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Chloroform: CASRN 67-66-3 (04/01/93)

Health risk assessment information on a chemical is included in IRIS only after a comprehensive review of chronic toxicity data by work groups composed of U.S. EPA scientists from several Program Offices. The summaries presented in Sections I and II represent a consensus reached in the review process. The other sections contain U.S. EPA information which is specific to a particular EPA program and has been subject to review procedures prescribed by that Program Office. The regulatory actions in Section IV may not be based on the most current risk assessment, or may be based on a current, but unreviewed, risk assessment, and may take into account factors other than health effects (e.g., treatment technology). When considering the use of regulatory action data for a particular situation, note the date of the regulatory action, the date of the most recent risk assessment relating to that action, and whether technological factors were considered. Background information and explanations of the methods used to derive the values given in IRIS are provided in the five Background Documents in Service Code 5, which correspond to Sections I through V of the chemical files.

STATUS OF DATA FOR Chloroform

File On-Line 01/31/87

Category (section)	Status	Last Revised
Oral RfD Assessment (I.A.)	on-line	09/01/92
Inhalation RfC Assessment (I.B.)	pending	
Carcinogenicity Assessment (II.)	on-line	03/01/91
Drinking Water Health Advisories (III.A.)	no data	
U.S. EPA Regulatory Actions (IV.)	on-line	04/01/92
Supplementary Data (V.)	on-line	01/31/87

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\_I. CHRONIC HEALTH HAZARD ASSESSMENTS FOR NONCARCINOGENIC EFFECTS

\_\_I.A. REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

Substance Name -- Chloroform  
CASRN -- 67-66-3  
Primary Synonym -- Trichloromethane  
Last Revised -- 09/01/92

The Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis, but may not exist for other toxic effects such as carcinogenicity. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to Background Document 1 in Service Code 5 for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of compounds which are also carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file when a review of that evaluation is completed.

\_\_I.A.1. ORAL RfD SUMMARY

Critical Effect	Experimental Doses*	UF	MF	RfD
Fatty cyst formation in liver	NOEL: none  LOAEL: 15 mg/kg/day	1000	1	1E-2 mg/kg/day
Dog, Chronic Oral Bioassay	(converted to 12.9 mg/kg/day)			

Heywood et al., 1979

\*Conversion Factors:  $15 \text{ mg/kg/day} \times 6 \text{ days}/7 \text{ days} = 12.9 \text{ mg/kg/day}$

\_\_I.A.2. PRINCIPAL AND SUPPORTING STUDIES (ORAL RfD)

Heywood, R., R.J. Sortwell, P.R.B. Noel, et al. 1979. Safety evaluation of toothpaste containing chloroform. III. Long-term study in beagle dogs. J. Environ. Pathol. Toxicol. 2: 835-851.

In this study beagle dogs were administered chloroform in a toothpaste base (0.5 mL of toothpaste base/kg/day) in gelatin capsules. A control group composed of 16 males and 16 females received the vehicle, and additional control groups of eight animals/sex were administered an alternative toothpaste or were left untreated. Experimental groups of eight male and eight female dogs received 15 or 30 mg chloroform/kg/day for 6 days/week. Treatment was continued for 7.5 years. Fatty cysts, considered to be treatment-related, were observed in livers of some dogs in both treatment groups. Nodules of altered hepatocytes were considered treatment-related but not dose-dependent. A dose-related increase in SGPT levels was noted and a less marked increase in SGOT was noted in the high-dose animals. The LOAEL was determined to be 12.9 mg/kg/day, and an RfD was set at 0.01 mg/kg/day.

#### \_\_\_I.A.3. UNCERTAINTY AND MODIFYING FACTORS (ORAL RfD)

UF -- Uncertainty factors of 10 each were applied to the LOAEL of 12.9 mg/kg/day to account for the interspecies conversion, protection of sensitive human subpopulations, and concern that the effect seen was a LOAEL and not a NOEL.

MF -- None

#### \_\_\_I.A.4. ADDITIONAL COMMENTS (ORAL RfD)

Chloroform is considered to be highly fetotoxic, but not teratogenic (Schwetz et al., 1974; Thompson et al., 1974).

A study in rats, using only one treatment dose (Palmer et al., 1979), identified 60 mg/kg/day by gavage as a LOAEL for decreased weight gain, plasma cholinesterase and relative liver weight. Other data in the literature (Jorgenson et al., 1982) also indicate changes in liver fat to be treatment-related.

#### \_\_\_I.A.5. CONFIDENCE IN THE ORAL RfD

Study -- Medium

Data Base -- Medium

RfD -- Medium



The critical study (Heywood et al., 1979) was of chronic duration, used a fairly large number of dogs, and measured multiple endpoints; however, only two treatment doses were used and no NOEL was determined. Therefore, confidence in the study is rated medium. Confidence in the data base is considered medium to low; several studies support the choice of a LOAEL, but a NOEL was not found. Confidence in the RfD is also considered medium to low.

\_\_\_I.A.6. EPA DOCUMENTATION AND REVIEW OF THE ORAL RfD

U.S. EPA. 1985. Drinking Water Criteria Document for Trihalomethanes. Office of Drinking Water, Washington, DC. (External Review Draft)

The 1985 Drinking Water Criteria Document for Trihalomethanes is currently undergoing Agency review.

Agency Work Group Review -- 12/02/85, 05/15/86

Verification Date -- 12/02/85

\_\_\_I.A.7. EPA CONTACTS (ORAL RfD)

Nancy Chiu / OST -- (202)260-7587

Michael L. Dourson / OHEA -- (513)569-7533

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\_\_\_I.B. REFERENCE CONCENTRATION FOR CHRONIC INHALATION EXPOSURE (RfC)

Substance Name -- Chloroform

CASRN -- 67-66-3

Primary Synonym -- Trichloromethane

A risk assessment for this substance/agent is under review by an EPA work group.









## \_\_II. CARCINOGENICITY ASSESSMENT FOR LIFETIME EXPOSURE

Substance Name -- Chloroform

CASRN -- 67-66-3

Primary Synonym -- Trichloromethane

Last Revised -- 03/01/91

Section II provides information on three aspects of the carcinogenic risk assessment for the agent in question: the U.S. EPA classification, and quantitative estimates of risk from oral exposure and from inhalation exposure. The classification reflects a weight-of-evidence judgment of the likelihood that the agent is a human carcinogen. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10,000, 1 in 100,000 or 1 in 1,000,000. Background Document 2 (Service Code 5) provides details on the rationale and methods used to derive the carcinogenicity values found in IRIS. Users are referred to Section I for information on long-term toxic effects other than carcinogenicity.

### \_\_II.A. EVIDENCE FOR CLASSIFICATION AS TO HUMAN CARCINOGENICITY

#### \_\_\_II.A.1. WEIGHT-OF-EVIDENCE CLASSIFICATION

Classification -- B2: probable human carcinogen

Basis -- Based on increased incidence of several tumor types in rats and three strains of mice

#### \_\_\_II.A.2. HUMAN CARCINOGENICITY DATA

Inadequate. There are no epidemiologic studies of chloroform itself. Chloroform and other trihalomethanes are formed from the interaction of chlorine with organic material found in water. Several ecological and case-control studies of populations consuming chlorinated drinking water in which chloroform was the major chlorinated organic show small significant increases in the risk of rectal bladder or colon cancer on an intermittent basis. Many



other suspected carcinogens were also present in these water supplies.

#### \_\_\_II.A.3. ANIMAL CARCINOGENICITY DATA

Sufficient. Chloroform has been tested for carcinogenicity in eight strains of mice, two strains of rats and in beagle dogs.

In a gavage bioassay (NCI, 1976), Osborne-Mendel rats and B6C3F1 mice were treated with chloroform in corn oil 5 times/week for 78 weeks. Fifty male rats received 90 or 125 mg/kg/day; females initially were treated with 125 or 250 mg/kg/day for 22 weeks and 90 or 180 mg/kg/day thereafter. Male mice received 100 or 200, raised to 150 or 300 mg/kg/day at 18 weeks; females were dosed with 200 or 400, raised to 250 or 500 mg/kg/day. A significant increase in kidney epithelial tumors was observed in male rats and highly significant increases in hepatocellular carcinomas in mice of both sexes. Liver nodular hyperplasia was observed in low-dose male mice not developing hepatocellular carcinoma. Hepatomas have also developed in female strain A mice and NLC mice gavaged with chloroform (Eschenbrenner and Miller, 1945; Rudali, 1967).

Jorgenson et al. (1985) administered chloroform (pesticide quality and distilled) in drinking water to male Osborne-Mendel rats and female B6C3F1 mice at concentrations of 200, 400, 900, and 1800 mg/L for 104 weeks. These concentrations were reported by the author to correspond to 19, 38, 81, and 160 mg/kg/day for rats and 34, 65, 130, and 263 mg/kg/day for mice. A significant increase in renal tumors in rats was observed in the highest dose group. The increase was dose related. The liver tumor incidence in female mice was not significantly increased. This study was specifically designed to measure the effects of low doses of chloroform.

Chloroform administered in toothpaste was not carcinogenic to male C57Bl, CBA, CF-1 or female ICI mice or to beagle dogs. Male ICI mice administered 60 mg/kg/day were found to have an increased incidence of kidney epithelial tumors (Roe et al., 1979; Heywood et al., 1979). A pulmonary tumor bioassay in strain A/St mice was negative as was one in which newborn C57X DBA2/F1 mice were treated s.c. on days 1 to 8 of life (Theiss et al., 1977; Roe et al., 1968).

#### \_\_\_II.A.4. SUPPORTING DATA FOR CARCINOGENICITY

The majority of tests for genotoxicity of chloroform have been negative. These negative findings include covalent binding to DNA, mutation in *Salmonella*, a *Drosophila* sex-linked recessive, tests for DNA damage a micro-



nucleus test, and transformation of BHK cells. By contrast one study demonstrated binding of radiolabeled chloroform to calf thymus DNA following metabolism by rat liver microsomes (DiRenzo, 1982). Chloroform caused mitotic recombination in *Saccharomyces* (Callen et al., 1980) and sister chromatid exchange in cultured human lymphocytes and in mouse bone marrow cells exposed in vivo (Morimoto and Koizumi, 1983).

The carcinogenicity of chloroform may be a function of its metabolism to phosgene, which is known to cross-link DNA. A host-mediated assay using mice indicated that chloroform was metabolized in vivo to a form mutagenic to *Salmonella* strain TA1537. Likewise urine extracts from chloroform-treated mice were mutagenic (Agustin and Lim-Sylianco, 1978).

Chloroform administered to mice in drinking water promoted growth and metastasis of Ehrlich ascites cells injected i.p. (Capel et al., 1979).

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## \_\_II.B. QUANTITATIVE ESTIMATE OF CARCINOGENIC RISK FROM ORAL EXPOSURE

### \_\_II.B.1. SUMMARY OF RISK ESTIMATES

Oral Slope Factor --  $6.1E-3$  per (mg/kg)/day

Drinking Water Unit Risk --  $1.7E-7$  per (ug/L)

Extrapolation Method -- Linearized multistage procedure, extra risk

Drinking Water Concentrations at Specified Risk Levels:

Risk Level	Concentration
E-4 (1 in 10,000)	$6E+2$ ug/L
E-5 (1 in 100,000)	$6E+1$ ug/L
E-6 (1 in 1,000,000)	$6E+0$ ug/L

### \_\_II.B.2. DOSE-RESPONSE DATA (CARCINOGENICITY, ORAL EXPOSURE)

Tumor Type -- all kidney tumors

Test Animals -- rat/Osborne-Mendel, male

Route -- drinking water



Reference -- Jorgensen et al., 1985

----- Dose -----		
Admin- istered (mg/L)	Human Equivalent (mg/kg/day)	Tumor Incidence
0	0	1/50
200	3.4	6/313
400	6.9	7/148
900	14.8	3/48
1800	28.9	7/50

\_\_\_II.B.3. ADDITIONAL COMMENTS (CARCINOGENICITY, ORAL EXPOSURE)

Historical control kidney tumor incidence was 5/301.

The unit risk should not be used if the water concentration exceeds 6E+4 ug/L, since above this concentration the unit risk may not be appropriate.

\_\_\_II.B.4. DISCUSSION OF CONFIDENCE (CARCINOGENICITY, ORAL EXPOSURE)

This assay was designed for detection and quantitation of effects at low dose; thus, large numbers of animals were treated and observed for their lifetime. Exposure route and vehicle is relevant to the medium for which the risk estimate was developed.

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\_\_\_II.C. QUANTITATIVE ESTIMATE OF CARCINOGENIC RISK FROM INHALATION EXPOSURE

\_\_\_II.C.1. SUMMARY OF RISK ESTIMATES

Inhalation Unit Risk -- 2.3E-5 per (ug/cu.m)

Extrapolation Method -- Linearized multistage procedure, extra risk

Air Concentrations at Specified Risk Levels:

Risk Level	Concentration
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E-4 (1 in 10,000)      4E+0 ug/cu.m  
 E-5 (1 in 100,000)    4E-1 ug/cu.m  
 E-6 (1 in 1,000,000) 4E-2 ug/cu.m

\_\_\_II.C.2. DOSE-RESPONSE DATA FOR CARCINOGENICITY, INHALATION EXPOSURE

Tumor Type -- hepatocellular carcinoma  
 Test Animals -- mouse, B6C3F1, female  
 Route -- oral, gavage  
 Reference -- NCI, 1976

----- Dose -----		Tumor
Admin-	Human	Incidence
istered	Equivalent	
(mg/kg/day)	(mg/kg/day)	
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Female

0	0	0/20
238	9.9	36/45
477	19.9	39/41

Male

0	0	1/18
138	6.2	18/50
277	12.5	44/45

\_\_\_II.C.3. ADDITIONAL COMMENTS (CARCINOGENICITY, INHALATION EXPOSURE)

This inhalation quantitative risk estimate is based on data from a gavage study. Above doses are TWA; body weights at the end of the assay were 35 g, males and 28 g, females. Vehicle control animals were run concurrently and housed with test animals. All treated animals experienced decreased body weight gain. Survival was reduced in high-dose males and in all treated females.

Experimental data for this compound support complete absorption of orally administered chloroform under conditions of this assay. There are no apparent species differences in this regard. Extrapolation of metabolism-dependent



carcinogenic responses from mice to humans on the basis of body surface area is supported by experimental data. The incidence data for both male and female mice were used to derive slope factors of  $3.3E-2$  and  $2.0E-1$  per (mg/kg)/day, respectively. The unit risk was prepared by taking a geometric mean of the slope factor and assuming 100% for low doses of chloroform in air.

The unit risk should not be used if the air concentration exceeds 400 ug/cu.m, since above this concentration the unit risk may not be appropriate.

#### \_\_\_II.C.4. DISCUSSION OF CONFIDENCE (CARCINOGENICITY, INHALATION EXPOSURE)

Adequate numbers of animals were treated and observed.

Risk estimates derived from male rat kidney tumor data ( $2.4E-2$ ) (NCI, 1976) and studies by Roe et al. (1979) ( $1.0E-1$ ) are generally supportive of the risk estimate.

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#### \_\_\_II.D. EPA DOCUMENTATION, REVIEW, AND CONTACTS (CARCINOGENICITY ASSESSMENT)

##### \_\_\_II.D.1. EPA DOCUMENTATION

U.S. EPA. 1985. Health Assessment Document for Chloroform. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Research Triangle Park, NC for the Office of Air Quality Planning and Standards. EPA 600/8-84-004F.

U.S. EPA. 1987. Drinking Water Criteria Document for Trihalomethanes. Office of Drinking Water, Washington, DC. Draft.

NCI (National Cancer Institute). 1976. Report on Carcinogenesis Bioassay of Chloroform. National Cancer Institute, Washington, DC. NTIS PB 264018.

##### \_\_\_II.D.2. REVIEW (CARCINOGENICITY ASSESSMENT)

The Health Assessment Document for Chloroform received extensive Agency and external review.



The Draft Drinking Water Criteria Document for Trihalomethanes has received external peer review.

Agency Work Group Review -- 10/29/86, 08/26/87

Verification Date -- 08/26/87

\_\_II.D.3. U.S. EPA CONTACTS (CARCINOGENICITY ASSESSMENT)

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\_III. HEALTH HAZARD ASSESSMENTS FOR VARIED EXPOSURE DURATIONS

\_\_III.A. DRINKING WATER HEALTH ADVISORIES

Substance Name -- Chloroform

CASRN -- 67-66-3

Primary Synonym -- Trichloromethane

Not available at this time.

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\_\_III.B. OTHER ASSESSMENTS

Substance Name -- Chloroform

CASRN -- 67-66-3

Primary Synonym -- Trichloromethane

Content to be determined.



\_IV. U.S. EPA REGULATORY ACTIONS

Substance Name -- Chloroform  
CASRN -- 67-66-3  
Primary Synonym -- Trichloromethane  
Last Revised -- 04/01/92

EPA risk assessments may be updated as new data are published and as assessment methodologies evolve. Regulatory actions are frequently not updated at the same time. Compare the dates for the regulatory actions in this section with the verification dates for the risk assessments in sections I and II, as this may explain inconsistencies. Also note that some regulatory actions consider factors not related to health risk, such as technical or economic feasibility. Such considerations are indicated for each action. In addition, not all of the regulatory actions listed in this section involve enforceable federal standards. Please direct any questions you may have concerning these regulatory actions to the U.S. EPA contact listed for that particular action. Users are strongly urged to read the background information on each regulatory action in Background Document 4 in Service Code 5.

\_\_IV.A. CLEAN AIR ACT (CAA)

No data available

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\_\_IV.B. SAFE DRINKING WATER ACT (SDWA)

\_\_\_IV.B.1. MAXIMUM CONTAMINANT LEVEL GOAL (MCLG) for Drinking Water

No data available

\_\_\_IV.B.2. MAXIMUM CONTAMINANT LEVEL (MCL) for Drinking Water

Value (status) -- 0.10 mg/L [total trihalomethanes\*] (Interim, 1979)





Considers technological or economic feasibility? -- YES

Discussion -- An interim MCL of 0.10 mg/L for total trihalomethanes\* is proposed based on chronic toxicity data for chloroform and existing technology and treatment methods. Chloroform produced central nervous system depression, hepatic, renal, teratogenic and carcinogenic effects at dose levels from 30 to 350 mg/kg.

\*Chloroform (67-66-3), dibromochloromethane (124-48-1), bromodichloromethane (75-27-4) and bromoform (75-25-2).

Monitoring requirements -- This MCL applies only to community water systems which serve a population of 10,000 or more individuals and which add a disinfectant (oxidant) to the water in any part of the drinking water treatment process. Monitoring frequency is dependent upon system size.

Analytical methodology -- Purge and trap gas chromatography (EPA 502.1).

Best available technology -- Granular activated carbon; powdered activated carbon; biological activated carbon; ion exchange.

Reference -- 44 FR 68624 (11/29/79)

EPA Contact -- Drinking Water Standards Division / OGWDW / (202) 260-7575 / FTS 260-7575; or Safe Drinking Water Hotline / (800) 426-4791

#### \_\_\_IV.B.3. SECONDARY MAXIMUM CONTAMINANT LEVEL (SMCL) for Drinking Water

No data available

#### \_\_\_IV.B.4. REQUIRED MONITORING OF "UNREGULATED" CONTAMINANTS

Status -- Listed (Final, 1987)

Discussion -- "Unregulated" contaminants are those contaminants for which EPA establishes a monitoring requirement but which do not have an associated final MCLG, MCL, or treatment technique. EPA may regulate these contaminants in the future.

Monitoring requirement -- Monitoring required for all water systems at a minimum frequency of once every 5 years.



Analytical methodology -- Gas chromatography (EPA 502.1, 502.2, 503.1); gas chromatographic/mass spectrometry (EPA 524.1, 524.2).

Reference -- 52 FR 25690 (07/08/87)

EPA Contact -- Drinking Water Standards Division / OGWDW /  
(202) 260-7575 / FTS 260-7575; or Safe Drinking Water Hotline / (800) 426-4791

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\_\_IV.C. CLEAN WATER ACT (CWA)

\_\_\_IV.C.1. AMBIENT WATER QUALITY CRITERIA, Human Health

Water and Fish Consumption: 1.9E-1 ug/L

Fish Consumption Only: 1.57E+1 ug/L

Considers technological or economic feasibility? -- NO

Discussion -- For the maximum protection from the potential carcinogenic properties of this chemical, the ambient water concentration should be zero. However, zero may not be obtainable at this time, so the recommended criteria represents an E-6 estimated incremental increase of cancer risk over a lifetime.

Reference -- 45 FR 79318 (11/28/80)

EPA Contact -- Criteria and Standards Division / OWRS  
(202)260-1315 / FTS 260-1315

\_\_\_IV.C.2. AMBIENT WATER QUALITY CRITERIA, Aquatic Organisms

Freshwater:

Acute LEC -- 2.89E+4 ug/L

Chronic LEC -- 1.24E+3 ug/L

Marine: None

Considers technological or economic feasibility? -- NO



Discussion -- The values that are indicated as "LEC" are not criteria, but are the lowest effect levels found in the literature. LECs are given when the minimum data required to derive water quality criteria are not available.

Reference -- 45 FR 79318 (11/28/80)

EPA Contact -- Criteria and Standards Division / OWRS  
(202)260-1315 / FTS 260-1315

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\_\_IV.D. FEDERAL INSECTICIDE, FUNGICIDE, AND RODENTICIDE ACT (FIFRA)

\_\_IV.D.1. PESTICIDE ACTIVE INGREDIENT, Registration Standard

No data available

\_\_IV.D.2. PESTICIDE ACTIVE INGREDIENT, Special Review

Action -- Final regulatory decision - PD4 (1983)

Considers technological or economic feasibility? -- YES

Summary of regulatory action -- The agency determined that applicator exposure had been reduced to a minimum as a result of label amendments. Registrants were required to submit data to establish tolerances of permissible residues on raw agricultural commodities. Compound returned to the registration process. Criterion of concern: oncogenicity.

Reference -- 48 FR 498 (01/05/83)

EPA Contact -- Special Review Branch / OPP  
(703)557-7400 / FTS 557-7400

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\_\_IV.E. TOXIC SUBSTANCES CONTROL ACT (TSCA)



No data available

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\_\_IV.F. RESOURCE CONSERVATION AND RECOVERY ACT (RCRA)

\_\_\_IV.F.1. RCRA APPENDIX IX, for Ground Water Monitoring

Status -- Listed

Reference -- 52 FR 25942 (07/09/87)

EPA Contact -- RCRA/Superfund Hotline  
(800)424-9346 / (202)260-3000 / FTS 260-3000

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\_\_IV.G. SUPERFUND (CERCLA)

\_\_\_IV.G.1. REPORTABLE QUANTITY (RQ) for Release into the Environment

Value (status) -- 10 pounds (Final, 1989)

Considers technological or economic feasibility? -- NO

Discussion -- The RQ for chloroform is based on potential carcinogenicity. Available data indicate a hazard ranking of medium based on a potency factor of 1.97 mg/kg/day and assignment to weight-of-evidence group B2. These correspond to an RQ of 10 pounds.

Reference -- 52 FR 8140 (03/16/87); 54 FR 33418 (08/14/89)

EPA Contact -- RCRA/Superfund Hotline  
(800)424-9346 / (202)260-3000 / FTS 260-3000

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\_V. SUPPLEMENTARY DATA





Substance Name -- Chloroform  
CASRN -- 67-66-3  
Primary Synonym -- Trichloromethane  
Last Revised -- 01/31/87

The information contained in this section (subsections A and B) has been extracted from the EPA Chemical Profiles Database, which has been compiled from a number of secondary sources and has not undergone formal Agency review. The complete reference listings for the citations in this section are provided in Service Code 5. The user is urged to read Background Document 5 in Service Code 5 for further information on the sources and limitations of the data presented here.

#### \_\_V.A. ACUTE HEALTH HAZARD INFORMATION

Toxicity -- Chloroform is classified as moderately toxic. A probable oral lethal dose for humans is 0.5 to 5 g/kg (between 1 ounce and 1 pint) for a 150-lb. person. The mean lethal dose is probably near 1 fluid ounce (44 g) (Gosselin et al., 1976). Also, it is a central nervous system depressant and a gastrointestinal irritant (Challen et al., 1958). Chloroform has caused rapid death attributable to cardiac arrest.

Medical Conditions Generally Aggravated by Exposure -- Not Found

Signs and Symptoms of Exposure -- Symptoms of acute exposure include fainting sensation, vomiting, dizziness, salivation, nausea, fatigue, and headache (ACGIH, 1971-1979). Other symptoms are respiratory depression, coma, kidney damage, and liver damage (IARC, 1972-1985). Liquid in the eye causes tearing and conjunctivitis (Grant, 1974). Symptoms of chronic exposure include loss of appetite, hallucinations, moodiness, and physical and mental sluggishness (NIOSH, 1974).

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#### \_\_V.B. PHYSICAL-CHEMICAL PROPERTIES

Chemical Formula -- CHCl3

Molecular Weight -- 119.39

Boiling Point -- 143F, 61.7C



Specific Gravity (H2O=1) -- 1.4832 at 20C/4C

Vapor Pressure (mmHg) -- 100 at 10.4C

Melting Point -- -82.3F, -63.5C

Vapor Density (AIR=1) -- 4.12

Evaporation Rate (Butyl acetate=1) -- (Carbon Tetrachloride = 1) 1.18

Solubility in Water -- 1 mL/200 mL at 25C

Flash Point [Method Used] -- None

Flammable Limits -- Not Found

Appearance and Odor -- Chloroform is a clear, colorless and mobile liquid with a characteristic odor.

Conditions or Materials to Avoid -- Chloroform develops acidity from prolonged exposure to air and light (General Electric Co., 1979, MSDS #315). Chloroform explodes when in contact with aluminum powder or magnesium powder or with alkali metals (e.g., lithium, sodium, and potassium) (NFPA, 1978) and dinitrogen tetroxide. Chloroform reacts vigorously with acetone in the presence of potassium hydroxide or calcium hydroxide (Bretherick, 1979). It is oxidized by strong oxidizers such as chromic acid, forming phosgene and chlorine (IARC, 1972-1985). Chloroform reacts vigorously with triisopropylphosphine (Bretherick, 1979).

Hazardous Decomposition or Byproducts -- When heated, chloroform emits hydrogen chloride, chlorine, and toxic and corrosive oxides of carbon and chlorine (General Electric Co., 1979, MSDS #315) and phosgene (ITI, 1982).

Use -- Chloroform is used as a grain fumigant; solvent for pesticides, adhesives (IARC, 1972-1985) fats, oils, rubbers, alkaloids, waxes (Merck, 1976); chemical intermediate for dyes and pesticides; and a component of cough syrups, toothpastes, and liniments (SRI, 1983). Not registered as a pesticide in the U.S. (USEPA/Pesticide Index, 1985).

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## \_VI. BIBLIOGRAPHY



Substance Name -- Chloroform  
CASRN -- 67-66-3  
Primary Synonym -- Trichloromethane  
Last Revised -- 07/01/92

\_\_VI.A. ORAL RfD REFERENCES

Heywood, R., R.J. Sortwell, P.R.B. Noel, et al. 1979. Safety evaluation of toothpaste containing chloroform. III. Long-term study in beagle dogs. J. Environ. Pathol. Toxicol. 2: 835-851.

Jorgenson, T.A., C.J. Rushbrook and D.C.L. Jones. 1982. Dose-response study of chloroform carcinogenesis in the mouse and rat: Status report. Environ. Health Perspect. 46: 141-149.

Palmer, A.K., A.E. Street, F.J.C. Roe, A.M. Worden and N.J. Van Abbe. 1979. Safety evaluation of toothpaste containing chloroform. II. Long-term studies in rats. J. Environ. Pathol. Toxicol. 2: 821-833.

Schwetz, B.A., B.J.K. Leong and P.J. Gehring. 1974. Embryo- and fetotoxicity of inhaled chloroform in rats. Toxicol. Appl. Pharmacol. 28: 442-451.

Thompson, D.J., S. D. Warner and V.B. Robinson. 1974. Teratology studies on orally administered chloroform in the rat and rabbit. Toxicol. Appl. Pharmacol. 29: 348-357.

U.S. EPA. 1985. Drinking Water Criteria Document for Trihalomethanes. Office of Drinking Water, Washington, DC. (External Review Draft)

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\_\_VI.B. INHALATION RfD REFERENCES

None

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\_\_VI.C. CARCINOGENICITY ASSESSMENT REFERENCES



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VI.D. DRINKING WATER HA REFERENCES

None

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VII. REVISION HISTORY

Substance Name -- Chloroform  
CASRN -- 67-66-3  
Primary Synonym -- Trichloromethane

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Date	Section	Description
03/01/88	I.A.1.	Dose conversion clarified
03/01/88	I.A.2.	LOAEL and RfD in text corrected
03/01/88	I.A.4.	Text revised
03/01/88	I.A.5.	Text revised
06/30/88	II.	Carcinogen summary on-line
06/30/88	I.A.7.	Primary contact changed
10/01/89	I.B.	Inhalation RfD now under review
06/01/90	IV.A.1.	Area code for EPA contact corrected
06/01/90	IV.F.1.	EPA contact changed
01/01/91	II.	Text edited
01/01/91	II.C.1.	Inhalation slope factor removed (global change)



02/01/91	II.C.3.	Information on extrapolation process included
02/01/91	II.C.4.	Text edited
03/01/91	II.D.3.	Primary contact changed
01/01/92	IV.	Regulatory actions updated
04/01/92	IV.A.1.	CAA regulatory action withdrawn
07/01/92	I.A.	Clarify Schwetz citation
07/01/92	VI.C.	Oral RfD references on-line
07/01/92	VI.C.	Carcinogenicity assessment references on-line
09/01/92	I.A.7.	Primary contact changed

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#### SYNONYMS

Substance Name -- Chloroform  
CASRN -- 67-66-3  
Primary Synonym -- Trichloromethane  
Last Revised -- 01/31/87

67-66-3  
Chloroform  
Formyl Trichloride  
Freon 20  
Methane Trichloride  
Methane, Trichloro-  
Methenyl Chloride  
Methenyl Trichloride  
Methyl Trichloride  
NCI-C02686  
R-20  
TCM  
Trichloroform  
Trichloromethane