LEVEL

5.1. No need for regulatory follow-up at EU level

Not applicable.

5.2. Other actions

Not applicable.

6. TENTATIVE PLAN FOR FOLLOW-UP ACTIONS (IF NECESSARY)

Indication of a tentative plan is not a formal commitment for the evaluating Member State. A formal commitment to prepare a REACH Annex XV dossier (SVHC, restrictions) and/or CLP Annex VI dossier shall be made via the Registry of Intentions.

Follow-up action	Date for intention	Actor
CLP Annex VI dossier	2021	Hungary

Part B. Substance evaluation

7. EVALUATION REPORT

7.1. Overview of the substance evaluation performed

1,2-dichlorobenzene was originally selected for substance evaluation in order to clarify the initial concerns on the following grounds:

- Suspected CMR (mutagenic property)- High (aggregated) tonnage- Wide dispersive use
- Other (acute toxicity for human health and bioaccumulation)

During the evaluation also other concerns were identified. The additional concerns were:

- Reproductive toxicity
- Skin sensitisation.

Table 4

EVALUATED ENDPOINTS	
Endpoint evaluated	**Outcome/conclusion**
Exposure to the environment	No further action.
Bioaccumulation	Concern was not substantiated.
Acute toxicity	Harmonised classification is warranted.
Reproductive toxicity	Concern was not substantiated.
Mutagenicity	Concern was not substantiated.
Skin sensitisation	Harmonised classification is warranted.

7.2. Procedure

1,2-dichlorobenzene has been selected for substance evaluation according to Article 44 of REACH Regulation for 2013, based upon the Justification Document prepared by the evaluating Member State. The Justification Document identified the above listed initial concerns which warranted a targeted substance evaluation of 1,2-dichlorobenzene.

In the course of the evaluation, the evaluating Member State concentrated on the above listed initial concerns and additional issues identified during the evaluation process, and in this way the evaluating Member State considers that all relevant endpoints have been addressed. While most of the endpoints were evaluated separately, the findings were aligned in the course of the evaluation.

The core documents used for the evaluation were the registration dossier, including the chemical safety reports and the exposure scenarios prepared by the Registrants, as well as further reports referenced by the registration dossier. Further to this, the evaluating Member State identified several relevant scientific studies and articles that were also considered in the course of the evaluation. The evaluating Member State exchanged information with the Registrant several times.

The evaluating Member State found the available data on several endpoints in the registration dossier insufficient, and, therefore, prepared a draft decision that has been sent to the Registrants on 29th April of 2014.

During the course of discussions in the 45th meeting of the Member States Committee the draft decision has been modified, considering that the Registrant provided some additional information regarding the uses and exposure scenarios, and he withdrew the professional use and several industrial uses of the substance. Due to these updates the substance has no wide dispersive use and no exposure of professional workers is expected, therefore, the concerns about inhalation toxicity and reproductive toxicity were not substantiated anymore.

In the final decision the Registrant was requested to conduct an *In vivo* Mammalian Alkaline Comet Assay (test method: OECD 489) combined with In vivo Mammalian Erythrocyte Micronucleus Test (test method: OECD 474) in Tier 1, and depending on the results, Mammalian Spermatogonial Chromosome Aberration Test (if Micronucleus test would be positive) and Transgenic Rodent Somatic and Germ Cell Gene Mutation Assay (if comet assay would be positive) in Tier 2.

The Registrant provided the requested Tier 1 study in 2018. Taking into account the new information gathered during the substance evaluation, the evaluating Member State was able to conclude on every concerned endpoints, therefore, conducting Tier 2 was not substantiated.

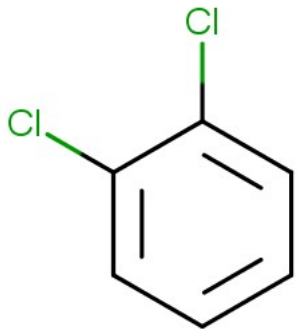
7.3. Identity of the substance

Table 5

SUBSTANCE IDENTITY	
Public name:	1,2-dichlorobenzene
EC number:	202-425-9
CAS number:	95-50-1
Index number in Annex VI of the CLP Regulation:	602-034-00-7
Molecular formula:	$C_6H_4Cl_2$
Molecular weight range:	147.002 g/mol
Synonyms:	o-dichlorobenzol, o-dichlorobenzene, ortho-dichlorobenzene, o-DCB, 1,2-Dichlorbenzol, 1,2-dichloro-benzene, 1,2-Dichlorobenzene, Benzene, 1,2-Dichloro-, Benzene, o-Dichloro-,

Type of substance ☒ Mono-constituent ☐ Multi-constituent ☐ UVCB

Structural formula:



7.4. Physico-chemical properties

Table 7

OVERVIEW OF PHYSICOCHEMICAL PROPERTIES	
Property	**Value**
Physical state at 20°C and 101.3 kPa	liquid
Vapour pressure	2.08 hPa @ 25°C
Water solubility	ca. 155.8 mg/L @ 25°C
Partition coefficient n-octanol/water (Log Pow)	ca. 3.433 @ 25°C
Flammability	non flammable
Explosive properties	non explosive
Oxidising properties	no
Viscosity	ca. 1.324 mPa @ 25°C
Boiling point	ca. 180.5 °C @ 1013.25 hPa
Density	ca. 1.3 g/cm³ @ 25°C

7.5. Manufacture and uses

7.5.1. Quantities

Table 8

AGGREGATED TONNAGE (PER YEAR)				
☐ 1 – 10 t	☐ 10 – 100 t	☐ 100 – 1000 t	☐ 1000- 10,000 t	☐ 10,000-50,000 t
☒ 50,000 – 100,000 t	☐ 100,000 – 500,000 t	☐ 500,000 – 1000,000 t	☐ > 1000,000 t	☐ Confidential

According to ECHA's dissemination site[2] 1,2-dichlorobenzene is manufactured and/or imported in the European Economic Area in 10 000 - 100 000 tonnes per year.

7.5.2. Overview of uses

The substance is used in formulation or re-packing, at industrial sites and in manufacturing. 1,2-dichlorobenzene is used in the following products: pH regulators and water treatment products, laboratory chemicals and heat transfer fluids.

Table 9

USES	Use(s)
Uses as intermediate	-
Formulation	Formulation into mixture
Uses at industrial sites	Use as intermediate Use as processing aid Solvent in polymer production Use in analytical laboratories Use as heat transfer fluids
Uses by professional workers	-
Consumer Uses	-
Article service life	-

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

According to the harmonised classification and labelling approved by the European Union, 1,2-dichlorobenzene is harmful if swallowed, causes skin irritation, causes serious eye irritation and may cause respiratory irritation. Furthermore, the substance is very toxic to aquatic life and it has long lasting effects.

Table 10

HARMONISED CLASSIFICATION ACCORDING TO ANNEX VI OF CLP REGULATION (REGULATION (EC) 1272/2008)							
Index No	**International Chemical Identification**	**EC No**	**CAS No**	**Classification**		**Spec. Conc. Limits, M-factors**	**Notes**
				Hazard Class and Category Code(s)	**Hazard statement code(s)**		
602-034-00-7	1,2-dichlorobenzene; o-dichlorobenzene	202-425-9	95-50-1	Acute Tox. 4* Skin Irrit. 2 Eye Irrit. 2 STOT SE 3	H302 H315 H319 H335	-	-

[2] 11/03/2018

				Aquatic Acute 1 Aquatic Chronic 1	H400 H410		

7.6.2. Self-classification

- In the registration(s):

In addition to the harmonised classification the substance is classified as Acute Tox. 4 (H332) and Skin Sens. 1B (H317).

Further to this, M-factor is assigned to Aquatic Acute 1 and Aquatic Chronic 1 hazard categories (M=1 in both cases).

7.7. Environmental fate properties

7.7.1. Degradation

7.7.1.1. Hydrolysis

The Registrant came to the conclusion that drastic circumstances (high basicity and temperature) are needed for changing the chlorine to hydroxyl group, therefore, the hydrolysis of 1,2-dichlorobenzene under environmental circumstances is unlikely.

The evaluating Member State agrees with the conclusion regarding the hydrolysis of 1,2-dichlorobenzene, because 1,2-dichlorobenzene belongs to the halo-hydrocarbons with low reactivity, therefore, it needs the presence of a base and high temperature for its hydrolysis. Consequently, the hydrolysis of 1,2-dichlorobenzene is unlikely under environmental circumstances.

7.7.1.2. Phototransformation/photolysis

Phototransformation in air

According to the registration dossier, the reaction of 1,2-dichlorobenzene with ozone and the nitrate radical is negligible, its immediate photolysis is unlikely. According to one of the publications, the estimated half-life of photo-oxidation is around 24 days. In another publication it reacts with the hydroxyl radicals that are produced in the atmosphere through photochemical ways. The calculated half-life in case of 4.2*10-13cm^3/(molecule*s) kOH value and the hydroxyl radical 5*105 molecule/cm3 tropospheric concentration is 38 ± 2 days (BUA report, 1990). The presence of 1,2-dichlorobenzene in rainwater indicates that it persists long enough to be returned to the earth´s surface by atmospheric wash out.

Taking into account the available, referred information, the evaluating Member State also found that 1,2-dichlorobenzene photodegrades in the atmosphere through OH-radicals that are produced through photochemical ways. The calculated half-life is 38 ± 2 days [kOH = 4.2*10-13 cm^3/(molecule*s); 5*105 OH molecule/cm3], calculated by Aopwin v1.92. The probability of immediate photolysis is low. 1,2-dichlorobenzene can return to the surface of the Earth through atmospheric washout, which is indicated by its presence in rainwater.

Phototransformation in water

The Registrant summarizes the phototransformation of 1,2-dichlorobenzene in water with reference to a report of BUA, and the half-life is estimated 12.8 days. (BUA report, 1990).

Based on the available reports, the evaluating Member State also found that the photolytic breakdown of 1,2-dichlorobenzene is possible in the top water layers due to the hydroxyl

radicals, and the estimated half-life (Goldach river, Germany) is 12.8 days (BUA report, 1990).

Phototransformation in soil

The Registrant declared that there are no data available for this endpoint.

The evaluating Member State considers this question as not particularly relevant and significant, since phototransformation in soil does not seem probable.

7.7.1.3. Biodegradation

Biodegradation in water

There is great variation in the reported results, with some studies indicating nearly zero biodegradation (Canton et al. 1985), while others report almost complete degradation (unpublished study report, 1985). One study of biodegradation is the OECD Test Guideline 301C with activated sludge exposed to 100 mg 1,2-dichlorobenzene under aerobic conditions for 28 days. The results showed that 1,2-dichlorobenzene is not readily biodegradable in anaerobic conditions (MITI 1992). Other studies showed 100% aerobic degradation of 1,2-dichlorobenzene by adapted microorganisms in the aquatic environment (Goltz et al. 1983, Weber et al. 1987).

Biodegradation in soil

Wang and Jones (1994a) investigated the behaviour and fate of a series of chloro substituted benzenes when spiked into soil (both "standard" soil and sewage sludge amended soil) using kinetic techniques over a 259 day test period. They found that, in general, the decrease in the chlorobenzene content of the soil could be described by a two-step first order kinetic model, indicating two elimination mechanisms.

Soils were either amended with sewage sludge or spiked with a mixed standard solution of chlorobenzenes, including 1,2-dichlorobenzene. Each soil treatment was investigated in four different experimental conditions: normal; sterilized; sterilized and shaded; and sterilized, shaded and sealed. In addition, there was a control, untreated soil. Each 1000 g (dry weight) soil was put in jars 20 cm tall and 10 cm in diameter except the soil in the sealed system. This system contained 60 g (dry weight) soil and was put in 100 mL glass bottles. All soils were placed in a glass house for 259 days where the temperature varied from 20 °C to 30 °C.

The study was not carried out according to a guideline and reported degradation in soil as a two-step process with a DT50 of 8.63 days reported for step 1 and a DT50 of 191 days reported for step 2. As a worst case, the DT50 in the second step (191 days) was taken to represent the DT50 of 1,2-dichlorobenzene in soil at 30°C. Therefore, the equivalent degradation rate at 12°C was calculated to be 806 days according to the EU-TGD (2003). Value used for CSA: Half-life in soil: 806 days at 12 °C.

After reviewing the available and relevant literature, the evaluating Member State accepts that the half-life of 1,2-dichlorobenzene (DT50) at 12 °C in soil is 806 days, since the worst case half-life was used in the calculations.

Concerning the biodegradation of 1,2-dichlorobenzene in water it can be stated that no biodegradation observed under the test conditions. Based on the available and relevant scientific information the evaluating Member State agrees with the conclusions of the Registrant and finds this conclusion acceptable since worst case was applied.

7.7.2. Environmental distribution

Adsorption/desorption

The log Koc value calculated on 20°C that was submitted in the registration dossier and was taken into account in the environmental exposure analysis by the Registrant was: 2,65 (as calculated by the SRC PCKOCWIN v1program). Based on this, it absorbs in the soil in to a small degree.

According to the available and relevant reports and publications, based on the Koc values measured and calculated in the experimental absorption studies (Log Koc: 2.43-3.6), 1,2-dichlorobenzene has a low-average absorption in the different soil types, but it can get to the groundwater with leaching (Chiou et al. 1979, Chiou et al. 1983, Curtis et al. 1986, Mackay et al. 1986, EPA Tech.). The half-life of 1,2-dichlorobenzene in groundwater is estimated to be 30-300 days (Health Canada 1993, NICNAS 2001, OECD 2001). It can absorb strongly in sediments in a water environment (Log Koc: 3.7-4.3) (HSDB 1996).

The evaluating Member State concludes that published log Koc values (2.43-3.6) indicate that 1,2-dichlorobenzene is likely to have a moderate sorption to soil and show slow migration to ground water. The substance is likely to have a strong adsorption to sediment.

Volatilisation

According to the Registrant, the Henry's Law constant values calculated with the EPICS method on different temperatures (10-30°C) are the following: 165 Pa m^3/mol (10°C), 145 Pa m^3/mol (15°C), 170 Pa m^3/mol (20°C), 159 Pa m3/mol (25°C) and 240 Pa m^3/mol (30°C). This indicated that the 1,2-dichlorobenzene easily evaporates from water, getting from the hydrosphere to the atmosphere.

The evaluating Member State came to the same conclusion, that in a water environment, based on the Henry's Law constants referred in the available and relevant reports, the 1,2-dichlorobenzene easily evaporates from water solutions. Evaporation is usually the fastest and shortest process, the sorption and bioaccumulation processes take longer time. Evaporation may lessen the absorption in sediments (EPA Tech., Lawrence 2006, Mackay et al., 1981).

Significant evaporation has to be expected from the soil surface, which may be tempered by absorption and leaching (NICNAS 2001, OECD 2001).

Evaporation is probably an important transport mechanism for the removal of 1,2-dichlorobenzene from the top layers of water and from the soil surface.

7.7.3. Bioaccumulation

Aquatic bioaccumulation

Based on the value of the octanol/water partition coefficient (log Pow=3.43) of 1,2-dichlorobenzene, bioaccumulation is possible. There are many studies and estimations about the bioaccumulation of 1,2-dichlorobenzene. (Casserly et al. 1983, Davis et al. 1983, MITI 1992, Oliver and Niimi 1983, Pereira et al. 1988).

The highest whole body BCF found was 19700 in green algae (Casserly et al. 1983), however the algae are not standard test organisms for the classification and investigation, and in this study the fraction adsorbing to the cells was not determined. The highest lipid content BCF found was 28840 in Blue Crab (Pereira et al. 1988). Some studies (Barrows et al. 1980 and Veith et al. 1980) show that when exposed organisms are moved to a clean environment, elimination is expected. The half-life for elimination from the tissues of bluegill sunfish was less than one day.

The BCF values of fishes are 142-560 (OECD 2001). In the key study (MITI 1992) the maximum BCF in terms of the whole body have been found to be 260 for 56 days. This study was conducted according to a method similar to the OECD Test Guideline 305. These BCF values are consistent with values obtained in other studies (Canton et al., 1985). The measured value in the MITI is far below the bioaccumulation criterion of > 2000 set in Annex XIII to REACH Regulation.

Terrestrial bioaccumulation

1,2-dichlorobenzenes can enter soil-plant systems through many routes, including atmospheric deposition, sewage sludge application to agricultural land, and through industrial activities (Wang and Jones 1994b).

Wang and Jones (1994c) studied the uptake of several chlorobenzene compounds in carrots grown in spiked and sewage-amended soils. The transfer of chlorobenzenes from soils to plants and the subsequent bioaccumulation is of interest because chlorobenzenes are ubiquitous in sewage sludge. Chlorobenzenes are also lipophilic and volatile compounds that can be taken up by plants by both root and foliage pathways. Carrots were grown for 100 days in control soil, chemically-spiked soil, and in low and high rate sludge-amended soils. 1,2-dichlorobenzene concentration in the soils did not remain constant throughout the growth period. BCF values are not traditional steady-state values since measurements were taken for only one time interval.

For the terrestrial food-chain, a BCF of 29.6 was calculated for earthworms (Neuhauser E. F. et al., 1986).

The evaluating Member State considers the available information relevant and appropriate to assess the bioaccumulative potential of 1,2-dichlorobenzene. Based on the measured (MITI 1992) BCF (260) for fish, 1,2-dichlorobenzene has bioaccumulation potential but this potential is limited.

7.8. Environmental hazard assessment

7.8.1. Aquatic compartment (including sediment)

Based on the registration dossier and other relevant scientific publications on the aquatic environment, the evaluating Member State confirmed that 1,2-dichlorobenzene is very toxic to aquatic invertebrates and toxic to algae and fish species as well.

1,2-dichlorobenzene has been tested on a wide range of aquatic organisms for all trophic levels. There are numerous acute data concerning aquatic toxicity of the substance, however chronic data are really rare. As worst case endpoint for the acute toxicity of 1,2-dichlorobenzene to freshwater fish and to algae, LC50 of 1.52 mg/L and EC50/LC50 of 2.2 mg/L value was chosen for Chemical Safety Assessment / for the derivation of PNEC.

Aquatic invertebrates proved to be the most sensitive organisms when they are exposed to 1,2- dichlorobenzene. Results for invertebrates from acute and chronic toxicity tests showed high toxicity, namely EC50 (48h) of 0.66 mg/L to *Ceriodaphnia dubia* and NOEC (based on the EC16 value) of 0.37 mg/L to *Daphnia magna.* (Regarding the NOEC of 0.37 mg/L the authors of the publication considered the EC16 value to be the NOEC in view of the fact that a 10-20% reduction in reproduction is within the range of natural variability.)

The freshwater PNEC is based on the no-observable-effect concentration of 0.37 mg/L obtained in a chronic toxicity test with *Daphnia magna*. Although this test was conducted over 14 days, whereas a 21-day-long test is prescribed in the OECD guideline 211, and EC16 value was chosen as NOEC, the reported endpoint of 0.37 mg/L was still lower than the NOEC of 0.63 mg/L obtained in a similar test with a 21 day exposure.

The reasoned opinion shows that 1.52 mg/L can be accepted to be taken into account for the derivation of PNEC in the aquatic compartment.

7.8.1.1. Fish

Short-term toxicity to fish

Short-term fish toxicity tests of 1,2-dichlorobenzene were performed on several species. In the available scientific publications the measured EC50s for fish range from 1.54 mg/L to 57 mg/L for 1,2-dichlorobenzene. The results of acute toxicity tests strongly depend on test organisms, on experimental conditions (open, closed or flow-through system). Due to the volatile property of the substance, the closed, but rather the flow-through systems are the most appropriate for the determination of effects. The lowest values of LC50 have been determined under the above mentioned conditions accordingly.

The most sensitive species based on the data available in the literature was the Rainbow trout (*Oncorynchus mykiss;* previous name: *Salmo gairdneri*).

As it is described in the paper of Calamari el al. (1983) the LC50 (24h) to the Rainbow trout was found to be 2.3 mg/L in a closed system.

In the paper of Call et al., (1983) the toxicity of targeted substance with the same species was demonstrated by an LC50 (96 h) of 1.58 mg/L and LC50 (144 h) of 1.54 mg/L. These experimental results were measured under well-defined conditions in a flow-through test system where the observations on fish were made daily for 6 days. The mortality and the behaviour of the fish and the test concentration were also monitored and measured daily.

The Rainbow trout was also tested by Ahmad et al., (1984). The LC50 (96h) was established to be 1.61 mg/L while the EC50 (96h) was found to be 1.55 mg/l based on mortality and the observation of abnormal swimming behaviour – usually loss of equilibrium – respectively.

Numerous additional relevant scientific studies had been published concerning the acute toxicity of 1,2-dichlorobenzene to other freshwater fish species. In these studies the acute toxicity of the substance was investigated with zebra fish (*Brachydanio rerio*; new name: *Danio rerio*), Fathead minnow (*Pimephales promelas)*, Bluegill sunfish (*Lepomis macrochirus)* under similar conditions, but none of them proved to be as sensitive as the Rainbow trout.

As it was reported in the WHO report (2004) in the studies with salt water species (with European flounder (*Platichthys flesus*) performed by Furay and Smith (1995) and in an other with Sheepshead Minnow (*Cyprinodon variegatus*) performed by Heitmuller et al., (1981) the LC50 (96h) was found to be 4.616 mg/L and 9.7 mg/L respectively.

In the paper of Dawson et al. (1977) the toxicity effect was examined on the salt-water species Tidewater silverside (*Menidia beryllina*) as well resulted in LC50 values of 7.3 mg/L after 96 h of exposure.

Although the data vary in a wide range of 1.54 to 57 mg/L, the LC50 values are more concurrent within one species as it can be seen from the table above. In the case of Rainbow trout the results remain in a tight range between 1.54 and 2.3 mg/L.

Data obtained from closed or flow-through test systems range from 1-10 mg/L whereas the data from open systems are much higher as it would be expected.

The available and reliable experimental data provide adequate basis for evaluating the short-term toxicity effect of 1,2-dichlorobenzene to fish.

In the course of the evaluation the evaluating Member State took into consideration one further scientific data related to short-term toxicity to fish: In the WHO report (2004) there is a reference published by Call et al., (1979) where the LC50 (96h) for the Rainbow trout

(*Oncorynchus mykiss)* was reported to be in the range of 1.52 and 1.58 mg/L. This is in line with the results in an other publication from the same authors (see above: Call et al., 1983). Although this cited publication (Call et al., 1979) is not available, the authors of both publications are the same, so following the precautionary approach it can be assumed as the minimum value of measured LC50s in the literature, and it can be proposed for further assessment.

The LC50 of 1.52 mg/L (Call et al., 1979) has been considered as the endpoint of acute tests. As it is the lowest LC50 data available in the literature it can be used as a worst case for the aquatic assessment of 1,2-dichlorobenzene.

Long-term toxicity to fish

No long-term fish test is available in the existing and available literature therefore, the chronic exposure and the no-observable-effect concentration (NOEC) cannot be assessed.

There were only two prolonged toxicity studies which are considered reliable (unpublished study report (1990), Könemann (1981) see results in table below) but they are not sufficient to evaluate chronic toxicity because the test duration was below 28 days thus the tests should be regarded acute.

The evaluating Member State deems that as the predicted environmental concentration in surface water is below the PNEC based on the endpoints of the available aquatic studies, therefore, further chronic fish study is not necessary.

7.8.1.2. Aquatic invertebrates

Short-term toxicity to aquatic invertebrates

As all the relevant scientific studies were assessed, invertebrates are the species most sensitive to 1,2-dichlorobenzene. The LC50 to 1,2-dichlorobenzene for aquatic invertebrates ranges from 0.66 to 10.3 mg/L.

The available toxicological data indicate that *Ceriodaphnia cf. Dubia* and *Daphnia magna* are the species most sensitive to 1,2-dichlorobenzene. (Rose et al., 1998, Calamari et al., 1983)

In the study performed by Rose et al. (1998) with *Ceriodaphnia cf. Dubia* according to standard methods the effective mean concentration (EC50) after 48-hour exposure was found to be 0.66 mg/L, which is the lowest endpoint in the available literature.

In the evaluating Member State's view these studies are reliable and sufficient as a key endpoint for further analysis for chemical safety assessment.

Long-term toxicity to aquatic invertebrates

The long term toxicity of 1,2-dichlorobenzene to *Daphnia magna* was investigated for 14 and 21 days by Calamari et al. in 1983 and Kühn et al. in 1989 respectively, and also by Hermens et al. (1984), in the latter with QSAR analysis.

In the 14 day toxicity study under semi-static conditions the lowest-observable-effect concentration (LOEC) and the effective mean concentration (14-d EC50) were 0.4 mg/L and 0.55 mg/L respectively (Calamari et al., 1983). The concentration of the test substance was determined at the start and frequently during the test. The loss of compound did not exceed 15% of the initial value.

The lowest endpoint after the 14 day exposure was an EC16 of 0.37 mg/L. This value was reported by the authors as the no effect concentrations due to the accepted hypothesis that the decrease of reproductive output under 20 % could be considered as the range of natural variability.

Although this test was conducted over 14 days whereas 21-day-long test is prescribed in the OECD Test Guideline 211 and EC16 value was chosen as NOEC, the reported endpoint of 0.37 mg/L was still lower than the NOEC of 0.63 mg/L obtained in a similar test with a 21-day exposure performed by Kühn et al. (1989).

In the study performed by Kühn et al. (1989) the chronic effect of 1,2-dichlorobenzene on daphnids was investigated over 21 days under semi-static conditions also, which is recommended, and the NOEC was determined to be at 0.63 mg/L based on reproduction. Although this test was conducted over more days, the reported NOEC of 0.63 mg/L was higher than the EC16 reported by Calamari et al. in 1983.

Therefore, as a worst case, the EC16 of 0.37 mg/L (Calamari et al., 1983) has been selected to represent the long term toxicity of 1,2-dichlorobenzene to aquatic invertebrates and it was taken into account for long-term toxicity to aquatic invertebrates for the derivation of PNEC.

7.8.1.3. Algae and aquatic plants

All the collected studies showed that algae, both fresh and saltwater, are considerably less sensitive to 1,2-dichlorobenzene toxicity than fish or invertebrates.

1,2-dichlorobenzene has been shown to cause growth inhibition to algae and cyanobacteria at exposure levels above 2 ppm.

With *Chlorella vulgaris, Selenastrum capricornutum* (now: *Pseudokirchneriella subcapitata*) and *Scenedesmus subspicatus* using different nutrient media Millington et al. (1988) determined the Lowest Observed Effect Concentration (LOEC) of the targeted substance after 5 days exposure.

With *Chlorella vulgaris* the observed 5-day LOEC values range from 5 mg/L to 100 mg/L with *Selenastrum capricornutum* from 10 to 80 mg/L and with *Scenedesmus subspicatus* from 50 to 100 mg/L for 1,2-dichlorobenzene influenced by the media.

Calamari et al., (1983) reported observed 96-hour ErC50 values for *Pseudokirchnerella subcapitata* to be 2.2 mg/L as the lowest endpoint (based on growth rate) for algae for 1,2-dichlorobenzene. In the laboratory study the exact NOEC could not be determined from the results, therefore, it was assessed that NOEC is below 0.88 mg/L. The ninety-six-hour EC100 was determined at 17.0 mg/L.

Although, several studies exist where growth inhibition of freshwater algae were observed, there is only one reliable study with cyanobacteria, namely with *Microcystis aeruginosa* reported in the BUA report where the cell-proliferation inhibition test resulted a value for the toxicity threshold of 53 mg/L (BUA report, 1990).

No chronic toxicity studies have been reported on chronic toxicity of chlorobenzene on any (fresh or saltwater) algae species, therefore, only the EC50/LC50 value can be determined for freshwater algae, which is 2.2 mg/L obtained from the study Calamari et al., (1983).

7.8.1.4. Sediment organisms

Though the adsorption of the chemical to sediment may take place, there are no ecotoxicity results available for freshwater sediment organisms exposed through the sediment.

Therefore, the PNEC sediment was calculated using the equilibrium partitioning method based on the PNEC freshwater.

The evaluating Member State has no information that would raise particular concern about this endpoint, and, therefore, accepts the conclusion made by the Registrant.

7.8.2. Terrestrial compartment

Toxicity to soil macro organisms

The results of the acute toxicity test for earthworm (*Eisenia fetida*) are taken into account for the effects on soil macro-organisms except arthropods for the derivation of PNEC:

Acute toxicity test of 1,2-dichlorobenzene was performed on earthworm (*Eisenia fetida*) as soil macro-organism. This test resulted LC50 (48h) 21 µg/cm^2 by Neuhauser (1985, 1986), the 95% confidence range was 19-23 µg/cm^2, following the OECD 207.

A terrestrial arthropod test is not available, but it is not needed, because an earthworm (annelid) acute toxicity test was performed.

The chemical attributes of 1,2-dichlorobenzene (volatility), its soil-water-air distribution % (2.8%-2.5%-94.6%) (OECD SIDS, 2001), and its medium mobility in soil support the conclusions reported by the Registrant regarding the toxic effect of 1,2-dichlorobenzene on soil macroorganisms.

The Registrant stated and evaluating Member State agrees that the earthworm test result cannot be considered suitable for PNEC soil calculation, since the test was a screening test and the result (LC50) was reported as µg/cm^2 of filter paper.

Toxicity to terrestrial plants

As it is stated by the Registrant, the PEC soil is below the PNEC, using the equilibrium partitioning method for the calculation. Consequently a terrestrial plant toxicity test is not required.

The evaluating Member State has not identified any particular concern about this endpoint.

Toxicity to soil micro-organisms

Walton et al. (1989a,b) studied the effects of 1,2-dichlorobenzene at 1000 mg/g on the respiration of soil bacteria at 1 g/kg dry soil to a silt loam soil and a sandy loam soil. The studies were undertaken in the dark at 20°C for 6 days instead of the recommended 28 days test duration according to the OECD 217. The Registrant stated that the reliability of the test result is weak because of the much shorter test duration.

Walton et al., (1989a,b) reported long term NOEC value for soil micro-organisms in two types of soil (silt loam soil and sandy loam soil) used at 1 g/kg 1,2-dichlorobenzene. In the first few days of the test the applied concentration led to lowering in CO_2 production, this effect appeared stronger in the soil with higher organic carbon content. Nevertheless, later (from the 4 to 6 days) the differences in the CO_2 production decreased and were no longer significant compared to control samples. The value of soil microorganisms long term EC10/LC10 or NOEC is 1000 mg/kg soil dw.

As referred in the relevant OECD SIDS dossier (2001), Meharg et al., (1998) reported that 1,2-dichlorobenzene did not show noxious effect on soil microorganisms up to levels of 50 µg/g. They also found that the biomass metabolic activity increased the degradation of the 1,2-dichlorobenzene.

In another test, Thompson et al., (1999) found significant decrease in hyphal fungal length at 65µg/g 1,2-dichlorobenzene concentration, soil bacteria were significantly more tolerant, the population decreases at 3.25 mg/g concentration of the 1,2-dichlorobenzene.

The evaluating Member State accepts the reported data and conclusions regarding the toxic effect of 1,2-dichlorobenzene on soil microorganisms.

7.8.3. Microbiological activity in sewage treatment systems

The available toxicological data (summarised in the table below) indicate that 1,2-dichlorobenzene has harmful effects on microorganisms, but the toxicity to microorganisms can be considered moderate.

Several studies of microorganisms ranging from a few hours to a couple of days duration have shown that the adverse effects of 1,2-dichlorobenzene can be observed above 2-3 mg/L (in Microtox tests) but in most cases this limit is above 50 mg/L.

As it is said in the Technical Guidance Document on risk assessment Part II., the Microtox test cannot be used for determination of the PNEC for microorganisms. This test must be considered as less relevant because it uses a salt-water species: *Vibrio fischeri*.

The function of the protozoa in STP is correlated to their growth. Therefore, values from ciliate growth inhibition tests, preferably with *Tetrahymena*, are relevant for the risk assessment for STPs (TGD II 2003) In a study by Yoshioka et al. (1985) using *Tetrahymena pyriformis* (Ciliate) 1,2-dichlorobenzene at 51 ppm cause 50% growth inhibition after 24 hours exposure.

The potential toxic action of 1,2-dichlorobenzene on water micro-organisms have been performed with *Pseudomonas putida* (bacteria), *Scenedesmus quadricauda* (green algae) and *Entosiphon sulcatum* (protozoa) (Bringmann and Kühn, 1980). (For *Scendesmus quadricauda* (green algae) the results can be found in the table of algae.) The toxicity thresholds (TT) for *Pseudomonas putida* (bacteria) and for *Entosiphon sulcatum* (protozoa) were determined to be 15 mg/L (after 16 hours) and at least 64 mg/L (72 hours) accordingly. Results of the cell multiplication inhibition test with *P. putida* (Bringmann and Kühn, 1980) can only be used for calculation of the PNEC for microorganisms in cases where no other test results employing mixed inoculate are available. However, in this case there are some bacteria tests with mixed cultures. For example, the inhibition of nitrification of *Nitrosomonas* bacteria exposed to 1,2-dichlorobenzene was investigated by Blum and Speece (1991) using a well-defined test method. The IC50 after 24 hour exposure was reported as 47 mg/L. In other publications the I(E)C50 of aquatic microorganisms was found to be much higher than 47 mg/L. In the paper of Yoshioka et al., (1986) using activated sludge bacteria according OECD TG 210, EC50(3h) of 100 mg/L was observed and in the study performed by Blum and Speece (1991) with aerobic heterotrophic culture IC50 of 910 mg/L was detected.

Therefore, an IC50 (24 h) of 47 mg/L has been selected for aquatic microorganisms by the Registrants as the key value for toxicity of microorganisms to 1,2-dichlorobenzene, since additional studies with lower endpoint cannot be considered as reliable as it has been explained in detail above.

Based on the available and relevant scientific information, the evaluating Member State concludes that the Registrant's judgement is relation to this endpoint is correct.

7.8.4. PNEC derivation and other hazard conclusions

7.8.4.1. PNEC water

The freshwater PNEC is based on the no-observable-effect concentration of 0.37 mg/L obtained in a reproduction toxicity test with Daphnia magna since no reliable NOEC value is available or could be quantified for fish species and for algae.

Although the Daphnia reproduction toxicity test was conducted over 14 days instead of 21 days, and EC16 value was chosen as NOEC, the reported endpoint of 0.37 mg/L was still lower than the NOEC of 0.63 mg/L obtained in a similar test with a 21-day exposure.

Therefore, on the basis of these considerations this value can be accepted to be taken into account for the calculation of PNEC in the aquatic compartment using an assessment factor of 100, as it was applied correctly by the Registrant.

Based on the observations made during the scientific evaluation of 1,2-dichlorobenzene, the evaluating Member State is of the opinion that the statements and the conclusions of the Registrant can be supported in the calculation of PNEC for the freshwater compartment.

7.8.4.2. PNEC sediment

Though the adsorption of 1,2-dichlorobenzene to sediment may take place there are no ecotoxicity results available for freshwater sediment organisms exposed through the sediment.

Therefore, the PNEC sediment was calculated using the equilibrium partitioning method based on the PNEC freshwater as recommended by ECHA (2008).

The PNEC resulted in 0.0385 mg/kg sediment wet weight corresponding to 0.177 mg/kg sediment dry weight.

The PNEC calculated with extrapolation method using partition coefficient resulted in 0.0385 mg/kg sediment wet weight corresponding to 0.177 mg/kg sediment dry weight, which is equal to the value given by the Registrant.

7.8.4.3. PNEC soil

The hazard assessment conclusion for the PNEC soil is 0.0333 mg/kg soil dw, using the equilibrium partitioning method.

The Registrant stated and the evaluating Member State agrees with it that according to the ECHA Guidance on Information Requirements and Chemical Safety Assessment, Chapter R10.6 recommendation, if only one relevant test result is available, the PNEC soil should be calculated using the equilibrium partitioning method. PNEC soil calculated 0.0333 mg/kg soil dw, so it was selected as the worst case.

7.8.4.4. PNEC for sewage treatment plant

The IC50 of Nitrosomonas after 24 hour exposure was 47 mg/L in the key study (Blum and Speece 1991). The test method of the study is equivalent to ISO DIS 9509 (Method for assessing the inhibition of nitrification of activated sludge microorganisms by chemicals and waste water) and an assessment factor of 10 was used for the calculation of PNEC.

PNEC for the STP microorganisms is 4.7 mg/L.

Table 11

PNEC DERIVATION AND OTHER HAZARD CONCLUSIONS		
Hazard assessment conclusion for the environment compartment	**Hazard conclusion**	**Remarks/Justification**
Freshwater	PNEC aqua (freshwater): 0.004 mg/L	Assessment factor: 100 Extrapolation method: assessment factor Aquatic invertebrates proved to be the most sensitive organisms when they are exposed to 1,2-dichlorobenzene. The freshwater PNEC is based on the no-observable-effect concentration of 0.37 mg/L obtained in a chronic toxicity test with *Daphnia magna*.
Marine water	PNEC aqua (marine waters): 0 mg/L	Assessment factor: 1000 Extrapolation method: assessment factor The marine water PNEC is based on the no-observable-effect concentration of 0.37 mg/L obtained in a chronic toxicity test with *Daphnia magna*.
Sediments (freshwater)	PNEC sediment (freshwater): 0.177 mg/kg sediment dw	Assessment factor: - Extrapolation method: equilibrium partitioning method There are no ecotoxicity results available for freshwater sediment organisms exposed through the sediment. Therefore, the PNEC sediment was calculated using the equilibrium partitioning method based on the PNEC freshwater.
Sediments (marine water)	PNEC sediment (marine water): 0.018 mg/kg sediment dw	Assessment factor: - Extrapolation method: equilibrium partitioning method the PNEC marine water sediment was calculated using the equilibrium partitioning method based on the PNEC freshwater
Sewage treatment plant	PNEC STP: 4.7 mg/L	Assessment factor: 10 Extrapolation method: -assessment factor The IC50 of Nitrosomonas after 24 hour exposure was 47 mg/L, and an assessment factor of 10 was used for the calculation of PNEC.
Soil	PNEC soil: 0.033 mg/kg soil dw	Assessment factor: - Extrapolation method: equilibrium partitioning method PNEC soil was calculated using the equilibrium partitioning method.
Air	no hazard identified	-

7.8.5. Conclusions for classification and labelling

1,2-dichlorobenzene has been tested on a wide range of aquatic organisms for all freshwater trophic levels. There are numerous acute data concerning aquatic toxicity. Reliable long-term tests with fish and algae are not available. Reliable chronic toxicity tests exist only for Daphnids. Therefore, the derivation of the freshwater PNEC is based on results of three acute tests for the three trophic levels and on the no-observable-effect concentration of 0.37 mg/L obtained in the chronic toxicity test with *Daphnia magna*. According to this information an assessment factor of 100 is applied in the extrapolation method of PNEC for water.

1,2-dichlorobenzene is very toxic to aquatic invertebrates and toxic to algae and fish species as well. The most sensitive species were the water fleas. In the study with *Ceriodaphnia dubia* the effective mean concentration (EC50) was found to be 0.66 mg/L, which is the lowest endpoint.

No data are available for sediment dwelling organisms. Therefore, the PNEC for sediment was calculated using the equilibrium partitioning method based on the PNEC for freshwater. The PNEC resulted in 0.0385 mg/kg sediment wet weight corresponding to 0.177 mg/kg sediment dry weight.

The toxic effect of 1,2-dichlorobenzene on water micro-organisms was investigated with a test method which is equivalent to ISO DIS 9509 (Method for assessing the inhibition of nitrification of activated sludge microorganisms by chemicals and waste water). In this study the IC50 of *Nitrosomonas* after 24 hour exposure was reported as 47 mg/L. An assessment factor of 10 can be used for the determination of the PNEC with this endpoint and the calculation of $PNEC_{STP}$ resulted in a value of 4.7 mg/L.

Two trophic levels were investigated for terrestrial ecosystem according to the available literature. However the reliabilities of these studies were low. Therefore, the PNEC soil should be calculated using the equilibrium partitioning method as 0.0333 mg/kg soil dw.

The evaluating Member State agrees to the relevant findings of the Registrant and considers that establishing the M-factor as 1 for both aquatic acute and aquatic chronic toxicity, as self-classified by the Registrant, seems to be justified.

7.9. Human Health hazard assessment

7.9.1. Toxicokinetics

1,2-dichlorobenzene is well absorbed via the oral route. For the purpose of performing the health assessments it will be assumed that 100% of an oral dose of any of the isomers is absorbed and that 60% of an inhalation dose is absorbed when exposure persists for longer than 1 to 3 hours (Astrand, 1975). In rats, absorption from the gastrointestinal tract seems to be complete at doses of 5 and 50 mg/kg bw but incomplete (83% absorption) at 250 mg/kg bw (Hissink et al., 1996). There are no quantitative data for the dermal and inhalation absorption of 1,2-dichlorobenzene in animals or absorption of the chemical via any route in humans (OECD SIDS, 2001).

The metabolism of 1,2-dichlorobenzene has been well studied in rats, mice and humans and found to be similar (OECD SIDS, 2001). The major site for the biotransformation of 1,2-dichlorobenzene is the liver. Metabolism proceeds predominately by cytochrome P450-mediated aromatic hydroxylation to dichlorophenol derivatives. The major cytochromes involved in the metabolism of 1,2-dichlorobenzene are CYP2B1/2 and CYP2E1, and – via their intermediate epoxides – 3,4-dichlorophenol (3,4-DCP) and 2,3-dichlorophenol (2,3-DCP) are formed as the primary metabolites, respectively (Den Besten et al., 1992; Valentovic et al., 1993a; 1993b). Secondary oxidation of the dichlorophenols produces the corresponding dichloro-hydroquinones and lesser amounts of 3,4- and 4,5-

dichlorocatechol. The hydroquinone and catechol species undergo autoxidation yielding the corresponding dichlorobenzoquinones (Den Besten et al., 1992). Following the administration of 1,2-dichlorobenzene to rabbits and rats, the major urinary metabolites identified were 2,3-DCP, 3,4-DCP and their glucuronide, sulfate and mercapturic acid derivatives (Azouz et al., 1955; Hissink et al., 1996).

All the three isomers have been detected in blood and in adipose tissues (Dowty et al., 1975, Morita et al., 1975; Morita and Ohi, 1975). 1,2-dichlorobenzene has been detected in Canadian mothers' milk at the mean level of 3 ng/g with a maximum of 29 ng/g (Mes *et al.*, 1986). Human exposure to 1,2-dichlorobenzene resulted in the following urinary metabolites being detected: 2,3-DCP, 3,4-DCP, 3,4-dichlorocatechol and 4,5-dichlorocatechol. Each of the metabolites was also present in conjugated form (Kumagai and Matsunaga, 1995).

The orto- and para- isomers of dichlorobenzene are lipophilic and can be expected to bioaccumulate to some extent, particularly in tissues with high fat content during prolonged continuous exposures (Ware, 1988). In rats, 1,2-dichlorobenzene is distributed primarily to the adipose tissue with lesser amounts detected in the kidneys, liver and plasma. 1,2-dichlorobenzene equivalents were bound to the kidneys, liver and plasma with covalent binding accounting for a substantial proportion of bound material (OECD SIDS, 2001). Non-specific covalent binding to the α2μ-globulin fraction of the rat kidney was observed (Charbonneau et al. 1989). Administration of a single dose of 1,2-dichlorobenzene by either the oral, intraperitoneal or intravenous route results in high initial tissue levels of 1,2-dichlorobenzene equivalents and peak tissue levels occur within 1 and 6 hours, depending on the method of administration, followed by rapid decline thereafter (Hissink et al., 1996a; 1996b; 1996c; Stine et al., 1991; Kato and Kimura, 1997).

On the basis of the available information the evaluating Member State did not identify any concern regarding the bioaccumulation of 1,2-dichlorobenzene in humans.

7.9.2. Acute toxicity and Corrosion/Irritation

Oral:

Several acute toxicity studies of 1,2-dichlorobenzene were referred in the registration dossier, however most of them were evaluated by the Registrant as not reliable.

A single dose oral toxicity study of 1,2-dichlorobenzene (Nagata et al., 2001) was conducted according to OECD Test Guideline 401. It was considered reliable by the Registrant as no deviation from the guideline was reported. Male Crj:CD(SD) rats were dosed with 0 (vehicle only), 500, 1000, or 2000 mg/kg bw of 1,2-dichlorobenzene. In addition, female Crj:CD(SD) rats were administered 2000 mg/kg bw in order to show that there were no gender-specific differences. According to the guideline, 5 animals per dose group and sex were used. Three male rats given 2000 mg/kg bw died during the study. The liver showed degeneration and/or necrosis of hepatocytes accentuated in the centrilobular area in dead animals and centrilobular hypertrophy of hepatocytes in survivors. Based on this study, the Registrant considered Acute Tox. 4 for oral toxicity as the proper classification of this endpoint of 1,2-dichlorobenzene.

The evaluating Member State found several other well-conducted acute toxicity studies referred in OECD SIDS Initial Assessment Report have shown hepatotoxicity, characterized by elevated plasma alanine aminotransferase and aspartate aminotransferase levels, the major systemic effect occurring at doses of 172 mg/kg bw (oral) or 147 mg/kg bw (intraperitoneal) or greater (Den Besten et al., 1991; Stine et al., 1991; Allis et al., 1992; Umemura et al., 1996). An increase in hepatic cell proliferation was observed following a single dose (300 mg/kg bw) along with hepatocyte swelling and necrosis (Umemura et al., 1996; OECD SIDS, 2001)

As liver effect were seen below the dose levels causing mortality in acute toxicity studies after a single exposure, and also the literature data proved acute hepatotoxic effect, the application of STOT SE Category 2 for hepatotoxicity seems justified.

In these studies no acute effects on kidney or other organs were reported.

Inhalation:

1,2-dichlorobenzene is an organic, colourless liquid with an aromatic odour. The vapour pressure of the registered substance at 25°C is 1.56 mm Hg (=2.08hPa=0,208kPa) and ca.1 mm Hg (=1.33hPa=0,133kPa) at ca. 20°C. The volatility is an important physico-chemical property of 1,2-dichlorobenzene and also based on the exposure considerations assessing the inhalation route of exposure is necessary.

The Registrant applied the Weight of Evidence approach to fulfil the data requirements for acute inhalation toxicity summarizing the published data about the acute inhalation effects of 1,2,-dichlorbenzene.

Based on the data published by Bonnet P et al. (1979) and Bonnet P et al. (1982) the inhalation LC50 was 7.56 mg/L and 9.36 mg/L in mice and rats, respectively. In rats the published data on signs of toxicity contained hypotension, somnolence, lacrimation and retarded body weight gain up to day 14 of the observation period. However, the autopsy of the surviving animals on day 14 of the observation period did not show observable findings in lung, liver or kidney.

In the OECD SIDS Report (2001) the critical effects from acute exposure to 1,2-dichlorobenzene in animals and humans are eye and respiratory irritation, reported at atmospheric levels at 100 ppm (602 mg/m^3) in humans. At high doses, 1,2-dichlorobenzene produces central nervous system effects in humans and test animals.

Considering these results and the Weight of Evidence approach, classification for Acute Toxicity Category 4 for inhalation seems justified.

Irritation:

1,2-dichlorobenzene has harmonised classification concerning its irritating properties, further to this, no indication of concern has been raised about this endpoint, therefore, irritation is not relevant for this substance evaluation.

Corrosivity:

An acute dermal irritation/corrosion study was conducted according to ETAD guideline and similar to OECD Guideline 404. The study was performed with 24h exposure period instead of 4h exposure period, observations after 24 h, 72h and 7 days was conducted.

Six New Zealand White rabbits were exposed to 0.5 mL 1,2-dichlorobenzene for 24 hours. Observation time points were 24h, 72h and 7 days after removal of the patch.

The mean erythema score between 24h and 72h was 1.56. Irritation was not fully reversible within 7 days. For the mean oedema score between 24h and 72h, a value of 1 was calculated. The effects were fully reversible within 7 days.

According to the study results the evaluating Member State concludes that 1,2-dichlorobenzene does not cause skin corrosion.

7.9.3. Sensitisation

Skin:

Mouse local lymphnode assay (LLNA) was performed with modifications according to the OECD Test Guidelines 429 and 406, EC Guideline 2004/73/EC (29th Adaptation of Guideline 67/548/EEC, B.42)/Health Effects Test Guideline and OPPTS 870.2600 (EPA) with compliance to GLP which was considered to be the key study by the Registrant for assuming the skin sensitisation properties of 1,2-dichlorobenzene. The test item was formulated in acetone/olive oil (4:1) and the following test item solution concentrations were administered: 0 (vehicle control), 2, 10 and 50%. There were increases of statistical significance regarding the weights of the draining lymph nodes and the cell counts in the high dose group compared to vehicle treated animals. The positive level is the increase of the cell count index by 0.4. EC1.4 for the cell counts was clearly exceeded at the high dose group, while the "positive level" of ear swelling has not been reached or exceeded in any dose group.

The sensitising potential is assumed from the increases in cell proliferation in the draining lymph nodes. Differentiation indices were calculated as the quotient of the relative lymph node reaction divided by the relative acute skin reaction were > 1 for the high dose group, i. e. 2.92 and the EC 1.4 value calculated was 32.09% for the test item indicating a specific activation of the cells of the immune system via dermal route after application of 50% 1,2-dichlorobenzene.

These data indicate that, in accordance with the classification proposed in the Technical Report No. 78 of the ECETOC, 1,2-dichlorobenzene has weak sensitising potential in mice after dermal application of a 50% concentration, consequently, the concentration of 10% can be accepted as the NOEL for the parameters investigated in this study with respect to skin sensitisation.

The evaluating Member State agreed that, based upon the above data, the self-classification of 1,2-dichlorobenzene for skin sensitisation category 1B is appropriate and harmonised classification is to be proposed as a risk management option at EU level.

Respiratory system:

The evaluating Member State found no indication of concern regarding the sensitising effects of 1,2-dichlorobenzene on the respiratory system.

7.9.4. Repeated dose toxicity

Oral:

The repeated dose toxicity of 1,2-dichlorobenzene was examined during a 13-week study of male and female rats (F344) administered 1,2-dichlorobenzene (0, 30, 60, 125, 250 or 500 mg/kg bw) 5 days/week by gavage. Only minimal hepatocellular necrosis was observed at 125 mg/kg/day in a few rats (National Toxicology Program (NTP), 1985).

Another 90-day toxicity study was conducted in Sprague-Dawley rats at doses of 25, 100 and 400 mg/kg/day in corn oil by gavage. This study identified a LOAEL of 100 mg/kg bw/day for changes in body and organ weight as well as pathological changes to the liver. A NOAEL of 25 mg/kg bw/day was identified from this study, considering that only kidney weights in females were statistically significantly increased, but with no consistent effects in histopathology, urinalysis or BUN (Robinson et al., 1991).

In the 2-year NTP carcinogenicity study no evidence of treatment-related liver pathology and no increase in serum enzymes (SGPT, GGPT, alkaline phosphatase) were observed in

rats given 60 or 120 mg/kg bw/day for rats in the 13-week subchronic segment of this NTP study. This can justify 60 mg/kg bw/day as a NOAEL.

Despite the relative closeness of the doses in the subchronic and chronic studies (see section 5.8), the only adverse effect found in the chronic exposure study in rats was a slightly reduced body weight gain in high-dose males.

Based on the repeated dose studies listed in the OECD SIDS Report, the NOAEL was 60 mg/kg bw/day, while the LOAEL was 120 mg/kg bw/day, the observed adverse effects included increases in liver and kidney weights and hepatotoxicity (OECD, 2001).

Considering the results of the repeated dose oral toxicity studies, the evaluating Member State concluded that no classification for STOT RE is justified taking into account the guidance values described in Guidance to Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures.

Inhalation:

The Registrant waived the performing of subchronic inhalation toxicity study (90 days) referring to Annex IX of the REACH Regulation stating that a subchronic toxicity study (90 days) does not need to be conducted if a reliable chronic toxicity study is available, provided that an appropriate species and route of administration were used. The Registrant referred to section "7.7 Carcinogenicity", an oral carcinogenicity study was conducted in rats and mice for 103 weeks (NTP, 1985). The Registrant considered that a route-to-route extrapolation was possible based on this oral carcinogenicity study, so a repeated dose toxicity study with inhalative exposure did not need to be conducted. It should be noted that the Registrant did not use the data from carcinogenicity study to derive DNEL value, the subchronic data from the above referred repeated dose toxicity study (NTP, 1985) were the basis of DNEL value.

Based on the OECD SIDS Report (OECD SIDS, 2001) in an inhalation 2-generation reproduction study in rats, the NOAEL and LOAEL based on kidney and liver effects for adult rats were 50 (0.3 mg/L) and 150 ppm (0.9 mg/L) respectively (unpublished study report, 1989).

As indicated in the update of the registration dossier wide dispersive use occurs no longer, and consumer and professional workers are not exposed to the substance, therefore, the evaluating Member State concludes that there is no concern regarding toxicity to liver and kidney via the inhalation route.

7.9.5. Mutagenicity

Human information:

Chromosome studies (Zapata-Gayon et al., 1982) were done in 8 males and 18 females who were accidentally exposed for 4 working days (i.e. 8 hr/day) to vapors of 1,2-dichlorobenzene. The chemical was spread in the basement of the one-floor laboratory building for pest control. There was no determination of the concentration of toxic vapors; the symptoms of most exposed individuals were consistent with those usually observed at concentrations above 100 ppm. The clinical symptoms in 10 individuals included headache, general malaise, dizziness and nausea. All persons had variable degrees of mucosal irritations. Peripheral blood was obtained from all 26 exposed individuals and 11 volunteers were used as controls. Cultures of peripheral blood were made according to the technique of Moorhead et al., (1960). Of the 1345 cells studied, 120 disclosed chromosomal aberrations (mean = 8.92%), whereas a control group of 11 healthy individuals revealed 19 cells with aberrations in 972 cells examined (mean = 2.02%). The main chromosomal alterations were 84 single breaks (6.25%) and 86 double breaks (6.39%). In the control group there were 2 single breaks (0.92%) and 10 double breaks (1.06%), with significant statistic values of $p < 0.001$ for the exposed group. Other chromosomal aberrations were

polyploidy and ring formation but these were not statistically significant. Chromosome studies conducted 6 months later in 15 persons of the exposed group disclosed a significant reduction of chromosomal aberrations, but the aberrations were still present more frequently as compared with the control group.

There are no data about acromatic lesions (gaps), whether they were included or excluded from the analysis of the total aberration yield.

There is no data about the purity of 1,2-dichlorobenzene used for pest control.

In vitro:

Ames test was performed with 1,2-dichlorobenzene on *Salmonella typhimurium* TA 100, TA 1535, TA 98, TA 1537 and E. coli WP2 uvrA with and without metabolic activation according to GLP. No mutagenic activity was observed. (Klimisch reliability factor 1) (unpublished study report, 2001). An earlier Ames test was performed on *Salmonella typhimurium* TA 100, TA 1535, TA 98, TA 1537, TA 1538 with and without metabolic activation. No mutagenic activity was observed. No data on GLP. (Klimisch reliability factor 2) (Shimizu M. et al. 1983)

Sister chromatid exchange (SCE) assay was performed with 1,2-dichlorobenzene on Chinese hamster ovary (CHO) cells by doses up to 59 µg/mL without metabolic activation and 500µg/mL with metabolic activation. Results were negative without metabolic activation and positive with metabolic activation. (Klimisch reliability factor 2) (Loveday K.S. 1990). Another sister chromatid exchange assay was performed on Chinese hamster ovary (CHO) cells as well. The result was again positive with metabolic activation. The lowest positive dose was 59 µg/mL (Klimisch reliability factor 2) (Tennant R.W. et al., 1987). No data on GLP was available for these assays.

Cytogenetic assay was performed on Chinese hamster ovary (CHO) cells by doses up to 202 µg/mL with and without metabolic activation. No mutagenic activity was observed. No data on GLP are available (Klimisch reliability factor 2) (Loveday K.S. et al. 1990). Another cytogenetic assay was also performed on Chinese hamster lung (CHL/IU) cells by doses up to 230 µg/mL without metabolic activation and up to 280 (and 270 µg/mL in confirmative test) with metabolic activation, according to GLP. Test results were negative (clastogenicity occurred only in the presence of expressed cytotoxicity) (Klimisch reliability factor 2) (Masumori S. et al., 2001).

Several mammalian cell gene mutation assays were performed with 1,2-dichlorobenzene giving varying results. In an assay (Klimisch reliability factor 2) on mouse lymphoma L5178Y cells performed by doses up to 130 µg/mL without metabolic activation and up to 78µg/mL with metabolic activation; the results were negative without metabolic activation, but positive with metabolic activation (Myhr B.C. et al. 1991). Another assay was also performed on mouse lymphoma L5178Y $tk^{+/-}$ cells by doses up to 79 µg/mL with and without metabolic activation. Again, the results were negative without metabolic activation and positive with metabolic activation (Klimisch reliability factor 2) (Kim et al., 2007). The result of another mammalian cell gene mutation assay performed on mouse lymphoma L5178Y cells was positive with metabolic activation. The lowest positive dose was 6.5 µg/mL (Klimisch reliability factor 2) (Tennant RW. et al., 1987). The mammalian cell gene mutation assay performed on Chinese hamster ovary cells (CHO/HGPRT) by doses up to 220 µg/mL gave negative results (Klimisch reliability factor 2) (Bioassay Systems. Corp. 1984). No data on GLP was available for any of these assays.

DNA-repair test on primary rat hepatocytes was performed at concentration of 89×10^{-5} M. No genotoxic activity was observed. No data on GLP was available. (Klimisch reliability factor 2) (Williams et al., 1989).

An assay on covalent binding to calf thymus DNA was performed with metabolic activation. The incubation mixture contained 2.5 µCi of ^{14}C-1,2-dichlorobenzene and 1.5 mg of calf thymus DNA.

The covalent binding index showed positive genotoxic effect. No data on GLP was available (Klimisch reliability factor 2) (Colacci A et al., 1990).

In vivo:

Micronucleus assay was performed on bone marrow cells of male mice by daily intraperitoneal injections for 3 days. Doses were 0, 50, 100, 200 mg/kg bw, and 0, 150, 250 mg/kg bw in the first and in the repeated tests, respectively. The initial test was positive by trend analysis (p=0.049) to 200 mg/kg but none of the dose groups were positive. The repeated test at 250 mg/kg was negative by trend analysis. Because of the relatively small increase in MN-PCE in the initial test and the lack of reproducibility, the overall results were considered negative. No data on GLP are available (Klimisch reliability factor 2) (Shelby et al., 1993).

Another micronucleus assay was performed on bone marrow cells of male mice by intraperitoneal administration. Four doses up to 2 x 375 mg/kg bw were tested. The test material was administered in 2 equal doses, 24 h apart. 1,2-dichlorobenzene gave dose dependent positive result. No data on GLP are available (Klimisch reliability factor 2) (Mohtashamipur et al., 1987).

Micronucleus assay was also performed on peripheral blood reticulocytes of mice by i.p. application. Doses were 153.5, 307.0, and 614 mg/kg. Sampling times were 36, 48 and 60 h after administration. The test material proved to be negative in this test. No data on GLP are available (Klimisch reliability factor 2.) (Kim et al. 2007).

Cytogenetic assay was performed on bone marrow cells of male rats, and 1, 0.2 and 0.04 g/kg/day was administered subcutaneously for 16 days. Six animals per dose were sacrificed after 1, 2, 4, 8 and 16 days of treatment. 1,2-dichlorobenzene at 1g/kg/day induced increased mortality, but exhibited no cytogenetic effects in the treated animals. No data on GLP are available (Klimisch reliability factor 2) (Reustle et al,. 1979).

Hepatic DNA damage was investigated by alkaline elution in female rats. Two doses of 150 mg/kg were given per os. The first dose was given 21 h before sacrificing the rats; the second dose 4h before sacrifice. In this test 1,2-dichlorobenzene gave negative results (Klimisch reliability factor 2) (Kitchin et al., 1992)

Somatic mutation and recombination assay was performed on Drosophila melanogaster eyes. In the first test the doses were 3.4 and 6.8 mM in the food, the results were negative. In the second test the doses were 5 and 10 mM in the food. 10 mM was toxic, 5 mM 1,2-dichlorobenzene proved to be weakly positive (Klimisch reliability factor 2) (Vogel et al., 1993).

In vivo binding to DNA was tested by intraperitoneal injection of ^{14}C-1,2-dichlorobenzene (127 µCi/kg body wt) in rats and mice. Animals were killed 22 h after injection. 1,2-dichlorobenzene bound covalently to DNA in all assayed organs (liver, kidney, lung, stomach) of rats and mice. The covalent binding index to liver DNA was typical to those carcinogens classified as weak initiators. No data on GLP (Klimisch reliability factor 1) (Colacci et al., 1990).

Due to the equivocal results an *in vivo* mammalian alkaline comet assay combined with an *in vivo* mammalian erythrocyte micronucleus test was performed.

The combined study was conducted according to OECD test guidelines 489 and 474. Wistar WI (Han) rats (SPF) were used as the test system. Young adult animals were selected for the study. The total number of animals used in the dose-range finding study was 4 and in the main study 25. In the main study 5 male rats were treated per sampling time in each treatment group. The body weights of the rats at the start of the treatment in the main study were within 20% of the sex mean.

In the main study male animals were dosed three times by oral gavage with vehicle (corn oil) or with 125, 250 and 500 mg 1,2-dichlorobenzene per kg body weight for three consecutive days. One positive control group was dosed twice by oral gavage with 200 mg ethyl methane sulfonate (EMS) per kg body weight for the comet assay and another with 20 mg cyclophosphamide (CP) per kg body weight for the micronucleus assay. In total 6 treatment groups were used, each consisting of 5 animals.

The animals of the two highest dose groups showed the following toxic signs after dosing: lethargy, rough coat and a hunched posture. In addition the group dosed with 500 mg/kg showed ataxia.

Considering the observations of clinical signs and the results of a study with Wistar rats treated by gavage with 1,2-dichlorobenzene (Hissink et al., 1996), where blood was sampled at different times after administration and 1,2-dichlorobenzene was detected in the blood. Therefore, this study can be accepted as an alternative evidence of exposure of the bone marrow.

Approximately 3-6 hours after the second dose of EMS and third dose of the vehicle or 1,2-dichlorobenzene the animals were sacrificed and bone marrow, liver, glandular stomach and duodenum were isolated for the micronucleus and comet assay. Single cell suspensions from bone marrow, liver, glandular stomach and duodenum were made followed by comet slide preparation. The slides were analyzed and the Tail Intensity (%) was assessed. Bone marrow smears were prepared for micronucleus analysis.

In the erythrocyte micronucleus test the number of micronucleated polychromatic erythrocytes was counted in at least 4000 polychromatic erythrocytes (with a maximum deviation of 5%). The ratio of polychromatic to normochromatic erythrocytes was determined by counting and differentiating at least the first 1000 erythrocytes at the same time. Micronuclei were only counted in polychromatic erythrocytes. The evaluation was made by light microscope after randomly coding the slides.

The mean number of micronucleated polychromatic erythrocytes scored in the treated groups was compared with the corresponding solvent control group. The animals of the treated groups showed no decrease in the ratio of polychromatic to normochromatic erythrocytes, which indicated a lack of toxic effects of 1,2-dichlorobenzene on the erythropoiesis. The animals of the groups treated with cyclophosphamide showed an expected decrease in the ratio of polychromatic to normochromatic erythrocytes, demonstrating toxic effects on erythropoiesis.

The incidence of micronucleated polychromatic erythrocytes in the bone marrow of all negative control animals was within the 95% control limits of the distribution of the historical negative control database. Cyclophosphamide, the positive control substance, induced a statistically significant increase in the number of micronucleated polychromatic erythrocytes. In addition, the number of micronucleated polychromatic erythrocytes found in the positive control animals was within the 95% control limits of the distribution of the historical positive control database.

Regarding the groups treated with 1,2-dichlorobenzene, no increase in the mean frequency of micronucleated polychromatic erythrocytes was observed in the bone marrow of treated animals compared to the vehicle treated animals.

It can be stated that 1,2-dichlorobenzene is not clastogenic or aneugenic in the erythrocyte micronucleus test of male rats up to a dose of 500 mg/kg (the maximum tolerated dose) under the experimental conditions.

With regard to the comet assay in the vehicle control group the mean Tail Intensity (%) in bone marrow, liver, duodenum and stomach was within the historical control data range. In parallel, the positive control EMS induced a statistically significant increase in the Tail Intensity (%) in bone marrow, liver, duodenum and stomach. In summary, it can be concluded that the comet assay in bone marrow, liver, duodenum and stomach is valid.

No statistically significant increase in the mean Tail Intensity (%) was observed in bone marrow and duodenum of male animals treated with 1,2-dichlorobenzene compared to the vehicle treated animals. In addition, no statistically significant increase in the mean Tail Intensity (%) was observed in liver cells of 1,2-dichlorobenzene-treated male animals at a dose of 125 and 250 mg/kg/day compared to the vehicle treated animals.

At 500 mg/kg a slight but statistically significant increase in the Tail Intensity (%) was observed (2.1-fold increase, $p<0.05$ Dunnett's t test) from 2.35% in the vehicle control to 4.87% at 500 mg/kg. A trend test was performed and a statistically significant trend was observed ($p<0.05$, non-parametric trend analysis by contrast). In stomach cells the 125 and 250 mg/kg treatment group showed a significant increase in mean Tail Intensity (%) from 23.85% in the vehicle control to 57.99% at 125 mg/kg (2.0-fold increase) and to 56.72% (2.4-fold increase) at 250 mg/kg ($p<0.05$ Dunnett's t test). At 500 mg/kg no statistically significant increase was observed. A trend test was performed and a statistically significant trend was observed ($p<0.05$, non-parametric trend analysis by contrast).

All rats were necropsied and part of the liver, stomach and duodenum was fixed. Microscopic examination was performed on the liver and stomach of all animals since an increase in DNA damage was observed in these two organs after treatment with dichlorobenzene.

The following substance-related microscopic findings were present:

In the liver centrilobular necrosis was present in all 1,2-dichlorobenzene treated groups in a dose dependent manner and up to a marked degree. Centrilobular mononuclear inflammatory cell infiltrate was present in all 1,2-dichlorobenzene treated groups in a dose dependent manner and up to moderate degree. In glandular stomach hypertrophy parietal cells were present in all 1,2-dichlorobenzene-treated groups in a dose dependent manner and up to slight degree. Among these findings the centrilobular necrosis in the liver is the only finding representing cell death and causing increased DNA damage.

In liver cells a slight increase in DNA damage in the comet assay was observed at 500 mg/kg. The Tail Intensity of 4.87% is clearly within the historical data control range of the comet assay in the liver. Histopathology showed that, at this dose, centrilobular necrosis was present up to a marked degree. It can be concluded that the DNA damage observed at 500 mg/kg is caused by necrosis.

In the stomach a statistically significant increase in DNA damage was observed at 125 and 250 mg/kg, but no dose response was established since no significant increase was observed at 500 mg/kg. Histopathological examination showed hypertrophy but no necrosis in the stomach at any of the tested concentrations. Thus DNA damage was observed after treatment but since this effect showed no dose response, the overall conclusion was equivocal and additional investigation in a comet assay in stomach was required.

A repeated alkaline comet assay was conducted to investigate the equivocal results in the first assay (unpublished study report, 2018b). The study investigated the same rat strain as the earlier study and the dosing regime and dose levels are identical with the doses investigated in the first study (125, 250 and 500 mg/kg/day). Systemic effects were observed, including reduction in body weight gain and clinical observations, which confirm that this study, as the earlier one, was conducted up to the maximum tolerated dose. In the repeated study - contrary to the first combined study - only liver, stomach and duodenum were investigated. The data obtained with the concurrent vehicle control (% Tail DNA) for liver, stomach and duodenum were within or close to the laboratory historical control ranges. The positive control showed clear, unequivocal increases in % Tail DNA.

1,2-dichlorobenzene did not induce any DNA damage in the liver when administered via oral gavage for 3 days to male rats up to and including 500 mg/kg/day. The animals treated with the substance did not show increases in % Tail DNA. The mean was 2.15% for the

negative control and 1.26, 0.36, and 1.20% for 1,2-dichlorobenzene dose levels 125, 250, and 500 mg/kg/day, respectively. The group mean values for animals treated with the substance were within the laboratory historical control range (0.06 to 2.10%). In the liver of animals receiving 1,2-dichlorobenzene at ≥ 125 mg/kg/day, there was centrilobular necrosis, single cell necrosis and/or degeneration, generally with mononuclear cell infiltrates and increased mitoses. Increased mitoses were also observed with the positive control EMS.

No DNA damage was induced in the stomach when administered via oral gavage for 3 days to male rats up to and including 500 mg/kg/day. The animals treated with 1,2-dichlorobenzene showed statistically significant decrease ($p = 0.042$) in mean of % Tail DNA at the high dose (500 mg/kg/day) which is considered biologically not relevant as there was decrease in mean of % Tail DNA compared to the vehicle control. The group mean of % Tail DNA (0.556%) obtained with this group (0.34 to 0.82%) were low and below the historical control range (1.13 to 14.66%).

1,2-dichlorobenzene caused increase in the mean of % Tail DNA in the duodenum, but this result is considered equivocal as the individual mean values for the 250 and 500 mg/kg/day groups were outside the historical control values. The individual mean values for control, 125, 250, and 500 mg/kg/day groups were 1.43, 0.43, 4.45, and 3.73%, respectively, and the historical control values were between 0.43 and 2.63 %. In the duodenum, findings observed in animals dosed with 1,2-dichlorobenzene at ≥ 250 mg/kg/day were similar to the findings in the positive control EMS group: decreased mitoses and/or staining in crypts.

In summary, increases in mean % Tail DNA above the historical control values for the mid and high dose groups lead to an equivocal result for duodenum.

Due to the equivocal results of the comet assay the Registrant submitted a Weight-of-Evidence (WoE) evaluation on potential mutagenicity after Tier 1 testing (*In vivo* Mammalian Alkaline COMET Assay, OECD 489, combined with *In vivo* Mammalian Erythrocyte Micronucleus Test (OECD 474). The WoE evaluation makes the following statements:

The initial concern on potential in vivo clastogenicity of 1,2-dichlorobenzene is mainly based on a study by Mohtashamipur et al., (1987). In this study the doses of 1,2-dichlorobenzene (0, 187, 375, 562 or 750 mg/kg bw) were halved in two, and administered 24 hours apart by intraperitoneal injections to male NMRI mice and the animals were sacrificed 6 hours after the final injection. At 30 hours after first exposure, a dose-dependent increase in micronuclei was observed in the femoral bone marrow of treated mice compared to control animals. This study had its limitations e.g. lack of data on substance purity, survival of animals, cytotoxicity.

The highest dose in the in vivo mammalian erythrocyte micronucleus assay (OECD 474) conducted by the Registrant was the maximum tolerated dose showing clear treatment related clinical signs indicating (indirect) proof of exposure. The group that was treated with cyclophosphamide showed an expected decrease in the ratio of polychromatic to normochromatic erythrocytes compared to the vehicle control, demonstrating toxic effects on erythropoiesis. In conclusion 1,2-dichlorobenzene is not clastogenic or aneugenic in the bone marrow micronucleus test of male rats up to a dose of 500 mg/kg (the maximum tolerated dose) under the experimental conditions.

The initial concern on potential mutagenicity of 1,2-dichlorobenzene is mainly based on studies by Colacci et al., (1990) and Zapata-Gayon et al., (1982). In the study by Colacci et al., (1990) 24 hours after intraperitoneal injection of radiolabelled 1,2-dichlorobenzene to male Wistar rats and BALB/c mice, covalent binding of radiolabel was detected in the DNA, RNA and proteins of liver, kidney, lung and stomach. The authors stated the covalent binding index to liver DNA to be 17 in rats and 50 in mice. Binding of 1,2-dichlorobenzene to proteins and RNA was higher than to DNA. The chemical nature of the DNA/RNA and protein binding was not investigated.

In a study by Zapata-Gayon et al., (1982) 26 individuals accidentally exposed to 1,2-dichlorobenzene for four days revealed a statistically significant (4.4-fold) increase in the frequency of chromosomal aberrations in peripheral blood lymphocytes as compared with a control group; after six months, chromosomal aberrations were still more frequent than in the control group. Clinical symptoms were reported such as headache, vertigo, nausea, malaise and most individuals reported eye, nose and throat irritation with one individual developing a partial facial oedema. There are no data about the purity of 1,2-dichlorobenzene, therefore, chromosomal aberrations could be caused by 1,2-dichlorobenzene or by impurities or by both of them.

Two in vivo comet assays were conducted by the Registrant (unpublished study report, 2018a and 2018b). In the first comet assay no genotoxic effect was observed in the bone marrow, duodenum and liver. In the stomach, the result was equivocal (unpublished study report, 2018a).

A repeated study was conducted to investigate the equivocal results in the first test in detail (unpublished study report, 2018b). The repeated study investigated the same rat strain as the earlier study and the dosing regime and dose levels are identical with the doses investigated in the first study (125, 250 and 500 mg/kg/day). Systemic effects observed included reduction in body weight gain and clinical observations, which confirm that this study, as the earlier study, was conducted at the maximum tolerated dose. The data obtained for 1,2-dichlorobenzene for increase in % Tail DNA in the duodenum are considered to be equivocal for the repeat study because the individual mean values for the 250 and 500 mg/kg/day groups were outside the historical control values.

MSCA considers that the values are not statistically significant, not dose dependent, only a limited number of historical control data are available for duodenum, the variability of the mid and high dose groups values are high, and the values are substantially lower than the values observed for the positive control group, this equivocal finding might be considered as biologically questionable.

Together with the negative results in the initial study, the remaining uncertainty on the equivocal result observation in the repeated experiment is low.

Based on the available data, the WoE evaluation, the exposure assessment and the fact that, after the dossier update on the uses, no professional use is expected, therefore, human exposure is not significant, the evaluating Member State concludes that 1,2-dichlorobenzene is not mutagenic and the concern for mutagenicity was removed.

7.9.6. Carcinogenicity

In vivo tumor initiation/promotion was evaluated with gamma-glutamyltranspeptidase (GGT) activity in male and female Sprague-Dawley rats. In a non-guideline experiment, one day after a 2/3 partial hepatectomy the rats were treated with diethylnitrosamine (a tumor initiator, 51 mg/kg bw) followed by two 1,2-dichlorobenzene injections (1st and 5th week, 147 mg/kg bw). After the last injection the rats were sacrificed and the incidence of GGT positive foci were analyzed. The number of foci and the morphology of the cells in treated groups were not significantly different from control groups (Herren-Freund and Pereira, 1986).

DNA repair assay which shows good correlation with carcinogenicity was performed on primary cultures of adult male F344 rat hepatocytes. 1,2-dichlorobenzene concentrations were 1 % (v/v) to 10^{-7} % (v/v). In adult rat-liver (ARL) eptihelial cell/transformation assay five marker assays were performed (GGT activity, growth in low calcium medium, growth in soft agar, increase in cell density at confluency and increase in 2DG uptake). 1,2-dichlorobenzene concentrations were 10^{-2} and $5*10^{-2}$ % (v/v).

No cytotoxicity was observed in hepatocytes and 1,2-dichlorbenzene induced a low anchorage independency in ARL cells, but it may occur through non-genotoxic mechanisms (Shimada, 1983).

The most relevant study was performed in the US NTP Programme (NTP report, 1985). In the 2-years (103 weeks) carcinogenicity study performed on male and female rats (F344/N) and mice ($B6C3F_1$) at concentrations of 60 and 120 mg/kg bw 1,2-dichlorobenzene five days per week. Non-neoplastic lesions in liver, kidney, bone marrow, spleen and thymus did not appear, and no evidence of treatment-related liver pathology was found. The incidence of pheochromocytomas was increased in low dose male rats, but the higher dose group exhibited lower occurrence of the premalignant cells than that observed in the control group. Statistically positive trends were detected in the incidence of mice with histiocytic lymphomas in case of treated groups, but the results were not biologically significant as both treated groups exhibited lower occurrence than the control. In rats, the incidence of undifferentiated leukemia was lower in the low-dose female group than in the control group. In the low dose treated group the testicular interstitial tumor appearance was slightly increased in rats and not examined in mice. (NTP report, 1985).

Also no significant changes in serum enzymes (SGPT, GGPT, alkaline phosphatase) were observed in rats treated 60 or 120 mg/kg bw/day in the 13-week subchronic segment of this NTP study.

Signs of carcinogenicity did not reveal in a study where male rats were orally treated during a 9 months' period with 1,2-dichlorobenzene, in extremely low concentrations of 0,001; 0,01; 0,1 mg/kg bw/day (Varshavskaya, 1968).

Other non-guideline experiments with 1,2-dichlorobenzene whose reliability is less than Klimisch 3 were performed and no signs of carcinogenicity were found (Ashby and Paton, 1995; Kitchin et al., 1992).

Based on the available information, no concern for the carcinogenic potential of 1,2-dichlorobenzene has been raised.

7.9.7. Toxicity to reproduction (effects on fertility and developmental toxicity)

Effects on fertility:

In a two-generation reproductive study 1,2-dichlorobenzene was administered in doses of 50, 150 or 400 ppm (equivalent to 305, 915 or 2440 mg/m^3). The route of administration was inhalation. The study however was not GLP compliant and following a compliance check decision by ECHA it was assigned by the Registrant a Klimisch reliability factor of 3 (not reliable). The Registrant concluded that this test is not suitable for assessing the potential effects of 1,2-dichlorobenzene regarding the endpoint of fertility, due to the following major deficiencies:

- Several essential examinations were missing from the study, considering OECD Guideline 416 (Sperm analyses in F0 and F1 adult rats, investigation of oestrous cycle, staging of ovarian follicles at histopathological examinations, histopathology of thyroid/parathyroids, adrenals and seminal/coagulation glands, individual pup weights, clinical signs by pup number, pup organ weights (F1 and F2), determination of implantation sites, prevention of sibling matings, determination of developmental milestones, detailed interpretation of effects and a statement of NOAEL estimation).
- The study lacks clear dose and route rationale.
- The concentrations were below the saturated vapour concentration and were determined without a standard method. Vapour pressure and actual concentration the selected concentrations appear not to be high enough to deliver a valid inhalation study.
- Although the atmosphere was generated by aerosolization there is no aerosol determination referred.

Taking into account the above listed deficiencies, the evaluating Member State concluded that this study report is not adequate for assessing the reproductive toxicity of 1,2-dichlorobenzene. Nevertheless, the effects observed in this study are still considered as indicative of concern, regardless of the actual dose levels. In adult animals, liver and kidney effects were seen and a significantly lower pup weight was observed during lactation in both F0 and F1 litters. This latter effect might be secondary to maternal toxicity, however, without an appropriate reproductive toxicity study, it is not possible to state that there would not be any effects on fertility, under the circumstances of the study.

A short abstract of an experiment is also available for 1,2-dichlorobenzene where male rats were exposed intraperitoneally to doses of 50, 100, 250, 300 or 800 mg/kg bw of test material (Murthy and Holovack, 1985). In this study rats were tested for sperm abnormalities by light microscopic observation of sperm suspensions. Morphological abnormalities were observed (banana heads, acrosomal defects, tail curlings and twisting) in a dose dependent percentage following single administration of the test material. Animals were sacrificed 10 days post exposure. There is no actual article and no further details of the study are available, therefore, the Klimisch reliability of these data is only 4 (not assignable). These data cannot be considered when assessing the reproductive toxicity of 1,2-dichlorobenzene, however, they cannot be completely disregarded either as they might be indicative of a specific toxic effect.

While considering the above mentioned equivocal findings, since the Registrant had declared the withdrawal of the professional use and several industrial uses of the substance, making wide dispersive use of 1,2-dichlorobenzene not probable and thus there is no realistic possibility of significant exposure which may cause reproductive toxicity, no concern regarding fertility was identified by the evaluating Member State.

Developmental toxicity:

There was only one reliable teratogenicity study for 1,2-dichlorobenzene (Hayes et al., 1985; Klimisch reliability factor: 2 – reliable with restrictions) available to the evaluating Member State. In this study the test material was administered via the inhalatory route to rats and rabbits. No data is available for the GLP compliance of the study. The animals were exposed to doses of 100, 200 or 400 ppm (equivalent to 0.6, 1.2, or 2.4 mg/L air) of 1,2-dichlorobenzene.

In rats maternal toxicity was present at all doses: mean body weight and food consumption were significantly lower compared to animals in the control group. An increase was observed in the absolute and relative liver weight of animals in the 400 ppm group and the relative liver weight in the 100 ppm group. The Registrant concluded that the maternal NOAEC was above 400 ppm. The only effect related to the treatment was a significant increase in the occurrence of delayed ossification of cervical vertebral centra in the highest dose group. No other significant dose dependent embryo- or fetotoxic effects were observed at any of the doses; the incidence of major malformations was not significantly increased. The NOAEC for teratogenicity and fetotoxicity were both above 400 ppm.

In rabbits a significant maternal weight loss was observed at all dose levels during the first 3 days of exposure. Liver and kidney weight were unaffected by treatment. The Registrant identified the maternal NOAEC as > 400 ppm (equivalent to 2.4 mg/L air). No significant dose dependent embryo- or fetotoxic effects were evident in the study. The ratio of male to female offspring was significantly different from a 50:50 distribution in the 200 ppm group, however, the sex ratio was not significantly altered in the 400 ppm group. The incidence of major malformations was not significantly increased in any of the exposed groups when compared to the control. The NOAECs for teratogenicity and fetotoxicity were both found to be above 400 ppm.

The above mentioned study (Hayes et al., 1985) has several minor deficiencies, however, it is acceptable as a key study and suitable for assessing the teratogenic potential of 1,2-

dichlorobenzene. Other literature references are also available, these results also seem to support the conclusion that 1,2-dichlorobenzene is not teratogenic in rats or rabbits.

In a supporting study performed on rats and rabbits (Hanley Jr. et al., 1981), where 1,2-dichlorobenzene was administered via inhalation in doses of 1.2, 2.4 or 3 mg/L, no significant effects on reproductive parameters were reported. Slight maternal toxicity was evident for rabbits: non-significant decrease in maternal weight gain and liver weight (absolute and relative) and slight hepatic changes at necropsy. Maternal toxicity was severe for rats: the symptoms included decreased body weight, body weight gain and food consumption, increases in the relative liver and kidney weights and signs of systemic toxicity at gross necropsy. Embryo lethality was observed only among the rats exhibiting the most severe signs of maternal toxicity. The Klimisch reliability factor of this study is 2.

A short abstract is also available (Ruddick et al., 1983, Klimisch reliability: 4). In this study the test material was administered to rats orally by gavage in doses of 50, 100 or 200 mg/kg bw/day. No teratogenic effects were found according to the abstract, which further supports the results obtained from more robust studies.

Several other secondary and less reliable literature data (Dorigan, 1976; John et al., 1984; Johnson et al., 1987; Gombar et al. 1991) have also been referred to by the Registrant, all of them concluding that 1,2-dichlorobenzene has no embryotoxic or teratogenic effects.

Despite the positive findings in the presented available studies, considering the fact that wide dispersive use of the substance is not probable, the evaluating Member State agrees that 1,2-dichlorobenzene raised no concern in relation to developmental toxicity.

7.9.8. Hazard assessment of physico-chemical properties

Not relevant for this evaluation.

7.9.9. Selection of the critical DNEL(s)/DMEL(s) and/or qualitative/semi-quantitative descriptors for critical health effects

The substance is used in closed system, the exposure is unsignificant and well controlled. No professional workers and consumers are exposed to 1,2-dichlorobenzene. Oral, dermal as well as inhalative exposure to the substance may occur. Oral exposure is unlikely to occur if industrial hygiene standards are applied. Consequently, oral exposure was not considered in the assessment of workers' exposure.

For the derivation of DNELs of 1,2-dichlorobenzene, a subchronic gavage (repeated dose) study in rats was evaluated. Based on this study the NOAEL value further used for derivations was 60 mg/kg bw (male and female rats).
For long-term inhalation or dermal route-systemic effects (worker) default extrapolation factors (assessment factors) were used.

The substance is classified as irritant to eye and skin (H315 and H319) and self-classified for skin sensitisation category 1B (H317). Therefore, it was not possible to derive a DNEL for local dermal effects (long-term and short-term) and as a conclusion the substance was classified to the medium hazard range. A qualitative – instead of a quantitative – risk assessment for local exposure (according to the ECHA recommendation) was performed. Notwithstanding most of the above processes are closed and the possibility of dermal contact was considered to be low, dermal exposure (and exposure to the eye) should be minimised by appropriate risk management measures (e.g. technical and organisational measures such as a good standard of general ventilation, minimisation of manual phases; usage of personal protective equipment).

7.9.10. Conclusions of the human health hazard assessment and related classification and labelling

The Registrant did not deviate from the current harmonised classification of 1,2-dichlorobenzene as Skin Irrit. 2, Eye Irrit. 2, STOT SE Category 3 for respiratory irritation and Acute Tox. 4 for oral toxicity. Although the latter classification is also in accordance with the findings of a reliable study selected as key study for the endpoint, the evaluating Member State found that, based upon the results of further studies considered as reliable, the application of STOT SE Category 2 for hepatotoxicity seems to be justified, as well.

The acute inhalation toxicity of 1,2-dichlorobenzene was assessed by the Registrant by using the Weight of Evidence approach considering the relevant published data. Considering the same results and the Weight of Evidence approach applied, the evaluating Member State supports the self-classification made by Registrant and considers that classification for Acute Toxicity Category 4 for inhalation of 1,2-dichlorobenzene seems to be justified.

Several oral repeated dose studies with a duration from 14 days to 2 years were conducted with 1,2-dichlorobenzene. Based on the results of the available repeated dose studies the NOAEL and LOAEL can be set. Considering the guidance values described in Guidance to CLP Regulation no classification for STOT RE is justified for the toxic effects observed after the exposure by oral route.

In addition to the above, the Registrant self-classified the substance for skin sensitisation. In this regard, the evaluating Member State concludes its evaluation as follows.

The Registrant performed a reliable, guideline conform test in order to investigate the skin sensitising properties. Based upon the results of this test the Registrant self-classified 1,2-dichlorobenzene as a weak skin sensitiser. The evaluating Member State has considered the findings of this study and found that the classification of 1,2-dichlorobenzene for skin sensitisation category 1B seems to be appropriate.

In conclusion, the assessment of the human health hazard endpoints confirmed the appropriateness of the substance's current harmonised classification supplemented by the abovementioned additional classification.

7.10. Assessment of endocrine disrupting (ED) properties

During the course of evaluation the evaluating Member State did not find any concern related to endocrine disrupting properties.

7.11. PBT and VPVB assessment

Persistence assessment

Based on the available and relevant scientific publications it can be stated that 1,2-dichlorobenzene is persistent, because 1,2 -dichlorobenzene is not readily biodegradable in water (MITI 1992), or only when microorganisms have been allowed to acclimatize to the presence of the substance (Goltz et al., 1983) (See also chapter 4.1.2.1).

Based on the study of Wang and Jones (1994) 1,2-dichlorobenzene is very persistent (vP), because its half-life in soil is 191 days. This value exceeds the vP criteria based on Annex XIII of REACH Regulation. (See also Chapter 4.1.2.2)

The available and referred studies are relevant and sufficient to assess the persistence of 1,2-dichlorobenzene and it can be concluded that 1,2-dichlorobenzene is persistent in the assessment of PBT properties.

Bioaccumulation assessment

There are many studies and estimates about the bioaccumulation of 1,2-dichlorbenzene (see chapter 4.3.1). Most of them deal with the fishes. The BCF values of fishes are 142-560. In the MITI examination the maximum BCF in terms of whole body have been found 260 for 56 days. This study was conducted according to a method similar to OECD Guideline 305. These BCF values are consistent with values obtained in other studies.

Additional publications exist for other organisms. The highest whole body BCF has been found of 19,700 in green alga (Casserly et al., 1983), but in this study the fraction adsorbing to the cells was not determined. Some studies (Barrows et al., 1980, Veith et al., 1980) show that when exposed organisms are moved to a clean environment, elimination is expected. The half-life for elimination from the tissues of bluegill sunfish was less than one day.

The highest lipid content BCF have been found of 28840 in blue crab. (Pereira et al., 1988). According to REACH Regulation Annex XII "The assessment of bioaccumulation shall be based on measured data on bioconcentration in aquatic species. Data from freshwater as well as marine water species can be used." Based on the Regulation it is obvious that the whole body BCF should be considered instead of the lipid fragment.

1,2-dichlorobenzene has bioaccumulation potential based on the measured (MITI 1992) BCF 260 of fish. This BCF value is consistent with values obtained in other studies.

However, the measured value in the MITI is far below the bioaccumulation criterion of >2000 set in Annex XIII to REACH. 1,2-dichlorobenzene is, therefore, not considered a bioaccumulative substance.

Consequently, 1,2-dichlorobenzene could not be classified as bioaccumulative in the assessment of PBT properties.

Toxicity assessment

1,2-dichlorobenzene has been tested on a wide range of aquatic organisms for all trophic levels.

There are numerous acute data concerning aquatic toxicity of the substance however chronic data are really scarce. No reliable long-term test with fish is available in the existing and available literature. The long term toxicity of 1,2-dichlorobenzene was investigated only on aquatic invertebrates.

In the study performed by Kühn et al., (1989) the chronic effect of 1,2-dichlorobenzene on daphnids was investigated over 21 days, which is recommended by the OECD guideline, and the NOEC was determined to be at 0.63 mg/L.

In the paper of Calamari et al., (1983) the lowest endpoint after the 14 day exposure was an EC16 of 0.37 mg/L. This value was reported by the authors as the no effect concentration due to the accepted hypothesis that the decrease of reproductive output under 20 % could be considered as the range of natural variability.

Although this test was conducted just over 14 days - in contrast with OECD guideline, where the 21-day exposure is recommended - the reported NOEC of 0.37 mg/L is lower than the NOEC reported by Kühn et al., (1989).

Therefore, as a worst case, the NOEC of 0.37 mg/L (Calamari et al., 1983) has been selected to represent the long term toxicity of 1,2-dichlorobenzene to aquatic invertebrates.

The long-term NOEC for freshwater organisms (namely 0.37 mg/L to *Daphnia magna*) is higher than 0.01 mg/L, so the substance is considered not to fulfill the toxicity criterion of the PBT assessment, therefore, 1,2-dichlorobenzene is not classified as toxic in the assessment of PBT properties.

7.12. Exposure assessment

Human health:

No professional workers and consumers are exposed to 1,2-dichlorobenze. In principle, oral, dermal as well as inhalative exposure to the substance may occur during the manufacture of the substance. Oral exposure is unlikely to occur if industrial hygiene standards are applied, consequently, oral exposure was not considered in the assessment of workers exposure.

The substance is classified as irritant to eye and skin (H315 and H319) and STOT SE Category 3 for respiratory irritation with an additional self-classification for skin sensitisation category 1B (H317). Therefore, it was not possible to derive a DNEL for local dermal effects (long-term and short-term) and as a conclusion the substance was classified to the medium hazard range. A qualitative – instead of a quantitative – risk assessment for local exposure (according to the ECHA recommendation) was performed.

Based on the applied risk management measures and operational conditions described in the qualitative (dermal) and quantitative (inhalation) risk assessment reports, no risk towards workers is expected.

Environment:

Production takes place in a closed system at a single industrial site. The discharge is continuous and wastewater is released to the on-site wastewater treatment plant. Direct emission to air also occurs. Direct release to soil is not expected. Indirect emission to soil compartment is considered only via deposition from the atmosphere, the sewage sludge from the on-site WWTP is incinerated.

The waste is considered hazardous and is sent to hazardous waste incineration plants. The opinion of the evaluating Member State is that the exposure assessment for waste stage made by the Registrant is acceptable, because of the process of manufacture, the most representative use patterns (use as an intermediate under strictly controlled conditions and processing aid) and the fact that wastes from all use scenarios are treated as hazardous waste.

When assessing the potential exposure to humans and the environment, the evaluating Member State found that considering the identified uses of the substance, the exposure scenarios prepared by the Registrant cover all possible exposures. The risk management measures are thoroughly identified and described.

Based on the exposure scenarios and other supporting information the evaluating Member State was able to assess the potential exposure of humans and the environment by 1,2-dichlorobenzene and established that when all specified risk management measures and operational conditions are in place and followed, then exposure is practically unlikely and can be considered as insignificant.

7.13. Risk characterisation

7.13.1. Human Health

7.13.1.1. Workers

Based on the calculated values of risk characterization ratios (<1,0 at every identified operations) there is no concern caused by the exposure of workers to the substance when all specified risk management measures and operational conditions are in place and followed. If not, exposure concentrations have to be monitored on a regular basis.

7.13.1.2. Consumers

Not relevant.

7.13.1.3. Indirect exposure of humans via the environment

Based upon the findings on possible environmental exposure indirect exposure of humans via the environment can practically be excluded.

7.13.2. Environment

1,2-dichlorobenzene fulfilled only the P (and vP) criterion of the PBT assessment. Therefore, the substance is not classified as a PBT or vPvB. Experimental data indicate that 1,2-dichlorobenzene is not biodegradable and hydrolytically stable under environmental conditions. In addition, its half-life in soil is 191 days at 25°C. The value of the octanol-water partition coefficient does not fulfil the B criterion. The measured BCF for fish was found to be 260. The lipid content BCF is much higher, but rapid elimination is expected in the environment. The long-term NOEC for freshwater organisms is greater than 0.01 mg/L and the current classification does not include risk phrases that indicate toxicity, so the substance is considered to not fulfil the toxicity criterion. No toxicity data are available for birds.
The environmental risk assessment indicates that 1,2-dichlorobenzene does not pose unacceptable risk to the environment, except for the use pattern of the processing aid by downstream users that shows an increased risk for the aquatic environment. However, there is a wide variety of operational conditions and controls for the different downstream users, some of them have a monitoring programme. The release of 1,2-dichlorobenzene to onsite or municipal STP will be monitored and the release limit is 0.035 mg/L according to the Registrant. In view of the evaluating Member State, a monitoring programme – especially in the case of greater users and release to municipal sewage treatment plant – can guarantee safe usage during processing aid operations by downstream users.

7.14. References

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7.15. Abbreviations

ARL	Adult rat liver
BCF	Bioconcentration factor
BUA	Beratergremium für umweltrelevante Altstoffe
BUN	Blood urea nitrogen
CAS	Chemical Abstracts Service
CHL	Chinese hamster lung
CHO	Chinese Hamster Ovary
CLP	Classification, labelling and packaging
CSA	Chemical Safety Assessment
CSR	Chemical Safety Report
DCB	1,2-dichlorobenzene
DMEL	Derived Minimal Effect Level
DNA	Deoxyribonucleic acid
DNEL	Derived No Effect Level
DT50	Half-life
DU	Downstream user
EC50	Effective concentration 50%
ECHA	European Chemicals Agency
EMS	Ethyl Methanesulfonate
EPA	Environmental Protection Agency
ERC	Environmental Release Category
GGT/GGPT	Gamma-glutamyltranspeptidase
GLP	Good Laboratory Practice
HSDB	Hazardous Substances Data Bank
IC50	Inhibition concentration 50%
IUCLID	International Uniform Chemical Information Database
LC50	Lethal Concentration 50%
LLNA	Local lymphnode assay
LOAEL	Lowest Observed Adverse Effect Level
LOEC	Lowest Observed Effect Concentration
MITI	Malaysia International Trade and Industry

MN-PCE	Micronucleated polychromatic erytrocyte
MSCA	Member State Competent Authority
NICNAS	National Industrial Chemicals Notification and Assessment Scheme
NOAEC	No Observed Adverse Effect Concentration
NOAEL	No Observed Adverse Effect Level
NOEC	No Observed Effect Concentration
NTP	National Toxicology Program
OECD	Organisation for Economic Co-operation and Development
PBT	Persistent Bioaccumulative and Toxic
PNEC	Predicted No Effect Concentration
QSAR	Quantitative Structure Activity Relationship
RMM	Risk management measurement
SEV	Substance Evaluation
SGPT	Alanin aminotransferase
SIAM	SIDS Initial Assessment Meeting
SIDS	Screening Information Data Set
SRC	Syracuse Research Corporation
STOT	Specific Target Organ Toxicity
STOT RE	Specific target organ toxicity — repeated exposure
STOT SE	Specific target organ toxicity — single exposure
STP	Sewage Treatment Plant
TGD	Technical Guidance Document
TT	Toxicity Threshold
UNEP	United Nations Environment Programme
vPvB	Very Persistent and Very Bioaccumulative
WHO	World Health Organization