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ANNEX XV REPORT

(TRANSITIONAL DOSSIER)

SUBMITTED BY: France
DATE: November 2008

SUBSTANCE NAME: Chloroform
IUPAC NAME: Chloroform
EC NUMBER: 200-663-8
CAS NUMBER: 67-66-3

A. SUMMARY

Chloroform is a priority substance on the 2nd priority list in the framework of Council Regulation (EEC) 793/93 on the Control and Evaluation of the Risks of Existing Substances.

Chloroform, produced by hydrochlorination of methanol or chlorination of methane, is used mainly as a raw material in the production of hydrochlorofluorocarbon-22 (HCFC-22). Chloroform is also used in other applications as solvent, especially in the pharmaceutical industry (for example in the extraction of penicillin and other antibiotics), as a chemical intermediate in the production of dyes, pesticides and other substances and also, but in a less extent, as a degreasing agent.

Under EC Council Regulation (EEC) No 793/93 of 23 March 1993 on the evaluation and control of the risks of existing substances, the environmental risk assessment for chloroform has been performed and the final report has been submitted in November 2007 for publication. The human health report has been submitted in May 2008.

Based on the environmental assessment, risks have been identified for the following uses and environmental compartments and the following conclusions have been drawn:

- Conclusion (iii) is applied to the use of chloroform as a solvent for all compartments.
- Conclusion (iii) is also applied to 4 production sites, to all uses and to unintended releases for the sewage compartment.

Based on these conclusions a risk reduction strategy for chloroform in the environment has been developed, discussed and agreed at the last risk reduction meeting in April 2008. It was proposed:

- That competent authorities in the Member States concerned should lay down, in the permits issued under Council Directive 96/61/EC, conditions, emission limit values or equivalent parameters or technical measures regarding chloroform, in order for the installations concerned to operate according to the best available techniques (BAT) taking into account the technical characteristic of the installations concerned, their geographical location and the local environmental conditions.
- That Member States should carefully monitor the implementation of BAT regarding chloroform and report any important developments to the Commission in the framework of the exchange of information on BAT.
- To facilitate permitting and monitoring under Council Directive 96/61/EC (Integrated Pollution Prevention and Control) the results of the risk assessment of chloroform should be taken into account for the ongoing work to develop guidance on ‘Best Available Techniques’ (BAT).

- For plant not covered by the IPPC directive, local emissions to the environment should, where necessary, be controlled by national rules or by permit to ensure that no risk for the environment is expected.

Based on the human health assessment, risks have been identified for the following uses and endpoints:

For workers, conclusion (iii) applies to:

- Manufacture of chloroform and HCFC 22 for acute toxicity (combined), irritation, RDT (inhalation and combined), carcinogenicity (inhalation and combined), fertility (combined) and development (inhalation and combined)
- Chloroform as intermediate or solvent in the synthesis of chemicals for acute toxicity (inhalation and combined), irritation, RDT (inhalation and combined), carcinogenicity (inhalation and combined), fertility (combined) and development (inhalation and combined). It is then recommended to update at community level occupational exposure limit values for chloroform according to Directive 98/24/EEC taking into account this risk assessment.

- For the human exposed via environment, conclusion (iii) applies to human exposed via the environment at local scale for RDT (local) via air, RDT and carcinogenicity via air, food and water. If correctly applied, measures recommended to avoid chloroform release in the environment should appropriately reduce the risk highlighted for the man exposed via environment at local scale.

Finally, the RAR left a conclusion open for mutagenicity. An annex XV classification and labelling dossier will be sent to ECHA before 31 December 2008 with, in particular, a Muta. Cat 3 and Repr. Cat. 3 proposal but the RAR should be updated as soon as the opinion of the Risk Assessment Committee on the French proposal is available.

Chloroform is also a by-product chemical associated with disinfection of swimming pool water; chloroform is originated by the reaction of disinfecting agents with organic substances and not intentionally used. Consequently, it was agreed that the Risk Characterisation of chloroform as a by-product chemical should not be presented in the Chloroform risk assessment but rather than in the Sodium Hypochlorite RAR. Any risk identified in scenario 3 for workers as swimming instructors, lifeguards, competitive swimmers and for consumers as child swimmers and adult swimmers **should be addressed in the Sodium Hypochlorite RAR** (results of RC for scenario 3 are presented in Annex 1 for information).

B. INFORMATION ON HAZARD AND RISK

B.1 Identity of the substance(s) and physical and chemical properties

B.1.1 Name and other identifiers of the substance(s)

This section was built with parts 1.1 of EU-RAR(2007). More details are available in the document joined in annex XV dossier.

Chemical Name: 1,1,1-Trichloromethane
EC (EINECS) Number: 200-663-8
CAS Number: 67-66-3
IUPAC Name: Chloroform

Other names:

- trichloromethane,
- Trichloroform
- formyl trichloride,
- Formylchlorid
- methane trichloride,
- methyl trichloride,
- methane, trichloro-
- methenyl trichloride,
- TCM,
- Freon 20,
- R-20 (Refrigerant),
- HCC 20
- UN 1888
- Chloräterid
- Methenylenchlorür
- Methenyl trichloride
- Methinchlorid
- Methylenchlorür
- ***List not exhaustive***

B.1.2 Composition of the substance(s)

This section was built with parts 1.1 and 1.2 of EU-RAR(2007). More details are available in the document joined in annex XV dossier.

Table B.1.2-1: Chloroform chemical description

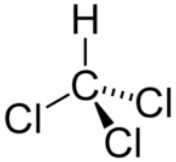
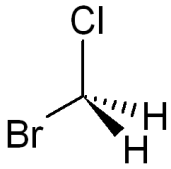
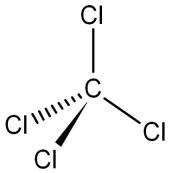
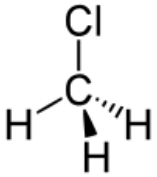
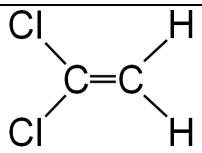
Main substance	
Chemical Name:	1,1,1-Trichloromethane
EINECS Number:	200-663-8
CAS Number:	67-66-3
IUPAC Name:	Chloroform
Molecular Formula:	$CHCl_3$
Structural Formula:	
Molecular Weight:	119.38 g/mol
Typical proportion %	≥ 99 % w/w
Real proportion (range) in %	Not available

Table B.1.2-2: Chloroform's impurities chemical description

Impurity 1	
Chemical Name:	chlorobromomethane
EINECS Number:	200-826-3
CAS Number:	74-97-5
IUPAC Name:	bromochloromethane
Molecular Formula:	CH_2BrCl
Structural Formula:	
Molecular Weight:	129.38
Typical proportion %	unknown
Real proportion (range) in %	
Impurity 2	
Chemical Name:	carbon tetrachloride
EINECS Number:	200-262-8
CAS Number:	56-23-5
IUPAC Name:	Carbon tetrachloride (Tetrachloromethane)
Molecular Formula:	CCl_4
Structural Formula:	
Molecular Weight:	153.82
Typical proportion %	unknown
Real proportion (range) in %	
Impurity 3	
Chemical Name:	chloromethane
EINECS Number:	
CAS Number:	74-87-3
IUPAC Name:	chloromethane
Molecular Formula:	CH_3Cl
Structural Formula:	
Molecular Weight:	50.49
Typical proportion %	< 0.005 % w/w
Real proportion (range) in %	

Impurity 4	
Chemical Name:	1,1-dichloroethylene
EINECS Number:	200-864-0
CAS Number:	75-35-4
IUPAC Name:	1,1-Dichloroethene
Molecular Formula:	$C_2H_2Cl_2$
Structural Formula:	
Molecular Weight:	96.95
Typical proportion %	< 0.002 % w/w
Real proportion (range) in %	
Additives	
Chemical Name:	confidential data
EINECS Number:	
CAS Number:	
IUPAC Name:	
Molecular Formula:	
Structural Formula:	
Molecular Weight:	
Typical proportion %	≤ 1 %
Real proportion (range) in %	

B.1.3 Physico-chemical properties

This section was built with part 1.3 of EU-RAR. More details are available in the document joined in annex XV dossier.

Chloroform is a volatile, heavy, colourless liquid. It is non-flammable and possesses a characteristic sweet odour.

Table B.1.3-1: Summary of physico-chemical properties of the substance

Property	**Value**
Molecular weight	119.5 g/mol
Melting point	- 63.5°C
Boiling point	61.3 °C
Relative density	1.48 at 20°C
Vapour pressure	209 hPa at 20°C
Partition coefficient	Log Kow 1.97
Henry's law constant	H=367 Pa.m3/mol at 25°C
Water solubility	8,700 mg/L at 23°C
Flash point	None
Flammability	no

B.1.4 Justification for grouping

No grouping proposed.

B.2 Manufacture and uses

This section is a summary of the information provided in the RAR already summarised in the RRS for the environment. For more details, refer to the chapter 2.1 of the RAR and chapter 2.2 of the RRS.

B.2.1 Manufacture and import of the substance

The production of chloroform is located at nine sites in the European Union (one of the ten sites stopped manufacturing chloroform in 2004). The total EU production volume was 302 800 tonnes in 2002. When taking into account imported and exported volumes, this annual tonnage is around **271,000**.

Two industrial processes are currently used to produce chloroform: hydrochlorination of methanol and chlorination of methane.
Hydrochlorination of methanol is a two-stage process in which methanol reacts primarily with hydrogen chloride and the resulting methyl chloride is then chlorinated using chlorine gas. The first reaction occurs in the vapour phase over a catalyst. The other chloromethanes are then formed by the thermal, non-catalytic chlorination of methylchloride. A simpler method for the production of chloroform involves the thermal, non-catalytic chlorination of methane. This one stage process is carried out at over 400°C and under a 200 kPa pressure to produce a mixture of all four chloromethanes. The ratio of products can be varied by controlling the feed rates of methane and chlorine and by recycling methane and unwanted lower halocarbons, e.g. methyl chloride.

B.2.2 Uses

Chloroform is mainly used as a raw material in the production of hydrochlorofluorocarbon-22 (HCFC 22), but also in other applications including production and extraction solvent, especially in the pharmaceutical industry (for example in the extraction of penicillin and other antibiotics). In some cases, chloroform is also used as a degreasing agent and as a chemical intermediate in the production of dyes, pesticides and other substances. Chloroform is registered in the USA for use as an insecticidal fumigant on stored grains and as mildew-fungicide for tobacco seedlings, but these applications aren't registered in the European Union. Elsewhere, unintended emissions of chloroform are observed in water chlorination processes or chlorination for paper bleaching (see section B.2.4.d for some details on uninteded releases of chloroform, see summary table of all life stages in section B.11).

B.2.2.1. Intermediate in HCFC-22 production

Chloroform is used mainly (**234,000** tpa in 2002, 86.3% of the net production) as a raw material in the production of hydrochlorofluorocarbon-22 (HCFC-22). Future trends in chloroform use should therefore depend, at least in part, on the trends of HCFC-22 manufacture.

This HCFC is an ozone depleting substance and its use has been controlled firstly under the Copenhagen Amendment (1992) to the Montreal Protocol on substances that deplete the ozone layer (1987): a freeze to 1989 consumption of HCFCs was agreed. The last regulation adopted on 29th September 2000 already set up a revised reduction program for the production of HCFCs (JOCE L. 244, September 29th, 2000); but in September 2007 at Montreal's Protocol's 20th Anniversary Celebrations, governments agreed to change again this program by freezing the production of HCFCs only in 2013 (at the average production levels in 2009-2010) and bringing forward the final phase-out date of these chemicals by 2020 in developed countries and more slowly in developing countries. This is detailed in the table below.

Table B.2.2-1: Montreal protocol Phasing-out program of HCFCs

Copenhagen Amendment (1992) to the Montreal Protocol (first plan)	Montreal's Protocol's 20th Anniversary Celebrations (2007) (revised plan)	
All countries	Developed countries	Developing countries
- Freeze: 1997 (to 1989 consumption levels) - 65% reduction by 2008; - 80% reduction by 2014; - 85% reduction by 2020; - Phase-out by 2025.	- Freeze: 2013 (to average production level of 2009-2010) - 75% reduction by 2010; - 90% reduction by 2015; - Phase-out by 2020.	- 10% reduction by 2015; - 35% reduction by 2020; - 67.5% reduction by 2025; - Phase-out by 2030.

In facts, in the 90s', the freeze of HCFCs consumption has been translated into a slight freeze in productions as shown in the following quantities of global HCFC-22

production: 213,700 t in 1990, 236,800 t in 1991, 245,700 t in 1992, 240,600 t in 1993 and 239,400 t in 1994.
Total HCFC-22 European production is estimated to have been approximately 150,000 tonnes in 1995 with 53,000 tonnes being sold for dispersive end uses (as refrigerant, fire-fighting material, foam blowing agent), 57,000 tonnes being used as chemical feedstock, the remainder being exported from the European Union. All the dispersive end uses of HCFC-22 may also be subjected to control in the next following years. This means that there may be a future reduction in demand for chloroform since HCFC-22 production is accounting for 96.5% of chloroform uses. However, this must be moderate because on the one hand the reduction of this production is slower than hoped initially and on the other hand other fluorocarbon productions using chloroform could grow.

At the European level, EU HCFC-22 production seems to have initiated a slight decrease during the last years: 150,000 t in 1995, 177,000 t in 1998; 169,000 t in 1999; 149,000 t in 2000; 140,000 t in 2001; 146,000 t in 2002. However, as there has been only a slight decrease in production since 1995, an average HCFC-22 production volume of 150,000 tpa has been used in the risk assessment.

The Ozone Depleting Substances (ODS) Regulation 2037/2000/EC (HCFC-22 is in group VIII of Annexe II), limiting and controlling the production, the import, the export, the use, the recycling, the destruction of these substances goes beyond the rules of the protocol of Montreal. However, western EU annual capacity for HCFC-22 was still reported, according to CEFIC, to be of 175,500 t in January 2001. Furthermore, the Regulation's major focus is to stop the use in refrigeration and air-conditioning equipment (in particular domestic refrigerators, freezers and building insulation foam, containing CFCs) and not the ones used as intermediate notably for polymer’s synthesis. The total Western European consumption of fluorocarbons was estimated 198,000 tonnes in 2005.

B.2.2.2. Solvent or/and other applications

In the pharmaceutical industry, chloroform is used as solvent for example in the extraction of penicillin and other antibiotics. Elsewhere, chloroform is is used as solvent or degreasing agent or chemical intermediate in industries like adhesives, pesticides, fats, oils, etc. In the manufacture of vinyl chloride /polyvinyl chloride (VC/PVC, IUPAC name: Polychloroethene) products and other chlorinated bulk chemicals, chloroform is a by-product. Similarly, chloroform is an important building block for fluorinated polymers and copolymers. Chloroform is also formed during the oxichlorination of ethylene by chlorine to produce ethylene dichloride (EDC), and during further steps to trichloroethylene and tetrachloroethylene.

The identification of the uses as intermediate or as solvent are all the time clear and should updated. However, it could be stated that, productions in 2002 were estimated 302,800 t, the export balance 31,800, the use as intermediate in HCFC-22 production 254,200, the use as solvent **8,700**, the other uses then HCFC-22 production and as solvent **8,100 tonnes**.

B.2.3 Uses advised against by the registrants

none

B.3 Classification and labelling

B.3.1 Classification in Annex I of Directive 67/548/EEC

According to Annex I of Directive 67/548/EEC, chloroform is classified as **harmful** and labelled as follows:

Table: Chloroform classification according to Directive 67/548/EEC

Symbol:		**Xn** [harmful]
R phrases:	1 % ≤ conc. < 5 %	**R 40** [Limited evidence of a carcinogenic effect]
	5% ≤ conc. < 20 %	**R 22** [Harmful if swallowed]
		R 40-48/20/22 [Harmful: danger of serious damage to health by prolonged exposure through inhalation and if swallowed]
	conc. ≥ 20 %	**R 22-38** [Irritating to skin]
		R 40-48/20/22
S-phrases:		**S 2** [Keep out of the reach of children]
		S 36/37 [Wear suitable protective clothing and gloves]

Revision of the classification of chloroform was discussed and agreed by the TC C&L in september 2007:

- The TC C&L agreed not to classify chloroform with Xi & R37 as the nasal effects reported were rather covered by Xn & R48/20.
- Further, the TC C&L agreed that R48/22 could be deleted as effects were only seen at high doses.
- They also agreed on classification with Repr. Cat. 3 & R63 based on the FR proposal.
- The narcotic effects that would be covered by Xn & R20 under the current system would trigger classification with STOT Single 3 under the CLP Regulation.

TCNES I'08 did not succeed in taking a decision on a conclusion on the endpoint mutagenicity as for a conclusion (ii) or (iii) there was not enough evidence which could be supported by the majority of the member states and for a conclusion (i) no

test proposal could be supported. Therefore the risk assessment of chloroform was not finalized for this endpoint under the ESR program and the conclusion was left open with regard to mutagenicity of chloroform. The classification for this endpoint should be submitted to ECHA before 31 December 2008.

Environmental classification: Chloroform is currently not classified as dangerous for the environment. Based on the outcome of the hazard assessment, the proposal of the rapporteur was not to classify chloroform as dangerous to the environment: The risk phrase R52/53 may apply based on acute toxicity data; however considering chronic toxicity results above 1 mg/L the escape clause cancels this proposal.

B.3.2 Classification in classification and labelling inventory/Industry's self classification(s) and labelling

No data available on industry's self classification

B.4 Environmental fate properties

For more details on this section, refer to chapter 3.1 of the environmental RAR.

B.4.1 Degradation

Hydrolysis

Pearson and McConnell, 1975 observed that chloroform hydrolyses in contact with water. Dilling *et al.*, 1975 determined experimentally a hydrolysis first order rate of 0.045 $month^{-1}$, which corresponds to a **half-life of 15 months at 25 °C**. The study was conducted for 12 months with a $CHCl_3$ concentration of 1 ppm in light proof pyrex tubes. The pH is not known.
Mabey and Mill, 1978and Jeffers *et al.*, 1989 measured lifetimes at different pH values. The half-life at **pH 7 was 1850 years at 25 °C**, at pH 9, 24 years and 0.24 years at pH 11. No acid catalysis was observed.

Conclusion: hydrolysis is an unimportant fate process at a neutral pH value.

Photolysis in water

Hubrich and Stuhl, 1980 and Dilling *et al.*, 1975 did not observe any photodegradation of chloroform in water. The test substance was exposed in air-saturated water for one year. No absorption of UV (> 175 nm) or visible light and no absorption under environmental conditions (> 290 nm) were determined.
Zepp *et al.*, 1987 estimated the first order rate by photoejected electrons near the surface water in a lake during July, assuming a concentration of dissolved organic carbon of 4 mg/L. With a first order rate of 1.3×10^{-3} h^{-1}, a half-life of 533 hours can be derived.
A lack of light absorption has been determined. The observed photolysis by Zepp *et al.*, 1987 is probably only important in the very upper surface layer and depends on the dissolved organic carbon content.

It is concluded that direct photolysis is not an important fate process.

Photodegradation in air

The rate of chloroform removal by reaction with hydroxyl radicals has been estimated by many different authors.
Pearson and McConnell, 1975 exposed 2000 - 4000 ppm chloroform in flasks filled with ambient air to diurnal and climatic variations in temperature and radiation. A half-life of 23 weeks (161 days) was determined, which was dramatically reduced in the presence of O or Cl atoms.
Spence *et al.*, 1976 determined a degradation of 75 % after 5 mn irradiation in presence of Cl radicals and air. Chloroform was exposed in a glass chamber with an optical path of 360 m.
Appleby *et al.*, 1976 irradiated a synthetic mixture of trichloroethylene, nitrogen oxide, water vapour and gasoline in Teflon bags. The light source was a fluorescent lamp designed to simulate light of the lower troposphere. Chloroform appeared within two hours of irradiation. The tropospheric stability of chloroform suggests that this compound must be considered as a secondary anthropogenic pollutant, a potential precursor of ozone destroying stratospheric chlorine atoms.
However, according to Building Research Establishment, 1994, chloroform may account for 0.4 % of the chlorine in the upper atmosphere. Once in the stratosphere, chloroform is attacked by hydroxyl radicals, although some may be photolysed by the lower wavelength radiation present to form ozone depleting species. Chloroform is not covered by the Montreal Protocol and its ozone depleting potential is thus thought to be lower than that of many CFCs.

Crutzen *et al.*, 1978 determined a rate constant of 4.0 x 10^{-10} cm^3/molecules.s at a sensitizer concentration of 400 molecules/cm^3 of O (1D) which is the concentration at 45 km altitude. This result is only relevant for the stratosphere.
Kloepffer and Daniel, 1990 calculated according to Atkinson, 1985 a rate constant of $\mathbf{k_{OH} = 1 \cdot 10^{-13}\ cm^3/molecules.s.}$ In a review of the atmospheric reactions of chloroform Atkinson, 1985 recommended a rate constant for reaction of hydroxyl radicals with chloroform of $\mathbf{k_{OH} = 1.03 \cdot 10^{-13}\ cm^3/molecules.s}$.

Using the specific degradation rate constant with OH radicals of $\mathbf{1.03 \cdot 10^{-13}\ cm^3/molecules.s}$, as recommended by Atkinson, 1985, and using a mean OH concentration of 500,000 molecules/cm^3, a pseudo first order rate constant for degradation in air can be derived:
$\mathbf{kdeg_{air}\ [OH] = 0.0044\ d^{-1}}$
Kloepffer and Daniel, 1990 calculated according to Atkinson, 1985 a rate constant of $\mathbf{k_{NO3} = 2.6 \cdot 10^{-16}\ cm^3/molecules.s.}$ Using a mean NO_3-radical concentration of $1 \cdot 10^8$ molecules/cm^3, a pseudo first order rate constant for degradation in air can be derived:
$\mathbf{kdeg_{air}\ [NO3-] = 0.0022\ d^{-1}}$

The overall degradation rate due to NO_3 and OH radical concentration is:
$\mathbf{kdeg_{air}\ [NO_3] + [OH] = 0.0066\ d^{-1}}$

An atmospheric **half-life of 105 days** can be deduced for chloroform.

Biodegradation

Aerobic biodegradation

in water:

The only study performed according to OECD Guideline 301 C (MITI, 1992) **did not show any biodegradation** after 14 days. The initial concentration was 100 mg/L and the test was performed at 25 °C.

Tabak *et al.*, 1981 found chloroform **degradable under aerobic conditions, with gradual adaptation**. Chloroform at concentrations of 5 and 10 mg/L was incubated at 25 °C for 7 days in static cultures inoculated with settled domestic wastewater. The screening was performed by a 7-day static incubation followed by 3 weekly subcultures. Part of the removal of chloroform was due to volatilisation. In this study, the potential for slow biodegradation with a long adaptation period has been reported, it has to be stressed however that an additional carbon source (5 mg/L yeast extract) has been used, also controls have been performed unsatisfactory, the abiotic one being carried out without biomass.

Bouwer *et al.*, 1981 tested chloroform in a concentration of 100 µg/L with primary sewage. Under the test conditions, 20 °C in the dark for 25 weeks, **no biodegradation** was observed. Even with lower initial concentrations (10 µg/L, 30 µg/L) no decomposition under the same conditions could be noticed.

Thomas *et al.*, 2000 found that unlike other trihalomethanes, chloroform added to aquifers does not degrade in either aerobic or anaerobic conditions. The decrease of chloroform that could be observed in wells over aquifer storage and recovery seasons was mainly due to dilution. In the same aquifer, no significant biodegradation of chloroform by the indigenous aquifer microorganisms was observed under aerobic or anaerobic conditions (Thomas *et al.*, 2000). The authors described the specific conditions in which biodegradation could be observed: aerobic degradation could occur through co-metabolism when sufficient quantity of oxydative co-metabolites (methane, ammonia) and the corresponding bacteria are present.

In conclusion, the results by Tabak *et al.*, 1981 could not be confirmed under more realistic conditions. Therefore, in this assessment, a first order rate constant for biodegradation in surface water of 0 d-1will be used.

in soil:

No results from standardised biodegradation systems for soil and sediment are available.

In a study performed on a sandy soil (Strand and Shippert, 1986), it was found that acclimation to an air-natural gas mixture stimulated the biological oxidation of chloroform to carbon dioxide. Acclimation of the soil was carried out for 3-8 weeks in an atmosphere of 1 % natural gas in air and around 200 ml of dechlorinated tap water/day constantly applied to the soil during this period. Degradation experiments were carried out using around 5 g of the acclimated soil and a chloroform concentration of 31 µg/kg wet soil. Incubations were performed at 22-25°C for 5 days. Chloroform oxidation continued up to 31 days but was inhibited by acetylene and high concentrations of methane, indicating that methane oxidising bacteria may catalyse chloroform oxidation. There was some chloroform oxidation observed in soils that were exposed only to ambient air (which may have included some hydrocarbons) but the rate in the natural gas enriched soils was four times greater.

In conclusion, these results demonstrate that degradation of chloroform occurs only under certain aerobic conditions by methane-utilising bacteria. However,

they cannot be used in the generic assessment. The first order rate constant for aerobic biodegradation in soil and sediment is 0 d-1.

Anaerobic biodegradation

in water:

The anaerobic primary degradation of chloroform was studied by Gosset, 1985 in batch studies with an inoculum based on municipal digested sludge at 35 degrees C. At a concentration of 5.1 mg/L, chloroform disappeared within 9 days. The main metabolite was dichloromethane (31%), which remained near constant for 21 days and then disappeared slowly over the remaining 60 days.

Further studies with radiolabelled chloroform indicated that most of the initial disappearance is due to mineralisation:

Initial $CHCl_3$ conc. (mg/L)	Duration of primary degr. (d)	Final CO_2 prod. (%)	CH_2Cl_2 prod. (%)
ca. 1.7	3	43.5	34.1
ca. 5	5	40.3	29.9
ca. 17	12	32.1	27.7

The quantity of CH_4 produced was negligible. Even at 1.7 mg/L, the gas production by the inoculum was inhibited by more than 60%, and by more than 80% at 17 mg/L.

Bouwer *et al.*, 1981 carried out a study on the degradation of chloroform with methanogenic bacteria over 112 days. At an initial concentration of 16 µg/L, 81 % of chloroform was degraded within two weeks. Degradation also occurred with initial concentrations of 34 µg/L (> 70% after 28 days) and 157 µg/L (43 % after 84 days). Degradation at the high concentration of 157 µg/L was less conclusive, but there appears to have been a gradual reduction in chloroform concentration. Removal percentages vary in an important way, as they are based on variable $CHCl_3$ measurements in controls.

Bouwer and McCarty, 1983 found that in seeded cultures under methanogenic conditions, chloroform was almost completely oxidised to CO_2. At initial concentrations of 15 and 40 µg/L a lag period of 40 and 20 days was observed respectively. ^{14}C-measurements confirmed the removal by biooxidation.

Rhee and Speece, 1992 carried out a study with methanogenic bacteria under optimised conditions in a continuous fed anaerobic reactor. The feed contained a primary substrate (either formate, acetate or propionate) so as to maintain a concentration of 2000 mg/L of substrate in the reactor. The concentration of $CHCl_3$ in the influent feed solution were 304, 1230 and 1960 mg/L in formate, acetate and proprionate enrichment cultures, respectively. The feed concentrations were chosen to produce a 50 % reduction in gas production. A degradation of 90, 89 and 93 % after 30 days of continuous operation was observed. The concentrations were monitored in the liquid and gas effluent. The removal by volatilisation was 6.2 - 10 % whereas the removal with the liquid effluent was < 0.08 %, corresponding to concentrations of <0.24, <0.98, <1.57 mg/L.

Fathepure and Vogel, 1991 determined a total decomposition of 83 % after two days in a sequential decomposition process in an anaerobic and aerobic column. A pre-adaptation of 4-6 weeks took place; the aerobic column was working for one year.

In conclusion, although a certain biodegradation can be mentioned to take place under some anaerobic conditions, chloroform is not considered readily biodegradable in water systems.

in sediment:
van Beelen and van Keulen, 1990 have also shown chloroform to be degraded to CO_2 using anaerobic methanogenic sediment. The inoculum was a 20 ml sediment suspension incubated for 64 days without any headspace. 63 % of radiolabelled chloroform at an initial concentration of 4 µg/L was biodegraded. Half-lives of 10 - 14 days at 10 °C and 2.6 days at 20 ° C have been determined. Based on the intermediate results, the biodegradation is supposed to follow 1st order kinetics.
Using an initial concentration of 400 µg/L the final percentage level in carbon dioxide and chloroform are similar to the values of the experiment using an initial concentration of 4 µg/L. However at other time intervals, the percentages of formed CO_2 were lower at the higher concentration. Based on the intermediate results, the biodegradation is supposed to follow logarithmic kinetics. Therefore the concentration of 400 µg/L was considered to be above the threshold for growth and adaptation.
van Beelen and van Vlaardingen, 1993 found that ^{14}C-labelled chloroform was mineralised to CO_2 when incubated at low concentrations (2.7-3.4 µg/L) in bottles containing no sandy fresh natural sediments at 20 °C. Chloroform was found to be mineralised in all samples with half-lives in the range 0.9 to 37 days. No mineralisation was observed in the majority of sandy sediment samples.

In conclusion, chloroform biodegradation is observed in anaerobic sediment. Based on these results, half-lives determined by van Beelen and van Keulen, 1990 are assumed to be valid for the anaerobic part of the sediment and the half-life value of 14 days will be considered here. The TGD proposes to assume that 90 % of the sediment is anaerobic and suggests, when only data is available for the anaerobic part, correcting the half-life value in order to take into consideration the aerobic fraction of the sediment compartment. Therefore, if we consider the whole sediment compartment (90 % anaerobic / 10 % aerobic), only 45 % of the chloroform is biodegraded in 14 days and the actual half-life in sediment is circa 15 days. This value of 15 days will be used in the assessment for the sediment.

The biodegradation rates for surface water, soil and sediment are therefore estimated, according to the procedure outlined in the TGD.

Table 0-1: Estimation of biodegradation rate constants in the different compartments

Compartment / medium	Biodegradation rate
Surface water	$k_{sw} = 0\ d^{-1}$
Sediment	$k_{sed} = 0.046\ d^{-1}$
Soil (aerobic)	$k_{soil} = 0\ d^{-1}$

B.4.2 Environmental distribution

Based on the physico-chemical properties of chloroform, the preferred target compartment in the environment at equilibrium is the air compartment (Building Research Establishment, 1994).

B.4.3 Bioaccumulation

Different bioaccumulation experiments were reviewed in the RAR. All of them were conducted in a flow through system, and most of them with a water concentration of 1000 µg/L. The BCF obtained fall in the range of 1.4 – 13, which is similar to the one obtained by MITI, 1992 (see reference in the RAR) in *Cyprinus carpio* with two different water concentrations. Therefore, a worst case BCF of 13 was used in the RAR.

B.4.4 Secondary poisoning

Because of the low bioaccumulation potential of chloroform (BCF = 13), the potential for secondary poisoning can be considered to be negligible.

B.5 Human health hazard assessment

For more details, refer to section 4.1.2 of the RAR (human health).

B.5.1 Toxicokinetics

This is a summary of the more detailed chapter 4.1.2.1 of the RAR.

Chloroform is well absorbed, metabolized and eliminated by mammals after oral, inhalation or dermal exposure. Chloroform is hence widely distributed in the entire organism, via blood circulation and, due to its liposolubility, preferentially in fatty tissues and in the brain.

The half-life of chloroform in humans has been calculated to be 7.9 hours following inhalation exposure (Gordon et al. 1988 in ATSDR 1997). Furthermore, an oral-exposure study found most of the chloroform dose being eliminated within 8 hours postexposure (Fry et al. 1972 in ATSDR 1997).

Chloroform is mainly metabolised in liver and both oxidative and reductive pathways of chloroform have been identified, although data *in vivo* are limited. The major metabolite is carbon dioxide, generated by oxidative pathway *in vivo*; this main pathway generates also reactive metabolites, including phosgene. The reductive pathway generates the dichloromethylcarbene free radical. Both pathways proceed through a cytochrome P450-dependent enzymatic activation step ant their balance depends on species, tissue, dose and oxygen tension. Phosgene is produced by oxidative dechlorination of chloroform to trichloromethanol, which spontaneously dehydrochlorinates (WHO, 2004).

The electrophilic metabolic phosgene binds covalently to nucleophilic components of tissue proteins and also interacts with other cellular nucleophiles and, to some extent, to the polar heads of phospholipids. Phosgene can also react with water to release carbon dioxide and hydrochloric acid.Available literature data show that chloroform toxicity is due to its metabolites: phosgene is supposed to be responsible for irreversible bindings to liver components (WHO, 2004).

Chloroform can cross the placenta, transplacental transfer has been reported in mice (Danielsson et al., 1986 in WHO, 1994) and in the fetal blood in rats (Withey and Karpinski, 1985 in WHO, 1994) and it is expected to appear in human colostrum and is excreted in mature breast milk (Lechner et al., 1988; Fisher et al., 1997 in Health Council of the Netherlands, 2000; Davidson *et al.*, 1982 in US EPA, 2004).

Considering the data reported, the animal inhalation, dermal and oral absorptions of chloroform are considered to be respectively 80%, 10% and 100%.

Data from human studies showed that 80% of the chloroform dose is absorbed via inhalation and 10% via dermal absorption. Oral absorption of chloroform is assumed to be 100%.

B.5.2 Acute toxicity

This is a summary of the more detailed chapter 4.1.2.2 of the RAR.

Chloroform acute toxicity data are available for inhalation and oral route in rats and mice and for the dermal route in rabbits. Some studies on clinical use and on accidental human exposure have also been reported.

Acute toxicity varies depending upon the strain, sex and vehicle. In mice the oral LD_{50} values range from 36 to 1366 mg chloroform/kg body weight, whereas for rats, they range from 450 to 2000 mg chloroform/kg body weight. Chloroform LC_{50} values of 6.2 g/m^3 and 9.2 g/m^3 have been reported for 6 h inhalation exposure in mice and rats respectively (WHO, 1994). Mice are more susceptible than rats to acute chloroform toxicity for both exposure routes. A systemic and local LOAEL of 1.0 g/kg has been reported in rabbits by dermal route for extensive necrosis of the skin and degenerative changes in the kidney tubules after chloroform exposure under occlusive conditions (Torkelson et al., 1976). An oral NOAEL of 30 mg/kg bw has been reported in rats for serum enzyme changes indicative of liver damage (Keegan *et al.*, 1998). A dose-dependent increase in the LI was present in the kidney of Osborne-Mendel rats given doses of 10 mg/kg (Templin et al., 1996b). The epithelial cells of the proximal tubules of the kidney cortex were the primary target cells for cytotoxicity and regenerative cell proliferation.

In general, chloroform elicits the same symptoms of toxicity in humans as in animals. The mean lethal oral dose for an adult is estimated to be about 45 g, but large interindividual differences in susceptibility occur. The human estimated inhalation LOAEC is ≤ 249 mg/m^3 (Verschueren, 1983 in WHO, 1994) and the oral LOAEL is <107 mg/kg (Winslow & Gerstner, 1978 in WHO, 1994). **Considered as key studies for risk characterisation**

Based on acute toxicity data, the proposed classification for chloroform is Harmful with the risk phrases R22: harmful if swallowed and R20: harmful by inhalation.

B.5.3 Irritation

This is a summary of the more detailed chapter 4.1.2.3 of the RAR.

Chloroform is an irritant substance for skin, eye and upper airways. Rabbit dermal studies showed slight to high irritation potency. In man, dermal contact with chloroform caused dermatitis. Severe eye irritation was observed in animals with liquid chloroform, reported effects are various but one rabbit study indicates slight but definite corneal injury. In man, eye contact with liquid chloroform caused temporary corneal epithelium injury. Mainly repeated dose studies have been reported for irritation, chloroform induced lesion and cell proliferation in the olfactory epithelium but also bone growth. In respiratory tract of mice and rats, inhaled chloroform induced lesions and cell proliferation in the olfactory epithelium and the nasal passage, the LOAEC reported in rats for enhanced bone growth and hypercellularity in the lamina propria of the ethmoid turbinates of the nose at the early time point (4 days) is 10 ppm (50 mg/m^3, Templin et al., 1996a). **Considered as key study for risk characterisation**

Table 0.2 Study summary for irritation

Animal species & strain	Number of animals	Doses	Result	Reference
Rabbit Dermal	Not reported	Liquid chloroform 24h, occlusive 10 applications for ears 2 applications for bellies	ear: hyperemia and exfoliation after 1 to 4 applications belly: slight hyperemia with moderate necrosis and eschar formation delayed healing of the skin	TORKELSON ET AL., 1976 IN WHO 2004
Rabbit, NZW Ocular	6	Undiluted chloroform, doses not specified	6/6 severe eye irritation, with mydriasis and keratitis 4/6 translucent zones in the cornea	Duprat et al., 1976
Rabbit Ocular	3	Undiluted chloroform, doses not specified 1 eye rinsed after 30s	Slight irritation of the conjunctiva slight but definite corneal injury	Torkelson et al., 1976
Rat, F344 Inhalation	10/sex/dose	vapour, 6h/d, 5d/week, 13 weeks 25, 50, 100, 200, 400 ppm	25 ppm (125 mg/m^3): mineralization and atrophy of the olfactory epithelium 200 ppm (1000 mg/m^3): necrosis of olfactory epithelium in males	Kasai et al., 2002
Rat, F344 Inhalation	10/sex/dose	vapour, 6h/d, 5d/week, 2 weeks 500, 1000, 2000, 4000, 8000 ppm	All doses desquamation, atrophy and disarrangement of the olfactory epithelium, edema of the lamina propria of the nasal cavity	Kasai et al., 2002
Rat, F344 Inhalation	Not reported	1.2, 3, 10, 29.5, 101, and 288 ppm 6 hr/day for 7 days	NOAEC= 3 ppm (15 mg/m^3) atrophy of Bowman's glands, new bone formation, and increased labeling index in S phase periosteal cells	Mery et al., 1994
Rat, F-344 rats Inhalation		0, 2, 10, 30, 90, or 300 ppm 6 h/day, 7 d/week or 5d/week, 13 weeks	Early time points (4 days) LOAEC= 10 ppm Enhanced bone growth, hypercellularity in the lamina propria 13 weeks LOAEC= 2 ppm Enhanced bone growth hypercellularity in the lamina propria of the ethmoid turbinates	Templin et al., 1996a

Animal species & strain	Number of animals	Doses	Result	Reference
Mouse, BDF1 Inhalation	10/sex/dose	vapour, 6h/d, 5d/week, 13 weeks 12, 25, 50, 100, 200 ppm	25 ppm (125 mg/m^3): degeneration of the olfactory epithelium in males 12 ppm (60 mg/m^3): thickening of the bone in nasal septum, eosinophilic changes of olfactory and respiratory epithelia in females	KASAI ET AL., 2002
Mouse, B6C3F1 Inhalation	10/sex/dose	vapour, 6h/d, 5d/week, 2 weeks 500, 1000, 2000, 4000, 8000 ppm	All doses atrophy and respiratory metaplasia of olfactory epithelium in males degeneration, necrosis and disarrangement of olfactory and respiratory epithelia in females	Kasai et al., 2002
Mouse, B6C3F1 Inhalation	Female	0.3, 2, 10, 30, and 90 ppm 6 h/d, 4 days	NOAEC = 90 ppm (441 mg/m^3) nasal lesions	Larson et al., 1996
Mouse, B6C3F1 Inhalation	Not reported	1.2, 3, 10, 29.5, 101, and 288 ppm 6 hr/day for 7 days	NOAEC= 3 ppm (15 mg/m^3) increased labeling index in S phase periosteal cells	Mery et al., 1994

The classification proposed according to the data available is Irritant with the risk phrases R38: irritating to skin, R36 irritating to eyes and R37 irritating to respiratory system.

B.5.4 Corrosivity

No data available.

B.5.5 Sensitisation

This part is totally extracted from 4.1.2.5 of the RAR.

No data were available for sensitisation and no occupational case of sensitisation was reported for workers/people exposed to chloroform in human studies.

A sensitisation test on chloroform was reported in a study in Japanese (Chiaki et al., 2002) the abstract only was available in English. This study was designed to evaluate the skin sensitizing potency of chloroform, and it was performed to further evaluate the differences between Guinea Pig Maximization Test (GPMT) and Local Lymph Node Assay (LLNA, RI Method). GPMT was conducted in accordance with Magnusson and Kligman Method. Chloroform and the immunopotentiator Freund's complete adjuvant were administered intradermally to 5 guinea pigs as primary sensitization (Day 1). One day after open application of 10% sodium lauryl sulfate

(SLS) to enhance sensitization (as secondary sensitization), chloroform was applied as an occlusive patch for 48 hours (Day 9, patch sensitization). For challenge, another 3 guinea pigs in the control group were used as a control group, and chloroform was applied to 5 guinea pigs in the sensitization group as an occlusive patch for 24 hours in the same manner (Day 22). Evaluation was according to the Draize criteria 48 and 72 hours after the start of challenge. Significant suppression of body weight gain ($P<0.01$) compared to the control group was seen at secondary sensitization (Day 9) after intradermal chloroform administration (Day 1). Extensive necrosis at the chloroform administration site was observed from the day after administration, and piloerection and decreased spontaneous movement were observed for 1 week following intradermal administration. In the evaluation at 48 and 72 hours after the start of challenge, erythema (score 1 or 2, slight to mild) was observed in all 8 animals including the control group. This reaction at the challenge site was observed until 8 days after the start of challenge, with a tendency for the erythema to become stronger over time in all 8 animals including the control group, confirming that chloroform, which is an organochlorine solvent, is a strongly irritant substance. Sensitization could not be definitely evaluated due to this strong irritation reaction, but since skin reactions were comparable in the chloroform sensitization group and the control group, chloroform sensitization was judged to be negative in GPMT.

On the other hand LLNA was conducted in accordance with Kimber Method. Hexyl cinnamic aldehyde (HCA) was used as the positive control substance in LLNA, and HCA was dissolved in chloroform or in acetone/olive oil solvent (AOO; acetone : olive oil = 4 : 1) to reach a concentration of 10%. Using 4 groups with 5 animals per group, chloroform, AOO, 10% HCA/chloroform or 10% HCA/AOO (25µL/ear) was applied to both auricles of the mice in each group for 3 consecutive days, and 3 days later the mice were euthanized by cervical dislocation 5 hours after ^{3}H-methyl thymidine was administered intravenously (250 µL, 2.96 MBq/mL) and the auricular lymph nodes were removed, in order to compare reactions to HCA with chloroform as vehicle and with AOO as vehicle. Then cells were isolated from the lymph nodes, cell suspensions prepared, and radioactivity was measured with a beta scintillation counter. Evaluation of LLNA was done by calculation of the Stimulation Index (SI). SI was obtained by dividing the mean measured value in each test substance administration groups by the mean measured value in the vehicle administration groups, the AOO and chloroform administration groups. SI for chloroform alone was obtained using the value for AOO as the vehicle administration group. Sensitization was judged to be positive if SI was 3 or more and there was statistically significant difference from the vehicle control group. In LLNA, chloroform showed higher levels of radioactivity than AOO. The lymphoproliferative activity is used as an index of sensitization in LLNA, but since primary irritation also activates lymph cell proliferation through inflammatory cytokine effects, the reactions are said to be difficult to differentiate. It is very likely that the reactions to chloroform seen in the present study were due to primary irritation rather than sensitization.

No classification is proposed for sensitisation.

B.5.6 Repeated dose toxicity

This part is a summary of the more detailed chapter 4.1.2.6 of the RAR.

Laboratory animal studies identify the liver kidneys and the nasal cavity as the key target organs of chloroform's toxic potential. The lowest reported oral LOAEL was 15 mg/kg/day in dog livers based on fatty cysts and elevated ALAT levels is a starting point for risk characterisation (Heywood et al., 1979 in US EPA, 2001). **Considered as key study for risk characterisation.**

For mice, reported oral LOAELs were 50 mg/kg bw/day for the hepatic effects and 37 mg/kg bw for renal effects (mineralization, hyperplasia and cytomegaly) (Condie *et al.*, 1983; Munson *et al.*, 1982 in WHO, 2004). The reported inhalation NOAEC for a 90 days sub-chronic exposure was 25 mg/m^3 (5 ppm) in male mice for the renal effects (vacuolation, basophilic appearance, tubule cell necrosis and enlarged cell nuclei) and a NOAEC of 25 mg/m^3 (5 ppm) was reported in male mice for hepatic effects (vacuolated hepatocytes and necrotic foci) (Templin et al., 1998). A chronic (104 weeks) inhalation NOAEC of 25 mg/m^3 (5ppm) was reported in mice for increased renal cytoplasmic basophilia in both exposed males and females, and increased atypical tubule hyperplasia and nuclear enlargement in the kidneys in the males (Yamamoto et al., 2002). **Considered as key study for risk characterisation.**

Nasal lesions have also been observed in rats and mice exposed by inhalation or via the oral route. Following a sub-chronic inhalation exposure, the lowest reported effect level was LOAEC= 9.8 mg/m^3 (2 ppm), which caused cellular degeneration and regenerative hyperplasia in nasal passage tissues of rats (Templin et al., 1996a). Lesions and cell proliferation in the olfactory epithelium and changes in the nasal passages were observed at LOAEL=34 mg/kg bw/d (Larson et al., 1995). **Considered as key studies for risk characterisation.** In human, limited data on repeated dose toxicity suggest that the liver and kidneys are the likely target organs.

Based on the data available for repeated dose toxicity, the classification proposed for chloroform is R48/20/22: danger of serious damage to health by prolonged exposure.

B.5.7 Mutagenicity

This part is a summary of the more detailed chapter 4.1.2.7 of the RAR.

Reviews by other groups:

Data on the mutagenicity of chloroform have recently been reviewed and evaluated by several groups: IARC, US EPA, ILSI and WHO. Most of the reviews concluded that chloroform is not a strong mutagen but a weak genotoxic effect was not excluded:

The International Life Sciences Institute (ILSI, 1997) performed a review of the available data on the mutagenicity of chloroform. ILIS committee concluded that no subset of observations points unequivocally to a specific genotoxic mode of action associated with chloroform, and that the preponderance of the evidence indicates that chloroform is not strongly mutagenic. The conclusion of IARC study on carcinogenic chemicals (1999) is that no data were available on the genetic and related effects of chloroform in humans. There is weak evidence for the genotoxicity of chloroform in experimental systems in vivo and in mammalian cells, fungi and yeast in vitro. It was not mutagenic to bacteria.

US EPA (2001) concluded that the weight of evidence indicates that even though a role for mutagenicity cannot be excluded with certainty, chloroform is not a strong mutagen and that neither chloroform nor its metabolites readily bind to DNA.

CICAD (2004) based on Environment Canada (2001) source document, concluded that most studies did not identify genotoxic potential for chloroform. Results from a few, non-standard studies indicate the possibility of a weak positive response in rats. Overall, however, the weight of evidence indicates that chloroform does not have significant genotoxic potential.

Studies presented in this report were chosen based on their reliability (1 or 2) according to Klimish scoring system. Although negative in vivo results are reported, several in vivo tests published in international rewiews demonstrated that chloroform could induce micronuclei and chromosomal aberrations. Positive results are observed in the target organ (kidney) or after at least three administrations in bone marrow cells, which might be consistent with a mechanism of oxidative damage due to glutathione depletion. Besides, it should be noted that MN and CA tests performed in rats were all positive whereas mixed results were observed in mice.

These studies suggest that chloroform is a slightly genotoxic compound in vivo and requires the classification as mutagenic compound category 3.

B.5.8 Carcinogenicity

This part is a summary of the more detailed chapter 4.1.2.8 of the RAR(2007).

According to US EPA, (2001) studies in animals reveal that chloroform can cause an increased incidence of kidney tumors in male rats or mice and an increased incidence of liver tumors in mice of either sex. These induced tumors responses are postulated to be secondary to sustained or repeated cytotoxicity and secondary regenerative hyperplasia, according to the dose levels tested. Two studies showed nasal lesion in rats or mice due to chloroform inhalation exposure. “The weight of the evidence indicates that a mutagenic mode of action via DNA reactivity is not a significant component of the chloroform carcinogenic process. The persistent cell proliferation presumably would lead to higher probabilities of spontaneous cell mutation and subsequent cancer (US EPA, 2001).”

There have been no reported studies of toxicity or cancer incidence in humans chronically exposed to chloroform (alone) via drinking water. Chlorinated drinking water typically contains chloroform, along with other trihalomethanes and a wide variety of other disinfection by-products. It should be noted that humans exposed to chloroform in drinking water are likely to be exposed both by direct ingestion and by inhalation of chloroform gas released from water into indoor air.

Although some studies have found increased risks of bladder cancer associated with long-term ingestion of chlorinated drinking-water and cumulative exposure to trihalomethanes, results were inconsistent between men and women and between smokers and non-smokers. Moreover, relevant studies contain little information on specific exposure, and it is not possible to attribute any excess risk specifically to chloroform. Specific risks may be due to other disinfection by-products, mixtures of by-products, other water contaminants, or other factors for which chlorinated

drinking-water or trihalomethanes may serve as a surrogate (WHO, 2004; IARC, 1999).

IARC, (1999) concluded there is inadequate evidence in humans for the carcinogenicity of chloroform but sufficient evidence in experimental animals for the carcinogenicity of chloroform. To conclude, the current human data are insufficient to establish a causal relationship between exposure to chloroform in drinking water and increased risk of cancer.

The NOAEC via inhalation for the kidney adenoma/carcinoma was identified at 5 ppm in mice, for nasal lesions a LOAEC of 5 ppm was determined (Yamamoto et al., 2002). Oral treatment with chloroform was associated with increased incidence of moderate to severe kidney lesions in CBA and CF/1 mice. NOAEL= 17 mg/kg bw (Roe et al., 1979). These values are considered as starting point for risk characterisation. **Considered as key studies for risk characterisation.**

Based on animal results the current classification for carcinogenicity of chloroform should be maintained: Category 3 with the risk phrases R40 limited evidence of carcinogenic effects.

B.5.9 Toxicity for reproduction

This part is a summary of the more detailed chapter 4.1.2.9 of the RAR.

Regarding fertility, only one author reported increased mice abnormal sperm following exposure to an air concentration of 400 or 800 ppm chloroform (estimated inhalation LOAEC = 400 ppm, Land *et al.*, 1979-1981). Otherwise, animal findings were epididymal lesions or increased right epipidymis weight (estimated oral NOAEC is 15.9 mg/kg, Chapin et al., 1997). **Considered as key studies for risk characterisation.**

As well, one occupational case study reported asthenospermia in association to chloroform exposure. No other adverse reproductive effect has been evidenced in the 90 days studies.

Concerning developmental toxicity, epidemiological studies of chloroform in drinking water no association was clearly established between exposure to chloroform and reduced fetal weight, stillbirth and cleft defects. Otherwise, we need to keep in mind that many of these epidemiological studies present limitations like the use of water concentration as the measure of exposure, which can lead to exposure misclassification.

By inhalation, the effects of chloroform on the various animals tested include effects on pregnancy rate, resorption rate, litter size and live fetuses. These effects have been observed with concentrations causing a decrease of maternal weight and food consumption. Other effects as fetal weight and CRL decrease, as well as skeletal and gross abnormalities or variations have been mentioned. They are summarized in the following table.

Table 0.3 Developmental toxicity data on different species

Reference	Protocol	Doses	Maternal effects	Developmental effects
Schwetz *et al.*, 1974	Sprague-Dawley rats *Inhalation* 0, 30, 100, 300 ppm 7 hr/day, gd 6-15	30 ppm	Reduced food consumption on gd 6-7 LOAEC =30 ppm based on reduced maternal body weight	Increased skeletal anomalies LOAEC =30 ppm based on increased skeletal anomalies
		100 ppm	Decreased body weight Reduced food consumption, increased relative liver weight	Increased gross anomalies
		300 ppm	Reduced food consumption, increased relative liver weight	Reduced pregnancy rate, decreased litter size, increased resorptions, altered sex ratio and decreased fetal weight and CRL
Baeder & Hoffman, 1988	Wistar rats *Inhalation* 0, 30, 100, 300 ppm 7 hr/day, gd 7-16	All concentrations	Reduced food consumption, reduced body weight LOEC = 30 ppm	Increased in completely resorbed litters, decreased CRL LOAEC = 30 ppm Decreased fetal weight (300 ppm only)
Baeder & Hoffman, 1991	Wistar rats *Inhalation* 0, 3, 10, 30 ppm 7 hr/day, gd 7-16	3 ppm	Reduced food consumption	Increased ossification variations
		10 ppm	Reduced body weight LOEC = 10 ppm	**NOAEC = 10 ppm based on decreased fetal weight & CRL**
		30 ppm		Decreased fetal weight and CRL
Thompson *et al.*, 1974	Sprague-Dawley rats Gavage 0, 20, 50, 126 mg/kg-day gd 6-15	50 mg/kg-day	Decreased food consumption, decreased weight gain	
		126 mg/kg-day		Increased implantations, decreased fetal weight
Ruddick *et al.*, 1983	Sprague-Dawley rats Intubation 0, 100, 200, 400 mg/kg-day gd 6-15	All doses	Decreased body weight, increased liver weight, decreased hematocrit, hemoglobin and red blood cells count	
		400 mg/kg/d	Increased kidney weight	Decreased fetal weight, increased of sternebrae aberrations and runting
Murray *et al.*, 1979	CF-1 mice *Inhalation* 0, 100 ppm 7 hr/day, gd 6-15,		Decreased weight gain, gd 1-7 or 8-15 Increased relative liver weight, gd 6-15 or 8-15	Decreased pregnancy rate, gd 1-7 or 6-15 Increased resorptions, gd 1-7

Reference	Protocol	Doses	Maternal effects	Developmental effects
	1-7 or 8-15			Decreased fetal weight and CRL, gd 1-7 or 8-15 Increased cleft palate, gd 8-15 Increased delayed ossification of sternebrae, gd 1-7 or 8-15
Thompson *et al.*, 1974	Rabbits Gavage 0, 20, 35, 50 mg/kg/d gd 6-18	All doses		Complete abortions
		20 mg/kg-day		**Decreased fetal weight LOAEL = 20 mg/kg/day**
		50 mg/kg-day	Death, decreased body weight gains	
Burkhalter & Balster, 1979	ICR mice 0, 31.1 mg/kg-day 3 weeks prior to mating, through mating, gestation and lactation, directly to weaned pups		Not discussed	Reduced postnatal weight gain Lower scores for forelimb placement on postnatal days 5 and 7
Chapin et al., 1997 NTP, 1988	Mice, continuous breeding study by gavage 0, 6.6, 15.9, 41.2 mg/kg-day		Reduced bw observed at the delivery of the 4th litter and on PND 14 of the 5th litter for 41.2 mg/kg-day group	No significant differences observed among groups for the number of litters per pair, litter size, proportion of live pups, sex ratio, or pup weight at birth

References in bold are selected as a starting point for risk characterisation

Based on the data available for fertility, effects are not sufficiently severe to justify a classification

Based on the data available for developmental toxicity, chloroform should be classified as Category 3 with the risk phrase R63 possible risk of harm to the unborn child

B.5.10 Other effects

None

B.5.11 Derivation of DNEL(s)/DMEL(s) or other quantitative or qualitative measure for dose response

Not derived.

B.6 Human health hazard assessment of physico-chemical properties

Hazard already assessed in the general human health hazard assessment.

B.6.1 Explosivity

B.6.2 Flammability

B.6.3 Oxidising properties

B.7 Environmental hazard assessment

B.7.1 Aquatic compartment (including sediment)

The following valid test results have been selected for the determination of a PNEC for freshwater.

- Fish: NOEC-6/9 months = 1.463 mg/L (*Oryzias latipes*)
- Invertebrate: NOEC-21d = 6.3 mg/L (*Daphnia magna*)
- Algae: 72h-EC 10 = 3.61 mg/L (*Chlamydomonas reinhardii)*

There are three long-term NOECs from species representing three trophic levels. Therefore, the PNEC is derived using an assessment factor of 10 to the lowest NOEC and

➢ **PNECaqua = 1.463 / 10 = 146 µg/L**

There are two methods of determination of $PNEC_{sed}$:

1) Determination of the $PNEC_{sed}$ using the sediment toxicity test

As three long-term ecotoxicity tests with benthic species representing different living and feeding conditions are available, an assessment factor of 10 should be applied to the lowest NOEC, which is the one from the test on the midge *Chironomus riparius*:
$PNEC_{sed}$ = 4.5 mg/kg / 10 = 450 µg/kg (dw)

2) Determination of the $PNEC_{sed}$ using the Equilibrium partitioning method

According to the TGD, $PNECsed(ww) = \frac{Ksusp-water}{RHOsusp} \cdot PNECaquatic * 1000$

Ksusp_water = suspended matter_water partition coefficient = 5.53 $m^3.m^{-3}$

Therefore: $PNEC_{sed}$ = 702 µg.kg^{-1} (ww)
$PNEC_{sed}$ = 3230 µg.kg^{-1} (dw)

The result with the Equilibrium partitioning method is much higher than the result based on the toxicity to *Chironomus riparius*. The value based on experimental results will be preferred:

➢ **PNECsed = 450 µg/kg (dw) = 97.8 µg/kg (ww)**

B.7.2 Terrestrial compartment

A $PNEC_{soil}$ has been derived using the equilibrium partitioning method. As micro-organisms are particularly sensitive to chloroform and represent relevant taxa for the soil compartment, the $PNEC_{STP}$ has been used instead of the $PNEC_{aqua}$. The $PNEC_{micro\text{-}organisms}$ is based on very short term tests relevant for the WWTP assessment but not for the soil compartment, consequently an additional factor of 10 has been used.

$$PNECsoil(ww) = \frac{Ksoil-water}{RHOsoil} \cdot \frac{PNECmicro-organisms \cdot 1000}{10}$$

Ksoil_water = soil _water partition coefficient = 5.77 $m^3.m^{-3}$

Therefore:

PNECsoil = 16.3 µg.kg^{-1} (ww) = 18.4 µg.kg^{-1} (dw)

B.7.3 Atmospheric compartment

The lowest test concentration at which effects were observed for visible symptoms and photosynthesis was 100 g/m^3. The test was however very short (3 hours) and this result could even not be used to assess an acute toxicity and derive a $PNEC_{air}$.

Elsewhere, the potential contribution of chloroform to climate change (Global Warning Potential = 0.0326), stratospheric ozone depletion (Stratospheric Ozone Depletion Potential = 0.0083), ground-level ozone formation (Photochemical Ozone Creation Potential = 8.14×10^{-13}) and acidification processes (No data and chemical alert) can be considered as negligible.

B.7.4 Microbiological activity in sewage treatment systems

The lower EC50 was found with *Nitrosomonas* bacteria, which convert ammonia nitrogen to nitrite as the first step of oxidation. The result to be considered for toxicity to micro-organisms is therefore: EC_{50} = 0.48 $mg.L^{-1}$. An assessment factor of 10 being applied to such results, the $PNEC_{micro\text{-}organisms}$ is therefore:

$PNEC_{micro\text{-}organisms}$ = 0.48 mg/L / 10 = 48 µg/L

B.7.5 Non compartment specific effects relevant for the food chain (secondary poisoning)

Since the bioaccumulation potential of chloroform seems low (BCF_{fish} = 13) and furthermore that no data regarding biomagnification were found, the potential for secondary poisoning can be considered to be negligible.

B.8 PBT and vPvB assessment

B.8.1 Assessment of PBT/vPvB properties – Comparison with criteria of Annex XIII

Would it be only by considering the criterion BCF which must be higher than 2000, with a BCF of 13 in fish (see section B.4.3) chloroform can't be regarded as a PBT substance or all the more a vPvB substance according to annexe XIII of Reach.

B.8.2 Emission characterisation

This section is not relevant, as chloroform is not a PBT or vPvB substance according to annexe XIII.

B.9 Exposure assessment

B.9.1 General discussion on releases and exposure

This section is a summary of the more detailed chapter 4.1.1 of the human health RAR (HH RAR updated in October 2008).

Humans may be exposed to chloroform at workplace and indirectly via the environment.
Chloroform is also a chemical by-product associated with disinfection of swimming pool water; chloroform is originated by the reaction of disinfecting agents with organic substances; the chloroform exposure will be assessed for workers as swimming instructors, lifeguards, competitive swimmers (they will be considered as workers) and for consumers as child swimmers and adult swimmers.
Workers are primarily exposed via inhalation and dermal routes (and ingestion route for competitive swimmers). Consumers in swimming pools are exposed by inhalation, dermal and ingestion routes.
For workers, there are two possible exposure pathways: from industrial processes and from the formation of chloroform in chlorinated swimming pool water.
In swimming pool, people are exposed to chloroform present in the water and in the air.
For the industrial activities, exposure may occur mainly during manufacture and use as intermediate for the production of chlorodifluoromethane (HCFC 22); chloroform is also used as a chemical intermediate or solvent in the synthesis of various chemicals and pharmaceuticals.
The vast majority of chloroform (95.4 %) is consumed as feedstock, in closed continuous processes, for the production of chlorodifluoromethane (HCFC 22, also known as refrigerant R 22). When the productions of chloroform and HCFC 22 are integrated in the same site, chloroform is supplied to the consuming units by pipeline inside the industrial site. In the other cases, transport to customer occurs by rail or truck tank or occasionally by vessel.
Chloroform is used in other applications (4.6 %) as feedstock (2.8%) or extraction solvent (1.8%), generally in batch processes, especially in the pharmaceutical industry (for example in the extraction of penicillin and other antibiotics) and in the production of dyes, pesticides and other substances. In these cases, chloroform is distributed in liquid form in tanks and drums and transported via rail or by road trucks.
General remark: The operations and tasks described hereafter are typical of standard chloroform production or handling facilities. There could be slight variations in the operating procedures but these will not affect the human exposure pathways and levels.
In view of data from literature source and data from European producers/importers, occupational exposure assessment was carried out through the three following main categories of scenarios:

- Scenario 1: the manufacture of chloroform and its use as an intermediate for the production of chlorodifluoromethane (both in closed continuous system);

- Scenario 2: its use as intermediate or solvent in the synthesis of various chemicals and pharmaceuticals (both in closed batch processes).
- Scenario 3: exposure of workers (swimming instructors, lifeguards, competitive swimmers) to chloroform in swimming pools.

B.9.2 Summary of the occupational exposure

It is assumed that the production and further processing is performed in closed system; dermal exposure for all scenarios is limited because of the very high vapour pressure of 20.9 kPa.

Table B.9.2-1 Summary of exposure data of chloroform (RWC : Reasonable Worst Case) concerning inhalation exposure relevant for occupational risk assessment

Scenario	Form of exposure	Activity	Duration	Frequency	Reasonable Worst Case	Method
1. Manufacture of chloroform and HCFC 22 (closed continuous process)	vapour	All functions, process operations, maintenance, filling, laboratory	Shift length : 8 h	Daily	1.15 ppm 5.6 mg/m^3	Workplace measurement
2. Chloroform as intermediate or solvent in the synthesis of chemicals (closed batch process)	vapour	All functions, process operations, maintenance, filling, laboratory	Shift length : 8 h	Daily	2 ppm 10 mg/m^3	Workplace measurement and expert judgment
3.1 Swimming instructor/lifeguard in a swimming pool	Vapour	Activity in the hall of the swimming pool	Shift length: 6 h	Daily (5 events / week)	0.027 ppm 0.136 mg/m^3	Workplace measurement
3.2 Competitive swimmers	Vapour	Regular training	Shift length: 4h	Daily (6 events / week)	0.042 ppm 0.206 mg/m^3	Workplace measurement

Table B.9.2-2 Summary of dermal exposure data of chloroform relevant for occupational risk assessment

Scenario	Form of exposure	Activity	Contact level (according to EASE model)	Level of exposure (mg/cm2/day)	Shift average Level of exposure (mg/kg/day)	Method
1. Manufacture of chloroform and HCFC 22 (closed continuous process)	liquid	All functions, process operations, maintenance, filling, laboratory	Intermittent	0.1-1 with shortened duration of dermal exposure (1)	42-420 with shortened duration of dermal exposure leading to 0.24 mg/kg/day (1)	EASE/ expert judgment
2. Chloroform as intermediate or solvent in the synthesis of chemicals (closed batch process)	liquid	All functions, process operations, maintenance, filling, laboratory	Intermittent	0.1-1 with shortened duration of dermal exposure (1)	42-420 with shortened duration of dermal exposure leading to 0.24 mg/kg/day (1)	EASE/ expert judgment
3.1 Swimming instructor/lifeguard in a swimming pool	Liquid	Activity in the hall of the swimming pool	No contact		0	Measurement and calculations
3.2 Competitive swimmers	Liquid	Regular training	Continual	Chloroform concentration in water = 0.98 mg/l	Chloroform concentration in water = 0.98 mg/l leading to 0.156 mg/kg/day	

(1) The EASE estimate is largely reduced because of the short duration time of dermal exposure. The retention time of pure chloroform is calculated to 4 seconds (order of magnitude)

Table B.9.2-3 Summary of ingestion exposure data of chloroform relevant for occupational risk assessment

Scenario	Form of exposure	Activity	Level of exposure (mg/l)	Systemic dose per day via ingestion (mg/kg/day)	Method
1. Manufacture of chloroform and HCFC 22 (closed continuous process)	liquid	All functions, process operations, maintenance, filling, laboratory	No concern	0	
2. Chloroform as intermediate or solvent in the synthesis of chemicals (closed batch process)	liquid	All functions, process operations, maintenance, filling, laboratory	No concern	0	
3.1 Swimming instructor/lifeguard in a swimming pool	Liquid	Activity in the hall of the swimming pool	No concern	0	Measurement and calculations
3.2 Competitive swimmers	Liquid	Regular training	Chloroform concentration in water = 0.98 mg/l	0.0056	

Exposure assumptions for scenarios 1 and 2:
A dermal absorption of chloroform through human skin of 10% is used to calculate the systemic dose per day via skin (mg/kg/day).
Human studies showed that the proportion of chloroform absorbed via inhalation ranged from 76 to 80% (Morgan et *al*., 1970 in WHO, 1994).

The systemic dose per day via inhalation is calculated with the following values:

- exposure duration = 8h
- inhalation rate = 1.25 m^3/h
- adult weight = 70 kg

Table B.9.2-4 Systemic doses per day via inhalation, via skin, via ingestion and total systemic dose for occupational risk assessment

Scenario	Systemic dose per day via inhalation (mg/kg/day)	Systemic dose per day via skin (mg/kg/day)	Systemic dose per day via ingestion (mg/kg/day)	Total systemic dose (mg/kg/day)
1. Manufacture of chloroform and HCFC 22 (closed continuous	1.25*8*5.6*0.8/70 = 0.64	16.8*0.1/70 = 0.024	0	0.66

Scenario	Systemic dose per day via inhalation (mg/kg/day)	Systemic dose per day via skin (mg/kg/day)	Systemic dose per day via ingestion (mg/kg/day)	Total systemic dose (mg/kg/day)
process)				
2. Chloroform as intermediate or solvent in the synthesis of chemicals (closed batch process)	1.25*8*10*0.8/70 = 1.14	16.8*0.1/70 = 0.024	0	1.164

B.9.3 Summary of the consumer exposure

As the use of chloroform is limited to professional and industrial applications through regulation, there is no direct consumer use of chloroform and consequently no direct public exposure is expected.

Chloroform is also a by-product chemical associated with disinfection of swimming pool water; chloroform is originated by the reaction of disinfecting agents with organic substances and not intentionally used. Consequently, it was agreed that the Risk Characterisation of chloroform as a by-product chemical should not be presented in the Chloroform risk assessment but rather than in the Sodium Hypochlorite RAR. Any risk identified in scenario 3 for workers as swimming instructors, lifeguards, competitive swimmers and for consumers as child swimmers and adult swimmers should be addressed in the Sodium Hypochlorite RAR (results of RC for scenario 3 are presented in Annex 1 of the RAR for information).

B.9.4 Summary of man exposed via environment

The estimation of the indirect exposure of humans via the environment is presented in the EUSES calculation file. The total daily intake based on the local environmental concentrations due to production and the different uses are presented in Table B.9.4-1.

Table B.9.4-1 Total daily intake due to local environmental exposures

Scenario	DOSE tot (mg/kg bw/day)
Production :	
Site A :	**6.73 E^{-3} mg.kg^{-1}.d^{-1}**
Site B :	9.87 E^{-5} mg.kg^{-1}.d^{-1}
Site C :	5.55 E^{-4} mg.kg^{-1}.d^{-1}
Site D :	3.68 E^{-3} mg.kg^{-1}.d^{-1}
Site E :	2.65 E^{-3} mg.kg^{-1}.d^{-1}
Site F :	1.96 E^{-3} mg.kg^{-1}.d^{-1}
Site G :	5.75 E^{-4} mg.kg^{-1}.d^{-1}
Site H :	7.93 E^{-4} mg.kg^{-1}.d^{-1}
Site I :	2.66 E^{-4} mg.kg^{-1}.d^{-1}
Site J :	5.19 E^{-3} mg.kg^{-1}.d^{-1}
HCFC Production	5.49 E^{-3} mg.kg^{-1}.d^{-1}
Dyes and Pesticide Production	1.17 E^{-3} mg.kg^{-1}.d^{-1}
Other applications	2.24 E^{-3} mg.kg^{-1}.d^{-1}
Uses as a solvent	**5.48 E^{-2} mg.kg^{-1}.d^{-1}**
Losses as a by-product during chemical manufacturing	1.71 E^{-2} mg.kg^{-1}.d^{-1}

Based on the regional concentrations, the total daily intake for humans is $8.07.10^{-5}$ mg/kg bw/d.

Exposure via air

In Section 3.1.3.4. of this report it is said that the **air concentration** of chloroform in urban areas never exceed 5 µg/m³.

Exposure via food and water

As far as the exposure to chloroform via drinking water, in the EU risk assessment of sodium hypochlorite (E.C., 2002), chloroform concentration in drinking water due to water chlorination was reported to be in the range of 11.7 – 13.4 µg/l (see section 3.1.1.3.2.1. of this report).

The highest indirect exposure is estimated for the production of chloroform and its use as a solvent. The human intakes via different routes due to the use of chloroform as a solvent estimated from EUSES are presented in Table 0.4.

Table 0.4 Different routes of intake from human exposure via the environment due to local and regional exposure (EUSES)

	Local exposure due to the use of chloroform as a solvent		Regional exposure	
	Predicted concentration	Estimated daily dose (mg/kg bw/d)	Predicted concentration	Estimated daily dose (mg/kg bw/d)
Drinking water	0.239 mg/L	0.00682	5.49×10^{-4} mg/L	1.57×10^{-5}
Fish	6.2 mg/kg	0.0102	10.8×10^{-3} mg/kg	1.77×10^{-5}
Leaf crops	1.75×10^{-3} mg/kg	0.00003	1.93×10^{-6} mg/kg	3.38×10^{-8}
Root crops	4.25×10^{-3} mg/kg	0.00002	1.09×10^{-3} mg/kg	6×10^{-6}
Meat	6.88×10^{-5} mg/kg	< 0.00001	1.14×10^{-7} mg/kg	4.92×10^{-10}
Milk	2.33×10^{-4} mg/kg	< 0.00001	3.88×10^{-7} mg/kg	3.11×10^{-9}
Air	0.132 mg/m^3	0.0377	0.145 µg/m^3	4.13×10^{-5}
Total daily dose (mg/kg bw/d)		0.0548		8.07×10^{-5}

The highest exposures are to be expected through intake of drinking water, intake of fish and through intake of air.

B.9.4 Other sources

This section is extracted from RRS (chapter 2.4).

Unitended formation of chloroform

Other emissions were mentioned in the RAR but no restriction for the moment is considered. These emissions are however listed here because risk strategies integrating several legislations (for example WFD + Reach) may take into account these other sources in order to proportionate their requirements:

Losses as by-product during chemical manufacturing
Chloroform is produced and emitted as a by-product in the manufacture of vinyl chloride /polyvinyl chloride (VC/PVC, IUPAC name: Polychloroethene) products and other chlorinated bulk chemicals. It is also formed during the oxichlorination of ethylene by chlorine to produce ethylene dichloride (EDC), and during further steps to trichloroethylene and tetrachloroethylene.

Water chlorination
Water is disinfected by chlorination in several different applications and chloroform is then produced by the aqueous reaction of chlorine with various organic compounds in water.
In **drinking water**, chloroform may be present in the raw water as a result of industrial effluents containing this chemical. In addition, chloroform is formed from other chlorinated compounds, reactions that may be enhanced by humic materials.

Water utilities are making efforts to avoid by-product formation in the disinfection processes, notably by adjusting or reducing chlorine inputs. However, this doesn't guarantee low levels of chloroform in municipalities in Europe. Thus, it was found that the concentration of chloroform in water samples collected in different quarters of a town were firstly strictly correlated with its concentration in treated water from the municipal water supply system serving the quarter, and secondly that even many samples were near the detection limit, some of them reached as high as 120 µg/l (Gromiec J.P., Romanowicz B., Wesołowski W., 1996. Chloroform concentration in drinking water of the Lódź municipal area. Rocz Panstw Zakl Hig.;47, 1, 69-76).

Swimming pool water has been reported as a source of chloroform. In France the swimming pools were mainly disinfected by using chlorinated compounds as dichloride or sodium or calcium hypochlorite. According to the more recent available data at the time of the risk assessment, no alternative to these chlorinated treatments are expected in the next years for public swimming pools. Levels of chloroform in water can range from 9 to 179 µg/l (Aggazzotti G, Fantuzzi G, Righi E, Predieri G., 1995. Environmental and biological monitoring of chloroform in indoor swimming pools, J. Chromatogr. A. 25, 710(1):181-90).

In France, effluents are usually not collected towards municipal waste water but rather towards the rainwater network. However, dispensations can be granted if swimming pool effluents are subjected to a preliminary treatment. It should be noted that new water is added to the public swimming pools at the minimum rate of 30 l/swimmer/day (an equivalent volume of effluents is thus generated), and a total draining of public swimming pools is made at least twice a year and of paddling pools once a week.

Cooling water in power plants and other industrial processes is often chlorinated to prevent the heat exchanger and condensing tubes becoming fouled, which would greatly reduce their efficiency. Again, the reaction between chlorine and organic material in the water may result in chloroform generation.

Pulp and paper bleaching

The most important potential for chloroform formation in water is occurring in the pulp and paper industry, where wood pulp is bleached with chlorine. Chloroform is then formed from the aqueous reaction of chlorine with organic substances in the wood pulp and is released to air during the bleaching process and the subsequent treatment of effluent, as in treated effluent and receiving waters.

However, the use of chlorine in paper industry should now decrease in France and most of other European countries, as chlorine-free papers ("totally chlorine-free" TCF or "elementally chlorine-free" ECF) are becoming preferred by customers.

Atmospheric reactions

The atmospheric degradation of high tonnage chlorinated solvents has been suggested as a major source of chloroform. Notably, both trichloroethylene and perchloroethylene have been implicated. This indirect source of chloroform is not yet estimated, especially as other chloroform releases into the atmosphere after physical or/and chemical reactions could also be listed:

- Chloroform has been measured in vehicle exhausts in the United States. Chloroform levels are 100 fold higher in vehicle exhausts of a car using leaded gasoline than in car using unleaded gasoline.
- Chloroform may be found in gases from wastewater sludge incinerators, chlorinated solvents incinerators and from disused or active landfill sites.

- Chloroform may be released during the use or storage of household products (for example cleaning products containing chloroform).

Chlorinated compounds transformation in groundwater

Chloroform may be formed in groundwater notably as the result of the degradation of carbon tetrachloride or other chlorinated compounds coming from atmospheric deposition or from contaminated field sites. Although chloroform breaks down slowly in water and can travel through soil to groundwater, the chlorinated compounds transformation is not expected to be a significant source of chloroform and was therefore not estimated in the risk assessment.

Natural sources of chloroform

Elsewhere, the origin of chloroform in the marine and terrestrial environment can be biogenic (microalgues, soil micro-organisms, forests …). The estimated emissions from anthropogenic sources may account only for less than 10% of the estimated total emissions from all sources (Laturnus F., Haselmann K.F., Borch T; Gron C., 2002. Terrestrial Natural Sources of Trichloromethane: An Overview. Biogeochemistry, Vol. 60, N°2, Biogeochemistry of Halomethanes, pp. 121-139).

B.9.5 Summary of environmental exposure assessment

Manufacturing

This section was built with part 3.1.1 of the RRS on the basis of the RAR information. More details can be found in section 3.1 of the RAR(env).

According to US-EPA (1984), losses don't differ between the two processes, therefore no distinction was made. There are ten major chloroform production sites in EU with an overall production of 302,800 tonnes in 2002. Among them, 4 sites (A, C, E, and J) have a PEC/PNEC ratio above 1. For site E, no risk is expected from chloroform production alone, but rather from its association with HCFC22 and dyes/pesticides productions. Thus, releases to wastewater - calculated using a removal value of 85.6% - are 2.5 Kg/d in the worst-case of chloroform production (site C) and 35.3 Kg/d when chloroform production is included in an integrated production (site E).

Use for HCFC-22 production

Ten HCFC-22 production sites were identified in EU15 accounting for 96.5% of the 234,600 tonnes used as intermediate. Emissions of chloroform to water compartments were available for 8 sites out of 10. Four of them led to PEC/PNEC ratios above 1. The highest production capacity is 35,000 t; with a release factor of 0.00006 kg per tonne of HCFC-22 produced, this site releases locally 7.0 kg chloroform per day to waste water.

Use for dyes and pesticides production

As information on the number of sites using chloroform for the production of dyes and pesticides was insufficient, the 10% rule was not applied and the total volume of 2,400 tonnes was used. Local release in wastewater is then 35 kg/d.

Other applications

Some confidential applications have been found for chloroform. No information was available so as to refine the exposure assessment. Consequently a generic scenario using A and B tables have been performed, leading to a local release estimate in wastewater of 33.2 kg/d.

Use as solvent

The estimated release of 278 kg/d is based on results of a monitoring campaign of effluents in France. The maximum release measured was 38.9 kg/d and the 90th percentile was then calculated to be 10 kg/d. By taking into account a removal of the substance in the STP of 85.6% (default value), releases in wastewater of 278 and 69 kg/d were respectively calculated. The PECsed has been calculated based on the PECwater, which is based on effluent monitoring in France.

B.10 Risk characterisation

B.10.1 Human health

Humans may be exposed to chloroform at workplace from the industrial production of chloroform or indirectly in swimming pools and via the environment. The use of chloroform is limited to professional and industrial applications through regulation (see **Erreur ! Source du renvoi introuvable.**), thus no direct consumer use of chloroform and consequently no direct public exposure is expected (see **Erreur ! Source du renvoi introuvable.**). The indirect consumer exposure results from the formation of chloroform in chlorinated drinking water and swimming pools.

Chloroform is well absorbed, metabolized and eliminated by mammals after oral, inhalation or dermal exposure. Chloroform is hence widely distributed in the entire organism, via blood circulation and, due to its liposolubility, preferentially in fatty tissues and in the brain. Nearly all tissues of the body are capable of metabolizing chloroform, but the rate of metabolism is greatest in liver, kidney cortex, and nasal mucosa.

Chloroform can cross the placenta, transplacental transfer has been reported in mice (Danielsson et al., 1986 in WHO, 1994) and in the fetal blood in rats (Withey and Karpinski, 1985 in WHO, 1994) and it is expected to appear in human colostrum and is excreted in mature breast milk (Lechner et al., 1988; Fisher et al., 1997 in Health Council of the Netherlands, 2000; Davidson *et al.*, 1982 in US EPA, 2004).

The estimated ingestion of chloroform via breast-milk was 0.043 mg, which did not exceed the US EPA non-cancer drinking water ingestion rates for children (Fisher et al., 1997).

Human studies showed that the proportion of chloroform absorbed via inhalation ranged from 76 to 80%. The very high volatility of the substance leads to considerable low retention times of the substance on the skin, consequently dermal adsorption requires submersion or contact with chloroform in liquid form, rather than vapour. Chloroform dermal absorption increases with the temperature and the vehicle used. Human studies have showed total absorbed doses of 7.8 and 1.6% when chloroform was administered in water and ethanol respectively, furthermore the contribution to the total body burden (oral + dermal) of an immersion in bath water containing low chloroform concentrations accounted for 18% at 40°C, 17-6% at 35°C and 1-7% at 30°C. The oral administration of chloroform resulted in almost 100% of the dose absorbed from the gastrointestinal tract.

Considering the data reported, the animal inhalation, dermal and oral absorptions of chloroform are considered to be respectively 80%, 10% and 100%. Data from human studies showed that 80% of the chloroform dose is absorbed via inhalation and 10% via dermal absorption. Oral absorption of chloroform is assumed to be 100% for risk characterisation.

Acute toxicity varies depending upon the strain, sex and vehicle. In mice the oral LD_{50} values range from 36 to 1366 mg chloroform/kg body weight, whereas for rats, they range from 450 to 2000 mg chloroform/kg body weight. Kidney damage induced in male mice are related to very sensitive strain, thus it is not considered relevant for risk characterisation.

Chloroform LC_{50} values of 6200 mg/m^3 and 9200 mg/m^3 have been reported for inhalation exposure in mice and rats respectively. Mice are more susceptible than rats to acute chloroform toxicity for both exposure routes. A systemic and local dermal LOAEL of 1.0 g/kg has been reported in rabbits for extensive necrosis of the skin and degenerative changes in the kidney tubules after chloroform exposure under occlusive conditions (Torkelson et al., 1976). An oral NOAEL of 30 mg/kg bw has been reported in rats for serum enzyme changes indicative of liver damage (Keegan *et al.*, 1998). A dose-dependent increase in the LI was present in the kidney of Osborne-Mendel rats given doses of 10 mg/kg (Templin et al., 1996b). The epithelial cells of the proximal tubules of the kidney cortex were the primary target cells for cytotoxicity and regenerative cell proliferation. The mean lethal oral dose for an adult is estimated to be about 45 g, the human inhalation LOAEC based on discomfort is ≤ 249 mg/m^3 (Verschueren, 1983 in WHO, 1994), orally a LOAEL <107 mg/kg has been determined on serious illness (WHO, 1994). However, large interindividual differences in susceptibility occur in human. NOAEL(C) and LOAEL(C) selected as starting point for risk characterisation are reported in **Erreur ! Source du renvoi introuvable.**.

Chloroform is an irritant substance for skin, eye and upper airways. Rabbit dermal studies showed slight to high irritation potency (LOAEL = 1000 mg/kg bw, Torkelson et al., 1976). In man, dermal contact with chloroform caused dermatitis. Severe eye irritation was observed in animals with liquid chloroform, reported effects are various but one rabbit study indicate slight but definitive corneal injury. In man, eye contact with liquid chloroform caused temporary corneal epithelium injury. Mainly repeated dose studies have been reported for irritation, chloroform induced lesion and cell proliferation in the olfactory epithelium but also bone growth. In respiratory tract of mice and rats, inhaled chloroform induced lesions and cell proliferation in the olfactory epithelium and the nasal passage, the LOAEC reported in rats for enhanced bone growth and hypercellularity in the lamina propria of the ethmoid turbinates of the nose at the early time point (4 days) is 10 ppm (50 mg/m^3, Templin et al., 1996a). No data have been reported for sensitisation with chloroform in human, an animal sensitisation test was reported but the validity of this study could not be assessed.

Laboratory animal studies identify the liver kidneys and the nasal cavity as the key target organs of chloroform's toxic potential. The lowest reported oral LOAEL was 15 mg/kg/day in dog livers based on fatty cysts and elevated ALAT levels is a starting point for risk characterisation (Heywood et al., 1979 in US EPA, 2001). For mice, reported oral LOAELs were 50 mg/kg bw/day for the hepatic effects and 37 mg/kg bw for renal effects (mineralization, hyperplasia and cytomegaly) (Condie *et al.*, 1983; Munson *et al.*, 1982 in WHO, 2004). The reported inhalation NOAEC for a 90 days sub-chronic exposure was 25 mg/m^3 (5 ppm) in male mice for the renal effects (vacuolation, basophilic appearance, tubule cell necrosis and enlarged cell nuclei) and a NOAEC of 25 mg/m^3 (5 ppm) was reported in male mice for hepatic effects (vacuolated hepatocytes and necrotic foci) (Templin et al., 1998). A chronic (104 weeks) inhalation NOAEC of 25 mg/m^3 (5ppm) was reported in mice for increased renal cytoplasmic basophilia in both exposed males and females, and increased atypical tubule hyperplasia and nuclear enlargement in the kidneys in the males (Yamamoto et al., 2002). Nasal lesions have also been observed in rats and mice exposed by inhalation or via the oral route. Following a sub-chronic inhalation exposure, the lowest reported effect level was LOAEC= 9.8 mg/m^3 (2 ppm), which caused cellular degeneration and regenerative hyperplasia in nasal passage tissues of

rats. Lesions and cell proliferation in the olfactory epithelium and changes in the nasal passages were observed at LOAEL=34 mg/kg bw/d (Larson et al., 1995). In human, limited data on repeated dose toxicity suggest that the liver and kidneys are the likely target organs. Human studies were poorly reported in the reviews so animal data were selected as the starting point for risk characterisation.

Data on the mutagenicity of chloroform have recently been reviewed and evaluated by several groups: IARC, US EPA, ILSI and WHO. Most of the reviews concluded that chloroform is not a strong mutagen but a weak genotoxic effect was not excluded. Studies presented in this report were chosen based on their reliability (1 or 2) according to Klimish scoring system. Although negative in vivo results are reported, several in vivo tests published in international rewiews demonstrated that chloroform could induce micronuclei and chromosomal aberrations. Positive results are observed in the target organ (kidney) or after at least three administrations in bone marrow cells, which might be consistent with a mechanism of oxidative damage due to glutathione depletion. Besides, it should be noted that MN and CA tests performed in rats were all positive whereas mixed results were observed in mice.

Studies in animals reveal that chloroform can cause an increased incidence of kidney tumors in male rats or mice and an increased incidence of liver tumors in mice of either sex. These induced tumors responses are postulated to be secondary to sustained or repeated cytotoxicity and secondary regenerative hyperplasia, according to the dose levels tested. For the renal effects in male mice the oral NOAEL was 17 mg/kg bw (Roe et al., 1979) and the inhalation NOAEC was 5 ppm (25 mg/m^3, Yamamoto et al., 2002).

Two studies showed nasal lesion in rats or mice due to chloroform inhalation, for nasal lesions a LOAEC of 5 ppm was determined (Yamamoto et al., 2002). The weight of evidence of chloroform weak genotoxicity is consistent with the hypothesis that the liver and kidney tumors induced depend on persistent cytotoxic and regenerative cell proliferation responses. The persistent cell proliferation presumably would lead to higher probabilities of spontaneous cell mutation and subsequent cancer.

There have been no reported studies of toxicity or cancer incidence in humans chronically exposed to chloroform (alone) via drinking water. Relevant studies contain little information on specific exposure, and it is not possible to attribute any excess risk specifically to chloroform.

Regarding fertility, only one author reported increased mice abnormal sperm following exposure to an air concentration of 400 or 800 ppm chloroform (estimated inhalation LOAEC = 400 ppm, Land *et al.*, 1979-1981). Otherwise, animal findings were epididymal lesions or increased right epipidymis weight (estimated oral NOAEC is 15.9 mg/kg, Chapin et al., 1997). As well, one occupational case study reported asthenospermia in association to chloroform exposure. No other adverse reproductive effect has been evidenced in the 90 days studies.

Concerning developmental toxicity, epidemiological studies of chloroform in drinking water no association was clearly established between exposure to chloroform and reduced fetal weight, stillbirth and cleft defects. Otherwise, we need to keep in mind that many of these epidemiological studies present limitations like the use of water concentration as the measure of exposure, which can lead to exposure misclassification.

By inhalation, the effects of chloroform on the various animals tested include effects on pregnancy rate, resorption rate, litter size and live fetuses. These effects have been observed with concentrations causing a decrease of maternal weight and food consumption. Other effects as fetal weight and CRL decrease, as well as skeletal and gross abnormalities or variations have been mentioned. An inhalation NOAEC of 10 ppm was based on decreased fetal weight & CRL (Baeder & Hoffman, 1991) and an oral LOAEL of 20 mg/kg/day was based on decreased fetal weight (Thompson et al., 1974).

Table 0.5 Summary of the selected NOAEL(C)s or LOAEL(C)s

Substance name	Inhalation (N(L)OAEC)	Dermal (N(L)OAEL)	Oral (N(L)OAEL)
Acute toxicity	LOAEC ≤ 249 mg/m³ 60 min, Man, Verschueren, 1983 in WHO, 1994	LOAEL= 1000 mg/kg bw 24h, Rabbit, Torkelson et al., 1976	LOAEL ≤ 107 mg/kg Single administration, Man, Winslow & Gerstner, 1978 in WHO, 1994 LOAEL = 10 mg/kg bw Single administration, Rat, Templin et al., 1996b
Irritation / corrositivity	LOAEC= 10 ppm - 50 mg/ m³ Early time pojnts (4 days), 90d, Rat, Templin et al., 1996a	-	-
Repeated dose toxicity (local)	LOAEC= 2 ppm - 10 mg/ m³ 90d, Rat, Templin et al., 1996a	-	LOAEL= 34 mg/kg bw 90d, Rat, Larson et al., 1995
Repeated dose toxicity (systemic)	NOAEC= 5 ppm - 25mg/ m³ 90d, Mouse, Templin et al., 1998; 104w, Yamamoto et al., 2002	-	LOAEL= 15 mg/kg bw 7.5y, Dog, Heywood et al., 1979
Carcinogenicity (local)	LOAEC= 5 ppm - 25 mg/ m³ 104w, Mouse, Yamamoto et al., 2002	-	-
Carcinogenicity	NOAEC= 5 ppm - 25 mg/ m³ 104w, Mouse, Yamamoto et al., 2002	-	NOAEL= 17 mg/kg bw 80w, Mouse, Roe et al., 1979
Fertility impairment	LOAEC= 400 ppm – 2000 mg/m³ 5d, Mouse, Land et al. 1979, in US EPA, 2004	-	NOAEL= 16 mg/kg bw 31w, Mouse, Chapin et al., 1997, in US EPA, 2004
Developmental toxicity	NOAEC= 10 ppm - 50 mg/m³ GD7-16 Rat, Baeder & Hoffman, 1991, in US EPA, 2004	-	LOAEL= 20 mg/kg-day GD6-18, Rabbit, Thompson *et al.*, 1974, in US EPA, 2004

B.10.1.1 Risk for workers

Chloroform is also a by-product chemical associated with disinfection of swimming pool water; chloroform is originated by the reaction of disinfecting agents with organic substances and not intentionally used. Consequently, it was agreed that the Risk Characterisation of chloroform as a by-product chemical should not be presented in the Chloroform risk assessment but rather than in the Sodium Hypochlorite RAR. Any risk identified in scenario 3 for workers as swimming instructors, lifeguards, competitive swimmers and for consumers as child swimmers and adult swimmers should be addressed in the Sodium Hypochlorite RAR (results of RC for scenario 3 are presented in Annex 1 of the RAR for information).

Summary of the risk characterisation for workers

		Acute toxicity			Local toxicity after single or repeated exposure			Sensitisation	Repeated dose toxicity Systemic			Mutagenicity	Carcinogenicity	Toxicity for reproduction,	
		Inhalation	Dermal	Combined	Inhalation	Dermal	Eye		Inhalation	Dermal	Combined			**Fertility**	**Development**
Scenario1: Chloroform used as intermediate (closed batch process)	MOS	44	148	5	10				2 (local) **4.5 (syst)**	342	12		4 427 16	357 667 24	9 567 21
	Concl.	**ii**	**ii**	**iii**	**iii**			**ii**	**iii**	**ii**	**iii**	**i**	**iii inh local iii inh ii dermal iii combi**	**ii inh ii dermal iii combi**	**iii inh ii dermal iii combi**
Scenario2: Chloroform used as solvent in the synthesis of chemicals (closed batch process)	MOS	25	148	3	5				1 (local) **2.5 (syst)**	342	7		3 427 9	200 667 14	5 567 12
	Concl.	**iii**	**ii**	**iii**	**iii**			**ii**	**iii**	**ii**	**iii**	**i**	**iii inh local iii inh ii dermal iii combi**	**ii inh ii dermal iii combi**	**iii inh ii dermal iii combi**

B.10.1.2. Risk for the consumers

As the use of chloroform is limited to professional and industrial applications through regulation, there is no direct consumer use of chloroform and consequently no direct public exposure is expected.

Chloroform is also a by-product chemical associated with disinfection of swimming pool water; chloroform is originated by the reaction of disinfecting agents with organic substances and not intentionally used. Consequently, it was agreed that the Risk Characterisation of chloroform as a by-product chemical should not be presented in the Chloroform risk assessment but rather than in the Sodium Hypochlorite RAR. Any risk identified in scenario 3 for workers as swimming instructors, lifeguards, competitive swimmers and for consumers as child swimmers and adult swimmers should be addressed in the Sodium Hypochlorite RAR (results of RC for scenario 3 are presented in Annex 1 of the RAR for information).

B.10.2 Risk for the environment

This section was built with part 3.3.2 of the RRS.

In the following sections, only exposure and risk assessments that have resulted in the identification of risk later on have been discussed in order to highlight the causes of this risk reduction strategy. Thus, the focus is only given on the water compartment with its 3 sub-compartments (surface Water, SEDiment and Sewage Treatment Plant. Table 3 summarises the identified risks for chloroform with the RCR (Risk Characterization Ratio = PEC/PNEC).

Water:

- The PEC/PNEC ratios obtained for surface water for chloroform are below 1 for all production sites. It can be concluded that there is no risk to aquatic organisms through production of chloroform **(conclusion ii)**.
- Only **the use of chloroform as a solvent** has a PEC/PNEC ratio above 1. Therefore, it can be concluded that there is a need for limiting the risks for this application **(conclusion iii).**

Sediment:

- For all production sites, PEC/PNEC-ratios are below 1. It can be concluded that there is no risk to sediment organisms through production of chloroform (**conclusion (ii)**).
- For all uses **except the use of chloroform as a solvent,** PEC/PNEC ratios are below 1 and a **conclusion (ii)** can be derived.
- Concerning the **use of chloroform as a solvent,** the risk identified for this application and the PEC/PNEC ratio is far above 1. Therefore, there is a need for limiting the risks for this application (**conclusion (iii)**).

Sewage treatment plant

- PEC/PNEC-ratios above 1 have been derived for four production sites, although specific information for these sites has been considered. PEC/PNEC-ratios above 1 have also been derived for uses where release estimates are based on effluent monitoring. (Using the 90-percentile value of the monitoring study, 10 kg/d after treatment, gives a PEC/PNEC ratio of 3.4).
- Therefore, a **conclusion (iii)** has to be derived **for production sites A, C, E and J**, for all uses and for unintended releases.

Table B.10.2-1: summary of identified environmental risks for chloroform – conclusion (iii)

Scenario	Environmental compartment	RCR
Uses as a solvent	Water	13.7
	Sediment	98.2
	Sewage treatment process	417
Production (sites A, C, E, J)	Sewage treatment process	1.3-24.2
HCFC production	Sewage treatment process	2.1
Dyes and pesticides production	Sewage treatment process	10.5
Other uses	Sewage treatment process	10.0
Unintended releases	Sewage treatment process	5.6

Some considerations about these conclusions (iii):

Chloroform production:

For production site E, specific information has been requested in order to check whether dyes and pesticides were actually produced on this site. As no data was provided by the producer, a worst-case scenario has been anticipated leading to a PEC/PNEC-ratio above 1. However, it should be specified that if no dyes and pesticides are actually produced on this site, this ratio would fall below 1 for site E.
Specific information on sewage treatment plant has later been provided by industry for site C and E. For site E, data confirm that no risk is expected from chloroform production alone at this site, but rather from integrated production of chloroform, HCFC22 and dyes/pesticides. For site C, data were in line with previous results showing that emissions have been realistically quantified.

HCFC-22 production:

The reduction of HCFC-22 production, which was largely the main use of chloroform as intermediate, could consequently reduce chloroform emissions in sewage compartment. However, the Montréal protocol and the ODS Regulation 2037/2000/EC concern only HCFC-22 used directly, for example as refrigerant, and could be counterpart by the growing production of fluorinated polymers and copolymers using HCFC-22 as intermediate. Whereas the consumption was around 176,000 tonnes in 2000, the total Western European consumption of fluorocarbons

was estimated 198,000 tonnes in 2005. This means that the complete stop of HCFC-22 could take more time and need over constraints to be achieved.

Use of chloroform as solvent:

The PEC_{water} value for this scenario is based on effluent monitoring in France. In this monitoring study, chloroform concentrations might come from other releases than the releases due to the specific use of chloroform as a solvent. The highest release value of 38.9 kg/d after treatment was used assuming that on-site biological treatment was performed and using an elimination rate of 85.6%. Using the 90-percentile value of the monitoring study (10 kg/d after treatment) would give a PEC/PNEC ratio of 3.4, which is still above 1.
The PEC_{sed} has been calculated based on the PEC_{water}, which is based on effluent monitoring in France.

Consideration of the risk towards STP:

It could be considered that microorganisms are able to adapt themselves to low chloroform concentrations. As 1) this was not clearly proven, 2) effluent are not systematically treated on-site by a acclimated consortia, and 3) because of monitoring of some peaks as high as 35.5 mg/l (see RAR page 27, Rhône-Alpes region in France in 2003) until now this reasoning cannot be considered as a solution.

Other compartments (conclusion (ii):

Terrestrial compartment:
As the worst case, the use as solvent, raised the PEC/PNEC ratio of 7.26 / 496=0.015, a general conclusion (ii) was drawn for the terrestrial compartment.

Atmospheric compartment:
Without any indication of biotic effects and since non-biotic effects are negligible in atmosphere, a **conclusion (ii)** was derived for this compartment based on a qualitative assessment.

Non compartment specific effect through the food chain:
Since bioaccumulation is low, a general **conclusion (ii**) was drawn for this compartment.

Table B.11-1: Inventory of the releases and PEC/PNEC ratios for chloroform during the various life stages.

Life stage			Sites	Estimated local release to wastewater[1]	**Clocal $_{eff}$ (µg/L) (PEC_{STP})**	**$PEC/PNEC_{STP}$**	**$PEClocal_{water}$ (µg/L)**	**$PEC/PNEC_{water}$**	**$PEClocal_{sed}$ dry weight [µg/kg]**	**$PEC/PNEC_{sed}$**
I	**Production (302,800 t in 2002) (271,000 net)**	Hydrochlorination of methanol or chlorination of methane	A	0.052 kg/d	124.8	**2.60**	0.96	0.007	21.3	0.047
			B[2]	0.014 kg/d	-	-	1.52	0.010	33.7	0.075
			C	2.5 kg/d	426.3	**8.88**	1.27	0.009	28	0.062
			D[3]	0.32 kg/d	25.6	0.42	0.89	0.006	19.7	0.044
			F[5]	0.98 kg/d	-	-	5.74	0.039	127	0.28
			G	7.53 kg/d	11.4	0.24	0.88	0.006	19.5	0.043
			H	10.08 kg/d	28.5	0.59	2.18	0.015	48.7	0.108
			I	0.074 kg/d	16.0	0.33	0.85	0.006	18.9	0.042
			J	0.28 kg/d	62.2	**1.30**	2.39	0.017	52.8	0.117
IIa	**Use as an intermediate (254,200 t in 2002)**	HCFC-22 production		7.0 kg/d worst case generic calculation *(site specific worst case: 0.57 kg/d)*	101.0	**2.1**	3.36	0.023	73.9	0.164
	(2,400 t in 2002)	Dyes and pesticides production		35.0 kg/d worst case generic calculation	504.0	**10.5**	13.4	0.092	297	0.660
	(5,700 in 2002)	Other applications (considered as confidential)		33.2 kg/d worst case generic calculation	478.0	**10**	12.8	0.088	282	0.628
IIb	**Use as a solvent (8,700 t in 2002)**	Extraction solvent in chemical and pharmaceutical industry		278 kg/d maximum measured release *(69 kg/d 90th percentile of measured releases)*	20.0	**417**	2001.9	**13.71**	44200	**98.2**
IIIa	**Unintended formation as by-product**	Losses as a by product during VC/PVC and other chlorinated products manufacturing		18.5 kg/d generic calculation	266.4	**5.6**	7.5	0.051	165	0.368
IIIb	**Unintended formation during water chlorination**	Drinking water Municipal wastewater Swimming pools Cooling water		*Diffuse source of chloroform → $PEC_{regional}$ calculations only*						

	Unintended formation during pulp and paper bleaching										
	Atmospheric reaction of high tonnage chlorinated solvents										
	Vehicle emissions										
	Landfills										
	Incineration processes										
	Natural sources										
	(Household products)			*Beyond the scope of this RRS*							
	Regional scale						0.828	0.0057		0.012	

[1] Releases to wastewater are calculated using measurements in effluents (C, D, G and J) or when no data was available 85.6% removal (A, E, H and I)
[2] No wastewater treatment Plant
[3] Releases of chloroform considering a simultaneous production of chloroform and HCFC 22 at the local scale
[4] Releases of chloroform considering a simultaneous production of chloroform, HCFC 22 and dyes / pesticides at the local scale
[5] Site F had stopped manufacturing chloroform in 2004 and is being dismantled

B.11 Summary of existing legal requirements and risk management measures proposed

B.11.1 For the environment

More details on the existing legal requirements, their efficiency and monitorability are available in section 4 of the risk reduction strategy for the environment which has been discussed and endorsed (as stated in the Handover ES/12b/2008 joined to the annex XV dossier) at the 15th risk reduction strategy meeting of the Member States for the implementation of council regulation (EEC) 793/93 on the evaluation and control of risks of existing substances in April 2008.

Finally, it has been recommended:

- That competent authorities in the Member States concerned should **lay down, in the permits issued under Council Directive 96/61/EC (IPPC, Integrated Pollution Prevention and Control, revised 2008/1/EC) conditions, emission limit values or equivalent parameters or technical measures regarding chloroform**, in order for the installations concerned to operate according to the best available techniques (BAT) taking into account the technical characteristic of the installations concerned, their geographical location and the local environmental conditions.
- That Member States should carefully **monitor the implementation of BAT regarding chloroform** and report any important developments to the Commission in the framework of the exchange of information on BAT.
- To **facilitate permitting and monitoring under Council Directive 96/61/EC (revised 2008/1/EC)** the results of the risk assessment of chloroform should be taken into account for the ongoing work to develop guidance on 'Best Available Techniques' (BAT).
- **For plant not covered by the IPPC directive**, local emissions to the environment should, where necessary, be **controlled by national rules or by permit** to ensure that no risk for the environment is expected.

B.11.2 For human health

B.11.2.1 Workers

Classification and labelling

See section B.3.1of this annex XV report.

As a result of its classification as hazardous substance, chloroform is subject to general regulations concerning its supply and handling.

Safety data sheets

In accordance with article 31 (title IV) of Regulation (EC) No 1907/2006, the supplier of a substance or a preparation that meets the criteria for classification as dangerous in accordance with Directives 67/548/EEC or 1999/45/EC shall provide the recipient of the substance or preparation with a safety data sheet compiled in accordance with Annex II.

The information system for hazardous substances and preparations in the form of labelling and the safety data sheets is considered sufficient in principle to provide the user with sufficient information for the selection of suitable occupational safety measures. The SDS should contain all relevant information from the risk assessment report.

Occupational safety and health regulations

At the European level, the following directives are primarily applicable as general regulations for occupational safety and health of workers in the production and use of chloroform:

- 98/24/EC on the protection of workers from the risk related to exposure to chemical agent at work.
- 89/656/EEC on the use of personal protective equipment
- 92/85/EEC on the safety and health of pregnant workers and workers who have recently given birth or are breastfeeding.
  Chloroform is included (substances labelled R40, R45, R46, and R47 under Directive 67/548/EEC) in Annex I of Directive 92/85/EEC, the non-exhaustive list of agents, processes and working conditions for which the employer must monitor the nature, degree and duration of exposure of workers in order to: assess any risks to the safety or health and any possible effect on the pregnancies or breastfeeding of workers, and decide what measures should be taken.
- Directive 94/33/EC on the protection of young people at work, 1994 O.J. (L 216) 12, 20 Aug 1994
  (Chloroform is included in the "Non-exhaustive list of agents, processes and work" against which young people must be protected (Substances and preparations classified according to Directives 67/548/EEC and 88/379/EEC as toxic (T), very toxic (T+), corrosive (C) or explosive (E).).

Only limited knowledge is available about the extent to which the EU member states have in each case transposed these basic requirements into national law.

Occupational exposure limits (OELs)

OELs apply to workplace air concentrations of chemicals. They are normally intended to protect workers against short-term adverse effects (irritation, acute effects) or long-term effects (e.g. on liver, lungs, kidneys, or chronic effects) after months or years of exposure. When applicable, a "short-term exposure limit" (STEL) may be proposed or imposed for the first ones, and/or a "time-weighted average" (TWA) for the second. The first value ordinarily refers to a 15 minutes or so duration, the second to a shift (generally considered as an 8-hour shift).

Table 0.6 details the OELs recommended for chloroform in various countries. They are provided for information and are not an indication of the level of control of exposure achieved in practice in workplaces.

Table 0.6 OEL values BGIA (2005)

	8-hour TWA		STEL, 15 min	
Country	mg/m^3	ppm	mg/m^3	ppm
EU*	**10**	**2**		
Austria	10	2		
Belgium[a]	10	2		
Denmark	10	2	20	4
France[c]	10	2	250	50
Germany (MAK)	2.5	0.5	10	2
Hungary	10		10	
Italy (+skin)	10	2		
Spain	10	2	-	-
Sweden	10	2	25	5
Switzerland[b]	2.5	0.5	5	1
United Kingdom[a]	10	2	-	
USA (OSHA)		-	240	50
USA (ACGIH)		10		

*Directive 2000/39/CE of 8 June 2000

a : values given by Belgium and UK in their comments on the RAR of chloroform (May 2007).

b: GESTIS International limit values 2008; http://bgia-online.hvbg.de/LIMITVALUE/WebForm_gw.aspx

c: Legally binding since 2006

The EU Directive 2000/39 proposed an Indicative Limit Value (ILV) for chloroform. The ILV is considered indicative for the limit of daily exposure for a worker which probably gives no rise to adverse health effects. The EU value, also noted ILV-TWA (for time weight average), is 10 mg/m3 on the basis of 8 h work, 40 h/week. This corresponds to a 2 ml/m³ (ppm) OEL value accepted in Europe.

Personal Protection Equipment (PPE) against dermal exposure

According to community Legislation, workers have to be provided with suitable PPE if their health is at risk due to exposure against chemicals. PPE that protects against the risks of chloroform is available and has to be indicated in the SDS. On account of the effects of chloroform, the use of suitable protective equipment is in general widely accepted and legally required, if exposure cannot be excluded by other technical or organisational measures.

Limitation on use

The Commission Directive 96/55/EC replacing the Directive 94/60/EC clarifies that chloroform may not be used in concentrations equal to or greater than 0.1% by weight in substances and preparations used in diffusive applications such as in surface cleaning and cleaning of fabrics. This provision entered into force on June 30th 1998.

Proposal:

Within the framework of workplace legislation an occupational exposure limit is an enforceable and effective means to make exposure control enforceable. If this OEL takes into account the risk assessment, it can also be considered to be an effective means for health protection in the workplace. It can be monitored by existing techniques of workplace measurement.

The OEL should reflect the critical exposure levels for the most critical effects (repeated dose toxicity, carcinogenicity and developmental toxicity) comprised between 0.7 and 1 mg/m^3. If exposures are controlled to this level this is an effective measure to reach the necessary level of protection.

Exposure reduction by technical and organisational measures and personal protection are foreseen in workplace legislation. The OEL is a practical and monitorable tool to make such exposure reduction enforceable and monitorable in the framework of worker protection legislation. The OEL will also trigger that personal protective equipment is provided if workplace concentrations exceed the OEL.

Given the conservative way of the exposure assessment (see RAR) for the chloroform, typical exposures and exposures representing good practice are probably lower than the worst-case exposure that has been taken for deriving concern during the risk assessment. This is particularly true for the chloroform production or in HCFC 22 plants were safety procedures are very strict because they are imposed by the use of very toxic chlorine or hydrogen fluoride gas. Technical and organisational measures seem to be possible to control the exposure to a level below the critical exposure level of 0.7-1 mg/m3.

The risk assessment has also resulted in concerns for several effects upon dermal exposure. There were no measurement data and dermal exposure has been assessed in a conservative way by the EASE model. It might be that real exposures are much lower assuming a protection factor of 90%.

The risks from dermal exposure cannot be reduced by the establishment of an OEL. Exposure can in principle be reduced by organisational measures that reduce the frequency, duration and area of exposure, by gloves and protective suits, by training to work cleanly and to use PPE correctly and by personal hygiene. Training, information and hygienic measures are foreseen in the framework of workplace legislation. As the scenarios assessed are within the chemical industry and only a limited number of skilled workforce is occupied, training, organisational measures and occupational hygiene in the framework of workplace legislation are regarded to be sufficient for limiting the risks in the industries and uses of chloroform, that have been assessed in the RAR.

It is then recommended to update at community level occupational exposure limit values for chloroform according to Directive 98/24/EEC taking into account this risk assessment.

At this time, considering the strictly conditions of uses already in place for the use of chloroform and considering the potential candidates for the substitution of chloroform (for ex. other chlorinated solvents with an equivalent toxicological profile), it is questionable that a restriction proposal is relevant.

B.11.2.2 Human exposed via environment

If correctly applied, measures recommended in section B.11.1 should appropriately reduce the risk highlighted in the RAR for the man exposed via environment.

G. STAKEHOLDER CONSULTATION

17 french manufacturers and users plants including **pharmaceutics, pesticides, paper, and plastic industries.**

H. OTHER INFORMATION

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All references are extracted from RAR or RRS. For more details, check the bibliography provided in these reports.