FOREWORD INTRODUCTION

VINYL CHLORIDE

CAS N°: 75-01-4

SIDS Initial Assessment Report

For

SIAM 13

Bern, Switzerland, 6-9 November 2001

1. Chemical Name:	Vinyl Chloride
2. CAS Number:	75014
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4. Shared Partnership with:	--
5. Roles/Responsibilities of the Partners:	--
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SIDS INITIAL ASSESSMENT PROFILE

CAS No.	75-01-4
Chemical Name	Vinyl Chloride
Structural Formula	CH_2=CHCl

RECOMMENDATIONS

This chemical is currently of low priority for further work in the SIDS Program as human exposures are controlled due to the chemical's genotoxicity and cancer hazard and based upon OECD risk reduction measures.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

The primary route of exposure for vinyl chloride is by inhalation. Vinyl chloride is rapidly and well absorbed following inhalation or oral exposure, and is bioactivated by the liver. The acute toxicity (rat oral LD_{50} >4000 mg/kg; rat and mouse inhalation LC_{50} 390,000 mg/m^3 and 294,000 mg/m^3 respectively) is low. Anesthetic effects have been reported in humans at levels of 12000 ppm (30,720 mg/m^3 for a five minute exposure period. The NOAEL for inhalation exposure to rats, rabbits, guinea pigs or dogs is 50 ppm (128 mg/m^3) for 6 months. For oral repeated dose, the critical target organ is the liver (liver cell polymorphism) with a lifetime NOAEL in the rat of 0.13 mg/kg/day. Vinyl chloride (and/or its metabolites) produces DNA adducts and has been positive in gene mutation and chromosomal aberration assays. Chromosomal aberrations have also been observed in peripheral lymphocytes of exposed workers in some studies. Long term exposure in experimental animals and humans causes liver cancer (angiosarcoma). Vinyl chloride is a known human carcinogen. Cancer of the lymphopoietic system, connective tissues, and soft tissue have been associated with vinyl chloride exposure in some studies, but not others. In a combined reproductive/developmental study in rats the NOAEL for reproductive/developmental effects was 1,100 ppm (2816 mg/m^3), the highest dose tested. Human studies have not linked vinyl chloride exposure with negative reproductive outcomes.

Environment

Vinyl Chloride has a vapor pressure of 3330 hPa at 20^{0}C, a water solubility value of 1.1 g/l at 20^{0}C and a log P_{ow} of 1.58 at 22^{0}C. In the soil and water microorganism study, vinyl chloride was biodegraded at 30% after 40 days and 99% after 108 days, and has a low bioaccumulation potential. Environmental releases of vinyl chloride are almost exclusively to the air compartment. Fugacity modeling indicates that of the vinyl chloride released >99% will remain in the air compartment. The dominant removal process in the atmosphere is photoxidation with a calculated half-life of 2.2 – 2.7 days. The 96 hour LC_{50} ranges from 210 to > 1000mg/l for fish (four studies). The estimated QSAR value for algae EC_{50} (96hr) is 118 mg/L and the LC_{50} (48 hr) for daphnia is 196 mg/L. Toxic concentrations of vinyl chloride are not expected to be reached in aquatic systems based on low emissions, low bioaccumulation potential and high volatility.

Exposure

Vinyl chloride is a gas, which is manufactured in closed systems as an industrial intermediate - mainly for the production of polyvinyl chloride (PVC) and vinyl copolymers. North American production capacity in 1999 was about 8.344 million metric tons and global capacity was 30.022 million metric tons. Workplace exposure is tightly controlled in the U.S. and other OECD countries. The most likely route for consumer and environmental exposure is inhalation of residual vinyl chloride monomer (VCM) present in PVC products, however, residual monomer levels in these products are highly regulated and tightly controlled to very low levels. Such products include food packaging, medical devices, PVC pipe, wire coatings, automotive interiors, exterior siding, interior vinyl floors,

wall and furniture coverings, and toys. Vinyl chloride is present in the air near production facilities generally at levels <0.1 mg/m^3, and in ground water generally below the 0.001 ppm detection limit.

NATURE OF FURTHER WORK RECOMMENDED

No recommendation.

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number: 75-01-4
IUPAC Name: Chlorothylene
Molecular Formula: C_2H_3Cl
Structural Formula: CH2=CHCl
Molecular Weight: --
Synonyms: vinyl chloride, (mono) chloroethylene, (mono) chloroethene, ethenyl chloride, chloroethene, 1-chloroethene, 1-chloroethylen and vinyl chloride monomer

1.2 Purity/Impurities/Additives

99.9% minimum

1.3 Physico-Chemical properties

Table 1 Summary of physico-chemical properties

Property	Value
Physical form of marketed product:	gas
Melting point:	-153.8 degrees C
Boiling point:	-14° C @ 1013 hPa
Density:	.964 g/cm^3 @ -10°C
Vapor pressure:	3330 hPa @ 20°C
Partition coefficient (Log Pow):	1.58 @ 22°C
Water solubility: Henry's law constant:	1.1 g/l @ 20° C 0.0278 m^3*atm/mol@ 24.8° C
Flash point:	-78° C (open cup)
Autoignition temperature:	473°C @ 1013 hPa
Flammability limits:	3.6 – 33 volume %

2 GENERAL INFORMATION ON EXPOSURE

Total estimated production capacity in the U.S. was estimated at 5.91 million metric tons (13 billion pounds) in early 1993 (C&EN, 1994; Syracuse Research, 1993). Estimated annual growth of vinyl chloride consumption is 4.5% (Jebens and Kishi 2000). The 1999 capacity in North America is estimated at 8.344 million metric tons (18.4 billion pounds), Western Europe 6.305 million metric tons (13.9 billion pounds), Japan 3.441 million metric tons (7.586 billion pounds), and other global regions 11.932 million metric tons (26.3 billion pounds). Worldwide production capacity in 1999 was approximately 30.022 million metric tons (66.186 billion pounds) (Jebens and Kishi, 2000).

In the United States, approximately 12 companies manufacture vinyl chloride in closed, continuous systems at about 12 different facilities (ATSDR, 1997) as an industrial intermediate. Vinyl chloride is used principally in the manufacture of polyvinyl chloride (PVC); smaller amounts are used to manufacture vinyl chloride-vinyl acetate and vinyl chloride-vinylidene chloride copolymers. According to the American Chemistry Council Vinyl Chloride Health Committee (which comprises the major U.S. manufacturers), >99.5% of vinyl chloride monomer is used to make polyvinyl chloride and various vinyl chloride derived copolymers, and the remainder (<0.5%) is used as a chemical feedstock for the manufacture of other chemicals.

A large proportion of vinyl chloride is converted at its manufacturing sites to PVC and vinyl chloride-derived copolymers. Nearly all vinyl chloride shipped to facilities off-site is also converted to polyvinyl chloride (PVC) or PVC copolymers. In many cases, vinyl chloride is transported by pipeline directly to the plant producing the polymer. The physical form of vinyl chloride is a neat liquid (99.9 % minimum purity) stored or transported under pressure.

PVC or vinyl chloride copolymers are used to make many different products, including PVC pipe, wire coatings, vinyl external siding for buildings, wall coverings, interior vinyl floor coverings, furniture coverings, toys, kitchen utensils, automotive car seat covers and interiors, wire coatings, materials for packaging (including food, drug and medical device packaging), films and resins. Exposures to residual monomer contained in these products are discussed further in Section 2.2.2.

2.1 Environmental Exposure and Fate

In the United States, vinyl chloride emissions are subject to required annual TRI (Toxic Release Inventory) reporting under Section 313 of the Emergency Planning and Community Right-to-know Act (EPCRA). The most recently available TRI data (1999), presented in Table 1, reported 848,576 lb emitted to the air, 106 lb to water and 405 lb to land or underground injection. Based on the US TRI numbers 0.0046% VCM produced is released into the air. This averages out to 55 pounds released/plant/day for a gas. Any gas released rapidly photodegrades due to the atmospheric half-life of ~2.5 days. The amount released between 1997 and 1999 decreased by 20% which indicates an ongoing commitment to reduce the emissions of vinyl chloride monomer.

The Mackay Level III fugacity model run with 100% release of vinyl chloride into air predicts that 99.98% of vinyl chloride emitted directly to the atmosphere will remain in the atmosphere, where the dominant removal process is reaction with atmospheric hydroxyl radicals (i.e., photooxidation). Perry has reported a second order rate constant of $k = 6.6 \pm 0.66 * 10^{-12}$ cm^3/molecule at 299.2°K for this reaction (Perry et al, 1977). From this rate constant an atmospheric half-life of 2.2-2.7 days can be calculated. These findings indicate that vinyl chloride photodegrades readily in the atmosphere.

With respect to the aqueous compartment, the Henry's law constant for vinyl chloride is 0.0278 m^3 * atm/mol @ 24.8° C (Gossett, 1987). In general, for chemicals with Henry's Law Constant values greater than 1.0×10^{-3} m^3 * atm/mol, volatilization from water to the atmosphere is rapid. Based on its large Henry's Law Constant and its high vapor pressure (3330 hPa @ 20°C), the 1997 ATSDR

Toxicological Profile for this chemical states that "the primary removal process for vinyl chloride from surface waters is volatilization into the atmosphere." According to Hill (1976), "A worst case system analysis of vinyl chloride behavior in aquatic systems suggests that unrealistically high levels of vinyl chloride inputs would be necessary to maintain significant concentrations in these systems. However, given extreme environmental conditions, aquatic sediments could exhibit long-term storage of low levels of vinyl chloride." Recent Toxic Release Inventory data presented above and in Table 1, however, do not indicate continuous or sizeable releases to the aquatic compartment. The partition coefficient (Log Pow) for vinyl chloride is 1.58 @ 22°C (Huels AG, 1981), suggesting that vinyl chloride will bioaccumulate to a very limited extent (EPA, 1982a). The 1997 Agency for Toxic Substances Disease Registry (ATSDR) Toxicological Profile for vinyl chloride reports a bioconcentration factor (BCF) for vinyl chloride of 5.1 (estimated from K_{ow} or water solubility), indicating limited bioconcentration in aquatic organisms. Vinyl chloride does not undergo rapid photolysis in water, since it does not absorb ultraviolet radiation above 218 nm (ATSDR, 1977; Hill, 1976)

The 1997 ATSDR Toxicological Profile reports that "a limited amount of existing data indicates that vinyl chloride is resistant to microbial degradation." The EPA (1977) observed no change in the biochemical oxygen demand in raw sewage seed vs raw sewage seed containing vinyl chloride at 20°C over a 25-day period. More recent biodegradation studies (not cited in the 1997 ATSDR report) indicate that biodegradation may occur (albeit slowly). A biodegradation study using soil-water microcosms from authentic aquifer microorganisms in sterile water containing vinyl chloride indicated an aerobic degradation rate of 30% in 40 days and 99% after 108 days (Davis and Carpenter, 1990). In this study, the half life was 60 days. Under anaerobic conditions using authentic soil-water aquifer microorganisms, degradation was 21% in one system after 70 days and 100% in another system (Freitag et al., 1985). However, under conditions that prevent volatilization, and in the absence of microcosms under varying pHs and temperatures, vinyl chloride is stable in water for periods greater than one year (Hill, 1976).

The soil adsorption coefficient K_{oc} = 56 (Lyman et al, 1990). This value (together with a water solubility of 1.1 g/l @ 20° C) (Huels AG, 1986; Dreher, 1986; Scherb, 1978) suggests that vinyl chloride possesses a reasonable degree of soil mobility.

In conclusion, vinyl chloride in soil possesses mobility, which increases its ability to biodegrade or volatilize. In water, volatilization to the atmosphere is the predominant process, and in the atmosphere, vinyl chloride undergoes photolysis with a calculated half-life ranging from 1.5 to 4 days.

Presence in the Environment in the United States

As can be seen from Table 1, air emissions account for ≥ 99% of total on-site emissions. In addition, total emissions have been steadily reduced by about 40% over the past dozen years, even as annual production has increased by about 35% (See Section 2).

Table 1. Vinyl Chloride Emissions Reported for the Toxic Release Inventory (TRI)[1]

Year	No.[2]	On-Site Emissions					Transfers to Off-Site Waste Mgmt.[3]	Total On- and Off-Site Emissions[3]
		Total Air Emissions[3]	Total Release to Water[3]	Under-ground Injection[3]	Total Releases to Land[3]	Total On-Site Emissions[3]		
1988	53	1,439,189	2051	53	4409	1,455,702	4,555	1,450,257
1995	48	1,044,665	525	33	1	1,045,224	15,645	1,060,869
1998	55	885,687	78	154	0	885,919	69,214	955,133
1999	51	848,576	106	405	1	849,088	14,015	863,103

[1] Source: EPA 1999 TRI Report
[2] Number Reporting
[3] In pounds

Atmospheric Monitoring

According to the 1997 ATSDR Toxicological Profile for vinyl chloride, "Air in rural/remote and urban/suburban areas of the United States typically contains no detectable amount (detection limit 0.001 ppm) of vinyl chloride" (EPA, 1982b; Grimsrud and Rasmussen 1975a,b; Harkov et al., 1984; Stephens et al., 1986; Wallace, 1984). Limited monitoring data indicate that in areas near vinyl chloride and PVC manufacturing facilities, the concentration of vinyl chloride in air typically ranges from trace levels to 105 ug/m^3 (0.041 ppm) (Fishbein, 1979). More recent monitoring near the fenceline of a vinyl chloride production site measured <0.06 (detection limit) – 34.16 ppb in one location (EPA, 1997-1998) and <0.06-10.01 ppb in a second location (EPA, 1998). Most measurements in these two locations were well below 1 ppb. Vinyl chloride has been detected at higher levels in dumpsite emissions, however, the source of these emissions was not from manufacture or use, but from degradation of other chemicals (Wood and Porter, 1987).

Groundwater and Drinking Water Monitoring

During the 1982 EPA Groundwater Supply Survey (Westrick et al., 1984), vinyl chloride was positively identified in only 0.74% of 945 groundwater supplies monitored throughout the United States (detection limit 0.001 ppm). The maximum concentration determined was 8.4 µg/l (0.0084 mg/l). Concentrations of vinyl chloride in drinking water wells and surface water in New York State were found to be 50 µg/l and 10 µg/l respectively (Burmaster, 1982). A high determination of 380 ug/l was obtained in groundwater in a nine state monitoring study (Dyksen and Hess, 1982). The weight of evidence (See ATSDR, 1997) suggests that this value is atypical.

Environmental Monitoring in Japan

According to a study issued by Japan's Ministry of the Environment in 1997, vinyl chloride monomer has been detected in river water within a range of 0.014 to 0.25 ppb (detection limit 0.011). Vinyl chloride was detected at levels above the detection limit in 12 out of 129 measuring points. Vinyl chloride was detected in air in 40 out of 53 measuring points at a range between 18-2000 ng/m^3 (detection limit 15 ng/ m^3). Data on industrial emissions of vinyl chloride monomer in Japan for 1997-1999 are given in Table 2.

Table 2. Vinyl chloride monomer emissions in Japan

		1997	1998	1999
Volume (1000 metric tons/yr)	Production	3,065	3,019	3,192
	Use	2,884	2,663	2,797
	Total	5,949	5,682	5,989
Emissions (metric tons/yr)	Production	349	323	281
	Use	1,740	1,459	1,339
	Total	2,089	1,782	1,620
Unit of Emission source (kg/metric ton)[1]	Production	0.114	0.107	0.088
	Use	0.603	0.548	0.479
	Total	0.351	0.314	0.271

[1] Calculation Method: Emissions (kg/yr)/Volume (metric tons/yr) (Production, use or total)

Source: Japan Chemical Industry Association

Environmental Regulation of Vinyl Chloride in the United States

The Environmental Protection Agency (EPA) regulates vinyl chloride in order to ensure protection of public health and the environment. The environmental statutes include the Clean Air Act (CAA), the Safe Drinking Water Act, the Resource Conservation and Recovery Act, and the Comprehensive Environmental Response, Compensation, and Liability Act.

Under Section 112 of the Clean Air Act, the EPA regulates vinyl chloride as a Hazardous Air Pollutant (HAP). The EPA's national emission standard for vinyl chloride requires that vinyl chloride emissions from vinyl chloride and polyvinyl chloride (PVC) production facilities not exceed an average of 10 ppm over a 3-hour period, with exceptions for emergency conditions (40 CFR §§ 61.60-61.71). Section 112 requires the EPA to regulate emissions of vinyl chloride more stringently, if it determines that a facility poses a significant residual risk to public health even though it is in compliance with the emission standard.

Under the Safe Drinking Water Act, the EPA has established a maximum contaminant level (MCL) of 0.002 mg/l. Under the Resource Conservation and Recovery Act (RCRA), heavy ends from the distillation of vinyl chloride are a listed hazardous waste (K020), as are a number of other waste streams (e.g., K174, K175). Any other solid waste at or above 0.2 mg/l in vinyl chloride content is considered to be a characteristic hazardous waste, and is regulated under RCRA. Such waste must meet Universal Treatment Standards (UTS) prior to disposal.

For further information, a more complete summary of the regulations for vinyl chloride may be obtained from the National Toxicology Program located in "The National Toxicology Program Ninth Report on Carcinogens."

2.2 Human Exposure

The potential sources of human exposure to vinyl chloride are to workers during manufacture and conversion to polymer, to consumers via residual monomer present in polymeric products, and to general populations through environmental exposure.

Non-occupational exposures to vinyl chloride are anticipated to be substantially lower than occupational exposures. This is because vinyl chloride is used as an initial chemical in manufacturing processes, but is only a minor residue in end products purchased by consumers. Inhalation is the primary route of exposure in such cases.

2.2.1 Occupational Exposure

Workplace exposures are tightly controlled in the industrialized nations. OECD countries in the ACGIH 2000 database list TLV's (TWA) ranging from 1-5 ppm. In the United States, workplace exposure is subject to regulation under the Occupational Safety and Health Act (OSHA) (29 CFR, Part 1910.1017) with an 8-hour Permissible Exposure Limit (PEL) of 1 ppm and a Short Term Exposure Limit (STEL) of 5 ppm. In addition, OSHA has established an action level (AL) of 0.5 ppm. Should workplace exposures exceed the AL, the employer is required to provide medical surveillance, protective clothing, respirators, warning signs, periodic exposure monitoring, and training for employees engaged in vinyl chloride and PVC operations in materials handling and emergency response procedures.

According to Jones (1981), "The National Institute for Occupational Safety and Health (NIOSH) began industrial hygiene studies of vinyl chloride exposed workers in early 1974." Three VC monomer plants, three VC polymerization plants, and seven PVC fabrication plants were surveyed. VC polymerization plant workers and workers in one job category in VC monomer plants were exposed to average levels above 1 ppm. The highest average exposure was 22 ppm. A NIOSH control technology study in 1977 showed that exposure levels in VC polymerization plants had been drastically reduced, but exposure levels above 1 ppm were still found in several cases (Jones, 1981.) Since 1977, steady improvements in manufacturing facilities, engineering controls and workplace practices have substantially reduced workplace exposures in the U.S. to below the OSHA action level of 0.5 ppm. NIOSH health hazard evaluation studies after1977 have primarily shown nondetectable levels of vinyl chloride.

The Environmental Protection Agency regulates waste products from vinyl chloride manufacture as hazardous waste and has established strict labeling requirements for containers that store waste or refined vinyl chloride product.

2.2.2 Consumer Exposure

Since vinyl chloride is an industrial intermediate that is chemically converted to polyvinyl chloride and copolymers, it is not sold in commercial/consumer formulations or products. Therefore exposure to vinyl chloride in commercial products is largely limited to residual vinyl chloride monomer in polyvinyl chloride products.

PVC plastics used for food contact packaging, drug and medical device products are regulated in the United States under the Federal Food, Drug and Cosmetic Act (FFDCA) as administered by the Food and Drug Administration (FDA). The FDA has determined a reasonable worst-case exposure estimate for vinyl chloride to be 25 nanograms average per day. The FDA stated that "because of numerous conservatisms in the estimate, lifetime-averaged individual exposure is expected to be substantially less than 25 nanograms per day" (FDA, 1986). The FDA has calculated that the individual lifetime risk of cancer from exposure to vinyl chloride monomer at 25 nanograms per day is less than 1 in 10 million. Thus the FDA concluded that "there is a reasonable certainty of no harm from the exposure to vinyl chloride monomer that may result from the use of vinyl chloride polymers in food packaging complying with the vinyl chloride limits set forth by the FDA" (FDA, 1986). Based on this analysis, the FDA withdrew its proposal to restrict the uses of vinyl chloride polymers in contact with food (51 Federal Register 4173 (1986). However, the FDA has banned the use of vinyl chloride as a propellant in aerosol cosmetic products (21 CFR §700.14) because

this type of use would result in possible harmful consumer exposure and other aerosol agents were available as substitutes.

CANTOX (1994) lists VCM exposures and states that "<1 ppm residual VCM in PVC products while modern medical grade PVC is believed to contain <10 ppb VCM (Van Dooren, 1991; Thomas and Ramstad 1992**)."**

Human exposure to vinyl chloride monomer in PVC plastics used in other, non-FDA regulated products (i.e. PVC pipe, vinyl coverings, automotive products) also is very low. Improved production techniques developed in the late 1970s and adopted by most PVC manufacturers by 1986 dramatically reduced the amount of vinyl chloride monomer (VCM) present in PVC. All PVC pipes and fittings used for potable water must meet the American National Standards Institute/National Sanitation Foundation, International. (ANSI/NSF) Standard 61 for residual vinyl chloride monomer (RVCM). The standard pass/fail value of 3.2 mg/kg corresponds to a theoretical extraction level in water of 1/10th the US EPA maximum contaminant level (MCL) of 0.002 mg/l for drinking water (McLellan, 2001). According to a NSF report on RVCM content of PVC sampled between January 1, 1998 through October 18, 2000, (McLellan, 2001) only 74 of 519 (14%) samples of PVC pipe and 21 of 178 (12%) samples of PVC fittings showed detectable levels of vinyl chloride monomer (detection level 0.1 mg/kg). The average RCVM value of all samples, considering non-detect samples as zero, is reported as 0.07 mg/kg for pipe and 0.03 mg/kg for fittings (McLellan, 2001).

In the case of wall covering applications, a study was conducted using PVC resin containing 1.2 ppm vinyl chloride monomer. This resin was mixed with 50 phr DOP and 1 phr of a Ca/ZN stabilizer only, and spread onto release paper at 1000 g/m^2 and gelled at only 150 degrees C for 30 sec. These gelation conditions would encourage retention of any monomer since 1) the formulation had an unnaturally high PVC level (the resin also having an unnaturally high PVC level), 2) the formulation was coated at an extremely high weight, and 3) the material was extremely under-processed. This material was then analyzed for VCM using headspace gas chromatography. No VCM was detected, using a detection limit of 10 ppb. The authors concluded that "clearly, since normal wall covering samples contain lower levels of polymer, generally have lower coating weights, and are processed under more severe conditions, the retention of VCM by wall covering samples is exceedingly unlikely" (Howick and McCarthy, 1996).

With respect to other indoor products made from PVC, the following is from the World Health Organization (WHO, 1999) "In a survey of PVC products carried out in 1976-77, the following indoor articles had a VC content of >0.05 ppm: bathroom tiles, piping, plastic bottle for table oil, and kitchen film. … The VC content of toys, kitchen utensils, food wrappings, wallpaper and car interiors was <0.05 ppm (German Environmental Office, 1978). In a more recent survey, VCM residues in various PVC samples were as follows: rigid water bottle (850 ppb), thin plasticized food film (3 ppb), monopolymer powder (10 ppb); copolymer film (15 ppb)" (Poy et al., 1987).

The Consumer Product Safety Commission (CPSC) has banned use of vinyl chloride as an ingredient or a propellant in self-pressurized products intended as suitable for household use (16 CFR §1500.17(a)(10)).

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

Limited information from animal studies indicates that vinyl chloride is rapidly and virtually completely absorbed following inhalation and oral exposure (ASTDR, 1997). Humans reportedly retain 42% of inhaled vinyl chloride (Krajewski et al., 1980). A study of rats showed absorption through the gastrointestinal tract. The portion of the dosage that was recovered in fecal matter was roughly 0.47% - 2.39%, indicative of the portion unabsorbed (Watanabe et al., 1978). Dermal absorption of gaseous vinyl chloride is not significant (Hefner et al., 1975). After a 2-2.5 hour exposure of rhesus monkeys to 800 and 7000 ppm, dermal absorption was estimated to be 0.031% and 0.023% of total bioavailable vinyl chloride, respectively.

In rats, absorbed vinyl chloride is primarily distributed to the liver and skin (Watanabe et al., 1976b). Metabolism is believed to proceed via three different pathways; the extent of which is dependent on vinyl chloride concentrations. At low concentrations, vinyl chloride is oxidized sequentially to 2-chloroethanol, 2-chloroacetaldehyde and 2-chloroacetic acid by alcohol dehydrogenase (ATSDR, 1988). At higher concentrations, vinyl chloride is metabolized by liver cytochrome P-450 IIE1 to the reactive oxirane, 2-chloroethylene oxide, and its rearrangement product 2-chloroacetaldehyde (Guengerich et al, 1991; Gwinner et al., 1983). Both 2-chloroethylene oxide and 2-chloroacetaldehyde have been shown to produce DNA adducts, which are thought to play a role in vinyl chloride toxicity (Oesch and Doerjer, 1982; Fedtke et al., 1989; Barbin et al. 1985, Swenberg et al., 1992).

The elimination of vinyl chloride follows first-order kinetics (ACGIH, 1991). The excretion pathway is governed by the extent of exposure, rather than the route of exposure. At low exposure levels, the majority is excreted into the urine (Watanabe et al., 1978). As an inhaled dose increases, the proportion of unmetabolized vinyl chloride exhaled increases.

3.1.2 Acute Toxicity

Studies in Animals

The oral LD_{50} (rat) is > 4000 mg/kg ((Hoechst AG, 1973). The inhalation (2h) LC_{50} for rat, mouse, rabbit and guinea pig are 390 mg/l, 294 mg/l, 595 mg/l and 595 mg/l, respectively (Prodan et al., 1975). Brief (30 minutes) exposures to concentrations of vinyl chloride ranging from 100,000 to 400,000 ppm have been shown to be fatal in rats, guinea pigs and mice (Mastromatteo et al., 1960). Symptoms of intoxication in rats and mice include muscular incoordination and twitching, narcosis and respiratory failure (Prodan et al., 1975; Mastromatteo et al., 1960). Although all of the acute inhalation toxicity studies are pre-1975, the weight of evidence allows the data to be used.

Studies in Humans

Inhalation at levels less than 8000 ppm for 5 minutes may be tolerated without developing symptoms of toxicity (Lester et al., 1963). Inhalation of concentrations ranging from 12000 to 20,000 ppm for 5 minutes may produce slight anesthetic effects including dizziness, headache and/or nausea (Lester et al, 1963). Deaths due to narcosis have been reported at undocumented concentrations (Danziger, 1960)

3.1.3 Irritation and Sensitisation

Intense salivation and lacrimation have been noted in rats, guinea pigs and rabbits exposed acutely to high concentrations (375 – 700 mg/l) of vinyl chloride gas (Prodan et al., 1975). When placed on skin or in eyes, liquid vinyl chloride may freeze tissue and produce a chemical burn as it evaporates, causing damage to the underlying tissue (Easter, 1994).

No information regarding the skin sensitization potential of vinyl chloride was located.

3.1.4 Repeated Dose Toxicity

Studies in Animals

Three oral toxicity studies and five inhalation studies were reviewed (Torkelson et al., 1961; Lester et al., 1963; Feron et al., 1975, 1979(a,b,c), 1981; Lee et al., 1977; Sokal et al., 1980; Til et al., 1991). The results are summarized in Tables 3 and 4. Oral administration of 30 mg/kg/day for 13 weeks or 0.13 mg/kg/day for 149 weeks produces no adverse effects in rats. Lifetime oral exposure to doses equal to or greater than 1.3 mg/kg/day is toxic to the liver.

The inhalation NOAEL in rats, rabbits, guinea pigs or dogs is 50 ppm for 6 months. Exposure of rats to 50 ppm for longer periods (10-12 months) is associated with decreased body weight, slightly increased mortality, and increased weights of some organs. Mice exposed to concentrations ≥ 50 ppm for 12 months exhibit changes in the liver and other organs. Long-term exposures (10-12 months) of concentrations greater than or equal to 200 ppm produce these types of changes in rabbits and rats.

Table 3. Summary of critical subchronic toxicity studies in animals

Test animals	Exposure	Effects	Reference
ORAL			
Rat (Wistar) 15/sex/group	Gavage in soybean oil 0, 30, 100 and 300 mg/kg once daily, 6 days/week for 13 weeks	NOEL = 30 mg/kg/day LOEL = 100 mg/kg/day 100 mg/kg/day - decreased leukocytes and blood sugar 300 mg/kg/day - Same effects as 100 mg/kg/day. Decreased serum GOT and GPT and urinary GOT. Increased liver/bw, adrenal/bw, hypertrophy of endoplasmic reticulum of liver	Feron et al. 1975
INHALATION			
Rat 12-15/sex/ group (study #1), 3-5/ sex/ (study #2)	0, 2% for 3 months (#1) 0, 5% for 19 days (#2)	NOEL < 2% 2 %- decreased white blood cells and spleen/bw ratio; increased liver/bw ratio; histopathologic changes in liver. 5%- increased red blood cells and liver/bw ratio; decreased white blood cells; histopathologic changes in liver.	Lester et al., 1963
10 rats/sex/ group (#1) 20-24 rats, 8-10 g. pigs, 1 dog, 3 rabbits/sex/ group (# 2) 24 rats, 12 g. pigs, 3 rabbits, 1 dog /sex/ group (# 3) 10 male rats/ group (# 4)	0 or 500 ppm , 7 hr/d, 5 day/wk for 4.5 mo (#1) 0, 100 or 200 ppm, for 7, 4, 2, 1 or 0.5 hr/day, 5 day/week for 6 mo (#2) 0 or 50 ppm, 7 hr/day, 5 day/week for 6 mo (#3) 0 or 50 ppm, 4, 2, or 1 hr/day, 5 day/week for 6 mo (#4)	500 ppm (#1) - liver and kidney cell changes 200 ppm, 7 hr/day (#2) - Rabbit - liver cell changes; Rat - increased liver/bw ratio NOEL (dog and guinea pig) - 200 ppm 100 ppm, 7 hr/day (#2) - Rat - increased liver/bw ratio (NOEL (rabbit) - 100 ppm NOEL (rat) - 50 ppm (#3) NOEL - 50 ppm (#4)	Torkelson et al, 1961

Table 4*. Summary of critical chronic toxicity/carcinogenicity studies in animals

Test animals	Exposure	Effects	Reference
ORAL			
Rat (Wistar) 60- 80/sex/ group	PVC powder with a high vinyl chloride monomer content in diet. 0, 1.7, 5.0, 14.1 mg/kg/day 135 weeks for males, 144 weeks for females	NOEL (systemic effects) < 1.7 mg/kg/day 1.7 mg/kg/day - liver cell changes, hepatocellular carcinoma 5.0 and 14.1 mg/kg/day - liver cell changes; hepatocellular carcinoma; hepatic, pulmonary, abdominal angiosarcoma; Zymbal gland tumors	Feron et al. 1981
Rat (Wistar) 100/sex/ all groups except 50/sex/group for highest dose	PVC powder with a high vinyl chloride monomer content in diet. 0, 0.014, 0.13, 1.3 mg/kg/day for 149 weeks	NOAEL (systemic effects) = 0.13 mg/kg/day LOAEL(systemic effects) = 1.3 mg/kg/day 1.3 mg/kg/day - increased mortality in females; liver cell changes; hepatocellular carcinoma; angiosarcoma	Til et al. 1991
INHALATION			
Rat (Wistar) 85 males/group	0, 50, 500, 20000 ppm 5 hr/day, 5 days/week, 10 months	NOEL (systemic effects) < 50 ppm 50 ppm - decreased body weight; increased organ weights; ultrastructural changes in liver 500 ppm - decreased body weight; increased organ weights; changes in spermatogenic epithelium; ultrastructural changes in liver 20000 ppm - similar changes as 500 ppm except no damage to spermatogenic epithelium	Sokal et al 1980
Rat (CD) Mouse (CD-1) 36/sex/dose	50, 250, 1000 ppm 6 hr/day, 5 days/week for 12 months	NOEL (systemic effects) < 50 ppm Rats - 50 ppm - increased mortality and DNA synthesis in liver; 250 ppm - increased mortality; angiosarcoma of liver; 1000 ppm - increased mortality; angiosarcoma of liver and lung; decreased body weight in females Mice - Increased mortality at all doses. Dose dependent increase in broncho-alveolar adenoma, mammary gland tumors, liver angiosarcoma	Lee et al., 1977
Rat (Wistar) 62/sex/group	5000 ppm 7 hr/day, 5 days/week for 52 weeks	Increased mortality; decreased body weight; hematological and clinical chemistry abnormalities; increased relative weights of liver, kidney and spleen and to a lesser extent, heart and lung; cellular changes in liver, spleen, heart, kidney and Zymbal glands; increased Zymbal glandsand nasal cavity carcinomas and liver angiosarcomas	Feron et al. 1979 a,b,c

*NOEL, LOEL and LOAEL refer only to systemic effects.

Studies in Humans

Past occupational exposure to several hundred ppm of vinyl chloride for periods ranging from one month to 3 years has been associated with development of "vinyl chloride disease" (ATSDR, 1990). Vinyl chloride disease is characterized by acroosteolysis, a condition characterized by lytic lesions of bones (primarily of fingers), scleroderma of the connective tissue in the fingers with dermal thickening, and a Raynaud-like condition with reversible arteriole constriction causing numbness, pallor and cyanosis of the fingers. The attribution of acroosteolysis to vinyl chloride exposure is based almost entirely on case reports and has been estimated to affect <3% of workers involved in the polymerization of vinyl chloride (Haustein and Ziegler, 1985; Black et al., 1986).

Long-term occupational exposure of workers to vinyl chloride prior to 1973 has been associated with cancer in humans. See section 3.1.6 for additional information.

3.1.5 Mutagenicity

Vinyl chloride has tested positive in a number of *in vitro* and *in vivo* mutagenicity and DNA damage and cytogenicity assays (Tables 6 and 7). Four well-conducted studies which describe mutagenesis and DNA damage in vivo and in vitro were examined in detail (Bartsch et al., 1975; Anderson et al., 1976; Drevon and Kuroki, 1979; Richardson et al., 1983). Although positive results have been reported without metabolic activation, employing a metabolic activation system enhances mutagenicity. Various reports suggest that the metabolites responsible for mutagenicity are 2-chloroethylene oxide and 2-chloroacetaldehyde (Huberman et al., 1975; Elmore et al., 1976; O'Neill et al., 1986; Loprieno et al., 1976, 1977; Drevon and Kuroki, 1979; McCann et al., 1975; Rannug et al., 1976). Both of these metabolites have been shown to produce DNA adducts, which are thought to play a role in development of carcinogenicity (Barbin and Bartsch, 1986; Oesch and Doerjer, 1982; Laib et al., 1985; Laib 1986; Fedtke et al., 1989; Barbin et al. 1985, Swenberg et al., 1992). In rats, the substitution mutations found at A:T base pairs in the ras and p53 genes are consistent with the promutagenic properties of the DNA adduct $1,N^6$-ethenoadenine formed from vinyl chloride metabolites (Barbin, 1999).

Table 6. Mutagenicity and DNA damage assays of vinyl chloride

Test System	**Mutagenicity**		**Other effects**	**Reference**
	Without metabolic activation	With metabolic activation		
S. typhimurium	+ - -	+ +		Malaveille et al., 1975; McCann et al., 1975; Andrews et al., 1976; Bartsch et al., 1976; Garro et al., 1976; Simmon et al., 1977; De Meester et al., 1980; Poncelet et al., 1980; Victorin and Stahlberg, 1988 Rannug et al., 1974; Elmore et al., 1976;
E. coli	-	+		Greim et al., 1975
Bacillus subtilis	-			Elmore et al., 1976
Schizosaccharomyces	-	+		Loprieno et al., 1976

pombe, Saccharomyces cerevisiae (host-mediated assay)				
Schizosaccharomyces pombe	-	+		Loprieno et al., 1977
Saccharomyces cerevisiae	-			Shahin, 1976
Neurospora crassa	-	-		Drozodowicz and Huang,1977
Yeast D7RAD in vitro and in vivo (spot test)			+	Eckardt et al., 1981
V79 Chinese hamster cells in vitro Tradescantia clone 4430	-	+	 +	Drevon and Kuroki, 1979 Van't Hof and Schairer, 1982
Drosophila or Mouse (DLT)			-	Verbugt and Vogel, 1977; Purchase et al., 1975; Anderson et al., 1976; Barbodej, 1976
Drosophila (SRL)			+	Verbugt and Vogel, 1977
Rats (DLT)			-	Short et al., 1977
Mice (spot test)			-	Peter and Ungvary,1980
Mice (DNA alkylation)			+	Osterman-Golkar et al.,1977
Mice (DNA SB)			+	Walles and Holmberg, 1984; Walles et al., 1988
Rats (DNA alkylation)			+	Green and Hathway, 1978; Laib et al., 1985
Rats (DNA adduct)			+	Laib et al., 1985; Laib 1986; Fedke et al., 1989; Ciroussel et al., 1990; Swenberg et al., 1992
Rats (DNA alkylation and RNA binding)			+	Laib and Bolt, 1977; Kappus et al., 1975
Human angiosarcomas of liver (point mutation)			+	Marion et al., 1991

DLT, dominant lethal test; SRL, sex-linked recessive lethal test; DNA SB, DNA strand breaks
Reproduced from Giri et al., 1995

Table 7. Cytogenetic assays of vinyl chloride

Test System	**End Point**	**Effect**	**Reference**
Mice	Micronuclei	+	Jenssen and Ramel, 1980; Richardson et al., 1983
Rat	Chromosome aberrations	+	Anderson and Richardson, 1981
Human lymphocytes in vivo	Micronuclei	+	Sinues et al., 1991
	Chromosome aberrations	+	Ducatman et al., 1975; Funes-Carvioto et al., 1975;

			Purchase et al., 1975, 1976, 1978; Szentesi et al., 1976; Heath et al., 1977; Hansteen et al., 1978; Fleig and Thiess, 1978; Kucerova et al., 1979; Anderson et al., 1980; Geryk and Zudova, 1986; Hrivnak et al., 1990; Fucic et al., 1990 a, b
	Chromosome aberrations	-	Kilian et al., 1975; Picciano et al., 1977; Fleig and Theiss, 1978; Rossner et al., 1980; De Jong et al., 1988
	Sister-chromatid exchange	+	Kucerova et al., 1979; Fucic et al., 1990 a, 1992; Sinues et al., 1991
	Sister-chromatid exchange	-	Anderson et al., 1981; Rossner et al., 1980
Human lymphocytes in vitro	Sister-chromatid exchange	+	Anderson et al., 1981

Reproduced from Giri et al., 1995

Vinyl chloride does not induce dominant lethal mutations in Drosophila, rats, or mice (Purchase et al., 1975; Verbugt and Vogel, 1977; Anderson et al., 1976; Bardodej, 1976; Short et al., 1977). It has been suggested that negative results in this test could be attributed to the inability of vinyl chloride or its active metabolites to reach germ cells in sufficient amounts to induce mutation (Purchase et al., 1975; Anderson et al., 1976; Short et al., 1977).

Chromosomal aberrations in human peripheral lymphocytes of exposed workers have been detected in many studies (Table 7) and breaks appear to be localized in specific chromosomes (Fucic et al., 1990b).

3.1.6 Carcinogenicity

Studies in Animals

Inhalation and ingestion of vinyl chloride produces cancer in laboratory animals. Results of a reviewed study by Til et al. (1991) indicate that lifetime oral exposure of rats to doses equal to or greater than 1.3 mg/kg/day is associated with development of hepatocellular carcinomas and angiosarcoma (a rare tumor of mesenchymal origin) of the liver (Table 4). Other reports indicate that mice exposed by inhalation to concentrations ≥ 50 ppm for 12 months develop broncho-alveolar adenoma, mammary gland tumors, and lung and liver angiosarcomas (Lee et al., 1977, 1978; Suzuki, 1983). Long-term inhalation of concentrations ≥ 250 ppm is also associated with development of angiosarcomas in rats (Lee et al., 1977,1978). Dose-dependent increases in the incidences of zymbal gland carcinomas, hepatocarcinomas, nephroblastomas, brain tumors, mammary tumors, and endocrine gland tumors also have been observed in long-term inhalation carcinogenicity bioassays of vinyl chloride in rats (Radike et al., 1981; Lee et al., 1978, Maltoni et al., 1981). Long-term inhalation of extremely high concentrations is associated with an increased incidence of bone, lung and skin cancer in rats (Viola et al., 1971).

Studies in Humans

Vinyl chloride is associated with liver cancer in humans and has been classified as a Group 1 carcinogen (carcinogenic to humans) by IARC, Category 1 (carcinogenic to man) by the EU and a Group A carcinogen (carcinogenic to humans) by the EPA (EPA, 1987). Occupational vinyl chloride exposure was first associated with development of liver cancer in 1974, when rare liver angiosarcomas were detected in three workers who worked in a vinyl chloride polymerization plant (Creech and Johnson, 1974). Worker cohorts employed in the vinyl chloride industry in the United States and Europe have been studied extensively over the last 25 years. The most recent updates were reviewed in detail (Mundt et al., 2000; Ward et al., 2000). These studies confirm earlier findings of an increased incidence of angiosarcoma in humans that are occupationally exposed.

Although results of some previous studies suggested that occupational exposure to vinyl chloride is associated with increased risk of respiratory disease, cancers of the lung, brain and hematopoetic/lymphocytic system, and malignant melanoma (Byren et al., 1976; Cordasco et al., 1980; Weber, 1981; Wong et al., 1991; Cooper, 1981; Tabershaw and Gaffey, 1974; Heldaas et al., 1984, 1987; Buffler et al., 1979; Smulevich et al., 1988; Waxweiler et al., 1976), the most recent cohort studies that were reviewed indicate that occupational exposure to vinyl chloride is not strongly associated with increased mortality risk from respiratory disease or cancers other than liver and biliary tract cancers (predominantly angiosarcomas)(Lewis et al., 1999; Mundt et al., 2000; Ward et al., 2000). Associations between vinyl chloride exposure and increased risk of mortality from cancers of connective and soft tissues or liver cirrhosis that were identified in one of these large cohort studies were not confirmed in the other. In reviewing the effects of exposure to vinyl chloride, both Doll (1988) and Storm and Rozman (1997) concluded that the evidence for induction of nonliver tumors was weak**.**

3.1.7 Reproduction/Developmental Toxicity

Studies in Animals

No studies employing oral exposure were located. Data from a 2-generation reproduction study via inhalation in rats (Huntingdon Life Sciences, 1998, 1999) and two developmental toxicity studies in animals exposed via inhalation (John et al., 1977; Ungvary et al., 1987) were reviewed. Data are summarized in Table 5.

Results of the combined reproductive-developmental study indicate that the NOAEL for reproductive or developmental toxicity is ≥ 1100 ppm in rats. The weight of evidence of the developmental studies indicates that vinyl chloride produces fetal toxicity only at exposures that produce maternal toxicity.

Table 5. Summary of critical reproductive and developmental toxicity studies in animals

Test animal	Exposure	Effects	Reference
REPRODUCTIVE			
Rat (Sprague-Dawley) 30/sex/group	0, 10, 100, 1100 ppm 6 hr/d, 5 d/week during premating; 6 hr/d, 7 d/week during gestation, lactation, postweaning	NOAEL (parental) = 10 ppm NOAEL (reproductive) ≥ 1100 ppm 100 and 1100 ppm - increased liver weight; liver changes in dams	Thornton, 2002; Huntingdon Life Sciences, 1999
DEVELOPMENTAL			
Rat (Sprague-Dawley) 25 per group	0, 10, 100, 1100 ppm, 6 hr/day, day 6-19 of gestation	NOAEL (parental) = 10 ppm NOAEL (developmental) ≥ 1100 ppm 100 ppm - increased kidney/bw ratio in dams 1100 ppm - increased kidney/bw, liver/bw ratio in dams	Thornton, 2002; Huntingdon Life Sciences, 1998
Rat (Sprague Dawley) Mouse (CF-1) Rabbit (NZ White) 16-28 per group	0, 500, 2500 ppm, 7 hr/day, day 6-15 of gestation (rat), day 6-18 of gestation (rabbit) 0, 50, 500 ppm, 7 hr/day, day 6-15 of gestation (mouse)	NOEL (parental) = 50 ppm (mouse), 500 ppm (rat) and 2500 ppm (rabbit). NOEL (developmental) = 500 ppm (mouse), 2500 ppm (rat, rabbit) Mouse - 500 ppm – decreased weight gain, feed consumption, liver weight, litter size, live fetuses, fetal weight; increased lethality, resorptions Rat - 500 ppm – decreased weight gain, corpora lutea, fetal body weight; 2500 ppm – decreased maternal food consumption; increased liver weight Rabbit - 500 ppm – decreased feed consumption, corpora lutea, implantation sites/dam. No effects at 2500 ppm.	John et al., 1977, 1981
Rat (CFY)	0, 4000 mg/m^3 (1500 ppm) for 24 hr/d on days 1-9, 8-14 or 14-21 of pregnancy	NOEL (maternal) < 4000 mg/m^3 NOAEL (developmental) = 4000 mg/m3 Decreased maternal weight gain when exposed on days 14-21; increased liver weight when exposed on days 1-9 or 8-14. Resorbed fetuses and fetal loss when exposed on days 1-9. No developmental changes.	Ungvary et al., 1978

Studies in Humans

Studies addressing the hypothesis that members of communities with nearby vinyl chloride polymerization facilities have significantly greater incidences of some forms of developmental toxicity have failed to demonstrate a statistically significant correlation between developmental toxicity and either parental occupation or proximity to the facility (ATSDR, 1997; Edmonds et al., 1978; Infante, 1976; Rosenman et al., 1989; Theriault et al., 1983). Results of both retrospective and prospective studies indicate that pregnancy outcomes of mothers occupationally exposed to vinyl chloride are not altered by exposure (Bao et al., 1988).

3.2 Initial Assessment for Human Health

Vinyl chloride is manufactured in closed systems as an industrial intermediate used predominately to produce polyvinyl chloride (PVC) and vinyl chloride copolymer. Workplace exposure is tightly controlled in the U.S. and other industrialized countries. Very low-level exposure to small amounts of residual monomer in products may also occur. Residual monomer levels in polyvinyl chloride plastics used in food contact, drug and medicinal purposes are tightly regulated Residual monomer levels for other polyvinyl chloride products (such as PVC piping) are also controlled to very low levels. Vinyl chloride has also been detected in the air near production facilities and in ground water, again generally at very low levels. Human occupational exposures to vinyl chloride in industrialized countries are limited to 1-5 ppm.

The primary route of exposure for vinyl chloride is by inhalation. Vinyl chloride is rapidly and well absorbed following inhalation or oral exposure, and is bioactivated by the liver. The acute toxicity (rat oral LD_{50} >4000 mg/kg; rat and mouse inhalation LC_{50} 390,000 mg/m^3 and 294,000 mg/m^3 respectively) is low. Anesthetic effects have been reported in humans at levels of 12000 ppm (30,720 mg/m^3 for a five minute exposure period. The NOAEL for inhalation exposure to rats, rabbits, guinea pigs or dogs is 50 ppm (128 mg/m^3) for 6 months. For oral repeated dose, the critical target organ is the liver (liver cell polymorphism) with a lifetime NOAEL in the rat of 0.13 mg/kg/day. Vinyl chloride (and/or its metabolites) produces DNA adducts and has been positive in gene mutation and chromosomal aberration assays. Chromosomal aberrations have also been observed in peripheral lymphocytes of exposed workers in some studies. Long term exposure in experimental animals and humans causes liver cancer (angiosarcoma). Vinyl chloride is a known human carcinogen. Cancer of the lymphopoietic system, connective tissues, and soft tissue have been associated with vinyl chloride exposure in some studies, but not others. In a combined reproductive/developmental study in rats the NOAEL for reproductive/developmental effects was 1,100 ppm (2816 mg/m^3), the highest dose tested. Human studies have not linked vinyl chloride exposure with negative reproductive outcomes. The data collected for SIDS elements were considered adequate for hazard identification.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

Vinyl chloride toxicity to algae and fish has been studied. Results are summarized in Table 8. The lowest 96-hour LC_{50} value for fish (*Brachydanio rerio)* in a closed system was 210 mg/l (analytical concentration) (Groeneveld, et al.1993). No green algal tests were located to predict growth inhibition or biomass after exposure to vinyl chloride for 72 or 96 hours. Exposure of green algae to 710 mg/l vinyl chloride for 192 hours causes growth inhibition (Bringmann and Kuehn, 1976). Using a chlorophyll fluorescence model developed with other organics, Brack et al. predicted the 48-hr EC_{50} to be 580 mg/l (Brack et al., 1998). Using SAR (ECOSAR, 2001), a 96-hour LC_{50} value of 191 mg/l for fish, a 96-hour EC_{50} value of 118 mg/l for algae, and a 48-hour LC_{50} value for Daphnia of 196 mg/l were estimated. ECOSAR was run using neutral organics since vinyl chloride behaves metabolically and biologically more like an alkane than a vinyl/allyl halide in aquatic systems. Toxic concentrations of vinyl chloride are not expected in aquatic systems based on low bioaccumulation potential (Lu et al., 1977) and extreme volatility. Based on vinyl chloride's physical chemical properties, it's nearly exclusive partitioning to the air compartment and its use pattern, the conduct of additional aquatic toxicity testing was not necessary.

Table 8. Effect of vinyl chloride on the environment

Organism	**Test**	**Result (mg/L)**	**Reference**
Plants			
Chlamydomonas reinhardtii (green algae)	Inhibition of fluorescence (est) - 2 hours	Toxicity threshold 580 mg/l[a]	Brack et al. (1998)
Scenedesmus quadricauda (green algae)	Growth inhibition - 192 hours	Toxicity threshold 710 mg/l	Bringmann and Kuehn (1976)
Fish			
Brachydanio rerio (Zebrafish)	OECD Guide-line 203 - 96 hours	NOEC: 128 mg/l LC50: 210 mg/l	Groeneveld et al. (1993)
Lepomis macrochirus (Bluegill sunfish)	Static - 96 hours	LC50: 1220 ppm	Industrial Bio-Test, 1971
Micopterus salmoides (Largemouth bass)	Static - 96 hours	LC50: 1060 ppm	Industrial Bio-Test, 1971
Esox lucius (Northern Pike)	Static - 10 day	LC100: 388 mg/l	Brown et al. (1977)

[a] For chlorinated hydrocarbons, toxicity can be predicted (within a factor of three) based on the Kows of 40 chemicals (r = 0.978). The theoretical toxicity threshold of vinyl chloride was calculated to be 580 mg/l (using a log Kow of 1.27)

4.2 Terrestrial Effects

No data on terrestrial toxicity of vinyl chloride were located.

4.3 Other Environmental Effects

Vinyl chloride toxicity toward bacteria has been studied with respect to *Pseudomonas putida.* The toxic threshold in aqueous medium (the concentration at which cell growth first became noticeably inhibited) was determined to be 135 mg/l (Bringmann and Kuehn, 1976).

4.4 Initial Assessment for the Environment

Results of well-conducted studies and SAR estimations show that vinyl chloride is slightly to moderately toxic to fish (96 hr LC_{50} value of 210 to > 1000mg/l for fish), algae (96- hr EC_{50} value of 118 mg/l), and Daphnia (48-hr LC_{50} value of 196 mg/l). The NOEL for the most sensitive species of fish is 128 mg/l.

As mentioned in the section on exposure, there is virtually no vinyl chloride released into water streams in the United States. Although vinyl chloride is mobile in soil, significant quantities are not expected to leach into groundwater in the United States, since very little vinyl chloride is released into soil. Any vinyl chloride in water streams would readily volatize and the bioaccumulation potential in aquatic organisms is low. These data indicate that the potential for toxicity to aquatic organisms is low.

5 RECOMMENDATIONS

It is recommended that vinyl chloride be considered low priority for further work.

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IUCLID Data Set

Existing Chemical	:	ID: 75-01-4
CAS No.	:	75-01-4
EINECS Name	:	chloroethylene
EINECS No.	:	200-831-0
TSCA Name	:	Ethene, chloro-
Molecular Formula	:	C2H3Cl

Producer Related Part

Company	:	The Dow Chemical Company
Creation date	:	07.12.2001

Substance Related Part

Company	:	The Dow Chemical Company
Creation date	:	07.12.2001
Memo	:	
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1. General Information **Id** 75-01-4
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1.0.1 OECD AND COMPANY INFORMATION

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Street	:	Bygdoy alle 2
Town	:	N-02400203 OSLO
Country	:	Norway
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Source	:	EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA) 11.02.2000

Type	:	
Name	:	SHELL FRANCE
Partner	:	
Date	:	
Street	:	89 bld Franklin Rooseve lt
Town	:	92564 Rueil Malmaison
Country	:	France
Phone	:	33 1 47.14.71.00
Telefax	:	33 1 47.14.82.99
Telex	:	SHELL 615013F
Cedex	:	
Source	:	EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA) 11.02.2000

Type	:	
Name	:	Solvay Kunststoffe GmbH
Partner	:	
Date	:	
Street	:	Postfach 110270
Town	:	42662 Solingen
Country	:	Germany
Phone	:	

1. General Information **Id** 75-01-4
Date 18.06.2002

Telefax :
Telex :
Cedex :
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000

Type :
Name : Solvay S.A.
Partner :
Date :
Street : Rue du Prince Albert 33
Town : 1050 Bruxelles
Country : Belgium
Phone :
Telefax :
Telex :
Cedex :
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000

Type :
Name : Viniclor S.A.
Partner :
Date :
Street : Avenida de Burgos 12 - 6
Town : 28036 Madrid
Country : Spain
Phone :
Telefax :
Telex :
Cedex :
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000

Type :
Name : Vinnolit Monomer GmbH
Partner :
Date :
Street : Gendorf
Town : 84504 Burgkirchen
Country : Germany
Phone : (0049) 8679-0
Telefax : (0049) 8679-5518
Telex :
Cedex :
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000

Type :
Name : Wacker - Chemie GmbH
Partner :
Date :
Street : Postfach 1260, Johannes-Hess-Strasse 24
Town : 84480 Burghausen
Country : Germany
Phone : 08677/83 4888
Telefax : 08677/83 5590
Telex :
Cedex :

1. General Information **Id** 75-01-4
Date 18.06.2002

Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000

Type :
Name : aee?ieeC ?a?EaeCeC
Partner :
Date :
Street : euieC
Town : 10044 ca??CeAiee?
Country : Greece
Phone : 031-750000
Telefax : (031)769897
Telex :
Cedex :
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000

1.0.2 LOCATION OF PRODUCTION SITE

1.0.3 IDENTITY OF RECIPIENTS

1.1 GENERAL SUBSTANCE INFORMATION

Substance type : organic
Physical status : gaseous
Purity : > 99.9 % w/w
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
29.05.2002

1.1.0 DETAILS ON TEMPLATE

1.1.1 SPECTRA

1.2 SYNONYMS

(Mono)chloroethene
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
21.04.1994

(Mono)chloroethylene
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
21.04.1994

1-Chlorethylen
Source : Hoechst AG Frankfurt/Main
Hoechst AG Frankfurt/Main
Celanese GmbH Frankfurt am Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
10.02.1994

1. General Information **Id** 75-01-4
Date 18.06.2002

1-Chloroethene
Source : Akzo Nobel Chemicals b.v. Amersfoort
BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
02.05.1994

1-Chloroethylene
Source : Akzo Nobel Chemicals b.v. Amersfoort
BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
02.05.1994

Chlorethen
Source : Hoechst AG Frankfurt/Main
Hoechst AG Frankfurt/Main
Celanese GmbH Frankfurt am Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
10.02.1994

Chloroethene
Source : Akzo Nobel Chemicals b.v. Amersfoort
BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
02.05.1994

Chloroethylene
Source : Akzo Nobel Chemicals b.v. Amersfoort
BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
Limburgse Vinyl Maatschappij Tessenderlo
Hoechst AG Frankfurt/Main
Celanese GmbH Frankfurt am Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
02.05.1994

ethylene monochloride
Source : Limburgse Vinyl Maatschappij Tessenderlo
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
16.05.1994

monochlorethylene
Source : Limburgse Vinyl Maatschappij Tessenderlo
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
16.05.1994

monochloroethene
Source : Neste Oy Chemicals Porvoo
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
17.05.1995

monochloroethylene
Source : Limburgse Vinyl Maatschappij Tessenderlo
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
16.05.1994

1. General Information **Id** 75-01-4
Date 18.06.2002

Monyl
Source : Hoechst AG Frankfurt/Main
Hoechst AG Frankfurt/Main
Celanese GmbH Frankfurt am Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
02.03.1994

vinyl chloride
Source : Neste Oy Chemicals Porvoo
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
17.05.1995

vinyl chloride monomer
Source : Limburgse Vinyl Maatschappij Tessenderlo
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
16.05.1994

1.3 IMPURITIES

1.4 ADDITIVES

1.5 QUANTITY

Production during the last 12 months :
Import during the last 12 months :
Quantity : more than 1 000 000 tonnes in
Result : In 1999 capacity in North America is estimated at 8.344 million metric tons (18.4 billion pounds), Western Europe 6.305 million metric tons (13.9 billion pounds), Japan 3.441 million metric tons (7.586 billion pounds), and other global regions 11.932 million metric tons (26.3 billion pounds). Worldwide production capacity in 1999 was approximately 30.022 million metric tons (66.186 billion pounds)
22.05.2002 (1)

1.6.1 LABELLING

Labelling : as in Directive 67/548/EEC
Symbols : F+T
Nota : D other RM: S
Specific limits : no data
R-Phrases : (45) May cause cancer
(12) Extremely flammable
S-Phrases : (53) Avoid exposure - obtain special instructions before use
(45) In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible)
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000

1. General Information **Id** 75-01-4
Date 18.06.2002

1.6.2 CLASSIFICATION

Classification : as in Directive 67/548/EEC
Class of danger : carcinogenic, category 1
R-Phrases : (45) May cause cancer
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000

Classification : as in Directive 67/548/EEC
Class of danger : extremely flammable
R-Phrases : (12) Extremely flammable
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000

1.7 USE PATTERN

Type : type
Category : Non dispersive use
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
29.05.2002

Type : type
Category : Use in closed system
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000

Type : industrial
Category : Basic industry: basic chemicals
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000

Type : industrial
Category : Chemical industry: used in synthesis
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000

Type : industrial
Category : Polymers industry
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000

Type : use
Category : Intermediates
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000

Type : use
Category : other: Monomer for production PVC
Source : EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
11.02.2000

1.7.1 TECHNOLOGY PRODUCTION/USE

1. General Information **Id** 75-01-4
Date 18.06.2002

1.8 OCCUPATIONAL EXPOSURE LIMIT VALUES

Type of limit : MAC (NL)
Limit value :
Remark : TWA 3 ppm over 1 year period.
Classified as carcinogenic to human.
A monitoring system must be available, giving a warning when the following concentrations will be reached: 30 ppm over 2 minutes; 20 ppm over 20 minutes; 15 ppm over 60 minutes. Respiration protection should be available when there is a risk of respiration of vinylchloride concentrations of 8 ppm or higher, over 1 hour.
Source : Akzo Nobel Chemicals b.v. Amersfoort
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
18.06.2002 (2)

Type of limit : MAK (DE)
Limit value : 3 other: ppm (vol/vol)
Country : Germany
Remark : Existing plants for VC and PVC production.
Source : EVC INTERNATIONAL SA/NV Bruxelles
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
30.05.1994 (3)

Type of limit : MAK (DE)
Limit value : 2 other: ppm (vol/vol)
Country : Germany
Remark : Otherwise.
Source : EVC INTERNATIONAL SA/NV Bruxelles
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
30.05.1994 (4)

Type of limit : MAK (DE)
Limit value :
Country : Germany
Remark : In Section III A 1 of the MAK-value list of 1988, VC is cited as a substance which, according to experience, may cause malignant tumors.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
08.12.1993

Type of limit : MEL (UK)
Limit value : 7 other: parts per million
Short term exposure
Limit value :
Schedule : 8 hour(s)
Frequency : 1 times
Remark : MEL(UK) also stipulates an overriding annual maximum exposure limit of 3 parts per million (time weighted average)
Source : Hydro Polymers Limited Newton Aycliffe, Co Durham
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
29.05.2002

Type of limit : TLV (US)
Limit value : 2.3 mg/m3
22.05.2002 (5) (6)

Type of limit : TRK (DE)
Limit value : 8 mg/m3

Short term exposure
Limit value : 32 mg/m3
Schedule : 15 minute(s)
Frequency : 4 times
Country : Germany
Remark : Limit value for existing plants for VC- and PVC -production
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
19.02.1997

Type of limit : TRK (DE)
Limit value : 5 mg/m3
Short term exposure
Limit value : 20 mg/m3
Schedule : 15 minute(s)
Frequency : 4 times
Country : Germany
Remark : Limit value for other plants
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
19.02.1997

Type of limit : TRK (DE)
Limit value : 8 mg/m3
Remark : annual average exposure < 1.5 mg/m3
Source : Wacker - Chemie GmbH Burghausen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
18.06.2002

Type of limit : other: TWA
Limit value : 5 ml/m3
Short term exposure
Limit value : 10 ml/m3
Schedule :
Frequency : times
Country : Finland
29.05.2002

Type of limit : other: MAC -ttg (NL)
Limit value : 3 other: ppm over 1 year
Source : Limburgse Vinyl Maatschappij Tessenderlo
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
10.05.1994 (7)

Type of limit : other: Norwegian
Limit value : 3 mg/m3
Source : Hydro Plast AB Stenungsund
NORSK Hydro a.s OSLO
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
15.04.1995

Type of limit : other: OEL (EEC)
Limit value : 3 other: ppm (vol/vol)
Country : United Kingdom
Source : EVC INTERNATIONAL SA/NV Bruxelles
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
30.05.1994 (8)

Type of limit : other: OEL (EEC)

1. General Information **Id** 75-01-4
Date 18.06.2002

Limit value : 3 other: ppm (vol/vol)
Country : Italy
Source : EVC INTERNATIONAL SA/NV Bruxelles
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
30.05.1994 (9)

Type of limit : other: VME
Limit value : 7.7 mg/m3
Country : France
Remark : Authorized value for industrial sites built before 1980
Source : Atochem Paris la Defense
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
17.02.1994 (10)

Type of limit : other: VME
Limit value : 2.6 mg/m3
Country : France
Remark : Authorized value for industrial sites built after 1980
Source : Atochem Paris la Defense
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
17.02.1994 (10)

1.9 SOURCE OF EXPOSURE

Memo : Release from production
Remark : VC production normally is a continuous process that is conducted in closed systems. Therefore no defined sources of atmospheric VC emissions occur. Additional exhaust-gas scrubbing measures have reduced the emission from point sources to drop below 0.0001 kg/t.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
19.02.1997 (11)

Memo : Release of residual monomers, trends
Remark : The main emission source for VC is freshly polymerized PVC itself which, after leaving the closed polymerization system, primarily releases its remaining monomer content into the atmosphere during drying, storage and processing. These emissions have been reduced by the introduction of intensive degasification processes between the polymerization and drying. The extent to which the monomer is removed depends on the PVC type. Furthermore, VC emissions have been reduced by the introduction of automatic pressurized water cleaners for removal of PVC crusts in the reactors.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
19.02.1997 (12) (13) (14) (11) (15)

Remark : Produced by degradation in the environment of several chlorinated compounds like trichloroethylene/perchloroethylene.
Source : Solvay S.A. Bruxelles
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
20.05.1994

Remark : The product is obtained via thermal cracking of 1,2-dichloroethane, distilled and condensed. It is transferred via piping or rail-tanks to the PVC polymerization plants.
Source : EVC INTERNATIONAL SA/NV Bruxelles

EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
26.05.1994

Remark : Inhalation
Skin contact
Source : Limburgse Vinyl Maatschappij Tessenderlo
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
10.05.1994

1.10.1 RECOMMENDATIONS/PRECAUTIONARY MEASURES

1.10.2 EMERGENCY MEASURES

1.11 PACKAGING

1.12 POSSIB. OF RENDERING SUBST. HARMLESS

1.13 STATEMENTS CONCERNING WASTE

1.14.1 WATER POLLUTION

Classified by : KBwS (DE)
Labelled by : KBwS (DE)
Class of danger : 2 (water polluting)
Country : Germany
Remark : Katalog-Nr. 462
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
19.02.1997 (16)

Classified by : KBwS (DE)
Labelled by :
Class of danger : 2 (water polluting)
Remark : Kenn-Nr. 462 (Wassergefahrdungsklasse - WGK)
Source : Hoechst AG Frankfurt/Main
Celanese GmbH Frankfurt am Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
30.01.1997 (17) (18)

Classified by : other: Hoechst AG
Labelled by : other: Hoechst AG
Class of danger : 2 (water polluting)
Source : Hoechst AG Frankfurt/Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
04.06.1994 (19)

1.14.2 MAJOR ACCIDENT HAZARDS

1. General Information **Id** 75-01-4
Date 18.06.2002

Legislation : Stoerfallverordnung (DE)
Substance listed : yes
No. in directive :
Remark : Stoerfall-Stoff-Nr. 315
Source : BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
08.08.1994 (20)

Legislation : Stoerfallverordnung (DE)
Substance listed : yes
No. in directive :
Remark : Nr. 54
Source : Hoechst AG Frankfurt/Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
04.06.1994 (21)

Legislation : Stoerfallverordnung (DE)
Substance listed : yes
No. in directive :
Country : Germany
Remark : Anhang II Nr. 315 (Vinylchlorid)
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
19.02.1997 (16)

Legislation : Stoerfallverordnung (DE)
Substance listed : yes
No. in directive :
Remark : Kenn-Nr. 315
Source : Hoechst AG Frankfurt/Main
Celanese GmbH Frankfurt am Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
25.11.1996 (21)

1.14.3 AIR POLLUTION

Classified by : TA-Luft (DE)
Labelled by : TA-Luft (DE)
Number : 2.3 (carcinogenic substances)
Class of danger : III
Source : BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
08.08.1994

Classified by : TA-Luft (DE)
Labelled by : TA-Luft (DE)
Number : 2.3 (carcinogenic substances)
Class of danger : III
Remark : Erlaubte Emission: 5 mg/m3; TA-Luft vom 27.02.1987
Source : Hoechst AG Frankfurt/Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
04.06.1994 (19)

Classified by : TA-Luft (DE)
Labelled by : TA-Luft (DE)

1. General Information **Id** 75-01-4
Date 18.06.2002

Number	:	2.3 (carcinogenic substances)
Class of danger	:	III
Country	:	Germany
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
19.02.1997		(16)
Classified by	:	TA-Luft (DE)
Labelled by	:	
Number	:	2.3 (carcinogenic substances)
Class of danger	:	III
Remark	:	Erlaubte Emission: 5 mg/m3; TA-Luft vom 27.02.1987
Source	:	Hoechst AG Frankfurt/Main Celanese GmbH Frankfurt am Main EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
30.01.1997		(18)

1.15 ADDITIONAL REMARKS

Remark	:	Wassergefahrdungsklasse (German water pollution classification): 2 (water polluting); Catalog no.: 462
Source	:	Akzo Nobel Chemicals b.v. Amersfoort EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
03.06.1994		
Remark	:	CONVERSION FACTORS (20 deg C, 101 kPa): 1 mg/m3 = 0.39 ppm 1 ppm = 2.56 mg/m3
Source	:	Solvay S.A. Bruxelles EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
28.02.1994		
Remark	:	For disposal, recover or recycle, if possible. Otherwise : evaporate. Do not use oxygen or compressed air for filling, discharging and handling the product. Keep containers tightly closed and in a cool, well ventilated place. Avoid electrostatic discharge generation. Extinguish any naked flames. Remove ignition sources. Avoid sparks. Do not smoke. Keep under nitrogen. International Transport Classification UN number : 1086 Class : 2.1 Packing group : - Proper shipping name : Vinyl chloride, inhibited. Sea (IMO) Marine pollutant : NO Symbol : Flammable gas. Rail/Road (ADR/RID) Class : 2 Item : 3 ?c) Symbol : Flammable gas. Proper shipping name : Vinyl chloride, inhibited.

Kemler plate : 239/1086

Air (IATA/IACO)
UN number : 1086
Class : 2.1
Packing group : -
Symbol : Flammable gas.

Source : SHELL FRANCE Rueil Malmaison
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
25.05.1994

Remark : IMO/IMDG Clase 2
N? ONU 1086 RID/TPF y ADR/TPC Clase 2,3?C

Source : AISCONDEL, S.A. Barcelona
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
02.06.1994

Remark : Transport information:
Substance transported from port storage terminal by road in 18 tonne tankers at an average frequency of 10 tankers per day. Control measures consist of use of dedicated purpose-built tankers travelling along routes authorised jointly by local regulatory authorities and emergency services.

Source : Hydro Polymers Limited Newton Aycliffe, Co Durham
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
27.05.1994

1.16 LAST LITERATURE SEARCH

Type of search Internal and external
Source : PCA Services, Inc. Kingsport, TN
13.01.2001

1.17 REVIEWS

Memo : ATSDR
20.05.2002 (22)

1.18 LISTINGS E.G. CHEMICAL INVENTORIES

2. Physico-Chemical Data

Id 75-01-4
Date 18.06.2002

2.1 MELTING POINT

Value : = -153.8 ° C
Decomposition : no at ° C
Sublimation : no
Method : other
Year : 1986
GLP : no data
Test substance :
Remark : Method not specified
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
15.05.2002 (23) (24)

Value : = -153.7 ° C
Sublimation :
Method : other: not specified
Year :
GLP : no data
Test substance :
Source : Elf Atochem
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (25)

Value : = -153.7 ° C
Source : Hoechst AG Frankfurt/Main
Celanese GmbH Frankfurt am Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (18)

2.2 BOILING POINT

Value : = -13.4 ° C at
Source : Hoechst AG Frankfurt/Main
Celanese GmbH Frankfurt am Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (18)

Value : = -13.4 ° C at
Source : Hoechst AG Frankfurt/Main
Celanese GmbH Frankfurt am Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (18)

Value : = -13.4 ° C at
Source : Hoechst AG Frankfurt/Main
Celanese GmbH Frankfurt am Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (18)

2.3 DENSITY

Type : density
Value : = .964 g/cm3 at -10° C
Method : other
Year : 1986
GLP : no data
Test substance :
Remark : Method not specified
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (23)

Type : density
Value : = .911 g/cm3 at 20° C
Method : other
Year : 1986
GLP : no data
Test substance :
Remark : Method not specified
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
15.05.2002 (23)

Type : density
Value : = .969 g/cm3 at -14.2° C
Method : other
Year : 1986
GLP : no data
Test substance :
Remark : Method not specified
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (24)

Type : density
Value : = .947 g/cm3 at 0° C
Method : other
Year : 1986
GLP : no data
Test substance :
Remark : Method not specified
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (23)

Type : density
Value : = .929 g/cm3 at 10° C
Method : other
Year : 1986
GLP : no data
Test substance :

Remark : Method not specified
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (23)

Type : density
Value : = 8 kg/m3 at 15° C
Method : other: not specified
Year :
GLP : no data
Test substance :
Remark : Type: Vapour density
Pressure: 2900 hPa
Source : Elf Atochem
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (26)

Type : density
Value : = .9106 g/cm3 at 20° C
Remark : Angaben beziehen sich auf die Flussigphase
Source : Hoechst AG Frankfurt/Main
Celanese GmbH Frankfurt am Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (18)

Type : relative density
Value : = 2.598 at 20° C
Remark : Relative Gasdichte bezogen auf Luft; bei 1013 hPa
Source : Hoechst AG Frankfurt/Main
Celanese GmbH Frankfurt am Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (18)

Type : density
Value : = .872 g/cm3 at 40° C
Method : other
Year : 1986
GLP : no data
Test substance :
Remark : Method not specified
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (23)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : = 3330 hPa at 20° C
Decomposition :

2. Physico-Chemical Data **Id** 75-01-4
Date 18.06.2002

Method other (measured)
Year : 1986
GLP : no data
Test substance :
Remark : Method not specified
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
12.04.2002 (24)

Value : = 510 hPa at -30° C
Decomposition :
Method other (measured)
Year : 1986
GLP : no data
Test substance :
Remark : Method not specified
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (24)

Value : = 780 hPa at -20° C
Decomposition :
Method other (measured)
Year : 1986
GLP : no data
Test substance :
Remark : Method not specified
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (24)

Value : = 1150 hPa at -10° C
Decomposition :
Method other (measured)
Year : 1986
GLP : no data
Test substance :
Remark : Method not specified
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (24)

Value : = 1180 hPa at -10° C
Decomposition :
Method other (measured)
Year : 1986
GLP : no data
Test substance :
Remark : Method not specified
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (23)

Value : = 1650 hPa at 0° C

2. Physico-Chemical Data **Id** 75-01-4
Date 18.06.2002

Decomposition :
Method other (measured)
Year : 1986
GLP : no data
Test substance :
Remark : Method not specified
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (24)

Value : = 1670 hPa at 0° C
Decomposition :
Method other (measured)
Year : 1986
GLP : no data
Test substance :
Remark : Method not specified
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (23)

Value : = 1750 hPa at 0° C
Decomposition :
Method other (calculated): not specified
Year :
GLP : no data
Test substance :
Source : Elf Atochem
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (26)

Value : = 2430 hPa at 10° C
Decomposition :
Method other (measured)
Year : 1986
GLP : no data
Test substance :
Remark : Method not specified
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (24)

Value : = 2450 hPa at 10° C
Decomposition :
Method other (measured)
Year : 1986
GLP : no data
Test substance :
Remark : Method not specified
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (23)

2. Physico-Chemical Data **Id** 75-01-4
Date 18.06.2002

Value : = 3330 hPa at 20° C
Source : Hoechst AG Frankfurt/Main
Celanese GmbH Frankfurt am Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (18)

Value : = 3400 hPa at 20° C
Decomposition :
Method other (calculated): not specified
Year :
GLP : no data
Test substance :
Source : Elf Atochem
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (26)

Value : = 4510 hPa at 30° C
Decomposition :
Method other (measured)
Year : 1986
GLP : no data
Test substance :
Remark : Method not specified
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (24)

Value : = 5980 hPa at 40° C
Decomposition :
Method other (measured)
Year : 1986
GLP : no data
Test substance :
Remark : Method not specified
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (23)

Value : = 6000 hPa at 40° C
Decomposition :
Method other (measured)
Year : 1986
GLP : no data
Test substance :
Remark : Method not specified
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (24)

Value : = 6250 hPa at 40° C
Source : Hoechst AG Frankfurt/Main
Celanese GmbH Frankfurt am Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
22.05.2002 (18)

Value : = 7600 hPa at 48° C
Decomposition :
Method other (calculated): not specified
Year :
GLP : no data
Test substance :
Source : Elf Atochem
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (26)

Value : = 7560 hPa at 50° C
Decomposition :
Method other (measured)
Year : 1986
GLP : no data
Test substance :
Remark : Method not specified
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (23)

2.5 PARTITION COEFFICIENT

Log pow : = 1.58 at 22° C
Method OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"
Year : 1981
GLP : no
Test substance :
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : VC 99.96 %
Impurities: Chloromethane (320 ppm) and n-Butan (54 ppm)
Reliability : (2) valid with restrictions
15.05.2002 (27)

Log pow : = 1.36 at ° C
Method other (calculated)
Year : 1989
GLP :
Test substance :
Remark : calculated according to Hansch and Leo 1979; Leo et al. 1988
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (28) (29)

2.6.1 WATER SOLUBILITY

Value : = 1.1 g/l at 20 ° C

2. Physico-Chemical Data **Id** 75-01-4
Date 18.06.2002

Qualitative : of low solubility
Pka : at 25 ° C
PH : at and ° C
Method : other: not specified
Year : 1986
GLP : no data
Test substance :
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
15.05.2002 (24) (30)

Value : = .95 other: weight % at 15 ° C
Qualitative :
Pka : at 25 ° C
PH : at and ° C
Method : other
Year : 1986
GLP : no data
Test substance :
Remark : Method: not specified.
Pressure: under th e vapour pressure of the liquid VC phase.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (23)

Value : = 2.72 g/l at 20 ° C
Qualitative :
Pka : at 25 ° C
PH : = 7 at and 20 ° C
Remark : 1013 mbar
Source : Hoechst AG Frankfurt/Main
Celanese GmbH Frankfurt am Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (18)

Value : = .915 other: weight % at 20.5 ° C
Qualitative :
Pka : at 25 ° C
PH : at and ° C
Method : other
Year : 1986
GLP : no data
Test substance :
Remark : Method: not specified.
Pressure: under the vapour pressure of the liquid VC phase.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (23)

Value : = 1.1 g/l at 25 ° C
Qualitative :
Pka : at 25 ° C
PH : at and ° C
Method : other: not specified
Year :

GLP : no data
Test substance :
Source : Elf Atochem
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (26)

Value : = .89 other: weight % at 29.5 ° C
Qualitative :
Pka : at 25 ° C
PH : at and ° C
Method : other
Year : 1986
GLP : no data
Test substance :
Remark : Method: not specified.
Pressure: under the vapour pressure of the liquid VC phase.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (23)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

Value : = -78 ° C
Type : open cup
Method : other
Year : 1986
GLP : no data
Test substance :
Remark : Method: open cup (according to Cleveland)
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (23) (24)

Value : = -78 ° C
Type : closed cup
Method : other: not specified
Year :
GLP : no data
Test substance :
Source : Elf Atochem
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (26)

Value : = -78 ° C
Type :
Source : Hoechst AG Frankfurt/Main
Celanese GmbH Frankfurt am Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (18)

2.8 AUTO FLAMMABILITY

Value : = 473 ° C at 1013 hPa
Method : other: not specified
Year :
GLP : no data
Test substance :
Source : Elf Atochem
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (26)

Value : = 410 ° C at
Remark : Zundtemperatur
Source : Hoechst AG Frankfurt/Main
Celanese GmbH Frankfurt am Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
29.05.2002 (18)

Value : ca. 472 ° C at
Method : Directive 84/449/EEC, A.15 "Auto-flammability of volatile liquids or gases"
Year : 1986
GLP : no data
Test substance :
Remark : according to DIN 51 794
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (23) (24)

2.9 FLAMMABILITY

Result : extremely flammable liquified gas
Method : other: not specified
Year :
GLP : no data
Test substance :
Remark : Formation of hydrogen chloride, carbon monoxide (corrosive and toxic)
Source : Elf Atochem
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (26)

Result : extremely flammable
Source : Hoechst AG Frankfurt/Main
Celanese GmbH Frankfurt am Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (18)

2. Physico-Chemical Data **Id** 75-01-4
Date 18.06.2002

2.10 EXPLOSIVE PROPERTIES

Result : other
Remark : Flammability limits: 3.6 - 33 Volume %
Source : Hoechst AG Frankfurt/Main
Celanese GmbH Frankfurt am Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (18)

2.11 OXIDIZING PROPERTIES

2.12 ADDITIONAL REMARKS

Memo : Critical temperature and pressure
Remark : Critical temperature: 156 degree C
Critical pressure: 55900 hPa
Source : Elf Atochem
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (26)

Memo : Explosive limits
Remark : Ignition Temperature (in Temperature Class T 2) according to the method of Nabert and Schoen (1980)
Explosive limit in air: 3.8...29.3 Vol-%
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (23)

Memo : Explosive limits
Remark : Explosive limits in air: 4...22 Vol-%
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (24)

Remark : Loslichkeit H2O in VC: 1.1 g/l bei 25 ?C und 1000 mbar Gefahrliche Reaktionen: mit Peroxiden, Sauerstoff - Polymerisation mit exothermer Warmetonung (H = -105.9 KJ/mol)
Loslich in fast allen org. Losemitteln, nicht in niedermolekularen Polyalkoholen.
Source : Hoechst AG Frankfurt/Main
Celanese GmbH Frankfurt am Main
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
25.11.1996 (18)

Remark : Decomposition products: Phosgene, Carbon monoxide and HCl
Source : Hoechst AG Frankfurt/Main
Celanese GmbH Frankfurt amMain
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
29.05.2002 (18)

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	other
Light spect.	:	>= 105 nm
Rel. intensity	:	based on Intensity of Sunlight
Indirect photolysis		
Sensitizer	:	
Conc. of sens.	:	
Rate constant	:	= cm3/(molecule*sec)
Degradation	:	% after
Deg. Product	:	
Method	:	other (measured)
Year	:	1977
GLP	:	no data
Test substance	:	other TS
Remark	:	A pseudo first order K of 3.3 * E-6 sec-1 (299.2 K) can be derived from the K reported by Atkinson (6.6 * E-12 cm3/molecule * sec) assuming a constant concentration of OH (1.0 * E6 molecules/cm3), and 12 hours of sunshine/day. By dividing the ln 2 by the pseudo rate constant, a T1/2 (299.2 K) of 2.4 d can be calculated. T1/2s of 3.2 d at 357.8 degrees K and 4.1 d at 422.5 degrees K can be similarly derived using the reported rate constants. A T1/2 of 2.4 d was determined by Crutzen (referenced in Atmospheric Chemistry, DG Goldberg (ed), Ann Arbor Press, 1982, p. 313-328)

Result	:	The rate constants for reaction of OH radicals with vinyl chloride were as follows:
		
		k = 6.6 $\pm$ 0.66 * E-12 cm3/molecule*sec at 299.2 degrees K;
		k = 5.01 $\pm$ 0.51 * E-12 cm3/molecule*sec at 357.8 degrees K;
		
		k = 3.95 $\pm$ 0.4 * E-12 cm3/molecule*sec at 422.5 degrees

Source	:	PCA Services, Inc PCA Services, Inc. Kingsport, TN
Test condition	:	OH radicals were produced by pulsed vacuum UV photolysis of H2O at wavelengths >= 1050 Angstrom. OH radical concentrations were monitored as a function of time after the flash by resonance fluorescence. The flash lamp was operated at discharge energies of 25-65 J per flash at repetition rates of one flash every 3 seconds and flash durations of <= 1 microsec. Decay curves of OH radicals were accumulated from 38-1200 flashes. OH radical concentrations were followed over at least 3 half-lives. Gas mixtures in reaction vessels were replenished every few flashes. The partial pressure of H2O in the reaction cells was typically 0.01 torr. Flows were monitored by calibrated flowmeters and gases were premixed before entering reaction vessels. The reactions of OH radicals (approximately 10*E11 molecules/cm3) with CH2=CHF, CH2=CHCl, and CH2=CHBr at concentrations ranging from 0-10*E13 molecules/cm3 were studied over the temperature range 299-426 degrees K at a total pressure of argon of 50 (CH2=CHCl and CH2=CHBr) or 100 torr (CH2=CHF)
Test substance	:	vinyl chloride >= 99.9% purity (0.006% methyl chloride)

3. Environmental Fate and Pathways **Id** 75-01-4
Date 18.06.2002

Reliability : (2) valid with restrictions
15.05.2002 (31)

Type : air
Light source : Xenon lamp
Light spect. : nm
Rel. intensity : based on Intensity of Sunlight
Conc. of subst. : 20 mg/l at degree C
Indirect photolysis
Sensitizer : other:NO (nitrogen oxide)
Conc. of sens. :
Rate constant : cm3/(molecule*sec)
Degradation : % after
Deg. Product : yes
Method : other (measured)
Year : 1977
GLP : no data
Test substance : no data
Deg. Product :

Remark :
The temperature at which the reaction took place and the wavelength of the xenon lamp were not stated

Result :
Vinyl chloride and ethyl chloride were decomposed to formaldehyde and HCl by irradiation with a xenon lamp in the presence of NO in air. The decomposition rate of vinyl chloride was faster than ethyl chloride. After irradiation for 10, 20, 40, or 60 min, the concentration of vinyl chloride decreased by approximately 25, 35, 40 and 45% in the absence of NO, by approximately 35, 45, 60 and 65% in the presence of 5 ppm NO, and by approximately 40, 65, 85 and 90% in the presence of 20 ppm NO.

Formation of formaldehyde was maximal (approximately 2700 ppm) after 60 minutes of irradiation with 20 ml/l (ppm) vinyl chloride. The concentration of HCl (approximately 10000 ppm) was highest after 120 minutes of irradiation with 20 ppm vinyl chloride. Lower maximal levels of formaldehyde (3 ppm) and HCl (75 ppm) were formed after 60-120 minutes of irradiation of 20 ppm ethyl chloride

Source :
PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Test condition :
Vinyl chloride or ethyl chloride (20 ml) and NO (0, 5 or 20 ml) were injected into reaction vessels (1 l) and irradiated with a xenon lamp for 1, 20, 20, 40, 60 or 120 min. Water (50 ml) was then injected into the vessels with a syringe. After standing for 20 minutues (with occasional shaking), the solutions were analyzed for formaldehyde and chloride ion using standard methods. Vinyl chloride and ethyl chloride concentrations were monitored using a gas chromatograph

Reliability : (2) valid with restrictions
12.01.2001 (32)

Type : air
Light source :
Light spect. : nm
Rel. intensity : based on Intensity of Sunlight
Indirect photolysis
Sensitizer : OH
Conc. of sens. : 500000 molecule/cm3

3. Environmental Fate and Pathways **Id** 75-01-4
Date 18.06.2002

Rate constant	:	= .0000000000068 cm3/(molecule*sec)
Degradation	:	= 50 % after 2.4 day
Deg. Product	:	
Method	:	other (measured)
Year	:	1984
GLP	:	no data
Test substance	:	no data
Remark	:	Average (atmospheric) OH-radical concentration according to Crutzen 1982; Method: Medium size smog chamber; determination of rate constant relative to ethene.
Result	:	Rate constant (measured): K (OH) = 6.8 $\pm$ 0.2 * E-12 cm3/molecule*sec Half-life (calculated): t 1/2 = 2.4 d
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

22.05.2002 (33) (34)

Type	:	water
Light source	:	other
Light spect.	:	> 300 nm
Rel. intensity	:	based on Intensity of Sunlight
Conc. of subst.	:	10 mg/l at degree C
Deg. Product	:	
Method	:	other (measured)
Year	:	1976
GLP	:	no data
Test substance	:	no data
Remark	:	Absorption of VC in water < 218 nm.
Result	:	No photolysis over a 90-hour period.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Hg-lamp; filtered (> 300 nm); Integrated intensity of the 300 - 370 nm light: ca. 8x more intense than midday-June sunlight (lat. 34 degree N) in the same spectral region.
Reliability	:	(2) valid with restrictions

22.05.2002 (35)

Type	:	water
Light source	:	
Light spect.	:	nm
Rel. intensity	:	based on Intensity of Sunlight
Conc. of subst.	:	10 mg/l at degree C
Deg. Product	:	
Method	:	other (measured)
Year	:	1976
GLP	:	no data
Test substance	:	
Result	:	No decomposition of VC during 20 h of irradiation.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Photolysis in unfiltered natural water from the Oconee River (GA, USA) and from the Okefenokee Swamp (GA, USA); in water containing 20 mg/l commercial humic acid.
Reliability	:	(2) valid with restrictions

22.05.2002 (35)

3. Environmental Fate and Pathways **Id** 75-01-4
Date 18.06.2002

Type : water
Light source : other
Light spect. : = 578 nm
Rel. intensity : based on Intensity of Sunlight
Conc. of subst. : 10 mg/l at degree C
Indirect photolysis
Sensitizer : other
Conc. of sens. :
Rate constant : cm3/(molecule*sec)
Degradation : % after
Deg. Product :
Method : other (measured)
Year : 1976
GLP : no data
Test substance : no data
Result : VC not readily degraded.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : Photosensitization with methylene blue (concentration: 1.0*E-4 M; generation of singlet oxygen).
Reliability : (2) valid with restrictions
22.05.2002 (35)

Type : water
Light source : other
Light spect. : = 313 nm
Rel. intensity : based on Intensity of Sunlight
Conc. of subst. : 10 mg/l at degree C
Indirect photolysis
Sensitizer : other
Conc. of sens. :
Rate constant : cm3/(molecule*sec)
Degradation : % after
Result : Rapid decomposition of VC (no kinetic data provided).
Disappearance quantum yield (313 nm): 0.75 (3.0 * E-2 M VC).
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : Photosensitization with acetone (concentration: 10 vol-%).
Reliability : (2) valid with restrictions
22.05.2002 (35)

Type : water
Light source :
Light spect. : nm
Rel. intensity : based on Intensity of Sunlight
Conc. of subst. : 10 mg/l at degree C
Indirect photolysis
Sensitizer : other
Conc. of sens. :
Rate constant : cm3/(molecule*sec)
Degradation : % after
Deg. Product :
Method : other (measured)
Year : 1976
GLP : no data
Test substance : no data
Result : Rapid disappearance of VC;
ca. 30 % degradation after 1 h;
ca. 80 % degradation after 3 h;

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : Photosensitization with H2O2 (generation of OH-radicals)
21.09.1993 (35)

3.1.2 STABILITY IN WATER

Type : abiotic
t1/2 pH4 : >= 1 year at degree C
t1/2 pH7 : at degree C
t1/2 pH9 : at degree C
t1/2 pH 6.1 : >= 1 year at degree C
Deg. Product :
Method : other
Year : 1976
GLP : no data
Test substance : other TS
Result :

Vinyl chloride was chemically stable in two natural water samples. It did not degrade after 41 hours of incubation at room temperature or 85 degrees C. In reaction mixtures at pH 3.0, 7.0 and 11.0, at 85 degrees C, no reaction was detected after 27 hours. No degradation of vinyl chloride was observed after 12 hours of incubation under oxidizing conditions at high temperature (85 degrees C). At elevated temperature vinyl chloride was degraded by H2O2. The reaction with H2O2 obeyed zero-order kinetics,

Extrapolation of the elevated temperature data to environmental conditions indicated a minimum T1/2 of at least one year. Extrapolation of pH data indicated a T1/2 on the order of years

Source :

PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Test condition :

The stability of vinyl chloride was tested in natural water from The Oconee River, GA, USA (pH = 6.1) and Okefenokee Swamp, GA, USA (pH 4.2). The Oconee River water sample was filtered through a 0.22 micron filter prior to use. A special reaction vessel designed to eliminate volatilization was used. The vessel was filled to the top with water an 20 ml of vinyl chloride was added. The filled vessel was placed in a constant temperature bath (room temperature or 85 degrees C) and removed at recorded intervals for analysis. The concentration of vinyl chloride at each time point was determined by comparison of glc peak heights using a vinyl-chloride carbon tetrachloride standard solution.

Reaction mixtures of varying pH (3.0, 7.0 and 11.0) were prepared to determine the effect of pH on the reaction. The effect of oxidation on the reaction was assessed by saturating the water with molecular O2 prior to adding vinyl chloride or by reacting H2O2 (10 mM) with vinyl chloride (0.1 mM) at 85 degrees C

Test substance :

Vinyl chloride was obtained from Matheson Chemical Company and used as received. Purity was not noted

Reliability : (2) valid with restrictions
13.01.2001 (36)

Type : Abiotic

t1/2 pH4 : at degree C
t1/2 pH7 : at degree C
t1/2 pH9 : at degree C
Remark : Hydrolysis over a pH range from 4.3 to 9.4 does not appear to be an important pathway for loss of VC from water. The hydrolytic half-life has been estimated to be less than 10 years at 25.5 degree C.
Source : Elf Atochem
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (37)

3.1.3 STABILITY IN SOIL

Type : other
Radiolabel :
Concentration :
Soil temp. : degree C
Soil humidity :
Soil classif. :
Year :
Remark : Chloroethylene is a gas and evaporates rapidly. It is also biologically degradable (see section 3.5)
Source : Solvay S.A., Bruxelles
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002

3.2 MONITORING DATA

Reliability : (2) valid with restrictions
28.05.2002 (38)

Reliability : (2) valid with restrictions
28.05.2002 (39)

Result : Vinyl chloride has been detected at higher levels in dumpsite emissions, however, the source of these emissions was not from manufacture or use, but from degradation of other chemicals.
Reliability : (2) valid with restrictions
28.05.2002 (40)

Result : Vinyl chloride was positively identified in only 0.74% of 945 groundwater supplies monitored throughout the United States (detection limit 0.001 ppm). The maximum concentration determined was 8.4 5g/l (0.0084 mg/l).
Reliability : (2) valid with restrictions
28.05.2002 (41)

Result : Concentrations of vinyl chloride in drinking water wells and surface water in New York State were found to be 50 5g/l and 10 5g/l respectively.
Reliability : (2) valid with restrictions
28.05.2002 (42)

Remark : The weight of evidence suggests that this value is atypical.

ATSDR. 1997. Toxicological profile for vinyl chloride. Public Health Service, US Department of Health and Human Services. ATSDR Toxicological Profiles. CRC Press, Inc.

Result : A high determination of 380 5g/l was obtained in groundwater in a nine state monitoring study.

Reliability : (2) valid with restrictions
28.05.2002 (43)

Result : PVC plastics used for food contact packaging, drug and medical device products are regulated in the United States under the Federal Food, Drug and Cosmetic Act (FFDCA) as administered by the Food and Drug Administration (FDA). The FDA has determined a reasonable worst-case exposure estimate for vinyl chloride to be 25 nanograms average per day. The FDA stated that "because of numerous conservatisms in the estimate, lifetime-averaged individual exposure is expected to be substantially less than 25 nanograms per day". The FDA has calculated that the individual lifetime risk of cancer from exposure to vinyl chloride monomer at 25 nanograms per day is less than 1 in 10 million. Thus the FDA concluded that "there is a reasonable certainty of no harm from the exposure to vinyl chloride monomer that may result from the use of vinyl chloride polymers in food packaging complying with the vinyl chloride limits set forth by the FDA".

Reliability : (2) valid with restrictions
28.05.2002 (44)

Result : <1 ppm residual VCM in PVC products while modern medical grade PVC is believed to contain <10 ppb VCM.

Reliability : (2) valid with restrictions
28.05.2002 (45)

Result : According to a NSF report on Residual Vinyl Chloride Monomer (RVCM) content of PVC sampled between January 1, 1998 through October 18, 2000, only 74 of 519 (14%) samples of PVC pipe and 21 of 178 (12%) samples of PVC fittings showed detectable levels of vinyl chloride monomer (detection level 0.1 mg/kg). The average RCVM value of all samples, considering non-detect samples as zero, is reported as 0.07 mg/kg for pipe and 0.03 mg/kg for fittings

Reliability : (2) valid with restrictions
28.05.2002 (46)

Method : In the case of wall covering applications, a study was conducted using PVC resin containing 1.2 ppm vinyl chloride monomer. This resin was mixed with 50 phr DOP and 1 phr of a Ca/ZN stabilizer only, and spread onto release paper at 1000 g/m2 and gelled at only 150 degrees C for 30 sec - gelation conditions that would encourage retention of any monomer since 1) the formulation had an unnaturally high PVC level (the resin also having an unnaturally high PVC level), 2) the formulation was coated at an extremely high weight and 3) the material was extremely under-processed. This material was then analyzed for VCM using headspace gas chromatography.

Result : No VCM was detected, the detection limit of the instrumentation being 10 ppb. The authors concluded that "clearly, since normal wall covering samples contain lower levels of polymer, generally have lower coating weights, and are processed under more severe conditions, the retention of VCM by wall covering samples is exceedingly unlikely".

Reliability : (2) valid with restrictions
28.05.2002 (47)

Result : In a survey of PVC products carried out in 1976-77, the following indoor

articles had a VC content of >0.05 ppm: bathroom tiles, piping, plastic bottle for table oil, and kitchen film. The VC content of toys, kitchen utensils, food wrappings, wallpaper and car interiors was <0.05 ppm.

Reliability : (2) valid with restrictions
28.05.2002 (48)

Result : VCM residues in various PVC samples were as follows: rigid water bottle (850 ppb), thin plasticized food film (3 ppb), monopolymer powder (10 ppb); copolymer film (15 ppb).

Reliability : (2) valid with restrictions
28.05.2002 (49)

Result : The Consumer Product Safety Commission (CPSC) has banned use of vinyl chloride as an ingredient or a propellant self-pressurized products intended as suitable for household use.

Reliability : (2) valid with restrictions
28.05.2002 (50)

Type of measurement : background concentration
Medium : air
Method :
Concentration :
Result : VC concentration in clean air regions in Germany (such as Westerwald, Schwarzwald, Lueneburger Heide, Bayrischer Wald; measured prior to 1977):
VC concentration in the Taunus area: 0.01 ug/m3.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (51) (52)

Type of measurement : background concentration
Medium : surface water
Method :
Concentration :
Result : VC concentration in water from the Rhine: max. concentration 1 ug/l.
VC concentration in Rhine tributaries in Nordrhein-West-falen: < 1 ug/l to 5 ug/l.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (53)

Type of measurement : background concentration
Medium : drinking water
Method :
Concentration :
Remark : More recent values of VCM found in PVC pipe are much lower (McLellan, 2001).
Result : In general, VC is not detectable in drinking water in the FRG. In some samples, maximum concentrations of up to 1.7 ug/l were observed. It is assumed, that this is caused by migration of VC from PVC pipes with an increased monomere content.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (54)

Type of measurement : background concentration

Medium : surface water
Method :
Concentration :
Remark : Highest levels of vinyl chloride in 1989-90 found in the river water (in ug/l) in Germany: Rhine: 0.031; Main: 0.008; Lippe: 0.40 (near an emission point); Ruhr: 0.060; Wupper: 0.069; Saale (ex-GDR): 69.
Source : Solvay S.A., Bruxelles
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (55)

Type of measurement : background concentration
Medium : ground water
Method :
Concentration :
Remark : Results from a survey throughout the USA indicate that vinyl chloride was positively identified (detection limit 1 ug/l) in only 0.74 of the ground water supplies.
Source : Solvay S.A., Bruxelles
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (56)

Type of measurement : background concentration
Medium : ground water
Method :
Concentration :
Remark : Concentration of vinyl chloride in 51 wells of the Berlin area is comprised between <1 to 110 ug/l (range).
Source : Solvay S.A., Bruxelles
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (57)

Type of measurement : concentration at contaminated site
Medium : air
Method :
Concentration :
Remark : Sampling at three different urban sites in New Jersey (USA): Newark, Elizabeth, Camden. All sites are located in highly industrialized areas. Continuous sampling: 24 hours continuous, 7d/w for 6 weeks during summer (July/August 1981) and winter (January/February 1982).
Result : No VC detected. Detection limit: 0.13 ug/m3
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (58)

Type of measurement : concentration at contaminated site
Medium : air
Method :
Concentration :
Result : VC concentration at different sites and times in Berlin city (Steglitz, Dahlem (residential area), Jungfernheide): n.d. (< 0.3 ug/m3) to 3.5 ug/m3 (mean values 0.3 to 0.4 ug/m3).
Source : Huels AG Marl

EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (51) (59)

Type of measurement : concentration at contaminated site
Medium : air
Method :
Concentration :
Result : VC immissions for various areas of Cologne during various time periods (1979 - 1986): 0 .5 to 15.3 ug/m3 (99th percentile: 5.8 to 68.8).
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
23.05.2002 (60) (61)

Type of measurement : concentration at contaminated site
Medium : air
Method :
Concentration :
Result : VC concentration in an industrial area (Ruhrgebiet-West): up to 113 ug/m3
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
23.05.2002 (52)

Type of measurement : concentration at contaminated site
Medium : air
Method :
Concentration :
Remark : Solvay S.A. suggests the following explanation: Such contamination could come from tri or perchloroethylene degradation or from PVC sludge residues.
Result : VC in the gas discharges of landfills: 34 mg/m3 (average value); 234 mg/m3 (maximum value)
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
23.05.2002 (62)

Type of measurement : concentration at contaminated site
Medium : ground water
Method :
Concentration :
Remark : It is supposed that VC is formed from tetrachloro- and trichloroethene under reducing conditions by soil bacteria.
Result : VC concentrations between n.d. (< 0.3 ug/l) and 1,040 ug/l were observed in samples of contaminated groundwater (sampling sites not specified).
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
23.05.2002 (63)

Type of measurement : concentration at contaminated site
Medium : ground water
Method :
Concentration :
Remark : It is supposed that VC is formed during the dry-cleaning process.
Result : 2,800 ug/l VC besides tetrachloroethylene (concentration not specified) were found in a narrow, ca. 1 km stretch of groundwater in a residential

area in North Bay Shore, Suffolk County, NY, USA. The contamination could be traced back to a dry-cleaning shop"s ditch.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
23.05.2002 (64)

Type of measurement : concentration at contaminated site
Medium : air
Method :
Concentration :
Result : VC concentration in Marl: 213 ug/m3
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
23.05.2002 (51)

Type of measurement : concentration at contaminated site
Medium : air
Method :
Concentration :
Result : VC concentration in an industrial area (Ruhrgebiet-West): 69 ug/m3 (99th percentile).
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
23.05.2002 (61)

Type of measurement : concentration at contaminated site
Medium : air
Method :
Concentration :
Result : VC concentration in the gaseous emissions of an Ohio (USA) landfill: 255 to 777 mg/m3.
(High concentrations are attributed to disposal of PVC sludge or PVC batches with high residual monomer content).
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
23.05.2002 (65)

Type of measurement : concentration at contaminated site
Medium : air
Method :
Concentration :
Result : VC concentration in landfill gases: 235 mg/m3
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
23.05.2002 (66)

Type of measurement : concentration at contaminated site
Medium : air
Method :
Concentration :
Result : VC concentration in gaseous emissions from landfills: 0.026 to 0.26 mg/m3.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
23.05.2002 (67)

Type of measurement : concentration at contaminated site
Medium : other: air and water
Method :
Concentration :
Remark : The concentration of vinyl chloride in the water effluents of VCM manufacture is presently (1993) under 1 mg/l. In air, the level of 5 ug/m3 (about 2 ppb) is obtained with an emission level of 200 g vinyl chloride per ton of PVC at a distance of 250 m from the plant.
Source : Solvay S.A., Bruxelles
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
23.05.2002 (68)

Type of measurement : concentration at contaminated site
Medium : air
Method :
Concentration :
Remark : At the Rafnes plant of Norsk Hydro, 95 % of measurements of vinyl chloride in the work environment are below 1 ppm (1043 measurements). Average emissions of vinyl chloride to air are about 25 kg/week.
Source : Solvay S.A., Bruxelles
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
23.05.2002 (69)

Type of measurement : other
Medium : air
Method :
Concentration :
Result : VC concentration in the municipality of Frankfurt/M. (for various periods): 1 to 22 ug/m3
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
23.05.2002 (51) (52) (70)

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : fugacity model level III
Media : other:air-water, soil, sediment
Air (level I) :
Water (level I) :
Soil (level I) :
Biota (level II / III) :
Soil (level II / III) : .02
Method : other:estimated
Year : 2000
Remark :
The Mackay model was run only on atmospheric emissions because the vast majority of vinyl chloride is emitted into the atmosphere. The 1998 TRI inventory listed emissions to water and soil as 78 lbs and 154 lbs, respectively.

The total persistence of vinyl chloride as determined by the model is governed primarily by the rate of atmospheric reaction with hydroxyl radical. A wide range of estimated half-lives (9.7 to 97 hours) was inputted into the model. The wide range of half-lives had no effect on the predicted overall distribution of vinyl chloride among air, soil and water

Result :

The Level III model predicted that 99.98% of vinyl chloride directly emitted to the atmosphere will stay in the atmosphere. The dominant removal process is reaction with atmospheric hydroxyl radical (T1/2 = 1.5 days). The total estimated persistence of vinyl chloride in the atmosphere is 34.2 hours. Less than 0.02% of the emitted vinyl chloride is predicted to migrate to the water, soil, or sediment compartments

Source :

PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Test condition :

A MacKay Level III Model (version 2.1) was run using a continuous emission of 1000 kg/hour vinyl chloride to the atmosphere. These data were estimated from 1998 TRI data, which indicated that 886,179 lbs of vinyl chloride were emitted to air. Physico-chemical properties were taken from the Environmental Fate and Pathways and Physico-chemical Data sections of the IUCLID data sheet for vinyl chloride (19-Feb-2000). An atmospheric half-life of 1.5 days was used (as estimated by Howard, Handbook of Environmental Fate and Exposure Data for Organic Chemicals, Vol. 1., 1989). The half-life in water, soil and sediment was estimated as 30 days (as estimated by Howard et al., Handbook of Environmental Degradation Rates, 1991)

Reliability : (1) valid without restriction
13.01.2001 (71)

Type : volatility
Media : water - air
Air (level I) :
Water (level I) :
Soil (level I) :
Biota (level II / III) :
Soil (level II / III) :
Method : other
Year : 1987
Remark :

Previous research revealed no interactive effects of organic mixtures on Henry's law constants. Concentrations of methanol less than 5% (39.6 g/l) also had no effect

Result :

Henry's Law Constants for vinyl chloride are as follows:

10.3 degrees C: 0.0147 m3*atm/mol (0.96 % CV)
17.5 degrees C: 0.0193 m3*atm/mol (3.48 % CV)
24.8 degrees C: 0.0278 m3*atm/mol (4.39 % CV)
34.6 degrees C: 0.0358 m3*atm/mol (1.48 % CV

Source :

PCA Service
PCA Services, Inc. Kingsport, TN

Test condition :

A modified EPICS procedure was used to measure Henry's Law Constants of 13 volatile C1 and C2 chlorinated hydrocarbons from 10 to 35 degrees C. The original EPICS procedure assumption of equal solute masses in individual bottles was eliminated, and differences in mass due to imperfect,

volumetric additions were accounted for through gravimetric means. Dilute aqueous mixtures of 3-6 solutes were employed as opposed to singular solutes. Methanol was present in the systems. Vinyl chloride (0.042 mg/l) was tested in a mixture containing chloromethane (0.042 mg/l), chloroethane (0.042 mg/l), cis-1,2-dichloroethylene (2.4 mg/l) and methanol (657 mg/l). All indicated concentrations are those added to high volume (100 ml EPICS systems) prior to partitioning into headspace. Added concentrations to low volume (25 ml system) were 4 times as large.

Henry's constants of three 100 ml systems and three 25 ml systems were measured in six 158.8 ml serum bottles. Distilled water (25 or 100 ml) was pipetted into each bottle, and bottles were sealed with Teflon/rubber septa and aluminum crimp caps. A 0.1 ml gas-tight syringe was used to deliver 20 microliters of the appropriate stock solution to each bottle. The exact amount of each solution added was determined by weighing the syringe before and after injection. The serum bottles were incubated (inverted and submerged) for 18-24 h at 10.0, 17.5, 24.8 or 34.6 degrees C in a reciprocating shaker bath. At various time points during the incubation, bottles were turned upright and headspace samples (0.5 ml) were obtained by inserting a side-port needle attached to a 1.0 ml gas-tight syringe (with a push-button valve) through the septum. The sample was immediately injected into a gas chromatograph for analysis

Reliability : (1) valid without restriction
13.01.2001 (72)

Type : adsorption
Media : water - soil
Air (level I) :
Water (level I) :
Soil (level I) :
Biota (level II / III) :
Soil (level II / III) :
Method : other: estimated
Year :
Result : A Koc of 56 was estimated in soil. VC will be expected to be highly mobile in soil.
Source : Elf Atochem
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
20.05.2002 (73)

Type : volatility
Media : water - air
Air (level I) :
Water (level I) :
Soil (level I) :
Biota (level II / III) :
Soil (level II / III) :
Method : other
Year : 1976
Result : Rate coefficients for O2 and VC gas exchange at four mixing levels:

Vortex depth (cm)	K O2 (/min)	K VC (/min)
0	-3.54*E-3 ± 2.28*E-4	-3.03*E-3 ± 2.74*E-4
1.5	-1.24*E-2 ± 1.45*E-3	-1.29*E-2 ± 1.22*E-3
5.0	-3.85*E-2 ± 1.16*E-2	-8.19*E-2 ± 1.06*E-3
10.0	-8.03*E-2 ± 3.86*E-2	-1.75*E-1 ± 7.88*E-2

measured: K VC/K O2 = 2.30 ± 0.31 (95 % confidence level)
calculated from ratio of molecular diameters:
K VC/K O2 = 0.83 and 0.87
(depending on the molecular diameters used for calculation) VC is exchanged with the atmosphere about twice as quickly as oxygen. Thus, the high volatility of VC leads to a rapid transfer from water into the atmosphere

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test condition : Nitrogen-sparged, deionized water (900 ml) and saturated VC solution (10 ml) were added to each of four beakers in an exhaust hood. The contents of the beakers 1, 2, 3, and 4, respectivly, were stirred to create vortices with depth of 0 (quiescent), 1.5 cm, 5 cm, 10 cm, respectively. O2 and VC concentrations were measured every 10 min for 180 min using a dissolved-oxygen meter and a gas chromatograph. (6 replications)

Reliability : (2) valid with restrictions
20.05.2002 (35)

Type : volatility
Media : water - air
Air (level I) :
Water (level I) :
Soil (level I) :
Biota (level II / III) :
Soil (level II / III) :
Method : other
Year :
Result : T 1/2 = 0.9 to 1.2 h
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test condition : Measurements were performed in a drainage canal of the "Vorfluteranlage Grosslappen" using water from the Isar-Schleissheimer Kanal (35 l/s; streaming velocity 0.5 m/s). VC was added at the entrance of the canal. Samples were drawn at 10m, 250 m, 750 m, and 1000m. Analysis by head-space method or pentane extraction and gas chromatography.

Reliability : (2) valid with restrictions
28.05.2002 (30)

Type : Volatility
Media : water – air
Air (level I) :
Water (level I) :
Soil (level I) :
Biota (level II / III) :
Soil (level II / III) :
Method : Other
Year : 1989
Result : Henry's Law Constant (calculated from the solubility at 15 degree C): H = 1.85 * E+3 Pa*m 3/mol
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
28.05.2002 (27)

Type : Volatility
Media : water – air
Air (level I) :
Water (level I) :
Soil (level I) :

Biota (level II / III) :
Soil (level II / III) :
Method : Other
Year : 1987
Result : Henry"""""s Law Constant (measured):
at 10.3 degree C: 1.47 * E+3 Pa * m3 / mol (CV = 0.96 %)
17.5 degree C: 1.93 * E+3 Pa * m3 / mol (CV = 3.48 %)
24.8 degree C: 2.78 * E+3 Pa * m3 / mol (CV = 4.39 %)
34.6 degree C: 3.58 * E+3 Pa * m3 / mol (CV = 1.48 %)
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : modified EPICS procedure with headspace analysis.
Reliability : (2) valid with restrictions
28.05.2002 (74)

Type : Volatility
Media : water – air
Air (level I) :
Water (level I) :
Soil (level I) :
Biota (level II / III) :
Soil (level II / III) :
Method : Other
Year : 1983
Result : 50 % of VC dissipates from an aqueous solution of 1 mg/l (1ppm) within 26 min, 90 % evaporates within 96 min.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
28.05.2002 (75)

Type : Volatility
Media : water – air
Air (level I) :
Water (level I) :
Soil (level I) :
Biota (level II / III) :
Soil (level II / III) :
Method : other
Year : 1988
Result : According to rough estimates, the half-lives for the evaporation of VC from water bodies is given as follows:
Pond: t 1/2 = 43.8 h
Lake: t 1/2 = 34.7 h
River: t 1/2 = 4.7 h
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
28.05.2002 (76)

3.3.2 DISTRIBUTION

Media : air - biota - sediment(s) - soil – water
Method : Calculation according Mackay, Level I
Year :
Result : Air: 99.985 %
Soil: 0.000 %

Water: 0.015 %
Sediment: 0.000 %
Biota: 0.000 %

Source : Huels AG, Marl
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test condition : Data used:
Molar mass: 62.50 g/mol
Log Pow: 1.58
Vapor pressure: 333000 Pa
Water solubility: 1.1 g/l

Equations used for additional data:
log Koc = 0.989 log Pow - 0.346

Volumes used:
Air: 6 000 000 000
Soil: 45 000
Water: 7 000 000
Sediment: 35 + 21 000
Biota: 7

Reliability : (2) valid with restrictions
28.05.2002

Media : water - air
Method : other (calculation)
Year :
Method : Best estimate model for the VC concentration in water and the cumulative loss to the air in a lake and in a stream.
Result : VC concentration in the sample stream and lake would be > 0.2 mg/l
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : VC concentration in input: 1 mg/l
fractional input: 10 % of total water volume
Reliability : (2) valid with restrictions
28.05.2002 (35)

Media : water - biota
Method : other (calculation)
Year : 1976
Method : Worst case estimate (stratified lake with simplistic food web); assumption: diffusion-limited exchange between water and unmixed lower sediment layers.
Result : Half-life time of VC in the sediment - benthic organism - predator - omnivore - cycle: t 1/2 = ca. 3 y;
VC concentration in the sediment approaches a steady-state value of 0.358 mg/l in about 15 y.
VC concentration in the benthic organisms reaches a steady state value of 0.013 mg/l in about 15 y.
VC concentrations in other organisms are less.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
28.05.2002 (35)

3.4 MODE OF DEGRADATION IN ACTUAL USE

Remark : In present installations, all offgases are collected or stripped and either recycled in the process or destructed in high performance incinerators.
Source : Solvay S.A., Bruxelles
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
28.05.2002 (68)

3.5 BIODEGRADATION

Type : aerobic
Inoculum : other:soil-water microcosms from authentic aquifer material
Contact time : 108 day
Degradation : = 99 % after 108 day
Result : readily biodegradable
Kinetic of test substance : 7 day = 25 **%**

40 day = 30 **%**
60 day = 50 **%**
90 day = 75 **%**
%
Control substance : other: sterile microcosms
Kinetic : 90 day = 0 **%**
108 day = 1 **%**
Deg. Product : yes
Method : other
Year : 1990
GLP : no data
Test substance : other TS
Deg. Product :
Result :

Analyses of soil: Solids contained little organic carbon (0.24 %) and were classified as sand based on low levels of silt and clay. The total number and number of viable microorganisms were 9.77 * E7 and 3.01 * E4, respectively.

Vinyl chloride degradation: Greater than 99% degradation of 1 ppm 14C - vinyl chloride occurred after 108 days. For 1 ppm and 0.1 ppm concentrations, approximately 65% and 50% of 14C was recovered as 14CO2, respectively. Less than 5% degradation occurred in controls

Source :

PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Test condition :

Source of Material: Material was collected from the northern bank of the South Canadian River from an area bordering a municipal landfill in Norman, OK. The site did not receive leachate from the landfill. The water table in the area was shallow (0.6-1.5 m below surface). Soil samples were taken from 0.5 to 1.0 m below the surface. Groundwater was collected by digging a hole 1-2 m deep and allowing the hole to fill.

Analyses of soil: Organic and inorganic contents of soil and soil texture were analyzed by standard methods. The total number of bacterial cells and number of viable microorganisms in soil was determined.

Test System: Microcosms were prepared containing 20 g (wet weight) of solids and 20 ml sterilized groundwater prepared in 30-ml sterile bottles.

Microcosms were sparged for 5 min with 100% O2 before adding vinyl chloride. An aqueous solution of vinyl chloride was added to yield concentrations of 0.1 or 1.0 ppm (wt/wt of soil and water). Resazurin (0.0002%) was added as a redox indicator. The system was sealed with a rubber septum and aluminum crimp seal. Samples were incubated at 20 degrees C in the dark and agitated (1 rpm).

Control: Autoclaved controls were included to monitor loss of test material and/or abiotic degradation.

Analyses of vinyl chloride and metabolites: 14C-vinyl chloride in the aqueous fraction was analyzed by HPLC. Total radioactivity in the aqueous fraction was determined by liquid scintillation counting. 14CO2 was collected by passing N2 gas (250 to 350 ml/min) through slurry mixtures which had been acidified with 200 microliters of concentrated phosphoric acid. Purged gas was collected in a series of two traps containing 10 ml 1N POH. Samples (1 ml) from combined traps were analyzed by liquid scintillation counting. CO2 production was confirmed by determining radioactivity in solution after addition of barium nitrate

Test substance :

14C vinyl chloride (specific activity 0.53 mCi/mmol) from Dupont, NEN Research Products, Boston MA

Reliability : (2) valid with restrictions
12.01.2001 (77)

Type : anaerobic
Inoculum : other:soil-water microcosms from authentic aquifer material
Contact time : 70 day
Degradation : % after
Result : other: 21% degradation in one system and 100% degradation in another
Control substance : other:sterile microcosms
Kinetic : **%**
%
Deg. Product : yes
Method : other
Year : 1999
GLP : no data
Test substance : other TS
Deg. Product :

Result :

NWIRP sediment: A 21% and 6% percent decline in vinyl chloride was observed in experimental and control microcosms by 70 days, respectively. Vinyl chloride was degraded to ethene (3 +/- 1%), CO2 (11+/- 2%) and CH4 (9 +/- 2%). Significant recovery of CO2, CH4, and ethane was observed within 5, 5, and 50 days, respectively. Metabolites were not detected in controls.

NAS sediment: A 98% and 13% percent decline in vinyl chloride was observed in experimental and control microcosms by 70 days, respectively. Vinyl chloride was degraded to ethene (10 +/- 1%), ethane (39 +/- 9%), CO2 (22 +/- 2%) and CH4 (22 +/- 1%). Significant recovery of CO2 and CH4 was observed immediately. Significant ethane accumulation was noted on day 50. Ethene concentrations declined as ethene was reduced to ethane. Ethene and ethane accounted for 50% of recovered radioactivity by the end of the study. Metabolites were not detected in controls

3. Environmental Fate and Pathways **Id** 75-01-4
Date 18.06.2002

Source :
PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Test condition :
Source of Material: From the Naval Weapons Industrial Reserve Plant (NWIRP), Dallas TX, and the Naval Air Station (NAS) Cecil Field, Jacksonville, FL. Sediments were collected from a shallow, freshwater lake (NWIRP) or a shallow, freshwater stream (NAS) that received groundwater contaminated with low concentrations (<= 20 ppb) of trichloroethene, dichloroethene and vinyl chloride. NWRIP sediment was a highly reduced, soft mud composed of clay and fine silt with vigorous methanogenesis. NAS sediment (a coarse grained sand with a 2-5% organic content) was collected near a site with continuous methane outgassing.

Test System: Anaerobic microcosms containing 15 g of saturated, methanogenic sediment under a helium atmosphere were prepared in 20-ml serum vials. The system was sealed with butyl rubber stoppers and flushed with an excess (1000 ml) of high purity helium. Experimental treatments were prepared in triplicate. Microcosms were preincubated for 5 days to establish methanogenesis before addition of 0.5 microCi of [1,2-14C] vinyl chloride. The initial dissolved concentration of vinyl chloride based on adsorption and Henry's law constant was 370 microgram/l and 630 microgram/l in NWIRP and NAS microcosms, respectively.

Control: Autoclaved controls (twice for 1 hr at 15 PSI and 121 degrees C were included to monitor loss of test material and/or abiotic degradation.

Analyses of vinyl chloride and metabolites: Headspace concentrations of vinyl chloride were monitored periodically by GC/FID. Sample volumes were replaced with helium. Formation of CH4, CO2, ethane and ethene were monitored continuously using GC/GRD. Measured concentrations were corrected for the loss of constituents due to headspace sample collection

Test substance :
[1,2-14C] vinyl chloride (NEN Dupont, Boston). Greater than 98% of total radioactivity was associated with vinyl chloride. Purity was > 99%

Reliability : (2) valid with restrictions
13.01.2001 (78)

Type : Aerobic
Inoculum : activated sludge, adapted
Contact time :
Degradation : = 21.5 % after 5 day
Result :
Deg. Product :
Method : other
Year : 1985
GLP : no data
Test substance : no data
Remark : Method not specified;
VC concentration: 0.05 mg/l;
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
28.05.2002 (79)

Type : Aerobic
Inoculum : Mycobacterium sp. (Bacteria)
Contact time :

Degradation	:	= 93 % after
Result	:	
Deg. Product	:	
Method	:	other
Year	:	1985
GLP	:	no data
Test substance	:	
Remark	:	Isolation of a strain of Mycobacterium (M. L1) that uses VC as sole source of carbon and energy from soil that had been contaminated with VC for several years. Affinity of the bacteria: KM ca. 100 ppm (1.75 uM) VC. Experiments were conducted to investigate removal of VC from waste gas by immobilized or growing cells, respectively. In the latter case VC was added to the fermenter as a 40 ml/min mixture of 1 % (V/V) VC in air. Under steady state conditions (dilution rate 0.012/h) 93 % of VC from the ingoing air was removed. In continuous culture batches, the bacterium mineralized 0.68 kg VC/m3*day. Evaluation of the carbon and chloride balance implied that VC was completely degraded. Degradation was accompanied by formation of HCl.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
28.05.2002		(80)

Type	:	Aerobic
Inoculum	:	other: mycobacterium
Contact time	:	
Degradation	:	= 93 % after
Result	:	
Source	:	Solvay S.A., Bruxelles Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Concentration: 1 % Fermentor
Reliability	:	(2) valid with restrictions
28.05.2002		(81)

Type	:	Aerobic
Inoculum	:	Other
Contact time	:	25 day
Degradation	:	% after
Result	:	under test conditions no biodegradation observed
Control substance	:	other: untreated bacteria
Kinetic	:	**%** **%**
Deg. Product	:	no
Method	:	
Year	:	1977
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	No change in biochemical oxygen demand between raw sewage seed and raw sewage seed plus vinyl chloride at 20 degrees C (as described in ATSDR, 1997).
29.05.2002		(82) (83)

Type : anaerobic
Inoculum : other bacteria
Deg. Product :
Method : other
Year : 1986
GLP : no data
Test substance : no data
Remark : A mixed culture of methane-utilizing bacteria (CL-M) isolated from sediments taken from a cattail marsh of a lake in Newton, Mass., that was enriched, but not especially adapted, completely degraded VC (as well as other chlorinated ethenes) at a concentration of 540 ug/l VC within 23 h under aerobic conditions. No volatile chlorinated compounds were formed.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
28.05.2002 (84)

Type : anaerobic
Inoculum : other: groundwater bacteria
Concentration : related to Test substance
related to
Remark : The initial concentration was 400 mg/m3 vinyl chloride in water. The half life was 4 weeks with sand and 10 weeks without sand.
Source : Solvay S.A., Bruxelles
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : 20 degree C, darkness
Reliability : (2) valid with restrictions
06.06.2002 (63)

Type : anaerobic
Inoculum : other: mycobacterium vaccae JOB5
Concentration : .888mg/l related to Test substance
related to
Contact time :
Degradation : = 100 % after
Result :
Source : Solvay S.A., Bruxelles
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : 2 hour incubation, grown on propane
Reliability : (2) valid with restrictions
28.05.2002 (85)

Type : anaerobic
Inoculum : other: water bacteria
Concentration : .29mg/l related to Test substance
related to
Remark : Methanotrophic culture. Result: 0.06 mg/l end concentration.
Source : Solvay S.A., Bruxelles
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : 12 days adaptation in fixed film packed bed reactor with 50 min retention time
Reliability : (2) valid with restrictions
28.05.2002 (86)

Type : anaerobic

Inoculum :
Remark : VC was approximately 50 % and 100 % degraded in 4 and 11 weeks, respectively, in the presence of sand by methanogenic organisms in laboratory scale experiments. In absence of sand, 20 % and 55 % degradation occured in 4 and 11 weeks, respectively.
Source : Elf Atochem
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
28.05.2002 (63)

Type : anaerobic
Inoculum :
Remark : Anaerobic degradation of tetrachloroethylene, trichloro-, dichloro- and chloroethene into ethane or ethene is experimentally observed in various conditions.
Source : Solvay S.A., Bruxelles
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
28.05.2002 (87) (88) (89) (90)

Remark : Several studies suggest the following mechanism for the microbial degradation of VC:

VC ----(oxidation by methane-monooxygenase)---->

chloroethylene oxide -----(rearrangement)------>

chloroacetaldehyde ---------(oxidation)-------->

chloroacetate ---(hydrolytic dehalogenation)--->

glycolate (------> normal cellular metabolism)
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
12.10.1993

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

Species : Other
Exposure period : 3 day at 26.7 degree C
Concentration : .25mg/l
Elimination :
Method : other
Year : 1977
GLP : no data
Test substance : other TS
Remark : 14C-labeled VC was evaluated in a closed model aquatic ecosystem and was allowed to pass through a model food chain. Transfer, biodegradation and bioaccumulation were studied. Due to the high vapour pressure, only 34 % of the VC were found in the water, while 65 % were found in the consumed air after 3 d of exposure. The following VC concentrations were determined by measuring the 14C-distribution:

Water 42 ug/kg
Oedogonium 1,307 ug/kg
Physa 1,225 ug/kg
Daphnia 621 ug/kg
Culex larvae 1,196 ug/kg
Gambusia 300 ug/kg
The authors concluded, that no substantial bioaccumulation of VC occurs and that the accumulation in the food chain is insignificant.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
28.05.2002 (91)

Species : other
Exposure period : at degree C
Concentration :
Elimination :
Method :
Year : 1985
GLP : no data
Test substance : other TS
Remark : Bioaccumulation was studied by application of 14C-labelled VC to algae (Chlorella fusca var. vacuolata), fish (Leuciscus idus), and activated sludge from a municipal sewage treatment plant. The following bioaccumulation factors (BFn) were reported:
Activated sludge BFn = 1,100 (n = 5 days)
Algae BFn = 40 (n = 1 day)
Fish BFn = <10 (n = 3 days)

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
28.05.2002 (79)

3.8 ADDITIONAL REMARKS

Remark : Migration of VC (residual monomer) from PVC packaging into foods is possible: VC was detected in soft drinks, alcoholic drinks, fats, oil, vinegar.
VC concentration in vinegar in the USA before 1975: n.d. to 8.4 ppm
VC concentration in edible fats stored in PVC containers: 21 ppb

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
28.05.2002 (54) (92)

Remark : Migration of VC from PVC packaging is probably negligible nowadays, since the residual monomer content of the polymer has been reduced. Solvay S.A. states that resudual monomer is now always < 10 ppb, in line e.g. with EEC Directive and other regulations.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
28.05.2002 (76)

Remark : Drinking water, after standing for 48 h in PVC pipes containing a VC residual monomer content of 500 ug/g, showed VC concentrations up to 30 ug/l.

Solvay S.A. states that as of 1994, residual monomer content in PVC pipes is < 0.5 ppm and no more 500 ppm (a factor of 1000 less).

In 2001, the levels of VCM present in PVC pipe is much lower (McLellan, 2001).

McLellan CJ. 2001. Test results of residual vinyl chloride monomer (RCM) measurements from polyvinyl (PVC) pipes and fittings. (NSF International)

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
28.05.2002 (93)

Remark : Tetrachloroethylene (PCE) can be transformed by reductive dehalogenation to trichloroethylene (TCE), dichloroethylene, and VC under aerobic conditions. In addition, 14C-PCE was at least partially mineralized to CO2 (24 % in a continuous flow fixed-film methanogenic column with a liquid detention time of 4 days; under different methanogenic conditions nearly quantitative conversion of PCE to VC was observed).

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
28.05.2002 (94)

Remark : Residual vinyl chloride in polyvinyl chloride used for packaging food in the EEC is limited to 1 ppm and there is also the requirement that vinyl chloride should be undetectable in the food so packaged, using an analytical method with a detection limit of 10 ppb. When last surveyed, in 1979, UK PVC-packaged foods easily complied with this requirement, with vinyl chloride levels in foods found to be less than 2 ppb.
A new survey was performed by ICI plc, Norsk-Hydro Polymers Ltd and MAFF Food Science Laboratories in the United Kingdom in 1986. A number of products (mostly mineral waters, orange drinks or vegetable oils) were purchased from supermarkets and subjected to analysis for vinyl chloride by headspace gas chromatography with flame-ionisation detection (GC/FID) (ICI). Detection limits achieved varied between the three laboratories, but were always less than 2 ppb. The ICI laboratories, using the EEC GC/FID method, found some samples of vetable oil apparently showing more than 2 ppb of vinyl chloride, but reanalysis of these samples using GC/MS demonstrated vinyl chloride levels of below 1 ppb.

Source : Norsk Hydro
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
28.05.2002 (95)

Remark : In France, controls of residual monomer in food packaging and content are performed regularly since 1975. Measurements performed in 1987 failed to detect traces of monomer (analytical thresholds: 0.1 to 0.5 ppm for materials, 2 to 3 ppb for liquids, 5 ppb for oils).

Source : Solvay S.A., Bruxelles
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
28.05.2002 (96)

Remark : Method: Analytical measurements, GC-MS method, performed in 1991.
GLP: No data

Medium: Bottled water
The migration of vinyl chloride into drinking water bottled into PVC was studied in relation to storage time. Vinyl chloride concentrations rose progressively in relation to the time after bottling to reach about 160 ng/l after 180 days. The migration was failry constant for the 4 first months and decreased thereafter. Levels in bottles taken from the Italian market were comprised between 10 to 83
ng/l.

Source : Solvay S.A., Bruxelles
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
28.05.2002 (97)

Result : Radiolabeled vinyl chloride was evaluated in laboratory model ecosystems for environmental fate, degradation pathways, bioconcentration, and food chain accumulation. The comparative effects of microsomal detoxications were evaluated using the inhibitor piperonyl butoxide. Vinyl chloride was not accumulated because of its high volatility

Reliability : (2) valid with restrictions
28.05.2002 (98)

4. Ecotoxicity **Id** 75-01-4
Date 18.06.2002

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	other: closed system
Species	:	Brachydanio rerio (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
Analytical monitoring	:	Yes
NOEC	:	c = 128
LC50	:	c = 210
Method	:	OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year	:	1992
GLP	:	Yes
Test substance	:	other TS
Result	:	

Nominal/measured concentrations: Measured concentrations were lower than nominal concentrations between day 0 and day 1 (nominal/analytical (mg/L), 31/21, 63/38, 125/70, 250/140 and 500/260). There was good agreement between nominal and analytical concentrations during last part of the experiment. Mean concentrations over 96 hour periods were 1.25 (control), 34.9, 59.4, 128, 220 and 388 mg/l.
Biological results were based on mean measured concentrations.

Mortality: No deaths or aberrant behavior were observed over 96 hours in controls or animals exposed to 34.9, 59.4 or 128 mg/l. Aberrant behavior was observed after 3 hrs of exposure to 220 or 388 mg/l. 70% mortality occurred in fish exposed to 220 mg/l by 96 hours. All fish exposed to 388 mg/l died within 48 hours. LC50.24h, LC50.48h, LC50.72h and LC50.96h were 240 mg/l, 210 mg/l, 210 mg/l and 210 mg/l, respectively. The minimum test concentration for 100% mortality was 388 mg/l. The NOEC based on mortality was 128 mg/l.

Length of Fish: Length of surviving fish was not altered by exposure to vinyl chloride.

Validity Measures: The pH ranged from 7.5-8.0. The dissolved oxygen concentration varied between 5.1 and 9.0 mg/l. The temperature ranged between 21.1 and 22.0 degrees C

Source :

PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Test condition :

Test Organisms: Brachydanio rerio originated from a commercial supplier in Ruinemans, Monfoort, The Netherlands. Fish were held in a plastic container (60 x 80 x 50 cm) containing 100 l reconstituted ISO-water which was continuously filtered. Temperature was maintained at 22 1 1: C. Fish were fed with Tetramin and waterfleas before initiating the test. The total weight of 20 fish was 4.2 g (0.21 g/fish)

Stock Solution: A Teflon-coated aluminum bag was filled with aerated ISO-water. Vinyl chloride was introduced via a plastic tube attached to the gas cylinder and a hypermodermic syringe attached to the bag via a septum. The amount of vinyl chloride added to the bag was determined by weighing it before and after gas introduction. Three different stock solutions of 1.0 g/l were prepared. One (15 liters) was used on day 0, the second (10 liters) on day 1, and the third (10 liters) on days 2 and 3.

Test Solution/ System:. Flasks (3200 ml) were partially filled with ISO-water

and and stock vinyl chloride solution was added (0, 100, 200, 400, 800 or 1600 ml) to make concentrations of 0, 31, 63, 125, 250 and 500 mg/l. Three test flasks (3200 ml) were prepared per concentration. Two fish were added to two of the flasks and 3 fish were added to the other. Flasks were then completely filled with ISO-water and tightly closed with aluminum caps with a rubber septum. Test solutions were renewed daily. Fish were not fed during the test.

Biological Observations and Measurements: Mortality and behavior and appearance of fish were noted 3, 24, 48, 72 and 96 hours after test initiation. Dead fish were removed every 24 hours. The length of the smallest and largest fish at each concentration was measured at the end of the test. Dissolved oxygen concentration, temperature and pH were measured in control flasks and flasks containing 500 mg/l before and after renewal at 24, 48, 72 and 96 hours (also at time 0 in controls).

Monitoring of Test Substance Concentration: Samples of test solutions (closed) were taken before and after renewal at 0, 24, 48, 72 and 96 hours and analyzed by gas chromatography. A calibration curve was prepared using standards of 0.984, 9.84, 98.4 and 984 mg vinyl chloride/liter DMSO.

Validity: The test was considered to be valid if the dissolved oxygen concentration was >= 60% of the air saturation value and control mortality was <= 10%.

Statistical Methods: LC50s were calculated using PROBIT of SAS. The NOEC was the highest test concentration that did not cause a significantly different response from controls during the test (Fisher's exact test)

Test substance :

Purity was > 99%. Water solubility was 1.1 g/l

Reliability : (1) valid without restriction

12.04.2002 (99)

Type : Static
Species : Lepomis macrochirus (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
Analytical monitoring : Yes
LC50 : c = 1220
Method : other
Year : 1971
GLP : no data
Test substance : other TS
Remark :

Methyl chloride, ethyl chloride, ethylene dichloride, and Toxaphene were also tested

Result :

The average concentrations of vinyl chloride measured in the test samples to which vinyl chloride was bubbled for 3, 5, 10, 15 and 18 minutes were 682, 576, 894, 1680, and 1760 ppm. There were no mortalities at the lower three concentrations and 100% mortality (within 6 hr) at the higher two concentrations. Dissolved O2 of test water for the higher two concentrations was 8.0 and 7.6 mg/L, respectively. The pH of the water was 7. The four-day Tolerance limit (TL)50 was 1220 ppm. The TL50 is equivalent to an LC50.

Source :

PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Test condition :

Healthy fingerlings with an average length ot 35 to 75 mm were used. All fish were kept under observation in large, aerated tanks at 18 degrees C for at least 10 days prior to testing, and were fed brine shrimp or minnows until 3 days prior to testing. All stock and test tanks contained reconstituted, deionized water to which 30 mg calcium sulfate, 30 mg magnesium sulfate, 48 mg sodium bicarbonate and 2 mg potassium chloride was added. Test vessels were lined with disposable polyethylene bags and filled with 12.5 l well-aerated water. 10 fish were added to each tank. After a 24 hour acclimation period, test material was bubbled into each tank for 3, 5, 10, 15, or 18 minutes. Water samples were taken at 1 minute and 1, 6, 24, 48, 72 and 96 hours after bubbling, and concentrations of test material in the samples were determined using a gas chromatograph. Fish were observed for 96 hours. The concentration of dissolved O2 and the pH of the test water was measured when mortalities occurred. The four-day median tolerance limit (TL50) was calculated using the method of Litchfield and Wilcoxon

Test substance :

Vinyl chloride from Ethyl Corporation. Purity was not noted

Reliability : (2) valid with restrictions
12.04.2002 (100)

Type : static
Species : Micropterus salmoides (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
Analytical monitoring : yes
LC50 : c = 1060
Method : other
Year : 1971
GLP : no data
Test substance : other TS
Remark :

Methyl chloride, ethyl chloride, ethylene dichloride, and Toxaphene were also tested

Result :

The average concentrations of vinyl chloride measured in the test samples to which vinyl chloride was bubbled for 3, 5, 10, 15 and 18 minutes were 647, 1024, 1596, 1221, and 2185 ppm, respevtively. The number of fish surviving exposure to 647, 1024 or 1596 ppm was 80%, 90% and 20%, respectively. Exposure to 1221 or 2185 ppm produced 100% lethality within 48 and 6 hr, respectively. Dissolved O2 of test water containing 1596, 1221 or 2185 ppm vinyl chloride was 4.1-5.8, 4.1-4.2, and 7.5 mg/L, respectively. The pH of the water containing these concentraion was 7. The 4 day Tolerance Limits (TL)50 was calculated as 1060 ppm. TL50 is identical to LC50.

Source :

PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Test condition :

Healthy fingerlings with an average length ot 35 to 75 mm were used. All fish were kept under observation in large, aerated tanks at 13 degrees C for at least 10 days prior to testing, and were fed brine shrimp or minnows until 3 days prior to testing. All stock and test tanks contained reconstituted, deionized water to which 30 mg calcium sulfate, 30 mg magnesium sulfate, 48 mg sodium bicarbonate and 2 mg potassium chloride was added. Test vessels were lined with disposable polyethylene bags and filled with 12.5 l well-aerated water. 10 fish were added to each tank. After a 24 hour acclimation period, test material was bubbled into each tank for 3, 5, 10, 15, or 18 minutes. Water samples were taken at 1

minute and 1, 6, 24, 48, 72 and 96 hours after bubbling, and concentrations of test material in the samples were determined using a gas chromatograph. Fish were observed for 96 hours. The concentration of dissolved O2 and the pH of the test water was measured when mortalities occurred. The four-day median tolerance limit (TL50) was calculated using the method of Litchfield and Wilcoxon

Test substance :

Vinyl chloride from Ethyl Corporation. Purity was not noted

Reliability : (2) valid with restrictions

12.04.2002 (100)

Type : Other
Species : Esox lucius (Fish, fresh water)
Exposure period : 10 day
Unit : mg/l
Analytical monitoring : Yes
LC100 : = 388
Method : other
Year : 1977
GLP : no data
Test substance : no data
Result :

100% mortality occurred over 10 days in fish exposed to vinyl chloride. One control fish died over a 73-day period. Exposed fish exhibited a loss of scales which was followed by appearance of gray-white skin ulcerations. The lack of neutrophils or ulcer-inducing bacteria in involved areas suggests that bacterial infection played no role in development of the lesions

Source :

PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Test condition :

Fifteen fish were exposed in the same tank. Vinyl chloride gas was bubbled continuously through the water to form a saturated solution (388 mg/l or 388 ppm). Fish were fed live minnows once per week. Fish ranged from 6 to 19 inches in length. Water was continuously filtered through Dynoflo filters with filter floss (changed ever 3 days). Control fish (20) were placed in an uncontaminated lake (Benedictine Lake, IL). Concentrations of VC were determined using a gas chromatograph

Reliability : (2) valid with restrictions

20.02.2001 (101)

Type : other: model
Species : other: fish
Exposure period : 96 hour(s)
Unit : mg/l
Analytical monitoring : No
LC50 : c = 191
Method : other: ECOSAR modeling
Year : 2001
GLP :
Test substance :
Remark : The ECOSAR program was run with the following inputs: SMILES: CCCl, Molecular formula: C2H5Cl1, Molecular Weight: 64.52, Log Kow: 1.36 (user entered); water solubility: 1290 mg/L (calculated). The formula for monochloroethane was used instead of vinyl chloride to force the program to calculate values based on a classification of vinyl chloride as a "neutral organic" instead of a "vinyl/allyl halide" Vinyl chloride behaves metabolically and biologically more like an alkane than a vinyl/allyl halide in

aquatic systems. ECOSAR values calculated on the classification of vinyl chloride as a neutral organic gives results consistent with measured values.

Reliability : (2) valid with restrictions
15.05.2002

Type : static
Species : Leuciscus idus melanotus (Fish, fresh water)
Exposure period : 48 hour(s)
Unit : mg/l
Analytical monitoring :
LC0 : = 250
LC50 : = 356
LC100 : = 438
Method : other: according to Mann, H.
Year :
GLP :
Test substance :
Remark : Under comparable conditions, in another laboratory it was found:
LC0 = 250 mg/l
LC50 = 406 mg/l
LC100= 500 mg/l
Source : Elf Atochem
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
28.05.2002 (102)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : other: model
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
Analytical monitoring : no
LC50 : c = 196
Method : other: ECOSAR 2001
Year : 2001
GLP :
Test substance : as prescribed by 1.1 - 1.4
Method : Class Neutral Organics used.
Result : The ECOSAR program was run with the following inputs: SMILES: CCCl, Molecular formula: C2H5Cl1, Molecular Weight: 64.52, Log Kow: 1.36 (user entered); water solubility: 1290 mg/L (calculated). The formula for monochloroethane was used instead of vinyl chloride to force the program to calculate values based on a classification of vinyl chloride as a "neutral organic" instead of a "vinyl/allyl halide" Vinyl chloride behaves metabolically and biologically more like an alkane than a vinyl/allyl halide in aquatic systems. ECOSAR values calculated on the classification of vinyl chloride as a neutral organic gives results consistent with measured values.
Reliability : (2) valid with restrictions
15.05.2002

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

4. Ecotoxicity **Id** 75-01-4
Date 18.06.2002

Species	:	Scenedesmus quadricauda (Algae)
Endpoint	:	biomass
Exposure period	:	192 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no
Toxic Limit Conc:	:	m = 710
Method	:	other:growth inhibition
Year	:	1976
GLP	:	no data
Test substance	:	no data
Remark	:	The density of vinyl chloride at 27 degrees C was calculated by PCA Services Inc. by linearly interpolating reported densities at 20 and 40 degrees C (0.911 g/ml and 0.872 g/ml, respectively)
Source	:	PCA Services, Inc PCA Services, Inc. Kingsport, TN
Test condition	:	Two series of 50-ml test solutions of vinyl chloride in twice-distilled, neutralized water (pH 7.0, 27 degrees C) were made up in 300-ml erlenmeyer flasks by means of serial dilution with concentrations of vinyl chloride successively decreasing by a factor of two. Volumes of stock vinyl chloride solution added to the flasks were 40 ml, 20 ml, 10 ml, 5 ml, 2.5 ml, 1.25 ml, 0.625 ml, 0.312 ml, 0.156 ml, 0.078 ml, 0.039 ml, 0.020, 0.010 ml and 0.005 ml. Based on a density of 0.893 g/ml at 27 degrees C, the final concentrations of vinyl chloride in each flask were 714400 mg/l, 357200 mg/l, 178600 mg/l, 89300 mg/l, 44650 mg/l, 22325 mg/l, 11162 mg/l, 5581 mg/l, 2791 mg/l, 1393 mg/l, 696 mg/l, 348 mg/l, 174 mg/l and 87 mg/l . One series of solutions served as a control for the light meter, while the second series contained standard solutions of Scenedesmus quadricauda with stock nutrients. Test solution containers were sealed as they were prepared. Inhibition of biomass growth was determined by measuring turbidity after the test period using a light meter. The TGK was determined using a half-log plot of light extinction versus concentration of vinyl chloride
Reliability	:	(2) valid with restrictions

13.01.2001 (103)

Species	:	Chlamydomonas reinhardtii (Algae)
Endpoint	:	other: chlorophyll A fluoresence
Exposure period	:	
Unit	:	mg/l
Analytical monitoring	:	
Toxicity Threshold:	:	c = 580
Method	:	other:estimation
Year	:	1998
GLP	:	no data
Test substance	:	other TS
Result	:	For chemicals exerting narcotic effects (ie all except H2S), toxicity could be predicted (within a factor of 3) based on the Kows of the chemicals. The theoretical toxicity threshold of vinyl chloride was calculated to be 580 mg/l (using a log Kow of 1.27). This is an estimated value based on studies with other chemicals.
Source	:	PCA Services, Inc PCA Services, Inc. Kingsport, TN
Test condition	:	Concentrations of approximately 40 chemicals found in leachates (including vinyl chloride) from three hazardous waste sites were

determined analytically. Leachates from the waste sites and 9 individual chemicals found in the leachates (H2S, toluene, 4-methyl-2-pentanone, trichloroethene, tetrachloroethene, 1,1,1-trichloroethane, ethyl benzene, m/p-xylene, and 1,2,4-trichlorobenzene) were tested for their ability to inhibit flourescence of Chlamydomonas reinhardtii (strain 11-32a SAG (+)). Algae were incubated with the leachates and/or chemicals for 2 hours at 20 degrees C in the dark in gas-tight, brown glass vessels. Fluoresence of algae was measured before and after an actinic light flash. The total area under the Kautsky curve during the first 400 ms after the flash was used as the toxicity parameter. The toxicity threshold (TT) was defined as the lowest concentration of a compound altering the area under the Kautsky curve by a threefold maximum standard deviation of control samples. Since standard deviations of controls were below 3.3%, the TT corresponded to a 10% alteration of the area under the curve.

The mathematical relationship between the log Kow of the tested compounds and the TT fit the following equation:

log TT = -0.95 log Kow +2.1 (r = 0.978)

This equation was used to derive theoretical toxicity thresholds of the components of the leachates that were not individually tested (including vinyl chloride)

Test substance :

Landfill leachates containing approximately 40 different chemicals (including vinyl chloride), H2S, toluene, 4-methyl-2-pentanone, trichloroethene, tetrachloroethene, 1,1,1-trichloroethane, ethyl benzene, m/p-xylene, 1,2,4-trichlorobenzen

Reliability : (2) valid with restrictions
15.05.2002 (104)

Species : other algae: green algae
Endpoint :
Exposure period : 96 hour(s)
Unit : mg/l
Analytical monitoring : no
EC50 : c = 118
Method : other: ECOSAR modeling
Year : 2001
GLP :
Test substance :
Remark : The ECOSAR program was run with the following inputs: SMILES: CCCl, Molecular formula: C2H5Cl1, Molecular Weight: 64.52, Log Kow: 1.36 (user entered); water solubility: 1290 mg/L (calculated). The formula for monochloroethane was used instead of vinyl chloride to force the program to calculate values based on a classification of vinyl chloride as a "neutral organic" instead of a "vinyl/allyl halide" Vinyl chloride behaves metabolically and biologically more like an alkane than a vinyl/allyl halide in aquatic systems. ECOSAR values calculated on the classification of vinyl chloride as a neutral organic gives results consistent with measured values.
Reliability : (2) valid with restrictions
29.05.2002

Species : Anacystis aeruginosa (Algae)
Endpoint :
Exposure period : 48 hour(s)
Unit : mg/l
Analytical monitoring : no data

4. Ecotoxicity **Id** 75-01-4
Date 18.06.2002

TT	:	= 105
Method	:	other: static, 27 degree C, pH 7.4
Year	:	1980
GLP	:	no data
Test substance	:	no data
Remark	:	TT = Toxicity Threshold
Source	:	Solvay S.A., Bruxelles Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

28.05.2002 (105)

Species	:	other algae: Chilomonas paramecium
Endpoint	:	growth rate
Exposure period	:	48 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no data
EC5	:	= 943
Method	:	other: static, 20 degree C, pH 6.9
Year	:	1980
GLP	:	no data
Test substance	:	
Source	:	Solvay S.A., Bruxelles Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

28.05.2002 (105)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type	:	aquatic
Species	:	Pseudomonas putida (Bacteria)
Exposure period	:	16 hour(s)
Unit	:	mg/l
Analytical monitoring	:	
EC5	:	>= 135
Source	:	Elf Atochem Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

20.05.2002 (106)

Type	:	aquatic
Species	:	activated sludge, domestic
Exposure period	:	
Unit	:	
Analytical monitoring	:	
Method	:	other
Year	:	1980
GLP	:	no data
Test substance	:	no data
Remark	:	The influence of VC on the aerobic step of waste water treatment plants was studied in a batch procedure termed "anaerobic toxicity assay" (ATA) and in a semicontinuous bioassay using a continuously stirred laboratory digester (1.5 l) at 35 degree C. In the ATA, 20 ml of sludge from a laboratory digester were added to 30 ml of a nutrient and buffer solution to which 0.1 ml of ethanol were added as substrate. In the semicontinuous

bioassay, digesters were initially seeded with digested municipal sludge.

In the ATA procedure, 5.4 mg/l VC was marginally inhibitory with respect to gas production, 32 mg/l were strongly inhibitory. A concentration of approximately 40 mg/l was required for 50 % inhibition over 3.5 days. In the semicontinuous digestion, even the highest concentration of VC (64 mg/l) did not cause adverse digester performance.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
28.05.2002 (107)

Type : aquatic
Species : Microcystis aeruginosa (Bacteria)
Exposure period : 7 day
Unit : mg/l
Analytical monitoring : no
EC3 : >= 105
Method :
Year :
GLP : no
Test substance :
Source : Elf Atochem
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
28.05.2002 (108)

Type : aquatic
Species : Uronema parduzci (Protozoa)
Exposure period : 72 hour(s)
Unit : mg/l
Analytical monitoring : no
EC5 : >= 1050
Method :
Year :
GLP : no
Test substance :
Source : Elf Atochem
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
28.05.2002 (109)

Type : aquatic
Species : other bacteria: anaerobic bacteria, unspecified
Exposure period : 1 day
Unit : mg/l
Analytical monitoring : no data
IC50 : = 40
Method : other: static, 35 degree C
Year :
GLP : no data
Test substance :
Remark : IC50 refers to gas production.
Strong inhibition at 32 mg/l, marginal inhibition at 5.4 mg/l
Source : Solvay S.A., Bruxelles
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
28.05.2002 (110)

4.5.1 CHRONIC TOXICITY TO FISH

Species	:	other
Endpoint	:	
Exposure period	:	
Unit	:	
Analytical monitoring	:	
Remark	:	Limited chronic impact due to high volatility and low log Pow of the compound is expected.
Source	:	Solvay S.A., Bruxelles Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

30.05.1994

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Species	:	other
Endpoint	:	
Exposure period	:	
Unit	:	
Analytical monitoring	:	
Remark	:	Limited chronic impact due to high volatility and low log Pow of the compound is expected.
Source	:	Solvay S.A., Bruxelles Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

30.05.1994

4.6.1 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

Species	:	other terrestrial plant
Endpoint	:	other
Exposure period	:	
Unit	:	
Method	:	other
Year	:	1982
GLP	:	no data
Test substance	:	no data
Remark	:	VC was rated as a weak mutagen in this test (exposure 6 h at 75 ppm (194 mg/m3) VC). Comparative open-field studies of industrial plants and "clean air areas" in the USA showed a clear dependence of the mutation rate on the test site. (No differentiations of the individual components)
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition	:	Tradescantia stamen hair test in clone 4430 (diploid interspecific hybrid of pink and blue flowering parents with blue being dominant). Visible marker used in the test: phenotypic change in pigmentation from blue to pink

(isolated or grouped pink cells in stamen hairs) in mature flowers. Material treated: fresh cuttings containing young inflorescences with 15 to 18 flower buds in a range of developmental stages. Following exposure, the cuttlings are grown in Hoagland's nutrient solution and flowers are analysed each day for 3 weeks. Induced pink-event rates are counted.

Reliability : (3) invalid
29.05.2002 (111) (112)

4.6.3 TOXICITY TO OTHER NON-MAMM. TERRESTRIAL SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5. Toxicity **Id** 75-01-4
Date 18.06.2002

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Value	:	> 4000 mg/kg bw
Method	:	other: no data
Year	:	1973
GLP	:	no
Test substance	:	other TS
Remark	:	Stamm: SPF-Wistar, Concentration: 50 ml/kg = ca. 4000 mg/kg Result: With the maximum quantity of 50 ml/kg body weight no animal died. Slight effects were noted. No additional information provided.
Source	:	Hoechst AG Frankfurt am Main Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	Vinyl chloride 8.6%ig was examined in Sesame oil.
Reliability	:	(2) valid with restrictions

20.05.2002 (113)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	70
Vehicle	:	
Exposure time	:	2 hour(s)
Value	:	= 390 mg/l
Method	:	other
Year	:	1975
GLP	:	no data
Test substance	:	no data
Remark	:	Concentration is based on nominal and not analytical. No additional information provided.
Result	:	Number of deaths at each dose: 375 mg/l (7/30), 400 mg/l (8/10), 425 mg/l (9/10), 500 mg/l (9/10), 525 mg/l (10/10). The majority of deaths at each dose occurred during the first hour of exposure. Clinical Signs: Death of animals preceded by excitement, contractions, convulsions, and respiratory excitement followed by failure. Necropsy Findings: General congestion of all internal organs. Potential Target Organs: Lungs, liver, kidney No additional information supplied.
Source	:	PCA Services, Inc PCA Services, Inc. Kingsport, TN
Test substance	:	

Test Organisms: Age, weight and source were not indicated

Number of animals per dose:30 animals were exposed to 15% (375.0 mg/l). Four groups of 10 animals each were exposed to 16% (400 mg/l), 17% (425.0 mg/l), 20% (500.0 mg/l), or 21% (525.0 mg/l).

Controls: None

Type of exposure: Exposure occurred according to Krakov's method in gas chambers of the Pravdintype (580 l). Gas was continuously stirred in the chamber by an inside pellet. Gas was measured volumetrically with a Zimmermann type spirometer. Animals were exposed for up to 2 hours.

Concentrations: 15% (375.0 mg/l),16% (400 mg/l), 17% (425.0 mg/l), 20% (500.0 mg/l), or 21% (525.0 mg/l).

Examinations: Clinical observations, necrops

Reliability : (2) valid with restrictions
21.05.2002 (114)

Type : LC50
Species : mouse
Strain :
Sex :
Number of animals : 446
Vehicle :
Exposure time : 2 hour(s)
Value : = 294 mg/l
Method : other
Year : 1975
GLP : no data
Test substance : no data
Remark :

Preliminary study in 100 animals exposed to 4.29-5.15% (107.25-128.75 mg/l) without ventilation showed LD100 =4.75% (118.75 mg/l Concentration is based on nominal and not analytical. No additional information provided.

Result :

Number of deaths at each dose: 225 mg/l (0/40), 250 mg/l (0/40), 275 mg/l (15/76), 287.5 mg/l (37/90), 300 mg/l (21/39), 325 mg/l (13/20), 350 mg/l (18/20), 362.5 mg/l (19/20), 375 mg/l (61/61), 500 mg/l (40/40).

Clinical Signs: Death of animals preceded by excitement, contractions, convulsions, and respiratory excitement followed by failure.

Necropsy Findings: General congestion of all internal organs.

Potential Target Organs: Lungs, liver, kidney

No additional information supplied.

Source :

PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Test substance :

Test Organisms: Age, weight and source were not indicated

Number of animals per dose: N=40, 40, 76, 90, 39, 20, 20, 20, 61 and 40 for exposure to 9% (225.0 mg/l), 10% (250.0 mg/l), 11% (275.0 mg/l), 11.5% (287.5 mg/l), 12% (300 mg/l), 13% (325.0 mg/l), 14% (350.0 mg/l),

14.5% (362.5 mg/l), 15% (375 mg/l) or 20% (500.0 mg/l), respectively

Controls: None

Type of exposure: Exposure occurred according to Krakov's method in gas chambers of the Pravdintype (580 l). Gas was continuously stirred in the chamber by an inside pellet.
Animals were exposed for up to 2 hours.

Concentrations: 9% (225.0 mg/l), 10% (250.0 mg/l), 11% (275.0 mg/l), 11.5% (287.5 mg/l), 12% (300 mg/l), 13% (325.0 mg/l), 14% (350.0 mg/l), 14.5% (362.5 mg/l), 15% (375 mg/l) and 20% (500.0 mg/l)

Examinations: Clinical observations , necrops

Reliability : (2) valid with restrictions
21.05.2002 (114)

Type : LC50
Species : rabbit
Strain :
Sex :
Number of animals : 20
Vehicle :
Exposure time : 2 hour(s)
Value : = 595 mg/l
Method : other
Year : 1975
GLP : no data
Test substance : no data
Remark : Concentration is based on nominal and not analytical. No additional information provided.
Result :

Number of deaths at each dose: 500 mg/l (0/4), 575 mg/l (1/4), 600 mg/l (2/4), 625 mg/l (3/4), 700 mg/l (4/4).

Clinical Signs: Death of animals preceded by excitement, contractions, convulsions, and respiratory excitement followed by failure.

Necropsy Findings: General congestion of all internal organs.

Potential Target Organs: Lungs, liver, kidney

No additional information supplied.

Source :

PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Test substance :

Test Organisms: Age, weight and source were not indicated

Number of animals per dose: Five groups of 4 animals each were exposed to 20% (500.0 mg/l), 23% (575.0 mg/l), 24% (600.0 mg/l), 25% (625.0 mg/l) or 28% (700.0 mg/l).

Type of exposure: Exposure occurred according to Krakov's method in gas chambers of the Pravdintype (580 l). Gas was continuously stirred in the chamber by an inside pellet.
Animals were exposed for up to 2 hours.

Concentrations: 20% (500.0 mg/l), 23% (575.0 mg/l), 24% (600.0 mg/l),

25% (625.0 mg/l) or 28% (700.0 mg/l).

Examinations: Clinical observations, necrops

Reliability : (2) valid with restrictions
21.05.2002 (114)

Type : LC50
Species : guinea pig
Strain :
Sex :
Number of animals : 30
Vehicle :
Exposure time : 2 hour(s)
Value : = 595 mg/l
Method : other
Year :
GLP : no data
Test substance : no data
Remark : Concentration is based on nominal and not analytical. No additional information provided.
Result :

Number of deaths at each dose: 500 mg/l (0/4), 575 mg/l (1/6), 600 mg/l (9/12), 650 mg/l (3/4), 700 mg/l (4/4). The majority of deaths occurred during first hour of exposure.

Clinical Signs: Death of animals preceded by excitement, contractions, convulsions, and respiratory excitement followed by failure.

Necropsy Findings: General congestion of all internal organs.

Potential Target Organs: Lungs, liver, kidney

No additional information supplied.

Source :

PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Test substance :

Test Organisms: Age, weight and source not indicated

Number of animals per dose: N= 4, 6, 12, 4 and 4 for exposure to 20% (500.0 mg/l), 23% (575.0 mg/l), 24% (600.0 mg/l), 26% (650.0 mg/l) or 28% (700.0 mg/l), respectively.

Type of exposure: Exposure occurred according to Krakov's method in gas chambers of the Pravdintype (580 l). Gas was continuously stirred in the chamber by an inside pellet.
Animals were exposed for up to 2 hours.

Concentrations: 20% (500.0 mg/l), 23% (575.0 mg/l), 24% (600.0 mg/l), 25% (625.0 mg/l) or 28% (700.0 mg/l).

Examinations: Clinical observations, necrops

Reliability : (2) valid with restrictions
21.05.2002 (114)

Type : other: 30 minute exposure
Species : rat
Strain :
Sex :

5. Toxicity **Id** 75-01-4
Date 18.06.2002

Number of animals	:	
Vehicle	:	
Exposure time	:	30 minute(s)
Method	:	
Year	:	1960
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Groups of 5 rats were exposed for 30 minutes to 0, 10, 20 or 30 per cent vinyl chloride in air. The concentration of vinyl chloride during the exposure was not measured. At the end of 30 minutes exposure the test animals were immediately removed to fresh air. Animals which died either during the exposure or after a delay period were autopsied soon after death. Two weeks after the exposure surviving test animals and controls were sacrificed and examined for gross pathological changes. Selected tissues including lungs, liver, kidney and heart from all animals, were preserved in formalin and sections stained with hematoxylin and eosin.
Result	:	100,000 ppm for 30 minutes: Increased motor activity after 10 minutes. Pronounced tremor, unsteady gait and muscular incoordination after 15 minutes. Rats were prostrate after 20 minutes and sedated after 30 minutes. All recovered within 5 minutes of cessation of exposure. Two weeks after exposure, slight congestion was still present in the lung following histopathological examination. 200,000 ppm for 30 minutes: Unconscious with rapid irregular breathing after 10 minutes. All recovered within 5 minutes of cessation of exposure. Congestion was noted two weeks after exposure in the lungs following gross and histopathological examination. 300,000 ppm for 30 minutes: Unconscious with rapid irregular breathing after 5 minutes. Breathing slow and shallow after 10 minutes. All animals were dead within 15 minutes. Congestion of the lungs, kidneys and liver was observed. In addition, hemorrhagic areas were observed in the lung.
Reliability	:	(2) valid with restrictions

12.04.2002 (115)

Type	:	other: 30 minute exposure
Species	:	mouse
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Exposure time	:	30 minute(s)
Method	:	
Year	:	1960
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Groups of 5 mice were exposed for 30 minutes to 0, 10, 20 or 30 per cent vinyl chloride in air. The concentration of vinyl chloride during the exposure was not measured. At the end of 30 minutes exposure the test animals were immediately removed to fresh air. Animals which died either during the exposure or after a delay period were autopsied soon after death. Two weeks after the exposure surviving test animals and controls were sacrificed and examined for gross pathological changes. Selected tissues including lungs, liver, kidney and heart from all animals, were preserved in formalin and sections stained with hematoxylin and eosin.
Result	:	100,000 ppm for 30 minutes:

Increased motor activity after 10 minutes. Pronounced tremor, unsteady gait and muscular incoordination after 15 minutes. Mice were prostrate after 20 minutes and sedated after 30 minutes. All recovered within 5 minutes of cessation of exposure. Two weeks after exposure, very slight engorgement of the pulmonary vessels in the lung and degenerative changes in the tubular epithelium of the kidney with hydropic swelling in one mouse were observed following histopathological examination.

200,000 ppm for 30 minutes:
Unconscious with rapid irregular breathing after 10 minutes. After cessation of exposure one mouse was dead. All others recovered within 5 minutes of cessation of exposure. Pulmonary congestion was evident on gross examination in the mouse that died during exposure. In the animals sacrificed two weeks after exposure, congestion was observed in the lungs following gross and histopathological examination.

300,000 ppm for 30 minutes:
Unconscious with rapid irregular breathing after 5 minutes. All animals were dead within 10 minutes. Congestion of the lungs, kidneys and liver was observed. In addition, hemorrhagic areas were observed in the lung.

Reliability : (2) valid with restrictions
12.04.2002 (115)

Type : other: 30 minute exposure
Species : guinea pig
Strain :
Sex :
Number of animals :
Vehicle :
Exposure time : 30 minute(s)
Method :
Year : 1960
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Method : Groups of 5 guinea pigs were exposed for 30 minutes to 0, 10, 20, 30 or 40 per cent vinyl chloride in air. The concentration of vinyl chloride during the exposure was not measured. At the end of 30 minutes exposure the test animals were immediately removed to fresh air. Animals which died either during the exposure or after a delay period were autopsied soon after death. Two weeks after the exposure surviving test animals and controls were sacrificed and examined for gross pathological changes. Selected tissues including lungs, liver, kidney and heart from all animals, were preserved in formalin and sections stained with hematoxylin and eosin.
Result : 100,000 ppm for 30 minutes:
Increased motor activity after 10 minutes. Pronounced tremor, unsteady gait and muscular incoordination after 15 minutes. After 30 minutes, guinea pigs were prostrate with tremors with one animal unconscious. All recovered within 5 minutes of cessation of exposure. Two weeks after exposure, lungs of treated animals were slightly more hyperemic than control animals.

200,000 ppm for 30 minutes:
Unconscious with marked twitching after 10 minutes. After 15 minutes, all animals were in deep narcosis with irregular and rapid respiration. After cessation of exposure, all recovered within 20 minutes. Pulmonary congestion was evident on gross and histopathologic examination.

300,000 ppm for 30 minutes:
Unconscious with twitching after 5 minutes. After 15 minutes, respirations

were slow and shallow. Twitching of extremities still noted. After 30 minutes, guinea pigs exhibited deep narcosis with slow, shallow breathing. After cessation of exposure, all recovered within 25 minutes. One guinea pig died within 24 hours following exposure with congestion of the lungs with hemorrhages and distended liver observed. Histopathologically, the liver of this animal showed severe fatty degeneration. In the surviving animals sacrificed two weeks after exposure, marked pulmonary congestion was present with hemorrhagic areas and edema. The liver of these animals gave the appearance of severe fatty degeneration but this was not confirmed with special stains.

400,000 ppm for 30 minutes:
Unconscious with slow, shallow breathing after 5 minutes. After 30 minutes, one guinea pig was dead and the remaining four were in deep narcosis. After cessation of exposure, the survivors recovered within 30 minutes. One of the four died within 24 hours of the exposure. The two which died showed marked congestion of the lungs with hemorrhages following gross and histopathological examination. In the surviving animals sacrificed two weeks after exposure, marked congestion of the lungs with hemorrhage was evident on both gross and microscopic examination.

Reliability : (2) valid with restrictions
12.04.2002 (115)

Type : LC50
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Exposure time : 2 hour(s)
Value : 200000 - 250000 ppm
Method : other: no data
Year : 1968
GLP : no
Test substance : other TS
Remark : Stamm: Wistar, weiblich
Source : Hoechst AG Frankfurt am Main
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : geprueft wurde monomeres Vinylchlorid
Reliability : (2) valid with restrictions
28.05.2002 (116)

Type : LC50
Species : mouse
Strain :
Sex :
Number of animals :
Vehicle :
Exposure time :
Method : other: no data
Year : 1927
GLP : no
Test substance : other TS
Source : Hoechst AG Frankfurt am Main
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test condition : geprueft wurde Vinylchlorid
Reliability : (4) not assignable

28.05.2002 (117)

Type	:	other
Species	:	mouse
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Exposure time	:	
Method	:	other
Year	:	1933
GLP	:	no data
Test substance	:	other TS
Remark	:	Minimal lethal concentration in mice after 10 min of exposure: 614 mg/l in air.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

28.05.2002 (118)

Type	:	other
Species	:	dog
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Exposure time	:	
Method	:	other
Year	:	1947
GLP	:	no data
Test substance	:	no data
Remark	:	Anesthesia was induced in dogs with VC at momentary concentrations of 50 Vol-% (Carr et al.: 15 - 90 %) in air. VC concentration was then reduced to 7 Vol-%. VC caused a rapid narcotic effect with rapid recuperation. Salivation, respiratory paralysis, and vomiting were observed after the narcosis. Severe cardiac arrhythmias and "incoordinated leg movements" occurred during narcosis.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

28.05.2002 (119) (120)

Type	:	LC50
Species	:	guinea pig
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Exposure time	:	2 hour(s)
Value	:	= 250000 ppm
Method	:	other: no data
Year	:	1968
GLP	:	no
Test substance	:	other TS
Remark	:	Examination of 2 animals
Source	:	Hoechst AG Frankfurt am Main Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

5. Toxicity **Id** 75-01-4
Date 18.06.2002

Test condition	:	monomeric vinyl chloride was examined
Reliability	:	(2) valid with restrictions
28.05.2002		(116)

Type	:	other
Species	:	guinea pig
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Exposure time	:	
Method	:	other
Year	:	1930
GLP	:	no data
Test substance	:	other TS
Remark	:	Applied VC concentrations: 0.5 to 40 %; Duration of exposure: 10 min to 8 h. Results: 40 % VC in air caused death within 10 - 20 min. Dissection of the animals revealed extensive blood congestion and edema of the lungs as well as hyperemia of the kidneys and liver.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
28.05.2002		(121)

5.1.3 ACUTE DERMAL TOXICITY

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	:	other
Concentration	:	
Exposure	:	
Exposure time	:	
Number of animals	:	
PDII	:	
Result	:	
EC classification	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	
Result	:	Liquid vinyl chloride would be expected to cause frostbite injury.
Reliability	:	(2) valid with restrictions
22.05.2002		(122)

5.2.2 EYE IRRITATION

Species	:	other
Concentration	:	
Dose	:	
Exposure Time	:	

Comment	:	
Number of animals	:	
Result	:	
EC classification	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	
Result	:	Liquid vinyl chloride would be expected to cause frostbite injury.
Reliability	:	(2) valid with restrictions

20.05.2002 (123)

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

Species	:	rat
Sex	:	male/female
Strain	:	Wistar
Route of admin.	:	oral feed
Exposure period	:	149 weeks (lifetime)
Frequency of treatment	:	4 consecutive hr/day (generally between 10 am and 2 pm)
Post obs. period	:	none
Doses	:	0.014, 0,13, 1.3 mg/kg bw
Control group	:	yes, concurrent vehicle
NOAEL	:	= .13 ml/kg bw
LOAEL	:	= 1.3 mg/kg bw
Method	:	other
Year	:	1991
GLP	:	no data
Test substance	:	other TS
Method	:	Study was conducted in accordance with generally accepted scientific principles
Remark	:	Reference dose for chronic oral exposure (RfD) and chronic inhalation exposure (RfC) are based on the NOAEL for liver cell polymorphism in this study (0.13 mg/kg/day) The toxicological significance of basophilic foci in low and mid-dose females is questionable because the incidence in controls (9%) was clearly lower than historical controls (18%). However, the incidence of basophilic foci in females from other studies performed during the same time period as the reported study ranged from 0-8%
Result	:	NOAEL (NOEL), LOAEL (LOEL): The NOAEL and LOAEL listed are for liver cell polymorphism. Actual dose received by dose level/sex: Food consumption and vinyl chloride (VC) concentrations were measured several times during feeding period to account for loss of VC through evaporation. Evaporative loss averaged 20 % over 4 hours. The ingested dose was adjusted downward by the amount of VC measured in feces to arrive at bioavailable doses. Mortality and time to death: Few deaths occurred before 72 weeks. The

mortality rate was similar in all groups (including controls) up to week 140. The mortality rate at week 149 of males was as follows: controls (80/100), 0.014 mg/kg (80/100), 0.13 mg/kg (82/100), 1.3 mg/kg (42/50). The mortality rate at week 149 of females was as follows: control (76/100), 0.014 mg/kg (77/100), 0.13 mg/kg (74/100), 1.3 mg/kg (45/50). The mortality rate of females treated with 1.3 mg/kg was significantly different from controls at week 149.

Clinical signs: No clincial signs were found in rats treated with 0.014 or 0.13 mg/kg. Nodules in liver were found upon palpation of females treated with 1.3 mg/kg. Body weight gain and food consumption were similar for all groups.

Laboratory Tests: No significant difference was observed between groups in glutathione content of liver at weeks 40 or 80.

Gross Pathology: A higher incidence of liver nodules suspected of being tumors was found in males and females treated with 1.3 mg/kg (7/50 and 8/50, respectively) vs. controls (1/100 and 2/100, respectively). There was a significantly higher incidence of cysts in livers of females treated with 1.3 mg/kg (33/50) vs. controls (17/100).

Histopathology of liver: Increased incidences of clear cell foci, basophilic foci, number of foci-bearing rats, hepatocellular carcinomas, and liver-cell polymorphism was noted in males treated with 1.3 mg/kg versus controls. Increased incidences of clear cell foci, basophilic foci, mixed cell foci, eosinophilic foci, number of foci-bearing rats, neoplastic nodules, cysts and liver-cell polymorphism were found in females treated with 1.3 mg/kg versus controls. One male and two females treated with 1.3 mg/kg developed angiosarcoma. Increased incidences of basophilic foci (26/96) and number of foci-bearing rats (31/96) were found in females treated with 0.13 mg/kg versus controls (9/98 and 19/98, respectively). Increased incidences of basophilic foci were found in females treated with 0.014 mg/kg versus controls (20/100 vs. 9/98, respectively)

Source **:**

PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Test condition **:**

Test Organisms: Newly weaned rats were obtained from the SPF Colony of the Central Institute for the Breeding of Laboratory Animals (TNO, Zeist, The Netherlands).

Number of animals per dose: 100 of each sex for the following dose groups: 0 mg/kg (control), 0.014 mg/kg, 0.13 mg/kg. 50 of each sex for the 1.3 mg/kg dose.

Administration/Exposure: PVC powder enriched with vinyl choride monomer (VCM) was added to a diet containing 1% PVC powder to provide 0.46, 4.6 and 46 ppm vinyl chloride (VC). Diets were prepared daily, immediately before being offered to rats.

Clinical Observations and Frequency: The number of deaths was recorded weekly. Body weight was determined at Weeks 2, 4, and once every 4 weeks thereafter. Food consumption was measured at Weeks 1-4, 11-12, and then every 12 weeks for periods of 2 weeks (e.g. wk 24-26, 36-38, etc) of 20 rats/sex/group.

Organs Examined at Necropsy: All surviving males and females were killed at 149 and 150 weeks, respectively. Several different organs and tissues (types not noted) were taken at necropsy. Liver (three pieces from three different lobes) and all grossly viable tumors or suspected tumors in abdominal cavity, Zymbal glands, and mammary glands were examined microscopically.

Satellite groups and reason for inclusion: Two additional groups of 5 animals/sex/dose were killed at weeks 40 and 80 and livers were assessesd for glutathione content.

Statistical Methods: The Fisher's exact probability test (one tailed) was performed on mortality data and microscopic lesions. The Chi-square test was performed on macroscopic lesions of liver

Test substance :

PVC powder enriched with vinyl chloride monomer.

Reliability : (1) valid without restriction
21.05.2002 (124)

Species	:	Rat
Sex	:	male/female
Strain	:	Other
Route of admin.	:	Inhalation
Exposure period	:	6 h/d, 5 d/wk
Frequency of treatment	:	up to 12 months
Post obs. period	:	
Doses	:	50, 250, 1000 ppm
Control group	:	yes
NOAEL	:	< 50 ppm
LOAEL	:	= 50 ppm
Method	:	other
Year	:	1977
GLP	:	no data
Test substance	:	other TS
Result	:	Time of death: Two females exposed to 50 ppm, 4 males and 10 females exposed to 250 ppm, and 8 males and 13 females exposed to 1000 ppm died or were terminated between 8 and 12 months due to moribund appearance. No deaths occurred in controls.

Body weight gain: Body weights of animals exposed to 50 or 250 ppm were not significantly different from controls throughout the study. The body weights of females exposed to 1000 ppm were less than controls after 4 weeks.

Laboratory Tests: No significant differences in hematology, clinical blood chemistry, pulmonary macrophage count, cytogenic analysis of bone marrow cultures, x-ray examination of extremities, collagen in liver and lung, urinary ALA, and serum alpha-fetoprotein or ALA synthetase were noted between animals exposed to vinyl chloride or controls.
DNA synthesis, as measured by 14C-thymidine incorporation into DNA, was significantly increased in the livers of male mice exposed to 50 ppm for 11 months.

Pathology: Hemangiosarcoma of liver was noted in 22/72 and 12/72 rats exposed to 1000 ppm or 250 ppm (respectively) for 9-12 months. Hemangiosarcoma was found in lungs of 13/72 rats exposed to 1000 ppm for 9-12 months. Hemangiosarcomas of both liver and lung were commonly

found in the same animals. Hemangiosarcomas were not found in control

Source :

PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Test condition :

Test Organisms: CD rats (aged 2 months) from Charles River (CD) were used.

Number of animals per dose: 36 rats of each sex (including control)

Administration/Exposure: Vinyl chloride gas was metered with rotameters into the chamber air supply. The lines and rotameter were heated to 37 degrees C to generate vapor and then to 40 degrees C to prevent condensation. The chamber concentration was monitored using a gas chromatograph with a flame ionization detector.

Doses: air (control), 50 ppm, 250 ppm, 1000 ppm

Clinical Observations: Body weight and food consumption were measured biweekly and weekly, respectively. RBC, reticulocyte, platelet, WBC and differential counts, nucleated RBC, hematocrit, hemoglobin, methemoglobin, prothrombin time, and Heinz bodies on 4 males and 4 females of each exposure group were determined at 1, 2, 3, 6, and 9 months. SGPT, BUN, SGOT, alkaline phosphatase, bilirubin, creatinine, LDH, alpha-HBDH, immunoglobulin IgA, IgB-A, IgB-B and IgM, total protein, albumin, and globulin in blood were determined for 4 males and 4 females in each exposure group at 1, 2, 3, 6, and 9 months. ALA in urine was also measured.

Macroscopic Necropsy: Animals were sacrificed when moribund, at scheduled intervals (see above), or after 12 months of exposure. The necropsy included examination of the brain, pituitary, thyroids, respiratory tract, alimentary canal, urogenital organs, thymus, heart, liver, pancreas, spleen, mesenteric lymph nodes, and body cavities. Brain, liver, kidneys, spleen and gonads were weighed.

Microscopic Necropsy: Tumors with adjacent normal tissues and whole or portions of other tissues were examined microscopically.

Other Examinations:Macrophage counts of pulmonary washings and cytogenetic analysis of bone marrow cultures were performed on controls and animals exposed to 1000 ppm. Limbs from the longest-exposed animals were examined for osteoporosis, malacia, bone tumors, changes in bone density, cortical thickness or striations within cortex, loss of cortex, or unusual trabecular pattern of bone. Hepatic aminolevulinic aicd (ALA) synthetase, alpha fetoprotein, collagen in liver and lung, and 14C-thymidine incorporation into DNA were measured

Test substance :

Vinyl choride gas (99.8% pure) from Matheson Products

Conclusion :

Rats were less sensitive to the toxic and carcinogenic effects of vinyl chloride than mice

Reliability : (1) valid without restriction
29.05.2002 (125)

Species : mouse
Sex : male/female
Strain : Abyssinian
Route of admin. : inhalation

5. Toxicity **Id** 75-01-4
Date 18.06.2002

Exposure period : up to 12 months
Frequency of treatment : 6 h/d, 5 d/wk
Post obs. period :
Doses : 50, 250, 1000 ppm
Control group : yes
NOAEL : < 50 ppm
LOAEL : = 50 ppm
Method : other
Year : 1977
GLP : no data
Test substance : other TS
Result :

Time of death: Two males and one female exposed to 1000 ppm were found dead between days 3 and 9 of exposure. Four males and 11 females exposed to 50 ppm, 7 males and 17 females exposed to 250 ppm, and 13 males and 21 females exposed to 1000 ppm were terminated between 6 months and the end of the exposure period due to moribund appearance. All animals exposed to 1000 ppm and all females exposed to 250 ppm died or were terminated at the end of 9 months. Two males and three females exposed to 50 ppm and two males exposed to 250 ppm died or were terminated during months 10-12. Two control males (total) died during exposure months 8 and 9

Body weight gain: Body weights of males or females exposed to 50 or 250 ppm were not significantly different from controls throughout the study. The body weight of males or females exposed to 1000 ppm declined during the 9th month, followed by sudden death.

Laboratory Tests: Increased DNA synthesis was observed in livers of male mice exposed to 50 ppm for 11 months (Table 1).

Table 1
14C-Thymidine incorporation into hepatic DNA of male mice exposed to VC for 11 months.

		14C Activity
VC level (ppm)	n	dpm mg DNA
0	8	2886+/-240
50	7	4232+/-463a

a Significantly different from control two-sample rank test.

Pathology: Mitotic figures were noted in livers of mice exposed to 50 or 1000 ppm between months 8 and 9 of exposure. This observation was not apparent in mice terminated at other times. Bronchoalveolar adenoma occurred in 48/72, 20/72 and 9/72 mice exposed to 1000 ppm, 250 ppm or 50 ppm (respectively) for up to 9 months. Hemangiosarcoma of liver was found in 31/72 and 21/72 mice exposed to 1000 ppm or 250 ppm (respectively) for up to 9 months. Hemangiosarcoma of other tissues was found in 8/72 mice exposed to 1000 ppm for 8 months. Mammary gland tumors (ductular adenocarcinoma, squamous cell carcinoma, and/or anaplastic cell carcinoma) were found in 13/36 and 3/36 females exposed to 1000 ppm or 250 ppm for 8 months. Squamous and/or anaplastic tumors metastasized to lungs of 9/36 females exposed to 50 ppm. Malignant lymphoma was observed in 5/72, 2/72 and 1/7 2 mice exposed to 1000, 250 or 50 ppm. Broncho-alveolar adenoma was noted in one control male mouse. No other tumors were found in controls

Source :

PCA Services, Inc

PCA Services, Inc. Kingsport, TN

Test condition :

Test Organisms: CD-1 mice (aged 2 months) from Charles River

Number of animals per dose: 36 mice of each sex (including control) were used in the study.

Administration/Exposure: Vinyl chloride gas was metered with rotameters into the chamber air supply. The lines and rotameter were heated to 37 degrees C to generate vapor and then to 40 degrees C to prevent condensation. The chamber concentration was monitored using a gas chromatograph with a flame ionization detector.

Doses: air (control), 50 ppm, 250 ppm, 1000 ppm

Clinical Observations and Frequency:
Body weight and food consumption were determined biweekly and weekly, respectively. RBC, reticulocyte, platelet, WBC and differential counts, nucleated RBC, hematocrit, hemoglobin, methemoglobin, Heinz bodies were determined on 4 males and 4 females of each exposure group at 1, 2, 3, 6, and 9 months. SGP and BUN in blood of 4 males and 4 females in each exposure group were determined at 1, 2, 3, 6, and 9 months. ALA concentration in urine was determined.

Macroscopic Necropsy: Animals were sacrificed when moribund, at scheduled intervals (see above), or after 12 months of exposure. The necropsy included examination of the brain, pituitary, thyroids, respiratory tract, alimentary canal, urogenital organs, thymus, heart, liver, pancreas, spleen, mesenteric lymph nodes, and body cavities. Brain, liver, kidneys, spleen and gonads were weighed.

Microscopic Necropsy: Tumors with adjacent normal tissues and whole or portions of other tissues were examined microscopically.

Other Examinations: Macrophage counts of pulmonary washings and cytogenetic analysis of bone marrow cultures were performed on controls and animals exposed to 1000 ppm. Limbs from the longest-exposed animals were examined for osteoporosis, malacia, bone tumors, changes in bone density, cortical thickness or striations within cortex, loss of cortex, or unusual trabecular pattern of bone. Hepatic aminolevulinic acid (ALA) synthetase, alpha fetoprotein and 14C-thymidine incorporation into DNA were measured

Test substance :

Vinyl chloride gas (99.8% pure) from Matheson Product

Conclusion :

Mice were more sensitive to the toxic effects of vinyl chloride than rats

Reliability : (1) valid without restriction
29.05.2002 (126)

Species : rat
Sex : male/female
Strain : Wistar
Route of admin. : inhalation
Exposure period : 12 months
Frequency of treatment : 7 hrs/day, 5 days/week
Post obs. period : none
Doses : 5000 ppm
Control group : yes

5. Toxicity **Id** 75-01-4
Date 18.06.2002

LOAEL	:	= 5000 ppm
Method	:	
Year	:	1979
GLP	:	no data
Test substance	:	
Method	:	Groups of 62 male and 62 female rats were exposed to 0 or 5000 ppm vinyl chloride monomer for 7 hrs/day, 5 days/week for up to 52 weeks. At weeks 4, 13, 26 and 52 hematology, clinical chemistry, liver and kidney function tests and urinalysis parameters were measured. Groups of 10 rats/sex were sacrificed after 4, 13, 26 and 52 weeks and subjected to a gross pathological examination. Selected organs (heart, kidney, liver, spleen, brain, gonads, thymus , pituitary, thyroid, adrenals and lungs) were weighed. Tissues were examined histopathologically.
Result	:	The first male rat from the 5000 ppm group died week 33 of the study. Thereafter, mortality among VCM-exposed rats gradually increased. At the end of the study, only 9 males and 10 females from the 5000 ppm group were still alive. Mean body weights for the 5000 ppm group were significantly lower than those of the controls throughout the study. Slight changes in hematological, clinical chemistry and urinalysis measurements were most notable after 26 or 52 weeks. Bromosulfophthalein retention was decreased in the 5000 ppm group at weeks 13, 26 and 52. Relative liver and kidney weights were nearly always significantly increased in both sexes at weeks 13, 26 and 52 and those of the spleen at weeks 26 and 52. The relative weights of the heart and lungs were slightly increased in the 5000 ppm group at week 52. Treatment-related pathological changes in organs other than the liver were not observed in animals killed after 4, 13 or 26 weeks. Hyperplastic changes were seen in the olfactory epithelium of the nasal cavity in 3 males after 52 weeks. Histopathologic changes were also noted in the Zymbal glands, lungs, kidneys, spleen and heart which may or may not have been VCM related. Grossly visible nodules were observed on approximately 80% of the VCM-exposed animals that died or were killed during the second half of the study. Nodules varied from solid and pale to cystic and hemorrhagic. Histopathologic changes were noted in the liver after 26 weeks and appeared to be more severe after 52 weeks.
Test substance	:	Vinyl chloride gas was supplied by Akzo Zout Chemie, Rotterdam, The Netherlands. Purity was not noted but would be expected to be comparable to Section 1.1-1.4. For study conducted at the same time period in this laboratory, test material from the same supplier was listed as: VC >= 99.97 % v/v (impurities: <2 ul/l acetylene, <15 ul/l monovinyl -acetylene, <10 ul/l 1,3-butadiene, <75 ul/l m ethylchloride, <50 ul/l ethylchloride, <1 ul/l chloroprene, <1 ul/l 1,1-dichloroethane, < 20 ul/l 1,2-dichloroethane, <5 mg/kg acetaldehyde, < 1 mg/kg HCl, <0.5 mg/kg Fe, <100 mg/kg water, <10 mg/kg evaporation residue). Reference: Feron, V.J., Hendriksen, C.F.M., Speek, A.J., Til, H.P., and Spit, B.J. (1981). Lifespan oral toxicity study of vinyl chloride in rats. Fd Cosmet Toxicol 19:317-333.
Reliability	:	(2) valid with restrictions
15.05.2002		(127) (128) (129)
Species	:	rat
Sex	:	male/female

5. Toxicity **Id** 75-01-4
Date 18.06.2002

Strain	:	no data
Route of admin.	:	inhalation
Exposure period	:	4.5 months
Frequency of treatment	:	7 h/d, 5 d/w
Post obs. period	:	none
Doses	:	500 ppm (1.28 mg/l)
Control group	:	yes, concurrent no treatment
Method	:	other
Year	:	1961
GLP	:	no data
Test substance	:	
Remark	:	Groups of 10 male and 10 female rats were exposed to 500 ppm for 7 hrs/day, 5 days/week for 4.5 months. Groups of 5 males and 5 females served as unexposed controls. At sacrifice, serum was saved to measure serum urea nitrogen, and alkaline phosphatase, serum glutamic pyruvic transaminase and serum glutamic oxalacetic transaminase activity. In addition, terminal organ weights were obtained and tissues (minimum kidney and liver) were saved for microscopic examination.
Result	:	Body weights of rats exposed to vinyl chloride were comparable to control values at the end of the study. Relative liver weights of rats exposed to 500 ppm were significantly increased in males and slightly increased in females. SUN and SGPT, SGOT and alkaline phosphatase activities were within normal limits. There were no grossly visible effects noted at necropsy. Histopathology: Liver: increased central lobular granular degeneration. Kidney: interstitial and tubular changes. No additional information provided.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

20.05.2002 (130)

Species	:	rat
Sex	:	male/female
Strain	:	no data
Route of admin.	:	inhalation
Exposure period	:	6 months (138 - 144 times in 204 days)
Frequency of treatment	:	7 h/d, 5 d/w
Post obs. period	:	
Doses	:	100 ppm (0.256 mg/l), 200 ppm (0.51 mg/l)
Control group	:	yes, concurrent no treatment
Method	:	other
Year	:	1961
GLP	:	no data
Test substance	:	
Remark	:	Groups of 12 male and female rats were exposed to 0 (unexposed), 0 (chamber control), 100 or 200 ppm for 7 hrs/day, 5 days/week for 6 months. Additional groups of 7-12 male and female rats from the 0 (unexposed), 0 (chamber control), 100 or 200 ppm group were maintained for 8 weeks after the last exposure as part of a recovery group. In addition, additional groups of 5 male rats were exposed to 100 or 200 ppm for 0.5, 1, 2 or 4 hours for the same exposure regimen. Urine was obtained for urinalysis. At sacrifice, serum was saved to measure serum urea nitrogen, and alkaline phosphatase, serum glutamic pyruvic transaminase and serum glutamic oxalacetic transaminase activity. Blood was collected for

hematological determinations. In addition, terminal organ weights (lung, heart, liver, kidney, spleen and testes) were obtained and tissues (minimum kidney and liver) were saved for microscopic examination.

Result : 200 ppm:
Appearance, mortality and growth were normal. Hematological, SUN and SGOT, SGPT and alkaline phosphatase activities and urinalysis were within normal limits. Relative liver weight of male and female rats exposed for 7 hours/day was significantly elevated and was slightly increased in rats exposed for 2 or 4 hours/day (Table 1). All other organ weights were within normal limits. There were no grossly visible lesions noted at necropsy. Histopathologic changes were not observed, including the liver.

In the recovery group, relative Liver weight values were still elevated 8 weeks after exposure. Some recovery had occurred.

100 ppm:
Appearance, mortality and growth were normal. Hematological, SUN and SGOT, SGPT and alkaline phosphatase activities and urinalysis were within normal limits. Relative liver weight of rats exposed for 7 hours/day was significantly elevated and was slightly increased in rats exposed for 2 or 4 hours/day (Table 1). All other organ weights were within normal limits. There were no grossly visible lesions noted at necropsy. Histopathologic changes were not observed, including the liver.

In the recovery group, relative Liver weight values were still elevated 8 weeks after exposure. Some recovery had occurred.

Table 1
Final body wt and relative liver weight of male rats exposed for 6 months.

Conc. ppm	Duration hr	Final Body Weight,g	Relative Liver Weight, g/100g
Unexposed control	7	343	2.45
Chamber control	7	356	2.52
200	7	341	2.85*
200	4	349	2.66
200	2	341	2.62
200	1	350	2.46
200	0.5	339	2.38
100	7	352	2.61*
100	4	360	2.62
100	2	331	2.64
100	1	387	2.52
100	0.5	363	2.42
Recovery Group:			
Unexposed control	7	354	2.43
Chamber control	7	393	2.41
200	7	385	2.59
100	7	376	2.53

* $p<0.05$

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
20.05.2002 (130)

Species : rat
Sex : male/female
Strain : no data

5. Toxicity **Id** 75-01-4
Date 18.06.2002

Route of admin. : inhalation
Exposure period : 6 months (130 times in 189 days)
Frequency of treatment : 7 h/d, 5 d/w
Post obs. period : none
Doses : 50 ppm (0.13 mg/l)
Control group : yes, concurrent no treatment
NOAEL : = 50 ppm
Method : other
Year : 1961
GLP : no data
Test substance :
Remark : Groups of 12 male and female rats were exposed to 0 unexposed), 0 (chamber control) or 50 ppm for 7 hrs/day, 5 days/week for 6 months. Additional groups of 12 male and female rats from the 0 (unexposed), 0 (chamber control), 100 or 200 ppm group were maintained for 6 weeks after the last exposure as part of a recovery group. In addition, additional groups of 10 male rats were exposed to 50 ppm for 1, 2 or 4 hours for the same exposure regimen. At sacrifice, serum was saved to measure serum urea nitrogen, and alkaline phosphatase, serum glutamic pyruvic transaminase and serum glutamic oxalacetic transaminase activity. Blood and urine were collected for hematological determinations and urinalysis, respectively. In addition, terminal organ weights (lung, heart, liver, kidney, spleen and testes) were obtained and tissues (minimum kidney and liver) were saved for microscopic examination.
Result : There was no effect on appearance, mortality, growth, hematology, clinical chemistry determinations, urinalysis , gross or histopathologic examination. Except for the kidney weight in female rats, all organ weights were comparable to control values. Since kidney weights were unaffected in previous studies at concentrations as high as 500 ppm, this apparent effect was considered to be an artifact. Liver weights are presented in Table 1.

Table 1
Final body wt and relative liver weight of male rats exposed for 6 months.

Conc. ppm	Duration hr	Final Body Weight,g	Relative Liver Weight, g/100g
Unexposed control	7	319	2.67
Chamber control	7	347	2.41
50	7	339	2.49
50	4	348	2.59
50	2	322	2.57
50	1	348	2.51

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
21.05.2002 (130)

Species : rat
Sex : male/female
Strain : Sherman
Route of admin. : inhalation
Exposure period : 3 months (90 days)
Frequency of treatment : 8 hr/day, 5 days/week
Post obs. period : none
Doses : 20,000 ppm

Control group	:	yes
LOAEL	:	= 20000 ppm
Method	:	
Year	:	1963
GLP	:	no data
Test substance	:	other TS: >99% pure
Method	:	Groups of 15 male and 15 female rats were exposed 8 hrs/day, 5 days/week to 0 or 20,000 ppm vinyl chloride for 3 months. All animals were weighed at approximately weekly intervals; hemoglobin levels were determined at monthly intervals. Blood was obtained for hemoglobin determinations prior to necropsy. Histopathologic examination of the liver, kidney and spleen was conducted on all animals.
Result	:	Five deaths occurred during the study (4 controls). Decreased white blood cells, increased liver/body weight ratios, and decreased spleen/body weight ratios were observed in animals exposed to vinyl chloride. Histologic examination of the liver revealed increased intracellular fat in rats exposed to vinyl chloride monomer.
Test condition	:	Animals were exposed in a 1100 L chamber with an airflow of 50 lpm. The concentration of gas was continuously monitored by a thermal conductivity meter calibrated for vinyl chloride versus air. The desired concentration was maintained with less than 5% deviation.
Reliability	:	(2) valid with restrictions

20.05.2002 (131)

Species	:	rat
Sex	:	male/female
Strain	:	Sherman
Route of admin.	:	inhalation
Exposure period	:	19 consecutive days
Frequency of treatment	:	8 hrs/day
Post obs. period	:	none
Doses	:	50,000 ppm
Control group	:	yes
LOAEL	:	= 50000 ppm
Method	:	
Year	:	1963
GLP	:	no data
Test substance	:	other TS: >99%
Method	:	Groups of 5 male and 5 female rats were exposed 8 hrs/day to 0 or 50,000 ppm vinyl chloride for 19 consecutive days. Blood was obtained for hemoglobin determinations and serum transaminase activity prior to necropsy. Histopathologic examination of the liver, kidney and spleen was conducted on all animals. No additional information supplied.
Result	:	Increased red blood cells, decreased white blood cells and increased liver/body weight ratios were observed in rats exposed to vinyl chloride. Histologic examination of kidney, liver and spleen revealed differences in the liver only. In the liver, marked swelling of the cells with large irregular vacuoles were observed in rats exposed to 50,000 ppm.
Test condition	:	Animals were exposed in a 1100 L chamber with an airflow of 50 lpm. The concentration of gas was continuously monitored by a thermal conductivity meter calibrated for vinyl chloride versus air. The desired concentration was maintained with less than 5% deviation.
Reliability	:	(2) valid with restrictions

20.05.2002 (131)

Species	:	rat

5. Toxicity **Id** 75-01-4
Date 18.06.2002

Sex	:	male/female
Strain	:	Wistar
Route of admin.	:	oral feed
Exposure period	:	4 hours/day
Frequency of treatment	:	daily
Post obs. period	:	
Doses	:	1.7, 5.0 and 14.1 mg VCM/kg/day
Control group	:	yes
LOAEL	:	= 1.7 mg/kg bw
Method	:	other: essentially follows OECD 453
Year	:	1981
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Groups of 60-80 males and 60-80 female rats were fed diets containing 10% PVC powder with varying concentrations of VCM at levels planned to provide daily intakes of 1, 3 or 10 mg VCM/kg body weight. The control group received 10% PVC with no measureable level of VCM. The various diets were prepared daily just prior to being offered to the rats. The diets were available to the rats each day for a period of four consecutive hours. After the 4-hour feeding the rats had no feed until the next day. In addition, a group of rats received 300 mg VCM/kg/day, 5 days/week, by oral gavage. For this group,the VCM was dissolved in soybean oil. Interim sacrifices of 10 male and 10 female rats from the control and two highest dose levels were performed after 26 and 52 weeks. The study was terminated when 75% of the control rats were dead, a point reached for males in week 135 and for females in week 144. Rats were weighed at weeks 1, 2, 4, 6, 8, 10 and 12 and at 4-week intervals thereafter. Feed consumption was measured 7 times during the study. Routine hematology determinations and urinalysis were conducted in weeks 13, 26, 52, 78 and 94. Clinical chemistry determinations were conducted in weeks 13, 26, 52 and 106 and included fasting blood glucose, blood urea nitrogen, serum total protein, serum albumin as well as serum alkaline phosphatase, glutamic-oxalacetic transaminase and glutamic-pyruvic transaminase activities. Animals alive after 135 weeks (males) or 144 weeks (females) were sacrificed and subjected to a gross examination. A thorough necropsy was performed and approximately 45 tissues were saved for histopathologic examination. A complete histopathologic examination was limited to 20 males and 20 females that survived to the end of the study or lived the longest. Histopathologic examination of all other rats was limited to the liver, Zymbal glands, lungs, kidneys, spleen, pituitary, thyroidk, adrenals, grossly visible tumors and organs containing gross lesions suspected of being tumors. For the interim sacrifices, clinical chemistry determinations were made. These included blood-clotting time, serum electrolytes, lactic dehydrogenase activity, serum alpha-foetoprotein, liver and kidney function tests. In action aminopyrine demethylase and aniline hydroxylase activities were measured in liver preparations. Liver and kidneys were weighed. Histopathological examination of the liver, kidneys and Zymbal glands was performed.
Remark	:	Mortality at the lowest dose, 1.7 mg VCM/kg/day, was comparable through 134 weeks. Between weeks 134 and 143, mortality in the female rats increased at a greater rate than controls.
Result	:	The mortality rate was higher in all VCM-treated groups than in the controls and increased with increasing VCM doses. The group receiving 300 mg/kg/day of VCM by oral gavage was terminated after 83 weeks. The 14.1 and 300 mg/kg groups were associated with shortened blood-clotting

times, slightly increased alpha-foetoprotein levels in blood serum, liver enlargement and increased hematopoietic activity in the spleen. Histopathologic changes noted in the liver at 1.7, 5.0 and 14.1 mg/kg/day were the only changes related to VCM ingestion.

Test substance : VC >= 99.97 % v/v (impurities: <2 ul/l acetylene, <15 ul/l monovinyl-acetylene, <10 ul/l 1,3-butadiene, <75 ul/l methylchloride, <50 ul/l ethylchloride, <1 ul/l chloroprene, <1 ul/l 1,1-dichloroethane, < 20 ul/l 1,2-dichloroethane, <5 mg/kg acetaldehyde, < 1 mg/kg HCl, <0.5 mg/kg Fe, <100 mg/kg water, <10 mg/kg evaporation residue).

Reliability : (2) valid with restrictions

21.05.2002 (132)

Species : rat
Sex : male/female
Strain : Wistar
Route of admin. : gavage
Exposure period :
Frequency of treatment : 6 days/week for 13 weeks
Post obs. period :
Doses : 30, 100 and 300 mg/kg/day
Control group : yes, concurrent vehicle
NOAEL : = 30 mg/kg
LOAEL : = 100 mg/kg
Method : other: essentially followed OECD 0408
Year : 1975
GLP : no
Test substance : as prescribed by 1.1 - 1.4
Method : Groups of 15 males and 15 females were administered 0, 30, 100 or 300 mg/kg vinyl chloride in soybean oil, 6 days/week for 13 weeks by gavage. Doses were adapted to mean body weights once/week. Individual body weights were recorded weekly and feed intake was measured during weeks 1-4 and 11 and 12. Standard hematologica and serum chemistry endpoints were determined in 10 males and 10 females of each group at termination. Kidney function and urinalyses were examined in week 13 in ten males and ten females of the control and high dose group. Rats were killed at week 14 and examined for gross changes. Heart, kidneys, liver, spleen, brain, gonads, thymus, thyroid and adrenals were weighed. Detailed microscopic examination of several organs was performed on high-dose and control animals. The liver was examined in rats treated with 30 or 100 mg/kg/day.

Result : Gavage administration of VCM solutions in soybean oil at levels up to 300 mg/kg/day did not cause any noticeable changes in appearance or behavior, body weight gain or feed intake. The total number of white blood cells and the sugar content of the blood were slightly decreased in the 100 and 300 mg/kg/day groups (Table 1). Serum GOT and GPT activities and of urinary GOT activity were decreased in males receiving 300 mg/kg/day. There were no other significant changes in the hematological or biochemical indices.

The relative liver weights in males and females showed a tendency to increase with increasing doses of VCM, but was only statistically significant at the highest dose level. In addition, a dose-related decrease in the relative adrenal weight occurred in males, but was only statistically significant at the highest dose level. The other organ weights recorded were closely comparable in all groups.

Minimal histologic changes in the liver, seen as one or a few foci of 40-70 hyperbasophilic hepatocytes occurred in one male and one female rats in both the 100 and 300 mg/kg/day groups. Electron microscopic examination of the liver showed hypertrophy of the endoplasmic reticulum in hepatocytes of animals given the highest dose. Lower dose levels were not examined.

Table 1
Summary results in animals orally gavaged with VCM in soybean oil

males

Parameter	mg/kg/day 0	30	100	300
total leucocytes (1000/mm3)	18.5	18.8	17.0	16.5
Blood sugar (mg/100 ml)	88	84	78**	77**
SGOT	228	217	224	201*
SGPT	53	49	48	45*
Rel Liver wt	3.51	3.60	3.74	3.76

females

Parameter	mg/kg/day 0	30	100	300
total leucocytes (1000/mm3)	17.3	17.6	14.6*	14.8*
Blood sugar (mg/100 ml)	89	88	74***	79**
SGOT	227	212	212	200
SGPT	42	38	38	39
Rel Liver wt	3.32	3.34	3.51	3.71***

Test substance : Vinyl chloride was dissolved in soybean oil. Solutions of vinyl chloride in soybean oil at room temperature were found to be stable. Soybean oil containing 5.6% vinyl chloride lost only 10% after 1 hour and 16 % after 4 hours. A 0.5% solution lost 25% after 24 hours. Gas chromatographic analysis of a 10% vinyl chloride solution in soybean oil stored at 37C for 8 days did not reveal any evidence of vinyl chloride oligomers or other reaction products of vinyl chloride with oil compounds.

Reliability : (2) valid with restrictions
20.05.2002 (133)

Species : rabbit
Sex : male/female
Strain : no data
Route of admin. : inhalation
Exposure period : 6 months (204 days)
Frequency of treatment : 7 h/d, 5 d/w
Post obs. period : none
Doses : 100 ppm (0.256 mg/l), 200 ppm (0.51 mg/l)
Control group : yes, concurrent no treatment
NOAEL : = 100 ppm
Method : other
Year : 1961
GLP : no data
Test substance :
Method : Groups of 3 male and 3 female rabbits were exposed to 0 (unexposed), 0 (chamber control), 100 or 200 ppm for 7 hrs/day, 5 days/week for 6 months. Growth and mortality records were maintained. At sacrifice, serum was obtained to measure urea nitrogen and alkaline phos phatase

and serum glutamic pyruvic transaminase activities. Terminal organ weights (lung, heart, liver, kidney, spleen and testes) were obtained and tissues (minimum kidney and liver) were saved for microscopic examination.

No further information supplied.

Result : 200 ppm:
All rabbits were normal in appearance, growth and mortality. Serum urea nitrogen and alkaline phosphatase and SGPT activities of rabbits exposed to 200 ppm were within acceptable limits. Gross pathology and relative organ weights were normal. Histopathologically, changes were noted only in the livers of rabbits of both sexes. In the males this was characterized by central lobular granular degeneration and necrosis with some foamy vacuolation. In the females, central lobular granular degeneration and necrosis with periportal cellular infiltration were observed.

100 ppm:
All rabbits were normal in appearance, growth and mortality. Serum urea nitrogen and alkaline phosphatase and SGPT activities of rabbits exposed to 100 ppm were within acceptable limits. Gross pathology, relative organ weights and histopathology were normal.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
21.05.2002 (130)

Species : rabbit
Sex : male/female
Strain : no data
Route of admin. : inhalation
Exposure period : 6 months (130 times in 189 days)
Frequency of treatment : 7 h/d, 5 d/w
Post obs. period : none
Doses : 50 ppm (0.13 mg/l)
Control group : yes, concurrent no treatment
Method : other
Year : 1961
GLP : no data
Test substance :
Method : Groups of 3 male and 3 female rabbits were exposed to 0 (unexposed), 0 (chamber exposed) and 50 ppm vinyl chloride for 7 hrs/day, 5 days/week for 6 months. Growth and mortality records were maintained. Urine was obtained at the end of the study. At sacrifice, serum was obtained to measure urea nitrogen and alkaline phosphatase and serum glutamic pyruvic transaminase activities. Terminal organ weights (lung, heart, liver, kidney, spleen and testes) were obtained and tissues (minimum kidney and liver) were saved for microscopic examination.

No further information supplied.

Result : All rabbits were normal in appearance, growth and mortality. Urine values were within acceptable limits. Serum urea nitrogen and alkaline phosphatase and SGPT activities of rabbits exposed to 50 ppm were within acceptable limits. Gross pathology, relative organ weights and histopathology were normal.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions

20.05.2002 (130)

Species	:	dog
Sex	:	male/female
Strain	:	no data
Route of admin.	:	inhalation
Exposure period	:	6 months (204 days)
Frequency of treatment	:	7 h/d, 5 d/w
Post obs. period	:	none
Doses	:	100 ppm (0.256 mg/l)
Control group	:	yes, concurrent no treatment
NOAEL	:	= 200 ppm
Method	:	other
Year	:	1961
GLP	:	no data
Test substance	:	
Method	:	Groups of 1 male and 1 female dogs were exposed to 0 (unexposed), 0 (chamber control), 100 or 200 ppm for 7 hrs/day, 5 days/week for 6 months. Growth and mortality records were maintained. The liver of each dog was biopsied prior to exposure and after 3.5 months of exposure, hence the liver of each dog served as it's own control. Pre-exposure and terminal hematological determinations were made on all dogs. Urine samples were obtained at the end of the study. At sacrifice, serum was obtained to measure urea nitrogen and alkaline phosphatase, serum glutamic pyruvic transaminase and serum glutamic oxalacetic transaminase activities. Terminal organ weights (lung, heart, liver, kidney, spleen and testes) were obtained and tissues (minimum kidney and liver) were saved for microscopic examination. No further information supplied.
Result	:	200 ppm: All dogs were normal in appearance, growth and mortality. Serum urea nitrogen and alkaline phosphatase, SGPT and SGOT activities of dogs exposed to 200 ppm were within acceptable limits. Hematological parameters, relative organ weights, gross pathology and histopathology were normal. 100 ppm: All dogs were normal in appearance, growth and mortality. Serum urea nitrogen and alkaline phosphatase, SGPT and SGOT activities of dogs exposed to 100 ppm were within acceptable limits. Hematological parameters, relative organ weights, gross pathology and histopathology were normal.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

21.05.2002 (130)

Species	:	dog
Sex	:	male/female
Strain	:	no data
Route of admin.	:	inhalation
Exposure period	:	6 months (130 times in 189 days)
Frequency of treatment	:	7 h/d, 5 d/w
Post obs. period	:	
Doses	:	50 ppm (0.13 mg/l)
Control group	:	yes, concurrent no treatment

Method : other
Year : 1961
GLP : no data
Test substance :
Method : Groups of 1 male and 1 female dogs were exposed to 0 (unexposed), 0 (chamber control) or 50 ppm for 7 hrs/day, 5 days/week for 6 months. Growth and mortality records were maintained. The liver of each dog was biopsied prior to exposure. Hematological determinations were made on all dogs after 3 months. Urine samples were obtained at the end of the study. At sacrifice, serum was obtained to measure urea nitrogen and alkaline phosphatase, serum glutamic pyruvic transaminase and serum glutamic oxalacetic transaminase activities. Terminal organ weights (lung, heart, liver, kidney, spleen and testes) were obtained and tissues (minimum kidney and liver) were saved for microscopic examination.

No further information supplied.
Result : All dogs were normal in appearance, growth and mortality. Serum urea nitrogen and alkaline phosphatase, SGPT and SGOT activities of dogs exposed to 50 ppm were within acceptable limits. Hematological parameters, relative organ weights, gross pathology and histopathology were normal.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
20.05.2002 (130)

Species : guinea pig
Sex : male/female
Strain : no data
Route of admin. : inhalation
Exposure period : 6 months (204 d)
Frequency of treatment : 7 h/d, 5 d/w
Post obs. period : none
Doses : 200 ppm, 100 ppm
Control group : yes, concurrent no treatment
Method : other
Year : 1961
GLP : no data
Test substance :
Method : Groups of 10 male and 8 female guinea pigs were exposed to 0 (unexposed), 0 (chamber control), 100 or 200 ppm for 7 hrs/day, 5 days/week for 6 months. Growth and mortality records were maintained. Terminal organ weights (lung, heart, liver, kidney, spleen and testes) were obtained and tissues (minimum kidney and liver) were saved for microscopic examination.

No further information supplied.
Result : 200 ppm:
All guinea pigs were normal in appearance, growth and mortality. Relative organ weights, gross pathology and histopathology were normal.

100 ppm:
All guinea pigs were normal in appearance, growth and mortality. Relative organ weights, gross pathology and histopathology were normal.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
20.05.2002 (130)

Species	:	guinea pig
Sex	:	male/female
Strain	:	no data
Route of admin.	:	inhalation
Exposure period	:	6 months (130 times in 189 days)
Frequency of treatment	:	7 h/d, 5 d/w
Post obs. period	:	none
Doses	:	50 ppm (0.13 mg/l)
Control group	:	yes, concurrent no treatment
Method	:	other
Year	:	1961
GLP	:	no data
Test substance	:	
Method	:	Groups of 12 male and 12 female guinea pigs were exposed to 0 (unexposed), 0 (chamber control) or 50 ppm for 7 hrs/day, 5 days/week for 6 months. Growth and mortality records were maintained. Terminal organ weights (lung, heart, liver, kidney, spleen and testes) were obtained and tissues (minimum kidney and liver) were saved for microscopic examination. No further information supplied.
Result	:	All guinea pigs were normal in appearance, growth and mortality. Relative organ weights, gross pathology and histopathology were normal.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

20.05.2002 (130)

Species	:	rat
Sex	:	male
Strain	:	Wistar
Route of admin.	:	inhalation
Exposure period	:	10 months
Frequency of treatment	:	5hr/day, 5 days/week
Post obs. period	:	
Doses	:	50, 500, 20000 ppm
Control group	:	yes
NOAEL	:	< 50 ppm
Method	:	
Year	:	1980
GLP	:	no data
Test substance	:	
Method	:	Male Wistar rats (2 months, 180-220 g) were divided into 4 groups of 85 animals each and were exposed to air or 50, 500, or 20000 ppm vinyl chloride for 10 months, 5 hours/day, 5 days/week. Vinyl chloride concentration in inhalation chambers was checked daily by gas chromatography. Body weight and behavior were recorded weekly. Before and during 1, 3, 6 and 10 months of exposure blood and urine samples were taken and analyzed. Five control rats and five exposed to 500 ppm and 20000 ppm were subjected to x-ray analysis. Seven treated rats per group and 10 or 11 control rats were sacrificed after 1.5, 3, 6, and 10 months of exposure and tissues were examined histologically. Livers from 4 treated rats per group and 6 controls were taken at 3, 6 and 10 months and were examined ultrastructurally. Differences between means were analyzed using the Student's t-test or Cox-Cohran's t-test depending on the ratio of population variances (F-test). Frequency data were analyzed by

the chi-square test.

Result : Rats exposed to any concentration of vinyl chloride lost weight over the course of the study. Relative weights of spleen, liver, kidneys, and heart were elevated in most groups of treated animals, and relative testes weights of high dose animals were elevated. There was no effect of treatment on bones. No histological changes in organs were observed before 6 months of exposure. Increased liver cell polymorphism and proliferation of reticulo-endothelial cells of the liver were observed in animals exposed to 500 or 20000 ppm for 6 months or more. These changes were observed after exposure to 50 ppm for 10 months. Damage to spermatological epithelium was noted in rats exposed to 500 ppm for 10 months. Ultrastructural changes in the liver were observed starting at 3 months in animals exposed vinyl chloride (any concentration). One rat exposed to 50 ppm and another exposed to 20000 ppm vinyl chloride for 10 months developed adenomatous nodular hyperplasia of the liver.

Test substance : Vinyl chloride gas was supplied by Chemical Plant, Tarnow Poland and was 99.7% pure

Reliability : (1) valid without restriction

20.05.2002 (134)

Species : rat
Sex : male
Strain : Wistar
Route of admin. : inhalation
Exposure period : 3.5 hours
Frequency of treatment : 5 days / week for 4 weeks
Post obs. period : 2 - 4 days and 13 days, respectively
Doses : 2.5 Vol. % = 25000 ppm
Control group : no
NOAEL : 25000 ppm
Method : other: no data
Year : 1968
GLP : no
Test substance : other TS
Remark : Five animals were exposed. Result: No changes in behavior; Feed consumption, weight development, hematological and urinary parameters were all normal.
Source : Hoechst AG Frankfurt am Main
Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : monomeric vinyl chloride was examined
Reliability : (2) valid with restrictions

28.05.2002 (116)

Species : rat
Sex : male
Strain : Wistar
Route of admin. : inhalation
Exposure period : 3,5 Stunden
Frequency of treatment : 5 Tage / Woche, 4 Wochen lang
Post obs. period : 2 - 4 Tage bzw. 13 Tage
Doses : 2,5 Vol. % = 25000 ppm
Control group : no
NOAEL : 25000 ppm
Method : other: keine Angaben
Year : 1968
GLP : no

Test substance	:	other TS
Remark	:	Five animals were exposed. Result: No changes in behavior; Feed consumption, weight development, hematological and urinary parameters were all normal.
Source	:	Hoechst AG Frankfurt/Main Celanese GmbH Frankfurt am Main EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	monomeric vinyl chloride was examined
Reliability	:	(2) valid with restrictions

28.05.2002 (135)

Species	:	cat
Sex	:	male
Strain	:	
Route of admin.	:	inhalation
Exposure period	:	3.5 hours
Frequency of treatment	:	5 days / week for 4 weeks
Post obs. period	:	2 - 4 days
Doses	:	2.5 Vol. % = 25000 ppm
Control group	:	no
Method	:	other: no data
Year	:	1968
GLP	:	no
Test substance	:	other TS
Remark	:	Two animals were exposed. Result: 1 cat died after 13 exposures with bronchitis and peribronchial pneumonia. The blood and urine parameters were normal. During the study, slight salivation was observed.
Source	:	Hoechst AG Frankfurt am Main Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	monomeric vinyl chloride was examined
Reliability	:	(2) valid with restrictions

28.05.2002 (116)

Species	:	dog
Sex	:	male
Strain	:	Beagle
Route of admin.	:	inhalation
Exposure period	:	3.5 hours
Frequency of treatment	:	5 days / week for 4 weeks
Post obs. period	:	2 - 4 and 13 days, respectively
Doses	:	5 Vol. % = 50000 ppm
Control group	:	no
Method	:	other: no data
Year	:	1968
GLP	:	no
Test substance	:	other TS
Remark	:	Two animals were exposed. Result: During the exposures, slight salivation was observed. There was a slight body weight gain. The blood and the urinary parameters were normal.
Source	:	Hoechst AG Frankfurt am Main Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	monomeric vinyl chloride was examined
Reliability	:	(2) valid with restrictions

28.05.2002 (116)

Species	:	guinea pig
Sex	:	
Strain	:	
Route of admin.	:	inhalation
Exposure period	:	3.5 hours
Frequency of treatment	:	5 days / week for 4 weeks
Post obs. period	:	2 - 4 and 13 days, respectively
Doses	:	2.5 Vol. % = 25000 ppm
Control group	:	no
NOAEL	:	25000 ppm
Method	:	other: no data
Year	:	1968
GLP	:	no
Test substance	:	other TS
Remark	:	Stroemendes Gemisch, an 5 Tieren; Ergebnis: Keine Verhaltensaenderungen; Futteraufnahme, Gewichtsentwicklung, Blutbild- und Urinuntersuchungen normal. Five animals were exposed. Result: No changes in behavior; Feed consumption, body weight development, hematology and urinary parameters were normal.
Source	:	Hoechst AG Frankfurt am Main Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	monomeric vinyl chloride was examined
Reliability	:	(2) valid with restrictions

28.05.2002 (116)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Ames test
System of testing	:	Salmonella typhimurium TA 1530, TA 1535, G-46, TA 1538
Concentration	:	0.2, 2 and 20% v/v vinyl chloride in air or 0.083 M vinyl chloride in medium
Cycotoxic conc.	:	> 20%
Metabolic activation	:	with and without
Result	:	positive
Method	:	other
Year	:	1975
GLP	:	no data
Test substance	:	other TS
Remark	:	The authors state that the inability of vinyl chloride in solution to cause mutagenesis may have been due to the rapid loss of vinyl chloride in the liquid phase by diffusion into the atmosphere. They do not present data in support of this hypothesis
Result	:	Without metabolic activation: Exposure to 0.2, 2 or 20% vinyl chloride for 48 hours in the absence of metabolic activation increased the mutation rate in all strains tested. TA 1530 showed the highest mutagenic response, with a 2.7, 7, or 15.5-fold increase over the spontaneous rate at the aforementioned concentrations. No significant increase in mutation rate was noted in TA 1538 cells after exposure to 20%. Bacterial survival at 20% was between 86 and 131%. With metabolic activation: The mutagenic response in all strains exposed

to 0.2, 2 or 20% vinyl chloride for 48 hours was enhanced by metabolic activation. TA 1530 showed the highest mutagenic response. After 6 hr of exposure to 20% vinyl chloride, the mutagenic response for the TA 1530 strain was enhanced 7-, 4- or 5-fold when fortified postmitochondrial liver fractions from humans, rats or mice were added. No enhancement of mutagenesis was noted when fractions from lung or kidney were added. Phenobarbitone pretreatment of rats or mice increased the rate of mutagenesis by up to 15-40%. No increase in mutation rate was noted in any strain incubated with 0.083 M vinyl chloride in the medium and liver supernatant from phenobarbital pre-treated mice.

Source :

PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Test condition :

Metabolic activation system: S9 supernatant or microsomal and soluble fractions from liver, lung and kidney of male BD-IV rats (n = 3-5, 100-130 g) and male OF-1 mice (n = 3-5, 30-35 g), or human liver (n = 4) was used. Additional groups of rats and mice received phenobarbitone sodium in their drinking water (1 mg/ml) for 7 days prior to preparation of tissue fractions.

Administration: Strains TA 1530 (6.8 x 10*E8), TA 1535 (3.3 x 10*E8) and TA 1538 (8.3 x 10*E8) were exposed to vinyl chloride (0, 0.2, 2 or 20% v/v) in air for 48 hr (37 degrees C) in the presence or absence of an NADPH generating system (pH 7.4) and S9 or microsomal fractions. Concentrations of vinyl chloride in the incubation medium after 6 hr were 0.04 mM, 0.4 mM and 4 mM. Exposure took place in dessicators in the dark. Bacterial survival was determined in parallel by seeding bacteria on a histidine-enriched medium. For shorter exposures vinyl chloride was removed under vacuum and replaced by air. Vinyl chloride (0.083 M) also was added to suspensions containing S-9 from PB-treated mice and G-46 or TA 1530 bacteria (2-4 x 10*E7) cells. These suspensions were incubated at 37 degrees C for 30 min under O2

Test substance :

Vinyl chloride (purity 99.9%) was contaminated with ethanol (30 ppm), water (20 ppm), methyl chloride (< 20 ppm) and non-volatile substances (< 5 ppm)

Reliability : (1) valid without restriction
16.05.2002 (136)

Type : Mammalian cell gene mutation assay
System of testing : V9 Chinese hamster cells
Concentration : 5 to 30% v/v in atmosphere
Cycotoxic conc. :
Metabolic activation : with and without
Result : positive
Method : other
Year : 1979
GLP : no data
Test substance : other TS
Result :

An increased rate of mutation or cytotoxicity over controls was not observed in cells exposed to vinyl chloride in the absence of S15. In cells suspended in liquid or agar containing S15 from phenobarbitone pretreated rats, exposure to 20% vinyl chloride induced a maximal mutation rate of 30% and 3% in AZA and OUA resistance, respectively. Maximal rates of mutation were observed at 5 hr in liquid incubation and 10-15 h in agar incubation. The mutation and survival rates of cells in liquid suspension that were treated with vinyl chloride (5-30 %) for 5 hours were dose-dependent. The mutation frequencies of cells exposed to 30% (51 AZA and

4 OUA resistant colonies) were 10-20 times greater than spontaneous rates. The percent survival of cells treated with 0, 5, 20 or 30% vinyl chloride for 5 hours was 100%, 90%, 70% and 50%, respectively

Source :

PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Test condition :

Cells (1.5 x 10*E6/plate) were incubated (in liquid suspension or 0.3% agar) with 0.75 ml S15 post-mitochondrial fraction from livers of BDVI or OF-1 male rats that had been treated with phenobarbitone (1 mg/ml) in drinking water for 7 days in the presence or absence of an NADPH-generating system. Plates were placed in an evacuated dessicator and exposed to 0, 5, 10, 20 or 30% v/v vinyl chloride. Additional plates were exposed to vinylidene chloride or chloroprene. Pressure was adjusted to atmospheric after 20-30 min. After exposure for 5, 10 or 15 hr (37 degrees C), vapor was removed under vacuum and replaced by air, cells were washed twice, and fresh medium was added. Cytotoxicity was determined by culturing 100 treated cells/dish for 7 days. Cells to be used in mutagenesis assays were plated at 2 x 10 *E4 and 10 *E5 cells per dish. After an expression period of 48 hr, 20 micrograms/ml 8-azaguanine (AZA) or 1mM ouabain (OUA) were added to the culture medium. Media were changed after 5-7 days. Cultures were fixed and stained with Giemsa after 12 and 14 days treatment with AZA or OUA, respectively

Test substance :

Vinyl chloride (purity 99.9%) contaminated with ethanol (30 ppm), water (20 ppm), methyl chloride (< 20 ppm) and non-volatile substances (< 5 ppm) was tested

Reliability : (1) valid without restriction
20.05.2002 (137) (138)

Type : Mammalian cell gene mutation assay
System of testing :
Concentration :
Cycotoxic conc. :
Metabolic activation :
Result :
Method :
Year : 1975
GLP : no data
Test substance : other TS: 2-chloroethylene oxide and 2-chloroacetaldehyde
Result : Chloroethylene oxide and 2-chloroacetaldehyde, two possibly carcinogenic metabolities of vinyl chloride in mammals, caused a dose-dependent induction of 8-azaguanine- and ouabain-resistant mutants in Chinese hamster V79 cells in vitro. Up to one-hundred-fold higher concentrations of 2-chloroethanol or monochloroacetic acid, a urinary vinyl chloride metabolite in rats and man, were inactive.
Reliability : (2) valid with restrictions
22.05.2002 (139)

Type : Ames test
System of testing : Salmonella typhimurium TA 1535, TA 100, TA 1537, TA 1538, TA 98
Concentration : 0.022 M VC in medium
Cycotoxic conc. :
Metabolic activation : no data
Result : negative
Method : other
Year : 1976
GLP : no data
Test substance : other TS

5. Toxicity **Id** 75-01-4
Date 18.06.2002

Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
20.05.2002		(140)
Type	:	Bacillus subtilis recombination assay
System of testing	:	B. subtilis strains 168 M, Hcr-9, FB-13, MC-1
Concentration	:	0.022 M
Cycotoxic conc.	:	
Metabolic activation	:	no data
Result	:	negative
Method	:	other
Year	:	1976
GLP	:	no data
Test substance	:	other TS
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
20.05.2002		(140)
Result	:	Reaction of CEO with cytidine gave the (hydrated) 2-oxoethyl derivative at the N-3 position prior to ring closure to 3,N4-ethenocytidine; 5-methylcytosine gave an analogous reaction. However, reactions of CEO or chloroacetaldehyde (CAA) with 3-methylcytidine - i.e., with the N-3 blocked as in double-stranded DNA (ds DNA) - were shown by GC-MS of the silylated products to give, at a much slower rate, a pattern of at least 17 adducts all of which contained chlorine. Based on MS fragmentation and considerations of positional, optical and cis/trans isomerism, the reaction products of the 3-methylcytosine moiety were assigned as cis/trans N4-(2-chlorovinyl)-3-methylcytosine which may have arisen from the corresponding N4-(1-hydroxy-2-chloroethyl) adduct. It is postulated that formation of these cytosine-N4 adducts would be more rapid in double-stranded DNA than in the model compound, and that the N4-(2-chlorovinyl) group may be a miscoding adduct.
Reliability	:	(2) valid with restrictions
22.05.2002		(141)
Type	:	Yeast gene mutation assay
System of testing	:	Schizosaccharomyces pompe (SP.198)
Concentration	:	5 and 50 % v/v VC in air
Cycotoxic conc.	:	
Metabolic activation	:	with and without
Result	:	positive
Method	:	other
Year	:	1976
GLP	:	no data
Test substance	:	other TS
Remark	:	Activating system: purified microsomes from mouse liver. Method: Test gas mixture bubbled through the suspension. Incubation for 30 min to 4 h at 37 degree C. VC concentration in the medium 16 and 48 mM, respectively. Results: mutagenic activity (foreward mutation) only when mouse liver microsomal preparations were added.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	VC (impurities: water 100 ppm, HCl 2 ppm, Fe3+ 0.5 ppm, acetaldehyde 5 ppm, acetylene 2 ppm, 1.3-butadiene 10 ppm, chloroprene 5 ppm)
Reliability	:	(2) valid with restrictions
20.05.2002		(142)

Type	:	Yeast gene mutation assay
System of testing	:	Schizosaccharomyces pompe (P1 strain)
Concentration	:	16 to 48 mM in medium
Cycotoxic conc.	:	
Metabolic activation	:	with and without
Result	:	positive
Method	:	other
Year	:	1977
GLP	:	no data
Test substance	:	other TS
Remark	:	Activating system: purified microsomes from mouse liver. Method: Test gas mixture bubbled through the suspension (with/without microsomal preparation added). Incubation for 1 h at 37 degree C. VC concentration in the medium 0, 16, 32, 48 mM, respectively. Results: VC mutagenic (foreward mutation) with microsomal preparation added.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	VC (impurities: water 100 ppm, HCl 2 ppm, Fe3+ 0.5 ppm, acetaldehyde 5 ppm, acetylene 2 ppm, 1.3-butadiene 10 ppm, chloroprene 5 ppm)
Reliability	:	(2) valid with restrictions

20.05.2002 (143)

Type	:	Yeast gene mutation assay
System of testing	:	Saccharomyces cerevisiae (D4)
Concentration	:	5 and 50 % v/v VC in air
Cycotoxic conc.	:	
Metabolic activation	:	with and without
Result	:	positive
Method	:	other
Year	:	1976
GLP	:	no data
Test substance	:	other TS
Remark	:	Method: Test gas mixture bubbled through the suspension. VC concentration in the medium 16 and 48 mM, respectively. Incubation for 30 min to 4 h at 37 degree C. Results: Mutagenic activity (gene conversion) in the presence of mouse liver microsomal preparations.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	VC (impurities: water 100 ppm, HCl 2 ppm, Fe3+ 0.5 ppm, acetaldehyde 5 ppm, acetylene 2 ppm, 1.3-butadiene 10 ppm, chloroprene 5 ppm).
Reliability	:	(2) valid with restrictions

20.05.2002 (142)

Type	:	other
System of testing	:	Host mediated assay with Schizosaccharomyces pompe (SP.198)
Concentration	:	700 mg/kg VC in olive oil (1.85 %)
Cycotoxic conc.	:	
Metabolic activation	:	without
Result	:	positive
Method	:	other
Year	:	1976
GLP	:	no data
Test substance	:	other TS
Remark	:	Method: 700 mg/kg VC in olive oil (1.85 %) fed to mice during 12 h. Schizosaccharomyces pompe inoculated into the peritoneal cavity and

culture of mutants from recovered peritoneal fluid.
Results: mutagenic activity observed.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : VC (impurities: water 100 ppm, HCl 2 ppm, Fe3+ 0.5 ppm, acetaldehyde 5 ppm, acetylene 2 ppm, 1.3-butadiene 10 ppm, chloroprene 5 ppm).
Reliability : (2) valid with restrictions
20.05.2002 (142)

Type : Yeast gene mutation assay
System of testing : Saccharomyces cerevisiae (D4)
Concentration : 16 to 48 mM in medium
Cycotoxic conc. :
Metabolic activation : with and without
Result : positive
Method : other
Year : 1977
GLP : no data
Test substance : other TS
Remark : Method: Test gas mixture bubbled through the suspension (with/without microsomal preparation added).
VC concentration in the medium 0, 16, 32, 48 mM, respectively.
Incubation for 1 h at 37 degree C.
Activation system: purified microsomes from mouse liver.

Results: positive (gene conversion) with microsomal preparation added.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : VC (impurities: water 100 ppm, HCl 2 ppm, Fe3+ 0.5 ppm, acetaldehyde 5 ppm, acetylene 2 ppm, 1.3-butadiene 10 ppm, chloroprene 5 ppm).
Reliability : (2) valid with restrictions
20.05.2002 (143)

Type : Ames test
System of testing : Salmonella typhimurium TA 100
Concentration : 20 % v/v VC in atmosphere for 3 to 9 h
Cycotoxic conc. :
Metabolic activation : with and without
Result : positive
Method : other
Year : 1975
GLP : no data
Test substance : other TS
Remark : Activation system: S-9 Mix or S-9 Mix + S-9 from the liver of phenobarbital or Aroclor-induced rats.
Results: Most of the mutagenic activity of VC is direct activity. Addition of the metabolic activator results in 2-fold increase.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : 99.9 % pure
Reliability : (2) valid with restrictions
20.05.2002 (144)

Type : Ames test
System of testing : Salmonella typhimurium TA 1535
Concentration : 2 % v/v VC in the atmosphere for 3 h
Cycotoxic conc. :
Metabolic activation : with and without
Result : positive

Method	:	other
Year	:	1976
GLP	:	no data
Test substance	:	other TS
Remark	:	Activation system: microsomal fraction (S9) from rat liver.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	high purity
Reliability	:	(2) valid with restrictions
20.05.2002		(145)

Type	:	other: DNA adducts
System of testing	:	
Concentration	:	
Cycotoxic conc.	:	
Metabolic activation	:	
Result	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	
Result	:	2-chloroethylene oxide and 2-chloroacetaldehyde have been shown to produce DNA adducts, which are thought to play a role in development of carcinogenicity.
Reliability	:	(2) valid with restrictions
22.05.2002		(146) (147) (148) (149)

Type	:	Ames test
System of testing	:	Salmonella typhimurium TA 1535, TA 1536, TA 1537, TA 1538
Concentration	:	20 % v/v VC in atmosphere for 75 min at 23 degree C
Cycotoxic conc.	:	
Metabolic activation	:	with and without
Result	:	positive
Method	:	other
Year	:	1974
GLP	:	no data
Test substance	:	other TS
Remark	:	Activation system: microsomal fraction (S9) from rat liver. Results: Positive only after metabolic activation in TA 1530 and TA 1535; negative in TA 1536, TA 1537, TA 1538.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	high purity
Reliability	:	(2) valid with restrictions
29.05.2002		(150)

Type	:	Ames test
System of testing	:	Salmonella typhimurium TA 1535
Concentration	:	0.4 to 15.4 % VC in air
Cycotoxic conc.	:	
Metabolic activation	:	with and without
Result	:	positive
Method	:	other
Year	:	1976
GLP	:	no data
Test substance	:	other TS
Remark	:	Activation system: Aroclore 1254-stimulated liver homogenate (species not specified)

Method: incubation for 72 h at 37 degree C in atmosphere containing VC.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : VC standard
Reliability : (2) valid with restrictions
29.05.2002 (151)

Type : Ames test
System of testing : Salmonella typhimurium TA 1530
Concentration : 75 % VC in air for 3h at 37 degree C
Cycotoxic conc. :
Metabolic activation : with and without
Result : positive
Method : other
Year : 1976
GLP : no data
Test substance : other TS
Remark : Activation system: rat or mouse liver microsomal preparations (S-9 supernatant) with or without induction by Aroclor or VC.
Comparison with activation by oxygen radicals produced by riboflavine in the presence of light.
Results: Metabolic activation seems to be negligible.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : 99.9 % pure
Reliability : (2) valid with restrictions
29.05.2002 (152)

Type : Ames test
System of testing : Salmonella typhimurium TA 1530, TA 1535, G-46
Concentration : 0.2, 2, 20 % (v/v) VC in air for 6 or 48 h at 37 degree C
Cycotoxic conc. :
Metabolic activation : with and without
Result : positive
Method : other
Year : 1975
GLP : no data
Test substance : other TS
Remark : Activation system: rat (female BD-IV), mouse (male OF-1), and human liver microsomal (S-9 and soluble) preparations.
Rats and mice with/without induction by phenobarbital.
VC concentration in medium: 4 * E-5 M, 4 * E-4 M, 4 * E-3 M, respectively.
Results: VC increases the number of revertants in strains TA 1530, TA 1535 and G-46 16, 12, or 5 times, respectively, over the spontaneous mutation rate.
When fortified S-9 liver fractions were added, the mutagenic response for TA 1530 was enhanced 7, 4, or 5 fold, respectively.
The VC metabolite chloroacetic acid showed only toxic effects, while chloroacetaldehyde, chloroethanol, and chloroethyleneoxide caused mutagenic response.
Chloroethyleneoxide has a strongly alkylating activity.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : 99.9 % pure
Reliability : (2) valid with restrictions
29.05.2002 (153)

Type : Ames test
System of testing : Salmonella typhimurium

Concentration :
Cycotoxic conc. :
Metabolic activation : with and without
Result : positive
Method :
Year : 1977
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Remark : Positive with and without metabolic activation as cited in a review by Giri et al., 1995.
Reliability : (2) valid with restrictions
16.05.2002 (154) (155)

Type : Ames test
System of testing : Salmonella typhimurium
Concentration :
Cycotoxic conc. :
Metabolic activation : with and without
Result : positive
Method :
Year : 1980
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Result : Positive with and without metabolic activation as cited in a review by Giri et al., 1995.
Reliability : (2) valid with restrictions
16.05.2002 (156) (154)

Type : Ames test
System of testing : Salmonella typhimurium
Concentration :
Cycotoxic conc. :
Metabolic activation : with and without
Result : positive
Method :
Year : 1980
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Result : Positive with and without metabolic activation as cited in a review by Giri et al., 1995.
Reliability : (2) valid with restrictions
29.05.2002 (154) (157)

Type : Ames test
System of testing : Salmonella typhimurium
Concentration :
Cycotoxic conc. :
Metabolic activation : with and without
Result : positive
Method :
Year : 1988
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Result : Positive with and without metabolic activation as cited in a review by Giri et al., 1995.
Reliability : (2) valid with restrictions
16.05.2002 (154) (158)

Type : Bacterial gene mutation assay

5. Toxicity **Id** 75-01-4
Date 18.06.2002

System of testing	:	E. coli strain K 12
Concentration	:	10.6 mM VC in test medium; incubation for 2 h at 37 degree C
Cycotoxic conc.	:	
Metabolic activation	:	with and without
Result	:	positive
Method	:	other
Year	:	1975
GLP	:	no data
Test substance	:	other TS
Remark	:	Activation system: Microsomal proteins from phenobarbital induced male mice. Results: Negative without metabolic activation. Positive with metabolic activation.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	VC > 99.9 % pure
Reliability	:	(2) valid with restrictions

20.05.2002 (159)

Type	:	Yeast gene mutation assay
System of testing	:	Saccharomyces cerevisiae
Concentration	:	
Cycotoxic conc.	:	
Metabolic activation	:	without
Result	:	negative
Method	:	
Year	:	1976
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Negative without metabolic activation as cited in a review by Giri et al., 1995.
Reliability	:	(2) valid with restrictions

16.05.2002 (154) (160)

Type	:	other: Spot test
System of testing	:	Yeast D7RAD
Concentration	:	
Cycotoxic conc.	:	
Metabolic activation	:	
Result	:	positive
Method	:	
Year	:	1981
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Increase in TRP+ revertants in cells incubated with vinyl chloride as cited in a review by Giri et al., 1995.
Reliability	:	(2) valid with restrictions

16.05.2002 (161) (154)

Type	:	other: Tradescantia clone 4430
System of testing	:	
Concentration	:	
Cycotoxic conc.	:	
Metabolic activation	:	
Result	:	positive
Method	:	
Year	:	1982
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Remark	:	Increased mutations in Tradescantia clone 4430 cells incubated with vinyl chloride as cited in a review by Giri et al., 1995.
Reliability	:	(2) valid with restrictions
16.05.2002		(154) (162)
Type	:	other
System of testing	:	Neurospora crassa strains Em a, 5297 (wild type) and nic-1,3416 (auxotrophic strain)
Concentration	:	various dilutions of VC (1.78 M) in ethanol or incubation of the test mixture in VC/air atmosphere
Cycotoxic conc.	:	
Metabolic activation	:	with and without
Result	:	negative
Method	:	other
Year	:	1977
GLP	:	no data
Test substance	:	other TS
Remark	:	Activation system: Liver microsomes, S -9 supernatant from uninduced Buffalo rats or S -9 fraction from phenobarbital induced rats. Method: Incubation for 3-4 h at room temperature or 3.5 h at 37 degree C.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	VC 99.9 % pure
Reliability	:	(2) valid with restrictions
29.05.2002		(163)
Type	:	other
System of testing	:	incubation of polyadenylic acid, rat liver microsomes, NADPH, VC
Concentration	:	
Cycotoxic conc.	:	
Metabolic activation	:	with
Result	:	positive
Method	:	other
Year	:	1978
GLP	:	no data
Test substance	:	no data
Remark	:	Test system: analysis of DNA adduct formation after in vitro incubation of polyadenylic or polycytidylic acid. Results: Formation of ethenoadenine and ethenocytidine moieties was observed.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
29.05.2002		(164)
Type	:	other
System of testing	:	Incubation of adenosine, mouse liver microsomes, NADPH producing enzymes with VC/oxygen
Concentration	:	
Cycotoxic conc.	:	
Metabolic activation	:	with and without
Result	:	positive
Method	:	other
Year	:	1975
GLP	:	no data
Test substance	:	other TS
Remark	:	Test system: Analysis of alkylation products Results: 1) Chloroethylene oxide was chemically and spectroscopically identified as a reaction product.

2) An alkylation product of adenosine is formed.
3) A similar product is formed during reaction of adenosine with chloroethylene oxide or 2-chloroacetaldehyde.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (165)

5.6 GENETIC TOXICITY 'IN VITRO'

Type : Micronucleus assay
Species : mouse
Sex : male/female
Strain : other: C57Bl/6J
Route of admin. : inhalation
Exposure period : 6 hr
Doses : 50000 ppm
Result :
Method : other
Year : 1983
GLP : no data
Test substance : other TS
Result :

The incidences of micronuclei in male and female mice exposed to vinyl chloride for 24 hours (24.6 and 25.0 /1000 PCE, respectively) were significantly greater than controls (2.6 and 1.2/1000 PCE, respectively). After 48 hours of exposure to vinyl chloride, an elevated incidence of micronuclei was observed only in males (7.2/1000 PCE vs. 2.2/1000 PCE in controls). Vinyl chloride was not cytotoxic at the level tested

Source :

PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Test condition :

Test animals and administration: Mice were obtained at 4-6 weeks old and held for 5 days prior to exposure. Forty animals (20/sex) were exposed to test atmosphere containing 50000 ppm vinyl chloride monomer or air for 6 hours. Test atmosphere was generated by mixing air at a rate of 150 l/min with 7.5 l/min of vinyl chloride monomer controlled by flow meters. Room air, control and test exposure chambers were monitored continuously for vinyl chloride by an infrared gas analyzer. Ten animals/sex/group were killed 24 hr and 48 hours after exposure.

Examination: Ten animals/sex/group were killed 24 hr and 48 hours after exposure by cervical dislocation. Femurs were removed and stripped clean of muscle, and the iliac end was removed. Marrow suspension was applied to microscope slides, which were stained, coded and scored blind. Five hundred polychromatic erythrocytes (PCE) were examined for each animal and the number containing micronuclei were scored. The ratio of polychromatic/mature erythrocytes was determined as a measure of cytotoxicity

Test substance :

Vinyl chloride monomer came from Cambrian Chemicals, Croydon, Surrey (GB). Purity was not listed

Reliability : (2) valid with restrictions
24.01.2001 (166)

Type : Cytogenetic assay

5. Toxicity **Id** 75-01-4
Date 18.06.2002

Species	:	Rat
Sex	:	male/female
Strain	:	Other
Route of admin.	:	Inhalation
Exposure period	:	7 h/d, 5 d/wk
Doses	:	50, 250, 1000 ppm
Result	:	negative
Method	:	other
Year	:	1977
GLP	:	no data
Test substance	:	other TS
Remark	:	The cytogenetic study reported here was not a stand alone study, but was a component of a repeated dose toxicity study described in Section 5.4
Result	:	There was no significant difference in the cytogenic analysis of bone marrow cultures between animals exposed to vinyl chloride or controls
Source	:	PCA Services, In PCA Services, Inc. Kingsport, TN
Test condition	:	Test Organisms: CD rats (aged 2 months) from Charles River (CD) were used. Number of animals per dose: 36 rats of each sex (including control) Administration/Exposure: Vinyl chloride gas was metered with rotameters into the chamber air supply. The lines and rotameter were heated to 37 degrees C to generate vapor and then to 40 degrees C to prevent condensation. The chamber concentration was monitored using a gas chromatograph with a flame ionization detector. Doses: air (control), 50 ppm, 250 ppm, 1000 ppm Experimental: Animals were sacrificed when moribund or at 12 months. A cytogenetic analysis of bone marrow cultures (as described by Tijo and Wang in: Human Chromosome Methodology, J. J. Yunis, Ed., Academic Press, New York, 1965) was performed on controls and animals exposed to 1000 ppm
Test substance	:	Vinyl choride gas (99.8% pure) from Matheson Products
Reliability	:	(2) valid with restrictions

20.05.2002 (126)

Type	:	Cytogenetic assay
Species	:	Mouse
Sex	:	male/female
Strain	:	Abyssinian
Route of admin.	:	Inhalation
Exposure period	:	7 h/d, 5 d/wk for up to 12 months
Doses	:	50, 250, 1000 ppm
Result	:	Negative
Method	:	other
Year	:	1977
GLP	:	no data
Test substance	:	other TS
Remark	:	The cytogenetic study reported here was not a stand alone study, but was a component of a repeated dose toxicity study described in Section 5.4

5. Toxicity **Id** 75-01-4
Date 18.06.2002

Result :
There was no significant difference in the cytogenic analysis of bone marrow cultures between animals exposed to vinyl chloride or controls

Source :
PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Test condition :
Test Organisms: CD-1 mice (aged 2 months) from Charles River

Number of animals per dose: 36 mice of each sex (including control) were used in the study.

Administration/Exposure: Vinyl chloride gas was metered with rotameters into the chamber air supply. The lines and rotameter were heated to 37 degrees C to generate vapor and then to 40 degrees C to prevent condensation. The chamber concentration was monitored using a gas chromatograph with a flame ionization detector.

Doses: air (control), 50 ppm, 250 ppm, 1000 ppm

Experimental: Animals were sacrificed when moribund or at 12 months. A cytogenetic analysis of bone marrow cultures (as described by Tijo and Wang in: Human Chromosome Methodology, J. J. Yunis, Ed., Academic Press, New York, 1965) was performed on controls and animals exposed to 1000 ppm

Test substance :
Vinyl choride gas (99.8% pure) from Matheson Products

Reliability : (2) valid with restrictions
24.01.2001 (126)

Type : Dominant lethal assay
Species : mouse
Sex : male
Strain : CD-1
Route of admin. : inhalation
Exposure period : 6 h/day for 5 days
Doses : 3000, 10000, 30000 ppm
Result : negative
Method : other
Year : 1976
GLP : no data
Test substance : other TS
Result :

Males: A significant increase in mortality was noted in males treated with 30000 ppm VC (9/20 vs. 0/20 in controls). No significant differences in the mating frequency of males treated with VC were found with respect to controls. There was a significant decrease in mating frequency of mice treated with EMS at week 1.

Females Mated with Vinyl Chloride-treated Males: The frequency of pregnancies remained high throughout the experiment in females mated with males treated with VC. The number of average total implants per pregnant female mated with mice treated with 0, 3000, 10000 or 30000 ppm VC ranged from 11.75 to 13.68, 11.56 to 13.56, 11.76 to 14.13, and 10.00 (the only value significantly different from control) to 13.67. There was no significant increase in the number of post-implantational early fetal deaths (as shown by the number of females with one or more early deaths, number of early deaths/pregnancy, or the number of early deaths/total implants/pregnancy). There also was no effect of vinyl chloride on fertility

or late deaths. The percentage of pre- and post-implantation dominant lethality in mice mated with males treated with the highest dose of VC was only significantly different from typical values (-14 to +12) at one time point (week 4, +19).

Females Mated with EMS or Cyclophosphamide-treated Males (positive controls): The frequency of pregnancy decreased in those mated with EMS-treated males at weeks 1 and 2. The number of implants per female, pregnancies with early deaths, and deaths per pregnancy in those mated with mice treated with cyclophosphamide or EMS were significantly different from control at week 1 and weeks 1 and 2, respectively. The number of early deaths/total implants/pregnancy in those mated with mice treated with cyclophosphamide or EMS was significantly different from control at weeks 1 and 2. The percentage of pre- and post-implantation dominant lethality in mice mated with males treated with cyclophosphamide or EMS was significantly different from typical values (-14 to +12) at week 1 (+62.3 and +95.9, respectively), week 2 (+49.3 and +51.3, respectively) and week 3 (+19.1, cyclophosphamide only)

Source :

PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Test condition :

Test animals and adminstration: Mice (CD-1) were obtained from Charles River, Manston, Kent. Groups of male mice (8-10 weeks old) of proven fertility were given 5 daily (6 hr) exposures of air (N=20), vinyl chloride (VC) at 3000 (N=20), 10000 (N=20) and 30000 ppm (N=20). Additional groups of mice were given either 200 mg/kg of cyclophosphamide by i.p. injection on day 5 (N=15) or 200 mg/kg ethyl methanesulphonate (EMS) in water for 5 days (N=25). The highest dose of VC was shown to be toxic in a previous test. Two undosed, virgin female mice (8-10 weeks old) were housed with a treated male of proven fertility (total of 106 males) for 5 days. Males were then housed without females for a week. The mating procedure was then repeated until the males had been mated at weekly intervals for 8 weeks with virgin, untreated females. Males were then killed and were not examined. Evidence of positive mating was not obtained. Female mice were killed 15 or 16 days after being housed with males.

Assessment: Uteri of female mice were examined for live implantations, early deaths and late deaths.

Statistical Procedures: A chi-square test was used to assess significant differences in frequency of successful mating and pregnancy, and the number of pregnancies with early deaths. Mean values of implantation data were adjusted to take the unequal number of pregnant females per male into account and were compared using ANOVA and a Dunnett's t test. Data for the number of early deaths per pregnancy and the percentage of total deaths recorded as early deaths per pregnancy were transformed prior to analysis by the variance ratio test

Test substance :

Vinyl chloride was obtained from Air Products Limited, Worsley, Walkden, Lanc

Conclusion :

Vinyl chloride is not mutagenic in the mouse at the stated exposure levels as measured by the dominant lethal test

Reliability : (2) valid with restrictions
25.01.2001 (167)

Type : other: DNA alkylation and adduct formation
Species : Rat

5. Toxicity **Id** 75-01-4
Date 18.06.2002

Sex	:	
Strain	:	
Route of admin.	:	
Exposure period	:	
Doses	:	
Result	:	Positive
Method	:	
Year	:	1985
GLP	:	no data
Test substance	:	other TS: [14C] vinyl chloride
Remark	:	N-2,N-3 ethenogaunine was detected in the liver of preweanling rats after exposure to [14C] vinyl chloride (as cited in a review by Giri et al., 1995).
Reliability	:	(2) valid with restrictions

20.05.2002 (154) (168)

Type	:	Other
Species	:	Rat
Sex	:	no data
Strain	:	Wistar
Route of admin.	:	Inhalation
Exposure period	:	5 h
Doses	:	dose not specified
Result	:	
Method	:	other
Year	:	1981
GLP	:	no data
Test substance	:	other TS
Remark	:	Method: Analysis of alkylation products of rat liver DNA and RNA. Exposure: 1) Rats exposed in vivo to 1,2-14C-VC; 2) Rat liver microsomes in vitro to 14C-VC.
Result	:	Etheno-derivatives of deoxyadenosine and deoxycytidine as well as 7-N-(2-oxoethyl)guanine are formed when rat liver microsomes are incubated with 14C-VC in vitro. 7-N-(2-oxoethyl)guanine is detected in DNA from the liver of rats exposed to 1,2-14C-VC in vivo. The results are related to formation of adducts from single-stranded and double-stranded DNA, respectively.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	1,2-14C-vinyl chloride, purity not specified
Reliability	:	(2) valid with restrictions

20.05.2002 (164) (169) (170) (171) (172)

Type	:	other: DNA alkylation and adduct formation
Species	:	Rat
Sex	:	
Strain	:	
Route of admin.	:	
Exposure period	:	
Doses	:	
Result	:	Positive
Method	:	
Year	:	1989
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	N-2,N-3 ethenogaunine was detected in the liver of preweanling rats after exposure to vinyl chloride (as cited in a review by Giri et al., 1995).
Reliability	:	(2) valid with restrictions

20.05.2002 (173) (154)

5. Toxicity **Id** 75-01-4
Date 18.06.2002

Type	:	other: DNA adduct formation
Species	:	Rat
Sex	:	
Strain	:	
Route of admin.	:	
Exposure period	:	
Doses	:	
Result	:	Positive
Method	:	
Year	:	1992
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Preweanling rats were exposed to 600 ppm (4 hrs/day) vinyl chloride for 5 days and DNA adducts in liver, lung and kidney were quantified. The liver had 3-8 times more DNA adducts than the lung or kidney. 7 -(2'-oxoethyl)guanine was the major adduct detected (as cited in a review by Giri et al., 1995).
Reliability	:	(2) valid with restrictions

20.05.2002 (154) (174)

Result	:	In rats, the substitution mutations found at A:T base pairs in the ras and p53 genes are consistent with the promutagenic properties of the DNA adduct 1,N6-ethenoadenine formed from vinyl chloride metabolites.
Reliability	:	(2) valid with restrictions

22.05.2002 (146)

Type	:	Drosophila SLRL test
Species	:	Drosophila melanogaster
Sex	:	Male
Strain	:	Other
Route of admin.	:	Inhalation
Exposure period	:	2 or 4 d
Doses	:	30 to 50 000 ppm (0.08 to 128 mg/l) VC in air
Result	:	
Method	:	other
Year	:	1977
GLP	:	no data
Test substance	:	other TS
Remark	:	Strain: Berlin K; mating of exposed males with Basc females. Exposure to 0, 30, 200, 850, 10 000, 30 000, or 50 000 ppm VC, respectively, for 2 or 4 days. Exposure to 30 ppm VC also for 17 days.
Result	:	Mutation frequency increased from 850 to 10 000 ppm VC and remained constant at concentrations above 10 000 ppm. Brooding analysis revealed that spermatocytes are particularly sensitive to killing by VC. Spermatogonia are less sensitive, presumably due to poorly developed ER. After prolonged exposure to 30 ppm mutation frequency was slightly (n.s.) enhanced. Thus, VC seems to show mutagenic activity even at very low concentrations.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	VC (impurities: 1 - 2 ppm acetylene, 1 ppm water, 82 ppm phenole).
Reliability	:	(2) valid with restrictions

20.05.2002 (175)

Type	:	Dominant lethal assay
Species	:	Drosophila melanogaster
Sex	:	
Strain	:	

5. Toxicity **Id** 75-01-4
Date 18.06.2002

Route of admin.	:	
Exposure period	:	
Doses	:	
Result	:	Negative
Method	:	
Year	:	1976
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	No increase in dominant lethal mutations as cited in a review by Giri et al., 1995.
Reliability	:	(2) valid with restrictions

20.05.2002 (176) (154)

Type	:	Dominant lethal assay
Species	:	Mouse
Sex	:	
Strain	:	
Route of admin.	:	
Exposure period	:	
Doses	:	
Result	:	Negative
Method	:	
Year	:	1976
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	No increase in dominant lethal mutations as cited in a review by Giri et al., 1995.
Reliability	:	(2) valid with restrictions

20.05.2002 (176) (154)

Type	:	Dominant lethal assay
Species	:	Rat
Sex	:	
Strain	:	
Route of admin.	:	
Exposure period	:	
Doses	:	
Result	:	Negative
Method	:	
Year	:	1977
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	No increase in dominant lethal mutations as cited in a review by Giri et al., 1995.
Reliability	:	(2) valid with restrictions

20.05.2002 (154) (177)

Result	:	A group of 67 workers occupationally exposed to VCM was examined for the presence and distribution of breaks along the chromosomal length. Breaks induced by VCM are not randomly distributed as had been expected in a normal population. According to our results there exist highly sensitive and highly resistant locations along the chromosomes to the actions of VCM.
Reliability	:	(2) valid with restrictions

22.05.2002 (178)

Type	:	Cytogenetic assay
Species	:	Chinese hamster
Sex	:	no data

Strain	:	no data
Route of admin.	:	Inhalation
Exposure period	:	4 h/d for 5 days
Doses	:	2 500 ppm (6.4 mg/l), 5 000 ppm (12.8 mg/l)
Result	:	
Method	:	other
Year	:	1978
GLP	:	no data
Test substance	:	no data
Result	:	Frequency of structural anomalies of chromosomes (inclusive/exclusive gaps) in b one marrow cells significantly higher than in the control group.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

16.05.2002 (179)

Type	:	Cytogenetic assay
Species	:	Chinese hamster
Sex	:	no data
Strain	:	no data
Route of admin.	:	i.p.
Exposure period	:	5 d
Doses	:	300 or 600 mg/kg b.w. (in olive oil)
Result	:	
Method	:	other
Year	:	1978
GLP	:	no data
Test substance	:	no data
Result	:	Frequency of structural anomalies of chromosomes (inclusive/exclusive gaps) in bone marrow cells significantly increased in treated group as compared to the control group.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

16.05.2002 (179)

Type	:	Cytogenetic assay
Species	:	Chinese hamster
Sex	:	male/female
Strain	:	no data
Route of admin.	:	Inhalation
Exposure period	:	6 to 24 h
Doses	:	1.25 % (32 mg/l), 2.5 % (64 mg/l), or 5 % (128 mg/l) in air
Result	:	
Method	:	other
Year	:	1980
GLP	:	no data
Test substance	:	other TS
Remark	:	Exposure: For analysis of chromosomal aberrations: 6, 12, or 24 h at 2.5 % (v/v) VC, or 24 h at 5 % (v/v) VC in air. For analysis of SCE: 6, 12, or 24 h at 1.25 or 2.5 % (v/v) VC in air.
Result	:	Percentage of chromosomal aberrations in bone marrow cells slightly increased in hamsters exposed to 2.5 % VC for 6 h. Distinct increase following 24 h exposure. High percentage of aberrations after exposure to 5 % VC for 24 h. Doubling of SCE frequency after exposure to 1.5 % VC for 6h. Increasing frequency with increasing dose and length of exposure.

5. Toxicity **Id** 75-01-4
Date 18.06.2002

Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	VC purity not specified
Reliability	:	(2) valid with restrictions
29.05.2002		(180)
Type	:	Cytogenetic assay
Species	:	rat
Sex	:	
Strain	:	
Route of admin.	:	
Exposure period	:	
Doses	:	
Result	:	positive
Method	:	
Year	:	1981
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	A significant increase in chromosomal abnormalities was observed in rats exposed to 1500 ppm, 6 hrs/day for 5 days by inhalation (as cited in a review by Giri et al., 1995).
Reliability	:	(2) valid with restrictions
16.05.2002		(181) (154)
Type	:	Dominant lethal assay
Species	:	Drosophila melanogaster
Sex	:	male
Strain	:	other
Route of admin.	:	inhalation
Exposure period	:	2 d
Doses	:	30 000 ppm (76.8 mg/l)
Result	:	
Method	:	other
Year	:	1977
GLP	:	no data
Test substance	:	other TS
Remark	:	Strain: Berlin K; mating of exposed males to Basc females.
Result	:	No mutagenicity observed.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	VC (impurities: 1 - 2 ppm acetylene, 1 ppm water, 82 ppm phenole).
Reliability	:	(2) valid with restrictions
16.05.2002		(175)
Type	:	Drosophila SLRL test
Species	:	Drosophila melanogaster
Sex	:	Male
Strain	:	Other
Route of admin.	:	Inhalation
Exposure period	:	3 h
Doses	:	1 %, 10 %, or 20 % (26 - 520 mg/l) VC in air
Result	:	
Method	:	other
Year	:	1978
GLP	:	no data
Test substance	:	other TS
Remark	:	Exposure: 3 h to 10 000, 100 000, or 200 000 ppm VC in the atmosphere. Induction: pretreatment with phenobarbiturate (1 % solution in water containing 1 % sucrose) for 24 h.

Strain: Karsnaes 60; mating of exposed males with Muller 5 females.
2. generation: mating of heterozygous females with Muller 5 males.

Result : Increased mutagenicity at lowest exposure concentration. No increase with concentration. Significant increase in mutagenicity by pretreatment with phenobarbiturate.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : 1) VC of high purity (impurities: trace amounts of isopropanol).
2) VC 99.995 % pure
Reliability : (2) valid with restrictions
29.05.2002 (182) (183)

Type : Micronucleus assay
Species : mouse
Sex :
Strain :
Route of admin. :
Exposure period :
Doses :
Result : positive
Method :
Year : 1980
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Remark : as cited in a review by Giri et al., 1995
Reliability : (2) valid with restrictions
16.05.2002 (154) (184)

Type : Mouse spot test
Species : mouse
Sex : female
Strain : other
Route of admin. : inhalation
Exposure period : 5 h on 10th day of gestation
Doses : 4,600 ppm (11.8 mg/l) in atmosphere
Result :
Method : other
Year : 1980
GLP : no data
Test substance : no data
Remark : Strain: female C57BL/6JHan mated to the Han rotated-bred males of the T-stock strain.
F1 offspring examined for mosaic coat colour at 3 - 5 weeks post partum.
Cyclophosphamide as positive control.
Result : Frequency of spots not significantly different from negative control. The results provide no evidence that VC causes gene mutation.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
16.05.2002 (185)

Type : other
Species : mouse
Sex : female
Strain : NMRI
Route of admin. : inhalation
Exposure period : 39 to 234 h (6 h/d, 5d/w)
Doses : 500 ppm (1.28 mg/l) in air
Result :

5. Toxicity **Id** 75-01-4
Date 18.06.2002

Method	:	other
Year	:	1984
GLP	:	no data
Test substance	:	other TS
Remark	:	Method: Determination of DNA-strand breaks (SSB). Exposure: 39, 60, 117, 234 h, respectively. Mice killed 2 h after exposure. Exposure 36, 114, 231 h, respectively. Mice killed 18 h after exposure. Control animals, exposed to air only, were killed after 36 h and 231 h, respectively.
Result	:	In animals killed 2 h after an exposure period of 117 h: increased levels of SSB in lungs, liver, kidney and possibly spleen. In spleen significant increase only after 234 h exposure. In animals killed 18 h after an exposure period of 36 h: SSB levels in kidney, lung, and liver had returned to normal values. In animals killed 18 h after an exposure period of 114 h and 231 h: SSB levels in kidney, lung, and liver remained elevated. SSB levels in brain elevated only in animals killed 18 h after an exposure period of 114 h.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	VC (>99.9 %)
Reliability	:	(2) valid with restrictions

16.05.2002 (186)

Type	:	other
Species	:	mouse
Sex	:	male
Strain	:	other
Route of admin.	:	inhalation
Exposure period	:	2.33 and 10 h, respectively
Doses	:	98 to 302 ppm*h
Result	:	
Method	:	other
Year	:	1977
GLP	:	no data
Test substance	:	other TS
Remark	:	Strains: CBA, BALB, ATL, respectively. Method: Analysis of DNA alkylation products in homogenates of liver and testes.
Result	:	VC is metabolically converted into a short-lived alkylating intermediate which introduces the 2-oxoethyl group onto nucleophilic sites in DNA and proteins. The main reactive metabolite is supposed to be chloroethylene oxide.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	1,2-14C -vinyl chloride (radiochemical purity 99 %)
Reliability	:	(2) valid with restrictions

16.05.2002 (187)

Type	:	other
Species	:	rat
Sex	:	male/female
Strain	:	Wistar
Route of admin.	:	oral feed
Exposure period	:	2 y
Doses	:	250 ppm (0.64 mg/l) in drinking water
Result	:	
Method	:	other
Year	:	1978

5. Toxicity **Id** 75-01-4
Date 18.06.2002

GLP	:	no data
Test substance	:	other TS
Remark	:	Materials studied: 1) DNA from liver homogenates from rats exposed to VC. 2) calf-thymus DNA modified by reaction with chloroacetaldehyde.
Result	:	Etheno-deoxyadenosine and etheno-deoxycytidine derivatives were identified in DNA hydrolysates from both experimental setups.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	VC purity not specified
Reliability	:	(2) valid with restrictions

16.05.2002 (188)

Type	:	other
Species	:	rat
Sex	:	male
Strain	:	Wistar
Route of admin.	:	inhalation
Exposure period	:	5 h
Doses	:	50 ppm (0.256 mg/l) initial concentration
Result	:	
Method	:	other
Year	:	1976
GLP	:	no data
Test substance	:	other TS
Remark	:	Materials studied: urine, brain, liver, spleen, kidney, adipose tissue, muscle.
Result	:	All physiological bases of rat liver RNA showed significant alkylation. Ethenoadenosine and ethenocytidine were identified. Uptake of VC by rats can be blocked with inhibitors of cytochrome-P-450-dependent microsomal drug metabolism (i.e. 3-bromophenyl-4(5)-imidazole or 6-nitro-1,2,3-benzo-thiadiazole). Uptake of VC is increased by pretreatment with DDT or clotrimazol. Immediately after exposure, highest levels were observed in liver and kidney. Metabolites were rapidly excreted (69.4 % within 24 h). Some metabolites remain in the tissue, presumably covalently bound to macromolecular structures.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	1,2-14C-vinyl chloride (99.9 % pure)
Reliability	:	(2) valid with restrictions

16.05.2002 (189) (164)

Type	:	other
Species	:	mouse
Sex	:	male
Strain	:	NMRI
Route of admin.	:	i.p.
Exposure period	:	4 h
Doses	:	162.5 mg/kg b.w. VC (in peanut oil)
Result	:	
Method	:	other
Year	:	1982
GLP	:	no data
Test substance	:	other TS
Remark	:	Method: Analysis of DNA and RNA alkylation. Materials studied: homogenates from spleen, pancreas, liver, kidney, lung, testis.
Result	:	RNA from spleen, pancreas, and liver, and DNA from spleen and liver contained highest amounts of radioactivity. Nucleic acids from the brain

were devoid of radioactivity. In kidney and liver RNA, a large part of the radioactivity was present as incorporated C1-fragments, but ethenocytidine, ethenoadenosine, and ethenoadenine were also present. In liver DNA incorporation of C1-fragments was insignificant. Binding mechanisms by RNA and DNA, respectively, presumably are different. The results are consistent with the ability of VC to act as a multipotent carcinogen by alkylation of DNA.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : (1,2-14C)-vinyl chloride (99 % purity)
Reliability : (2) valid with restrictions
29.05.2002 (190)

Type : other: DNA Single-Strand Breaks
Species : mouse
Sex :
Strain :
Route of admin. :
Exposure period :
Doses :
Result : positive
Method :
Year : 1988
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Remark : NMRI female mice were exposed to 100, 250 and 500 ppm vinyl chloride by inhalation. Liver cell nuclei were prepared and DNA single strand breaks were determined by the DNA unwinding technique. Vinyl chloride induced single strand breaks in a dose-dependent manner. About 80% of the damage was repaired within 20 hours (as cited in a review by Giri et al., 1995).
Reliability : (2) valid with restrictions
16.05.2002 (154) (191)

Type : other: DNA adduct formation
Species : rat
Sex :
Strain :
Route of admin. :
Exposure period :
Doses :
Result : positive
Method :
Year : 1990
GLP : no data
Test substance : as prescribed by 1.1 - 1.4
Remark : Increased levels of 1,N6-ethenodeoxyadenosine and 3,N4-ethenodeoxycytidine were measured in DNA of several organs in rats exposed to vinyl chloride (as cited in a review by Giri et al., 1995).
Reliability : (2) valid with restrictions
16.05.2002 (192) (154)

Type :
Species : other: Yeast D7RAD
Sex :
Strain :
Route of admin. :
Exposure period :
Doses :

5. Toxicity **Id** 75-01-4
Date 18.06.2002

Result	:	positive
Method	:	
Year	:	1981
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	A small but significant increase in TRP+ convertants occurred in mice treated with vinyl chloride and incubated with yeast strain 7RAD cells as cited in a review by Giri et al., 1995.
Reliability	:	(2) valid with restrictions

16.05.2002 (193) (154)

5.7 CARCINOGENITY

Species	:	rat
Sex	:	male/female
Strain	:	Wistar
Route of admin.	:	oral feed
Exposure period	:	149 weks
Frequency of treatment	:	4 consecutive hr/day (generally between 10 am and 2 pm)
Post. obs. period	:	none
Doses	:	0.014, 0,13, 1.3 mg/kg bw
Result	:	positive
Control group	:	yes, concurrent vehicle
Method	:	other
Year	:	1991
GLP	:	no data
Test substance	:	other TS
Method	:	Study was conducted in accordance with generally accepted scientific principles.
Remark	:	This summary describes carcinogenicity data from the repeated dose toxicity study by the same author in Section 5.4
Result	:	An increased incidence of hepatocellular carcinoma was noted in males treated with 1.3 mg/kg (3/49) versus controls (0/99). 1/49 males and 2/49 females treated with 1.3 mg/kg developed angiosarcoma (vs. 0 in controls)
Source	:	PCA Services, Inc PCA Services, Inc. Kingsport, TN
Test condition	:	Test Organisms: Newly weaned rats were obtained from the SPF Colony of the Central Institute for the Breeding of Laboratory Animals (TNO, Zeist, The Netherlands). Number of animals per dose: 100 of each sex for the following dose groups: 0 mg/kg (control), 0.014 mg/kg, 0.13 mg/kg. 50 of each sex for the 1.3 mg/kg dose. Administration/Exposure: PVC powder enriched with vinyl choride monomer (VCM) was added to a diet containing 1% PVC powder to provide 0.46, 4.6 and 46 ppm vinyl chloride (VC). Diets were prepared daily, immediately before being offered to rats. Clinical Observations and Frequency: The number of deaths was recorded weekly. Body weight was determined at Weeks 2, 4, and once every 4 weeks thereafter. Food consumption was measured at Weeks 1-4, 11-12,

and then every 12 weeks for periods of 2 weeks (e.g. wk 24-26, 36-38, etc) of 20 rats/sex/group.

Organs Examined at Necropsy: All surviving males and females were killed at 149 and 150 weeks, respectively. Several different organs and tissues (types not noted) were taken at necropsy. Liver (three pieces from three different lobes) and all grossly viable tumors or suspected tumors in abdominal cavity, Zymbal glands, and mammary glands were examined microscopically

Test substance : PVC powder enriched with vinyl chloride monomer
Reliability : (1) valid without restriction
20.05.2002 (124)

Species : Rat
Sex : male/female
Strain : Other
Route of admin. : Inhalation
Exposure period : 12 m
Frequency of treatment : 6h/d, 5 d/w
Post. obs. period :
Doses : 50, 250, and 1,000 ppm VC (0.128, 0.64, 2.56 mg/l)
Result :
Control group : yes, concurrent no treatment
Method : other
Year : 1978
GLP : no data
Test substance : other TS
Remark : Serial sacrifice after 1, 2, 3, 6, and 9 m.
Strain: CD rats (Carles River).
Result : Number of hemangiosarcomas:
in liver: 250 ppm VC: 2/36 (male), 10/34 (female)
1000 ppm VC: 6/36 (male), 15/36 (female)
in lungs: 250 ppm VC: 0/36 (m ale), 3/34 (female)
1000 ppm VC: 4/34 (male), 9/36 (female)
other organs:
50 ppm VC: 1/36 (male), 1/36 (female)
250 ppm VC: 2/36 (male), 0/34 (female)
1000 ppm VC: 0/34 (male), 1/36 (female)

Other tumors found occasionally:
bronchioloalveolar adenoma of the lung; reticuloendothelial cell carcinoma or hepatoma of the liver; ductular adenocarcinoma or fibroadenoma of the mammary gland (female); malignant lymphoma; adenoma of the kidney; squamous carcinoma, keratoacanthoma, fibroma of the skin; adenocarcinoma of sebaceous glands; chromophobe cell tumor of the pituitary.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : VC 99.8 % pure
Reliability : (2) valid with restrictions
20.05.2002 (194) (195)

Species : Rat
Sex : male/female
Strain : Wistar
Route of admin. : Inhalation
Exposure period : 7 hours/day, 5 days/week

5. Toxicity **Id** 75-01-4
Date 18.06.2002

Frequency of treatment :
Post. obs. period :
Doses : 5000 ppm
Result :
Control group : Yes
Method :
Year : 1979
GLP : no data
Test substance :
Method : Groups of 62 male and 62 female rats were exposed to 0 or 5000 ppm vinyl chloride monomer for 7 hrs/day, 5 days/week for up to 52 weeks. At weeks 4, 13, 26 and 52 hematology, clinical chemistry, liver and kidney function tests and urinalysis parameters were measured. Groups of 10 rats/sex were sacrificed after 4, 13, 26 and 52 weeks and subjected to a gross pathological examination. Selected organs (heart, kidney, liver, spleen, brain, gonads, thymus, pituitary, thyroid, adrenals and lungs) were weighed. Tissues were examined histopathologically.
Result : An increased number of tumors were observed in the Zymbal gland, nasal cavity and liver (Table 1). Tumors in the brain and kidneys were metastases from nasal or lung tumors.

Table 1

Site, type and incidence of tumors in rats exposed to 5000 ppm VCM for up to 52 weeks

	Tumor Incidence			
	Males		Females	
Site and tumor type	0	5000	0	5000
Liver				
neoplastic nodule	0	0	0	1
carcinoma	0	1	0	1
angiosarcoma	0	3	0	6
Zymbal glands				
papilloma	0	2	0	0
squamous cell carcinoma	0	5	0	3
adeno-squamous carcinoma	0	0	0	1
Lungs				
papillary adenoma	0	0	0	1
mesenchymal tumor type	0	0	0	1
Brain				
malignant ependymoma	0	1	0	0
nasal cavity carcinoma metastases	0	6	0	2
mesenchymal lung tumor metastasis	0	0	0	1
Nasal cavity				
olfactory epithelium carcinoma	0	9	0	9
carcino-sarcoma	0	0	0	1
esthesioneouroepithelioma	0	1	0	0
Kidneys				
mesenchymal lung tumor metastasis	0	0	0	1
Ovaries				
Granulosa cell tumor			1	0

Test substance : Vinyl chloride gas was supplied by Akzo Zout Chemie, Rotterdam, The Netherlands. Purity was not noted but would be expected to be

comparable to Section 1.1-1.4.

Other studies in the same laboratory at the same time (Feron et al., 1981) reported: VC >= 99.97 % v/v (impurities: <2 ul/l acetylene, <15 ul/l monovinyl-acetylene, <10 ul/l 1,3-butadiene, <75 ul/l methylchloride, <50 ul/l ethylchloride, <1 ul/l chloroprene, <1 ul/l 1,1-dichloroethane, < 20 ul/l 1,2-dichloroethane, <5 mg/kg acetaldehyde, < 1 mg/kg HCl, <0.5 mg/kg Fe, <100 mg/kg water, <10 mg/kg evaporation residue).

Reliability : (2) valid with restrictions
14.05.2002 (127) (128) (129)

Species : mouse
Sex : male
Strain : CD-1
Route of admin. : inhalation
Exposure period : 4 weeks
Frequency of treatment : 6 h/d, 5 d/w
Post. obs. period : sacrifice at 0, 12, 40 to 41 weeks after exposure
Doses : 1 ppm (0.0026 mg/l), 19 ppm (0.0486 mg/l), 100 ppm (0.256 mg/l), 300 ppm (0.768 mg/l), 600 ppm (1.536 mg/l)
Result :
Control group : yes, concurrent no treatment
Method : other
Year : 1983
GLP : no data
Test substance : other TS
Result : A dose-response relationship for the incidence of alveologenic tumors was observed. The latency period is inversely related to dose. Haemangiosarcomas were observed both, in the subcutaneous connective tissue of the ear and liver.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : VC > 99 % pure
Reliability : (2) valid with restrictions
20.05.2002 (196) (197)

Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : inhalation
Exposure period : 52 weeks
Frequency of treatment : 4 h/d, 5 d/w,
Post. obs. period : animals sacrificed at 68 weeks (BT 6) or 135 weeks
Doses : 30000 to 5 ppm (76.8 to 0.013 mg/l)
Result :
Control group : yes, concurrent no treatment
Method : other
Year : 1984
GLP : no data
Test substance : other TS
Remark : Concentrations:
Study BT 1: 10,000 ppm (25.6 mg/l), 6,000 ppm (15.36 mg/l),
2,500 ppm (6.4 mg/l), 500 ppm (1.28 mg/l),
250 ppm (0.64 mg/l), 50 ppm (0.128 mg/l) VC,
untreated control, 2,500 ppm vinyle acetate.
Termination of the experiment: 135 weeks.
Study BT 2: 200 ppm (0.51 mg/l), 150 ppm (0.38 mg/l),

100 ppm (0.256 mg/l) VC, untreated control.
Termination of the experiment: 143 weeks.
Study BT 6: (repetition of Viola""s experiment)
30,000 ppm (76.8 mg/l) VC.
Termination of the experiment: 68 weeks.
Study BT 9: (repetition of lowest dose group of BT 1;
5 times the number of animals used in BT 1).
50 ppm (0.128 mg/l) VC.
Study BT 15: 25 ppm (0.064 mg/l), 10 ppm (0.026 mg/l),
5 ppm (0.013 mg/l), 1 ppm (0.0026 mg/l) VC.
Termination of the experiment: 147 weeks.

Result : BT 1: Clear dose-response relation for Zymbal gland tumors (> 25 ppm)and hepatic angiosarcomas (> 50 ppm); less clear for hepatomas, nephroblastomas, and brain tumors, although increased incidence appeared treatment related. 1 haemangiosarcoma in a female rat at 50 ppm. Tumors of mammary gland, forestomach, papillomas, leukemias randomly distributed in test and control groups.

BT 2: Haemangiosarcomas and nephroblastomas in treated animals only.
Zymbal gland carcinomas in females in treated groups at all dose levels and in controls.
A few hepatomas occurred late during the experiment in both sexes at the highest dose and in male control animals.
Mammary gland tumors, leukemias, and forestomach papillomas randomly distributed in test and control groups.

BT 6 (repetition of Viola""s experiment):
Zymbal gland carcinomas as in Viola""s experim ent.
High incidence of angiosarcomas and forestomach tumors (isolated observation not repeated in later experiments).
No bone or cartilaginous tumors.

BT 9: Incidence of hepatic angiosarcomas in females 6 times that found in males.
Zymbal gland and brain tumors also treatment related but no sex differences observed.

BT 15: Zymbal gland carcinomas in all treated groups and in 2 males of the control group.
Angiosarcomas in both sexes at the highest concentration and predominantly in females.
At highest concentration 1 hepatoma (female) and 1 nephroblastoma (male).
No brain tumors.

The average latency period for treatment-induced tumors was reduced significantly.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test substance : Maximum level of impurities: H2O 10 ppm, acetaldehyde 5 ppm, acetylene 2 ppm, allene 5 ppm, butane 8 ppm, 1,3-butadiene 10 ppm, chlorophene 10 ppm, diacetylene 4 ppm, vinyl acetylene 10 ppm, propine 3 ppm, methylchloride 100 ppm.

Reliability : (2) valid with restrictions
20.05.2002 (198) (199) (200) (201) (202)

Species : Rat
Sex : Male
Strain : Sprague-Dawley

5. Toxicity **Id** 75-01-4
Date 18.06.2002

Route of admin.	:	Inhalation
Exposure period	:	12 months
Frequency of treatment	:	4 h/d, 5 d/w
Post. obs. period	:	termination of the study 2.5 years after first exposure
Doses	:	600 ppm (1.54 mg/l) VC, +- ingestion of 5 % ethanol (v/v) in water
Result	:	
Control group	:	yes, concurrent no treatment
Method	:	other
Year	:	1981
GLP	:	no data
Test substance	:	other TS
Remark	:	Exposure groups: 1) VC in air; 2) VC (in air) + ethanol (ingestion); 3) filtered air + ethanol (ingestion); 4) filtered air. Ethanol ingestion started 4 weeks prior to VC inhalation. Ethanol ingestion in drinking water (5 % v/v) ad lib. for life.
Result	:	Lesions in liver: hepatocellular carcinoma, angiosarcoma, hyperplastic nodules. Endocrine tumors (seminoma (ethanol), thyroid (VC/ethanol), adrenal tumors); number of pituitary tumors increased in treated groups above control levels; pancreatic (beta-cell) tumors (ethanol). Other tumors: lymphosarcomas (increased in VC and VC/ethanol), fibroma and fibrosarcoma, glioma, tumors of kidney, epidermis, excretory pancreas, parathyroid. In some cases more than 1 angiosarcoma or hepatocellular carcinoma developed in an animal. First death from an angiosarcoma after 9 months (VC/ethanol) and 12 months (VC). Incidence of liver tumors increased by concurrent treatment with ethanol: liver angiosarcoma: 23 % (VC), 50 % (VC/ethanol); hepatocellular carcinoma: 44 % (VC), 60 % (VC/ethanol). Ethanol acts as cocarcinogen in relation to VC induced tumors of the liver.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	VC 99.9 % purity
Reliability	:	(2) valid with restrictions

20.05.2002 (203)

Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	17 weeks
Frequency of treatment	:	4 h/d, 5 d/w
Post. obs. period	:	final sacrifice after 156 weeks
Doses	:	50 to 10,000 ppm (0.128 to 25.6 mg/l)
Result	:	
Control group	:	yes, concurrent no treatment
Method	:	other
Year	:	1979
GLP	:	no data
Test substance	:	other TS
Remark	:	Study BT 3 Concentrations: 10,000 ppm (25.6 mg/l), 6,000 ppm (15.36 mg/l), 2,500 ppm (6.4 mg/l), 500 ppm (1,28 mg/l), 250 ppm (0.64 mg/l), 50 ppm (0.128 mg/), untreated controls.
Result	:	Mammary tumors, Zymbal gland tumors, nephroblastomas and hepatic

angiosarcomas in high dose groups; shorter exposure time is sufficient to induce treatment related tumors.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test substance : Maximum level of impurities: H2O 10 ppm, acetaldehyde 5 ppm, acetylene 2 ppm, allene 5 ppm, butane 8 ppm, 1,3-butadiene 10 ppm, chlorophene 10 ppm, diacetylene 4 ppm, vinyl acetylene 10 ppm, propine 3 ppm, methylchloride 100 ppm.

Reliability : (2) valid with restrictions
20.05.2002 (201) (202)

Species : rat
Sex : male/female
Strain : Wistar
Route of admin. : oral feed
Exposure period : lifespan
Frequency of treatment : diet provided 4 h/d, 5 d/w, no other food for the next 20 h
Post. obs. period : final sacrifice at week 135 (males) and week 144 (females)
Doses : actual dose: 1.7, 5.0, 14.1, mg/ kg b.w. and day as monomer in PVC powder. 300 mg/kg b.w. and day (10 %) in soya-bean oil by gavage as positive control
Result :
Control group : yes, concurrent vehicle
Method : other: essentially follows OECD 453
Year : 1981
GLP : no data
Test substance : other TS
Method : Groups of 60-80 males and 60-80 female rats were fed diets containing 10% PVC powder with varying concentrations of VCM at levels planned to provide daily intakes of 1, 3 or 10 mg VCM/kg body weight. The control group received 10% PVC with no measureable level of VCM. The various diets were prepared daily just prior to being offered to the rats. The diets were available to the rats each day for a period of four consecutive hours. After the 4-hour feeding the rats had no feed until the next day. In addition, a group of rats received 300 mg VCM/kg/day, 5 days/week, by oral gavage. For this group, the VCM was dissolved in soybean oil. Interim sacrifices of 10 male and 10 female rats from the control and two highest dose levels were performed after 26 and 52 weeks. The study was terminated when 75% of the control rats were dead, a point reached for males in week 135 and for females in week 144.

Rats were weighed at weeks 1, 2, 4, 6, 8, 10 and 12 and at 4-week intervals thereafter. Feed consumption was measured 7 times during the study. Routine hematology determinations and urinalysis were conducted in weeks 13, 26, 52, 78 and 94. Clinical chemistry determinations were conducted in weeks 13, 26, 52 and 106 and included fasting blood glucose, blood urea nitrogen, serum total protein, serum albumin as well as serum alkaline phosphatase, glutamic-oxalacetic transaminase and glutamic-pyruvic transaminase activities. Animals alive after 135 weeks (males) or 144 weeks (females) were sacrificed and subjected to a gross examination. A thorough necropsy was performed and approximately 45 tissues were saved for histopathologic examination. A complete histopathologic examination was limited to 20 males and 20 females that survived to the end of the study or lived the longest. Histopathologic examination of all other rats was limited to the liver, Zymbal glands, lungs, kidneys, spleen, pituitary, thyroidk, adrenals, grossly visible tumors and organs containing gross lesions suspected of being tumors.

For the interim sacrifices, clinical chemistry determinations were made. These included blood-clotting time, serum electrolytes, lactic dehydrogenase activity, serum alpha-foetoprotein, liver and kidney function tests. In action aminopyrine demeth ylase and aniline hydroxylase activities were measured in liver preparations. Liver and kidneys were weighed. Histopathological examination of the liver, kidneys and Zymbal glands was performed.

Remark : Negative control group housed in a room separate from that used for the experimental groups to avoid contamination by inhalation of VC.

Result : A variety of neoplastic treatment-related liver lesions was found at each of the VC levels (Table 1). The tumor response in the liver seemed to shift from a predominance of angiosarcomas at the highest dose level (males: 27%; 27% in positive control; females: 9 %; 29 % in positive control) via a mixture of angiosarcomas and hepatocellular tumors at the intermediate levels to the exclusive development of hepatocellular tumors at the lowest VC level (predominantly in females). Angiosarcomas were also found in the lungs and extrahepatic in the abdomen but there was no dose-response relationship and the difference was statistically signifcant only in females at the lowest dose level.

Other tumors observed: tumors of Zymbal glands, abdominal mesotheliomas, adenocarcinomas of the mammary glands. There was a dose-dependent increase in the incidence of liver hemangiosarcomas starting from 5 mg/kg b.w./day. Males were more sensitive than females. There was a dose-response relationship for the incidence of hepatocellular carcinomas (all dosages). Females were more sensitive than males. NOAEL < 1.7 mg/kg b.w./day.

Table 1
Selected cancer type and incidence of rats fed VCM

Males

	mg VCM/kg/day				
Type and incidence	0	1.7	5.0	14.1	300
Liver					
neoplastic nodule	0	1	7**	23***	3
carcinoma	0	1	2	8**	1
angiosarcoma	0	0	6*	27***	27
Lungs					
angiosarcoma	0	0	4*	19***	19
Zymbal glands					
squamous-cell carcinoma	0	0	2	0	1
Abdomen					
mesothelioma	3	1	7	8	1
Thyroid					
parafollicular cell adenoma	4	12*	10	3	3
Pituitary					
adenoma	12	25**	6	2**	0
carcinoma	1	0	1	0	0

Females

	mg VCM/kg/day				
Type and incidence	0	1.7	5.0	14.1	300
Liver					
neoplastic nodule	2	26**	39***	44***	2
carcinoma	0	4	19***	29***	0

angiosarcoma	0	0	2	9**	29
Lungs					
angiosarcoma	0	0	1	5*	23
Zymbal glands					
squamous-cell carcinoma	0	0	0	0	1
Abdomen					
mesothelioma	1	6*	3	3	0
Thyroid					
parafollicular cell adenoma	7	10	3	2	0
Pituitary					
adenoma	14	16	10	5*	3
carcinoma	3	0	2	0	0

* p<0.05; ** p<0.01; *** p<0.001

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test substance : VC >= 99.97 % v/v (impurities: <2 ul/l acetylene, <15 ul/l monovinyl-acetylene, <10 ul/l 1,3-butadiene, <75 ul/l methylchloride, <50 ul/l ethylchloride, <1 ul/l chloroprene, <1 ul/l 1,1-dichloroethane, < 20 ul/l 1,2-dichloroethane, <5 mg/kg acetaldehyde, < 1 mg/kg HCl, <0.5 mg/kg Fe, <100 mg/kg water, <10 mg/kg evaporation residue).

Reliability : (1) valid without restriction

20.05.2002 (198) (204)

Species : rat
Sex : male
Strain : Wistar
Route of admin. : inhalation
Exposure period : 12 months
Frequency of treatment : 4 h/d, 5 d/w
Post. obs. period :
Doses : 3 % v/v VC (30,000 ppm; 76.8 mg/l)
Result :
Control group : yes, concurrent no treatment
Method : other
Year : 1971
GLP : no data
Test substance : other TS
Remark : 26 animals exposed, 25 animals in untreated control group. Survival time 280 to 380 days.

Result : First tumors after 10 months of treatment. 14 animals with epidermoid carcinoma, 2 with mucoepidermoid carcinoma, 1 with papilloma of the skin; 5 animals with adenocarcinoma, 1 with adenoacanthoma, 1 with squamous cell carcinoma of the lungs; 5 animals with osteochondroma of bones. No hemangiosarcomas reported. No tumors in the control group.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test substance : VC, 99 % purity, assumed to contain insignificant amounts of various non-carcinogenic contaminants.

Reliability : (2) valid with restrictions

20.05.2002 (205)

Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : gavage
Exposure period : 52 to 59 weeks

Frequency of treatment	:	1/d, 4-5 d/w
Post. obs. period	:	final sacrifice after 136 weeks
Doses	:	0.03 to 50 mg/kg b.w. in olive oil
Result	:	
Control group	:	yes, concurrent vehicle
Method	:	other
Year	:	1979
GLP	:	no data
Test substance	:	other TS
Remark	:	Study BT 11: Concentrations: 50, 16.65, 3.33 mg/kg b.w. duration of treatment 52 weeks. Study BT 27: Concentrations: 1, 0.3, 0.03 mg/kg b.w. duration of treatment 52 to 59 weeks.
Result	:	Study BT 11: 50 mg/kg b.w.: 1 nephroblastoma, 2 Zymbal gland carcinomas (both sexes); haemangiosarcomas in 25 % of animals (both sexes). 16.65 mg/kg b.w.: Haemangiosarcomas in 20 % of female and in 1 male animals; No treatment-related tumors in lowest dose group. Study BT 27: 1 mg/kg b.w.: hepatic angiosarcomas in 1 male and 2 females; no other treatment-related tumors. No treatment-related tumors in lower dose groups.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	Maximum level of impurities: H2O 10 ppm, acetaldehyde 5 ppm, acetylene 2 ppm, allene 5 ppm, butane 8 ppm, 1,3-butadiene 10 ppm, chlorophene 10 ppm, diacetylene 4 ppm, vinyl acetylene 10 ppm, propine 3 ppm, methyl chloride 100 ppm.
Reliability	:	(2) valid with restrictions
29.05.2002		(198) (199) (200) (201) (202)
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	i.p.
Exposure period	:	life time
Frequency of treatment	:	once or 2, 3, or 4 times at 2 months interval
Post. obs. period	:	final sacrifice after 144 weeks
Doses	:	4.25 mg in 1 cc olive oil
Result	:	
Control group	:	yes, concurrent vehicle
Method	:	other
Year	:	1977
GLP	:	no data
Test substance	:	other TS
Result	:	Study BT 12 1 nephroblastoma, 1 subcutaneous angiosarcoma observed.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	Maximum level of impurities: H2O 10 ppm, acetaldehyde 5 ppm, acetylene 2 ppm, allene 5 ppm, butane 8 ppm, 1,3-butadiene 10 ppm, chlorophene 10 ppm, diacetylene 4 ppm, vinyl acetylene 10 ppm, propine 3 ppm,

methylechloride 100 ppm.

Reliability : (2) valid with restrictions
29.05.2002 (198) (201) (202)

Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	24 w
Frequency of treatment	:	7 h/d, 5 d/w
Post. obs. period	:	
Doses	:	940 ppm (2.41 mg/l)
Result	:	
Control group	:	yes, concurrent no treatment
Method	:	other
Year	:	1981
GLP	:	no data
Test substance	:	no data
Remark	:	Four differently aged sets of animals were exposed: 6 w, 17-18 w, 32-33 w, 51-53 w, respectively. Similarely aged groups of untreated animals were kept as untreated controls. Serial sacrifices at 3, 6, and 9 months, respectively. Final sacrifice 43 weeks after onset of the exposure.
Result	:	No statistically significant differences in hematological or clinical chemistry measurements between exposed and untreated animals. Tumor types: Most frequently angiosarcoma of the liver (occasionally in other organs), pituitary adenoma, mammary tumors; in few exposed or unexposed animals zymbal gland tumors, tumors of the brain. Incidence of angiosarcomas is higher and tumors occur earlier in older animals of both sexes. Females are more susceptible than males.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

29.05.2002 (206)

Species	:	rat
Sex	:	male
Strain	:	Wistar
Route of admin.	:	inhalation
Exposure period	:	52 weeks
Frequency of treatment	:	4 h/d, 5 d/w
Post. obs. period	:	Animals sacrificed at 165 weeks
Doses	:	50 to 10,000 ppm (0.128 to 25.6 mg/l) VC
Result	:	
Control group	:	yes, concurrent no treatment
Method	:	other
Year	:	1979
GLP	:	no data
Test substance	:	other TS
Remark	:	Study BT 7 Concentrations: 10,000 ppm 25.6 mg/l), 6,000 ppm 15.36 mg/l), 2,500 ppm (6.4 mg/l), 500 ppm (1.28 mg/l), 250 ppm (0.64 mg/l), 50 ppm (0.128 mg/l), untreated control.
Result	:	Results closely similar to those obtained in males in experiment BT 1. Clearly dose-related incidence of hepatic angiosarcomas. No dose-relation

for Zymbal gland carcinomas, nephroblastomas, hepatomas, and brain tumors. Few mammary adenocarcinomas, skin carcinomas, and leukemias randomly in test and control groups. With the exception of hepatic angiosarcomas, the incidence of tumors was lower than in the comparable groups of experiment BT 1.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test substance : Maximum level of impurities: H2O 10 ppm, acetaldehyde 5 ppm, acetylene 2 ppm, allene 5 ppm, butane 8 ppm, 1,3-butadiene 10 ppm, chlorophene 10 ppm, diacetylene 4 ppm, vinyl acetylene 10 ppm, propine 3 ppm, methylchloride 100 ppm.

Reliability : (2) valid with restrictions
29.05.2002 (198) (207) (200) (201)

Species : rat
Sex : male
Strain : Wistar
Route of admin. : inhalation
Exposure period : 52 weeks
Frequency of treatment : 4 h/d, 5 d/w
Post. obs. period : sacrifice 82 weeks after end of exposure
Doses : 1 ppm (0.0026 mg/l)
Result :
Control group : yes, concurrent no treatment
Method : other
Year : 1979
GLP : no data
Test substance : other TS
Remark : Study BT 17
Number of animals: 120 males.

Result : Three extra-hepatic angiosarcomas.
One hepatoma.
Zymbal gland tumors in treated and control group.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test substance : Maximum level of impurities: H2O 10 ppm, acetaldehyde 5 ppm, acetylene 2 ppm, allene 5 ppm, butane 8 ppm, 1,3-butadiene 10 ppm, chlorophene 10 ppm, diacetylene 4 ppm, vinyl acetylene 10 ppm, propine 3 ppm, methylchloride 100 ppm.

Reliability : (2) valid with restrictions
29.05.2002 (198) (201) (202)

Species : rat
Sex : male
Strain : Sprague-Dawley
Route of admin. : inhalation
Exposure period : 5 to 25 weeks
Frequency of treatment : 1-4 h/d, 1-5 d/w
Post. obs. period : final sacrifice after 154 weeks
Doses : 6,000 ppm (15.36 mg/l), 10,000 ppm (25.6 mg/l)
Result :
Control group : yes, concurrent no treatment
Method : other
Year : 1979
GLP : no data
Test substance : other TS
Remark : Study BT 10

Exposure: 4 h/d, 5 d/w, 5 w
4 h/d, 1 d/w, 25 w
1 h/d, 4 d/w, 25 w

Result : High incidence of mammary tumors, Zymbal gland tumors; some nephroblastomas, forestomach tumors, skin carcinomas, and subcutaneous sarcomas; some hepatic and non-hepatic angiosarcomas even after short exposure regimen. Even the shortest exposure is sufficient to induce treatment related tumors.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : Maximum level of impurities: H2O 10 ppm, acetaldehyde 5 ppm, acetylene 2 ppm, allene 5 ppm, butane 8 ppm, 1,3-butadiene 10 ppm, chlorophene 10 ppm, diacetylene 4 ppm, vinyl acetylene 10 ppm, propine 3 ppm, methylchloride 100 ppm.
Reliability : (2) valid with restrictions
29.05.2002 (201) (202)

Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : inhalation
Exposure period : 7 d (transplacental: 12th to 18th gestational day)
Frequency of treatment : 4 h/d
Post. obs. period : final sacrifice after 143 weeks
Doses : 6,000 ppm (15.36 mg/l), 10,000 ppm (25.6 mg/l)
Result :
Control group : no
Method : other
Year : 1979
GLP : no data
Test substance : other TS
Remark : Study BT 5
No controls available.
Result : No increase in any of the type of tumors that were found to be increased in previous experiments. Thus, there is no evidence that VC could act as transplacental carcinogen.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : Maximum level of impurities: H2O 10 ppm, acetaldehyde 5 ppm, acetylene 2 ppm, allene 5 ppm, butane 8 ppm, 1,3-butadiene 10 ppm, chlorophene 10 ppm, diacetylene 4 ppm, vinyl acetylene 10 ppm, propine 3 ppm, methylchloride 100 ppm.
Reliability : (2) valid with restrictions
29.05.2002 (198) (201) (202)

Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : inhalation
Exposure period : 1 - 4 h/d, 1 - 5 d/w, 5 - 25 weeks
Frequency of treatment : 4 h/d, 5 d/w
Post. obs. period : final sacrifice after 13 weeks
Doses : 6,000 ppm (15.36 mg/l), 10,000 ppm (25.6 mg/l)
Result :
Control group : yes, concurrent no treatment
Method : other
Year : 1979

5. Toxicity **Id** 75-01-4
Date 18.06.2002

GLP	:	no data
Test substance	:	other TS
Remark	:	Study BT 14 (in newborne rats) Exposure: 4 h/d, 5 d/w, 5 w 4 h/d, 1 d/w, 25 w 1 h/d, 4 d/w, 25 w
Result	:	A low incidence of hepatic hemangiosarcomas and hepatomas was found in animals treated during the first 5 weeks of postnatal life. Mammary tumors and Zymbla gland tumors also increased. Dams that were treated for the same length of time with the same concentration did not develop tumors referrable to VC exposure.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	Maximum level of impurities: H2O 10 ppm, acetaldehyde 5 ppm, acetylene 2 ppm, allene 5 ppm, butane 8 ppm, 1,3-butadiene 10 ppm, chlorophene 10 ppm, diacetylene 4 ppm, vinyl acetylene 10 ppm, propine 3 ppm, methylchloride 100 ppm.
Reliability	:	(2) valid with restrictions
29.05.2002		(198) (201) (202)

Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	15 or 76 weeks, transplacental (starting 12th gestational day) and postnatal
Frequency of treatment	:	4- 7 h/d, 5 d/w
Post. obs. period	:	final sacrifice after 150 weeks
Doses	:	2,500 ppm (6.4 mg/l)
Result	:	
Control group	:	yes, concurrent no treatment
Method	:	other
Year	:	1984
GLP	:	no data
Test substance	:	other TS
Remark	:	Study BT 4001 and 4006 Exposure: Pregnant rats were exposed from the 12th day of pregnancy for 4 - 7 h/d, 5 d/w, for 76 weeks. The newly-borne rats were exposed similarly for 15 or 76 weeks.
Result	:	A high incidence of hepatic hemangiosarcomas and hepatomas occurred in all treated groups. Also high incidence of mammary tumors, Zymbal gland tumors, some nephroblastomas, some fores tomach tumors, few cutaneous and subcutaneous tumors.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	Maximum level of impurities: H2O 10 ppm, acetaldehyde 5 ppm, acetylene 2 ppm, allene 5 ppm, butane 8 ppm, 1,3-butadiene 10 ppm, chlorophene 10 ppm, diacetylene 4 ppm, vinyl acetylene 10 ppm, propine 3 ppm, methylechloride 100 ppm.
Reliability	:	(2) valid with restrictions
29.05.2002		(198) (201)

Species	:	rat
Sex	:	male/female
Strain	:	other
Route of admin.	:	inhalation
Exposure period	:	1 times 1 hour, 2 w, or 20 w

5. Toxicity **Id** 75-01-4
Date 18.06.2002

Frequency of treatment	:	1 h/d, 5 d/w
Post. obs. period	:	sacrifice 8 to 26 months after onset of the experiment
Doses	:	50 to 500 or 50 to 50,000 ppm VC
Result	:	
Control group	:	yes, concurrent no treatment
Method	:	other
Year	:	1981
GLP	:	no data
Test substance	:	no data
Remark	:	Strains and exposure: 1) Fisher 344: 1 h to 50 ppm (0.128 mg/l), 500 ppm (1.28 mg/l), 5,000 ppm (12.8 mg/l) or 50,000 ppm (128 mg/l) VC. 2) Fisher 344: 1 h/d, 5 d/w, 2 weeks, 500 ppm (1.28 mg/l) VC. 3) Fisher 344: 1 h/d, 5 d/w, 20 weeks, 50 ppm (0.128 mg/l) VC. 4) Sprague-Dawlay/Wistar: 1 h/d, 5 d/w, 10 weeks, 50 ppm (0.128 mg/l) or 500 ppm (1.28 mg/l) VC, respectively (= parents from a reproduction study). Sacrifice 8 to 24 months after exposure.
Result	:	No chemically induced tumor response in any of the groups.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions

29.05.2002 (208)

Species	:	rat
Sex	:	male/female
Strain	:	Wistar
Route of admin.	:	inhalation
Exposure period	:	5, 11, 17, 47, 83 days, either transplacentally, neonatally or from an age of 7 or 21 days onwards
Frequency of treatment	:	8 h/d, 7 d/w
Post. obs. period	:	sacrifice at age of 4 months
Doses	:	2,000 ppm (5.12 mg/l)
Result	:	
Control group	:	yes, concurrent no treatment
Method	:	other
Year	:	1985
GLP	:	no data
Test substance	:	other TS
Remark	:	Method: Evaluation of livers for ATPase-deficient foci. Transplacental exposure from day 1 after conception until birth. Also daily exposure of partially hepatectomized rats starting 24 h after surgery for 70 days.
Result	:	No increase in ATPase-deficient foci after transplacental exposure or exposure from day 1 through 5. Foci area was steeply increased when newborn rats were exposed for 11 and 17 days, but no further increase by exposure for 47 or 83 days. Only few foci when exposure started 2 1 days after birth. Exposure of adult rats did not result in more foci than in untreated controls. Induction of pre-neoplastic hepatocellular lesions in rats by VC is restricted to a well defined period (day 7 - 21) in early lifetime of the animals. This period is characterized by the beginning of rapid liver growth.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

5. Toxicity **Id** 75-01-4
Date 18.06.2002

Test substance	:	VC 99 % chemical purity
Reliability	:	(2) valid with restrictions
29.05.2002		(209)
Species	:	rat
Sex	:	male/female
Strain	:	other
Route of admin.	:	inhalation
Exposure period	:	3 to 10 weeks starting on day 1 or day 3 after birth
Frequency of treatment	:	8 h/d, 5 d/w
Post. obs. period	:	1 or 10 weeks
Doses	:	2.500 ppm (0.0064 mg/l) to 2,000 ppm (5.12 mg/l)
Result	:	
Control group	:	yes, concurrent no treatment
Method	:	other
Year	:	1985
GLP	:	no data
Test substance	:	other TS
Remark	:	Method: Evaluation of the dose dependence of the quantity of ATPase-deficient hepatocellular foci after subchronic exposure to VC. Exposure of neonatal Wistar rats starting on day 1 after birth for 10 weeks to 10 ppm (0.026 mg/l), 40 ppm (0.1 mg/l), 70 ppm (0.179 mg/l), 150 ppm (0.384 mg/l), 2,000 ppm (5.12 mg/l) VC in air. Postexposure period 1 week. Exposure of neonatal Wistar or Sprague-Dawley rats starting on day 3 after birth for 3 weeks to 2.5 ppm (0.0064 mg/l), 5 ppm (0.013 mg/l), 10 ppm (0.0256 mg/l), 20 ppm (0.0512 mg/l), 40 ppm (0.102 mg/l) and 80 ppm (0.205 mg/l) VC in air. Postexposure period 10 weeks. Strain: Wistar or Sprague-Dawley.
Result	:	Both sets of experiments revealed a straight linear relationship between the dose of VC and the % foci area induced. Within the dose range investigated, no obvious threshold for the induction of pre-neoplastic foci by VC was observed.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	VC 99 % chemical purity
Reliability	:	(2) valid with restrictions
29.05.2002		(210)
Species	:	mouse
Sex	:	male/female
Strain	:	Swiss
Route of admin.	:	inhalation
Exposure period	:	30 weeks
Frequency of treatment	:	4 h/d, 5 d/w
Post. obs. period	:	final sacrifice after 81 weeks
Doses	:	50 to 10,000 ppm (0.128 to 25.6 mg/l) VC
Result	:	
Contrd group	:	yes, concurrent no treatment
Method	:	other
Year	:	1979
GLP	:	no data
Test substance	:	other TS
Remark	:	Study BT 4 Concentrations: 10,000 ppm (25.6 mg/l), 6,000 ppm (15.36 mg/l), 2,500 ppm (6.4 mg/l), 500 ppm (1.28 mg/l), 250 ppm (0.64 mg/l), 50 ppm (0.13

mg/l).

Result : Mortality increased with increasing exposure level in the treated groups.
Clear increase in the incidence of hepatic haemangiosarcomas, pulmonary adenocarcinomas, and mammary gland tumors.
Dose-response relationship not clearly evident, presumably due to the increased mortality.
Dose-related shortening of the average latency period, particularly for pulmonary adenomas and mammary gland tumors.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test substance : Maximum level of impurities: H2O 10 ppm, acetaldehyde 5 ppm, acetylene 2 ppm, allene 5 ppm, butane 8 ppm, 1,3-butadiene 10 ppm, chlorophene 10 ppm, diacetylene 4 ppm, vinyl acetylene 10 ppm, propine 3 ppm, methyl chloride 100 ppm.

Reliability : (2) valid with restrictions
29.05.2002 (198) (200) (201) (202)

Species : mouse
Sex : male/female
Strain : CD-1
Route of admin. : inhalation
Exposure period : 9 months
Frequency of treatment : 7 h/d, 5 d/w
Post. obs. period : 9 months
Doses : 50 to 2,500 ppm
Result :
Control group : yes, concurrent no treatment
Method : other
Year : 1975
GLP : no data
Test substance : no data
Remark : Doses: 2,500 ppm (6,4 mg/l), 200 ppm (0.51 mg/l), 50 ppm (0.128 mg/l).
Result : (interim report)
Tumor types observed: alveologenic adenomas, hepatic angiosarcomas, mammary gland adeno-squamous carcinomas.
A dose-dependent increase in incidence of all tumor types was found after 18 months.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (211)

Species : mouse
Sex : male/female
Strain : CD-1
Route of admin. : inhalation
Exposure period : 12 months (serial sacrifices after 1, 2, 3, 6, 9 months)
Frequency of treatment : 6 h/d, 5 d/w
Post. obs. period :
Doses : 50 to 1,000 ppm
Result :
Control group : yes, concurrent no treatment
Method : other
Year : 1978
GLP : no data
Test substance : other TS
Remark : Doses: 1,000 ppm (2.56 mg/l), 250 ppm (0.64 mg/l), 50 ppm (0.128 mg/l).

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Result	:	Tumor types: Bronchioloalveolar adenomas, mammary tumors (ductular adenocarcinoma, squamous and anaplastic cell carcinomas), hemangiosarcomas of the liver (rarely other organs). The incidence and severity of these tumors increased with concentration of VC and length of exposure.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	VC 99.8 % pure
Reliability	:	(2) valid with restrictions
29.05.2002		(212)
Species	:	Mouse
Sex	:	male/female
Strain	:	NMRI
Route of admin.	:	Inhalation
Exposure period	:	26 or 52 weeks
Frequency of treatment	:	6 h/d, 5
Post. obs. period	:	sacrifice 26 to 56 weeks after onset of the experiment
Doses	:	50 ppm (0.128 mg/l) or 500 ppm (1.28 mg/ml) VC
Result	:	
Control group	:	yes, concurrent no treatment
Method	:	other
Year	:	1976
GLP	:	no data
Test substance	:	no data
Remark	:	Exposure: 50 ppm (0.128 mg/l) VC for 52 weeks or 500 ppm (1.28 mg/l) VC for 26 weeks , respectively.
Result	:	Tumor types: Alveologenic adenomas of the lungs, haemangiosarcomas in fat tissue as well as few benign and malignant tumors at various sites. Only one haemangiosarcoma of the liver was noted. Severe general deterioration of health in animals exposed to 500 ppm VC even after 26 weeks. All animals exposed to 500 ppm VC developed tumors; 71 % of the animals exposed to 50 pp VC were bearing tumors. The proportion of tumors of vascular origin is higher at lower dose levels. The frequency of all tumors, number of tumor foci and size of foci in both groups suggested a dose-dependent carcinogenic effect of VC.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability	:	(2) valid with restrictions
29.05.2002		(213)
Species	:	mouse
Sex	:	male/female
Strain	:	other
Route of admin.	:	inhalation
Exposure period	:	1 times 1 h, 2 w, 20w
Frequency of treatment	:	1 h/d, 5 d/w
Post. obs. period	:	sacrifice 8 to 24 months after exposure
Doses	:	50 to 50,000 ppm, or 50 to 500 ppm, respectively
Result	:	
Control group	:	yes, concurrent no treatment
Method	:	other
Year	:	1981
GLP	:	no data
Test substance	:	no data
Remark	:	Strains and Exposure: 1) ICR Swiss mice: 1 h, 50 ppm (0.128 mg/l), 500 ppm (1.28 mg/l), 5,000

ppm 12.8 mg/l), 50,000 ppm 128 mg/l) VC.
2) A/J mice: 1 h/d, 5 d/w, 2 w, 500 ppm (1.28 mg/l) VC.
3) A/J mice: 1 h/d, 5 d/w, 20 w, 50 ppm (0.128 mg/l) VC. Sacrifice 18 to 20 m after exposure.

Result : A definite dose-dependent increase of the incidence of lung tumors was determined after a single as well as after repeated exposures. The applied total dose from repeated exposures induced more tumors than that administered as a single dose.
Males seemed to be more prone to induction of pneumonitis (1 times 50,000 ppm) than females.
There was an increase in bronchiolo-alveolar adenomas, especially in males after a single exposure to high doses (i.e. 5,000 or 50,000 ppm).
Other than lung tumors: rather sporadically.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (214)

Species : mouse
Sex : male
Strain : CD-1
Route of admin. : inhalation
Exposure period : 5 to 6 months
Frequency of treatment : 5 h/d, 5 d/w
Post. obs. period : 2 to 37 d
Doses : 2,500 ppm (6.4 mg/l), 6,000 ppm (15.36 mg/l)
Result :
Control group : yes, concurrent no treatment
Method : other
Year : 1978
GLP : no data
Test substance : no data

Result : Pulmonary (alveologenic) tumors were observed in 26 of 27 experimental animals.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (215)

Species : hamster
Sex : male
Strain : other
Route of admin. : inhalation
Exposure period : 30 weeks
Frequency of treatment : 4 h/d, 5 d/w
Post. obs. period : 79 weeks
Doses : 50 to 10,000 ppm (0.128 - 25.6 mg/l)
Result :
Control group : yes, concurrent no treatment
Method : other
Year : 1979
GLP : no data
Test substance : other TS

Remark : Study BT 8
Strain: Syrian golden hamster
Concentrations: 10,000 ppm (25.6 mg/l), 6,000 ppm (15.36 mg/l), 2,500 ppm (6.4 mg/l), 500 ppm (1.28 mg/l), 250 ppm (0.64 mg/l), 50 ppm (0.128

		mg/l) VC, untreated control
Result	:	A few haemangiosarcomas, melanomas, Zymbal gland tumors, and forestomach papillomas were observed in treated animals. All tumors treatment related (questionable for melanomas). All tumors appeared after 36 weeks of treatment. No dose-response relationship was observed.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	Maximum level of impurities: H2O 10 ppm, acetaldehyde 5 ppm, acetylene 2 ppm, allene 5 ppm, butane 8 ppm, 1,3-butadiene 10 ppm, chlorophene 10 ppm, diacetylene 4 ppm, vinyl acetylene 10 ppm, propine 3 ppm, methylchloride 100 ppm.
Reliability	:	(2) valid with restrictions
29.05.2002		(198) (200) (201) (202)
Species	:	rat
Sex	:	male/female
Strain	:	Wistar
Route of admin.	:	oral feed
Exposure period	:	lifespan
Frequency of treatment	:	4 h/d, 5 d/w; no food during 20 hours
Post. obs. period	:	final sacrifice after 149 weeks
Doses	:	actual dose: 0.014, 0.13, 1.3 mg/kg b.w./day VC monomer in PVC
Result	:	
Control group	:	yes, concurrent no treatment
Method	:	other
Year	:	1983
GLP	:	yes
Test substance	:	other TS
Result	:	A statistically signifcant increase in the incidence of liver nodules (presumed to be hepatomas) was the only neoplastic response to administration of VC levels below 1.3 mg/kg b.w/day. Hepatocellular carcinomas and hepatic angiosarcomas (1 male, 2 females) were found at the highest dose in small numbers. No Zymbal gland tumors observed; no significant affect on the incidence of mammary gland tumors and abdominal mesotheliomas. NOAEL: 0.13 mg VC/kg b.w./day with respect to the induction of tumors.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	VC >= 99.97 % (impurities: acetylene 2 ul/l, mono-vinylacetylene 15 ul/l, 1,3-butadiene 10 ul/l, methyl chloride 75 ul/l, ethyl chloride 50 ul/l, chloroprene 1 ul/l, 1,1 -dichloroethane 1 ul/l, 1,2-dichloroethane 20 ul/l, acetaldehyde 5 mg/kg, HCl 1 mg/kg, Fe 0.5 mg/kg, H2O 100 mg/kg, evaporation residue 10 mg/kg). PVC powder (Carina S 65-02; VC content 3 ppm). The PVC powder was freed of VC by heating in the vacuum (residual VC content < 0.2 ppm).
Reliability	:	(2) valid with restrictions
29.05.2002		(198) (216)
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	s.c.
Exposure period	:	life time
Frequency of treatment	:	1 injection
Post. obs. period	:	final sacrifice after 145 weeks

Doses	:	4.25 mg in 1 ml olive oil
Result	:	
Control group	:	yes, concurrent vehicle
Method	:	other
Year	:	1977
GLP	:	no data
Test substance	:	other TS
Result	:	Study BT 13 1 nephroblastoma observed in a male.
Source	:	Huels AG Marl EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance	:	Maximum level of impurities: H2O 10 ppm, acetaldehyde 5 ppm, acetylene 2 ppm, allene 5 ppm, butane 8 ppm, 1,3-butadiene 10 ppm, chlorophene 10 ppm, diacetylene 4 ppm, vinyl acetylene 10 ppm, propine 3 ppm, methylchloride 100 ppm.
Reliability	:	(2) valid with restrictions

29.05.2002 (198) (201) (202)

5.8 TOXICITY TO REPRODUCTION

Type	:	Two generation study
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	Females: premating period to gestation day 20, and lactation day 4 until sacrifice. F1 pups selected to become P2 generation were exposed from postnatal day 26 until all litters were weaned. Males (both generations): parallel to females
Frequency of treatment	:	6 hr/d, 5 d/wk during premating; 6 hr/d, 7 d/wk during mating, gestation, lacation, and postweaning.
Premating exposure period		
Male	:	10 weeks prior to mating
Female	:	10 weeks prior to mating
Duration of test	:	
Doses	:	10, 100, 1100 ppm
Control group	:	yes
NOAEL Parental	:	= 10 ppm
NOAEL F1 Offspr.	:	= 1100 ppm
NOAEL F2 Offspr.	:	= 1100 ppm
Method	:	other: Study was designed to meet or exceed guidelines of EPA, TSCA, OECD, and EEC.
Year	:	1997
GLP	:	yes
Test substance	:	other TS
Remark	:	US EPA Integrated Risk Information System (IRIS) reviewed this study and considered 10 ppm as the NOAEL for parental effects in both males and females. Increased liver weights and centrilobular hypertrophy are considered a nonadverse adaptive response.
Result	:	NOAEL (NOEL), LOAEL (LOEL): NOAEL for reproductive effects > 1100 ppm. Parental (F0 and F1) Toxic Effects by Dose Level: No effect of exposure was noted on mortality, physical examination, body weight or body weight gain, food consumption, mating indices, pregnancy rate, male fertility,

gestation length, parturition data, or litter size. Effects on organs were limited to liver. Liver weights were significantly increased (by 13-20%) in F0 males exposed to 10, 100 and 1100 ppm and F1 males exposed to 100 and 1100 ppm (Table 1). The relative liver weight in F0 males exposed to 10 ppm was comparable to control F1 male weights and thus was not considered to be VCM-related. Dose-related centrilobular hypertrophy, considered to be a compensatory reaction, occurred in F0 and F1 males exposed to 100 or 1100 ppm and females exposed to 10, 100 or 1100 ppm (Table 2). Increased incidences of altered hepatocellular foci (basophilic, acidophilic and clear well) were observed in livers of F1 males and females exposed to 100 or 1100 ppm.

Offspring (F1 and F2) Toxic Effects by Dose Level: No adverse effect of vinyl chloride exposure on pup survival or growth, sex distribution, age for vaginal opening or preputial separation was found. Organ weights were not affected by exposure.

Table 1
Relative liver weights for the F0 and F1 generation

	ppm VCM			
Generation/sex	Control	10	100	1100
F0 males	2.83±0.26	3.05±0.29*	3.09±0.20*	3.26±0.19**
F1 males	2.98±0.33	3.01±0.19	3.32±0.36**	3.38±0.19**
F0 females	3.31±0.32	3.34±0.36	3.40±0.30	3.55±0.31
F1 females	3.54±0.66	3.37±0.42	3.60±0.45	3.74±0.38

* p<0.05; ** p<0.01.

Table 2
Summary of F0 and F1 generation liver histopathology

	ppm VCM			
	0	10	100	1100
F0 generation				
male rats				
centrilobular hypertrophy	0	0	15	30
acidophilic foci	0	0	0	1
basophilic foci	0	0	0	1
female rats				
centrilobular hypertrophy	0	2	26	30
F1 generation				
male rats				
centrilobular hypertrophy	0	0	19	30
acidophilic foci	1	0	4	5
basophilic foci	0	0	0	8
clear cell foci	0	0	0	5
female rats				
centrilobular hypertrophy	0	6	30	30
acidophilic foci	0	0	0	8
basophilic foci	0	0	1	11

N = 30 for each dose level

Source :

PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Test condition :

Test Organisms: Thirty animals/sex/group (for both P1 and P2 generation) began exposure at approximately 6 weeks of age. Males and females ranged in weight from 207-273 g and 137-177 g, respectively.

Mating Procedures: One male and one female rat from the same exposure group were co-housed nightly until evidence of mating (microscopic observation of sperm in vaginal smear and/or copulation plug in vagina) or for 14 consectutive days. Unmated females were randomly redistributed to a sexually active male rat within the same exposure group for an additional 6 days. P2 animals were randomly chosen from a pool of F1 pups (2/litter) that had been exposed to the same concentration as parents. For the P2 generation, care was taken to avoid brother-sister cohabitations. Once mated, females were housed individually for the remainder of gestation

Test substance :

Vinyl chloride was supplied by the Geon Company, Pedricktown, NJ (Lot #1). Purity was > 99.9%

Reliability : (1) valid without restriction
14.05.2002 (217) (218)

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	Day 6-19 of gestation
Frequency of treatment	:	
Duration of test	:	20 days
Doses	:	10, 100, 1100 ppm
Control group	:	yes
NOAEL Maternalt.	:	= 10 ppm
NOAEL Teratogen	:	= 1100 ppm
Method	:	other: Study was designed to meet or exceed guidelines of EPA, TSCA, OECD, and EEC.
Year	:	1991
GLP	:	yes
Test substance	:	other TS
Remark	:	

The exposure portion of this study was performed concurrently with the two-generation reproduction study described in Section 5.

Result :

Vinyl chloride concentrations: The exposure concentrations determined by IR and gas spectrometry were 10.8 +/- 1.1, 102 +/- 10, and 1110 +/- 43 ppm, respectively.

Maternal toxicity: No mortalities occurred in any group.
Pregnancy rate for the control, 10, 100 and 1100 ppm groups were 92, 96, 88 and 96, respectively (ns). Slight changes in body weight gain seen in treated animals were not treatment-related (Table 1). No maternal toxicity was observed at the 10 ppm level. Increases in relative kidney weight occurred in those exposed to 100 or 1100 ppm (0.006 +/- 0.0005 in both groups vs. 0.005 +/- 0.004 in control), and increased relative liver weight was noted at 1100 ppm (0.043 +/- 0.0024 vs. 0.041 +/- 0.0023 in control). There was no effect of treatment on pre- and post-implantation loss or the number of corpora lutea, implants, fetuses, or resorptions.

Fetal toxicity: There was no effect of treatment on sex ratio, fetal body weight (Table 1), or number or type of malformations (Table 2) observed.

Table 1
Body weight gains and litter size in female rats exposed to VCM

	ppm VCM			
Parameter	0	10	100	1100
Body weight gain gestation days 6-20	110±13.5	100±13.8*	101±14.0	99±10.4*
Implantation sites	14.2±1.38	12.9±1.80	13.1±2.55	13.3±2.30
Live fetuses	13.8±1.64	12.4±1.84	12.9±2.57	12.7±2.27
Fetal body weight	3.4±0.17	3.4±0.17	3.4±0.22	3.3±0.22

* $p<0.05$

Table 2
Fetal malformations following exposure to VCM

	ppm VCM			
Parameter	0	10	100	1100
Number examined, fetuses (litters)				
gross	318 (23)	297 (24)	283 (22)	305 (24)
soft tissue	167 (23)	155 (24)	147 (22)	158 (24)
skeletals	151 (23)	142 (24)	136 (22)	147 (24)
Gross				
cranio-rachischisis	0	0	0	1 (1)
Soft tissue				
distended lateral ventrides	0	0	1 (1)	0
Skeletals				
Malformations	0	0	0	0

Source :

PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Test condition :

After a 2-week acclimation period, females rats were mated with males. Females were considered to have mated if sperm was observed microscopically in the vaginal smear and/or a vaginal plug was observed. The day on which evidence of mating was observed was defined as Day 0 of gestation. Rats weighed an average of 213 g on gestation day 0. Vinyl chloride (0, 10, 100, 1100 ppm) was administered via whole body inhalation (6 hr/d) to 100 mated female rats (25/group) during gestation days 6-19. Exposure concentrations were verfied analytically. Animals were observed twice daily and given detailed physical exams daily on days 0 and 6-20. Body weights were recorded on days 0, 6, 9, 12, 15 and 20 of gestation and food consumption was recorded over days 0-6, 6-9, -9-12, 12-15, and 15-20. Animals were sacrificed on day 20 and given a postmortem examination which included wieghing of the gravid uterus, kidneys, and liver. The ovaries were evaluated for the number of corpora lutea and uteri for implants. Fetuses were removed, weighed, sexed, and evaluated for external abnormalities. One half were processed for visceral examination and the other for skeletal examination

Test substance :

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Vinyl chloride was supplied by the Geon Company, Pedricktown, NJ (Lot #1). Purity was > 99.9%

Reliability : (1) valid without restriction
21.05.2002 (219) (218)

Species	:	rat
Sex	:	female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	Day 6-15 of gestation
Frequency of treatment	:	7 hr/d
Duration of test	:	Day 21 of gestation
Doses	:	500 ppm, 2500 ppm w/wo 15% ethanol
Control group	:	yes, concurrent no treatment
NOAEL Maternalt.	:	< 500 ppm
NOAEL Teratogen	:	= 2500 ppm
Method	:	other
Year	:	1977
GLP	:	no data
Test substance	:	other TS
Remark	:	

The authors did not consider effects seen at 2500 ppm to be significant, and concluded that 2500 ppm produced no adverse developmental effects. Effects noted at 500 ppm VC were not considered to be of significance since they were not observed at 2500 ppm and controls for the 500 ppm group had lower values for variables in question compared to controls for the 2500 ppm VC group

Result :

NOAEL (NOEL), LOAEL (LOEL): The NOAEL for developmental toxicity was 2500 ppm.

Maternal Toxic Effects by Dose Level: Decreased weight gain was found in rats exposed to 500 ppm Vinyl chloride (VCM) (Table 1). Decreased feed consumption and increased absolute and relative liver weight were found in animals exposed to 2500 ppm VCM. There was no significant effect of exposure on maternal death.

Reproductive Indices: There was no significant effect of exposure on the number of litters, number of implantation sites/dam, number of implanations or litters resorbed, or percent pregnant. The number of corpora lutea/dam and pregnancy wastage (the number of corpora lutea minus the number of implants) decreased in rats exposed to 500 ppm VCM, but not 2500 ppm VCM (Table 2).

Fetal Data: No significant effect of exposure on number of live fetuses/litter, sex ratio, or overall incidence of gross, soft tissue or skeletal anomalies was noted. A significant decrease in fetal body weight and an increase in crown-rump length were observed in animals exposed to 500 ppm VCM but not 2500 ppm VCM (Table 2). The incidence of unilateral or bilateral dilated ureters increased in animals exposed to 2500 ppm VCM but not 2500 ppm VCM + ethanol (Table 3). An increased incidence of rib spurs was noted in animals exposed to 500 VCM but not 2500 ppm VCM.

In general, effects were augmented in animals exposed to VCM and ethanol.

Table 1
Maternal weight gain, liver weights and feed consumption in rats exposed to VCM

	ppm VCM	
Parameters	0	500
Number of dams	28	31
Weight gain days 6-21	148±11	125±19*
Relative liver weight, mg/g	36.5±4.1	37.1±2.6
Feed consumption days 6-15	21±2	22±2

	ppm VCM		
Parameters	0	2500	2500^
Number of dams	19	16	16
Weight gain days 6-21	127±15	138±23	120±15**
Relative liver weight, mg/g	34.4±3.3	37.8±2.6*	42.1±2.4**
Feed consumption days 6-15	22±2	21±2*	13±2**

^ also treated with 15% ethanol in drinking water
* p<0.05 from control; ** p<0.05 from VCM alone

Table 2
Observations made during C-section of rats exposed to VCM

	ppm VCM	
Parameters	0	500
Number of dams	28	31
Corpora lutea/dam	15+3	13+2*
Fetal body weight, g	5.67±0.29	5.44±0.38*
Fetal crown-rump length, mm	42.6±1.2	43.6±0.8*

	ppm VCM		
Parameters	0	2500	2500^
Number of dams	19	16	16
Corpora lutea/dam	14±2	15±2*	14±2**
Fetal body weight, g	5.59±0.27	5.62±0.29	5.34±0.32**
Fetal crown-rump length, mm	43.6±1.5	43.3±1.1	42.4±0.9**

^ also treated with 15% ethanol in drinking water
* p<0.05 from control; ** p<0.05 from VCM alone

Table 3
Incidence of skeletal malformations of rats exposed to VCM

	ppm VCM	
Parameters	0	500
Number examined, fetuses (litters)		
gross	339 (28)	387 (31)
soft tissue	113 (28)	129 (31)
skeletals	337 (28)	387 (31)
fetuses affected (%) (litters affected, %)		
gross anomalies		
omphalocele	0	1 (3)
soft tissue		
micropthalmia	0	0
dilated ureter (uni or bilateral)	2 (7)	2 (6)
small kidney	0	0

skeletal tissue		
sternebrae		
unfused	0	1 (6)
ribs		
spurs	1 (4)	9 (52)*
vertebrae		
missing cervical centra	0.3 (4)	2 (16)
skull		
delayed ossification	16 (61)	12 (61)
unfused	0	0

Parameters	ppm VCM 0	2500	2500^
Number examined, fetuses (litters)			
gross	229 (19)	214 (16)	188 (16)
soft tissue	76 (19)	73 (16)	63 (16)
skeletals	229 (19)	214 (16)	188 (16)
fetuses affected (%) (litters affected, %)			
gross anomalies			
omphalocele	0.4 (5)	0	0.5 (6)
soft tissue			
micropthalmia	0	0	2 (6)
dilated ureter (uni or bilateral)	5 (10)	27 (50)*	5 (19)**
small kidney	0	0	2 (6)
skeletal tissue			
sternebrae			
unfused	3 (32)	0.5 (6)	1 (12)
ribs			
spurs	0.4 (5)	0	0.5 (6)
vertebrae			
missing cervical centra	14 (68)	12 (69)	35 (69)
skull			
delayed ossification	18 (58)	6 (31)	3 (25)
unfused	53 (90)	3 (12)	2 (12)

^ also treated with 15% ethanol in drinking water
* p<0.05 from control; ** p<0.05 from VCM alone

Source :

PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Test condition :

Test Organisms: Twenty eight animals (controls) were exposed to air and 31 anim als were exposed to 500 ppm vinyl chloride (VC) by inhalation in the first experiment. Nineteen animals (controls) were exposed to air, 16 animals were exposed to 2500 ppm VC by inhalation, and 16 animals were exposed to 2500 ppm VC by inhalation plus 15% ethanol in drinking water in the second experiment. Rats weighed approximately 250 g at study initiation.

Test Conditions: Exposure was conducted in 3.5 cubic meter chambers. The atmosphere was generated by diluting gaseous vinyl chloride with filtered room air. The actual exposure concentration was measured with infrared spectrophotometer. The day on which a vaginal plug or sperm was seen in a vaginal smear was considered to be Day 0 of pregnancy. Animals were sacrificed on day 21 of gestation.

Param eters Assessed During Study: Food consumption (every 3 days), body weight (Days 6,10,16 and 21), number and position of live, dead and

resorbed fetuses, sex, weight and length (crown-rump) and external and skeletal condition of fetuses were measured. Soft tissues of one-third of each litter were examined microscopically.

Statistical Methods: The Fishers exact probability test was used to evaluate the incidence of resorption among litters. Body weights, body measurements and maternal liver weights were analyzed using ANOVA and a Dunnett's test. The incidence of fetal anomalies was analyzed using a Wilcoxon test.

Test substance :

Inhibited vinyl chloride monomer from Matheson Gas Products, Joliet, IL

Conclusion :

Rats are not as suceptible to toxic effects of vinyl chloride as mice

Reliability : (2) valid with restrictions
15.05.2002 (220)

Species	:	mouse
Sex	:	female
Strain	:	other: CF-1
Route of admin.	:	inhalation
Exposure period	:	Day 6-15 of gestation
Frequency of treatment	:	7 hr/d
Duration of test	:	Day 18 of gestation
Doses	:	50 ppm, 500 ppm w/wo 15% ethanol
Control group	:	yes, concurrent no treatment
NOAEL Maternalt.	:	= 50 ppm
NOAEL Teratogen	:	= 500 ppm
Method	:	other
Year	:	1977
GLP	:	no data
Test substance	:	other TS

Remark :

The authors concluded that none of the fetal effects noted at 500 ppm were adverse. Although the number of resorptions in mice treated with 500 ppm was greater than concurrent controls, it was not greater than historical controls

Result :

Maternal Toxic Effects by Dose Level: Decreased weight gain occurred in mice exposed to 500 ppm VCM (compared to control) (Table 1). Decreased feed consumption was observed in animals exposed to 500 ppm VCM (compared to control). Decreased absolute liver weight occurred in mice exposed to 500 ppm VCM (compared to control). Seventeen percent of mice exposed to 500 ppm VCM died (compared to 0% of controls).

Reproductive Indices: There was an increase in the incidence of resorptions in mice exposed to 500 ppm VCM (13% vs. 7% in controls) (Table 2). Litter size was reduced in mice exposed to 500 ppm VCM.

Fetal Data: Decreased numbers of live fetuses/litter and fetal weight occurred in mice exposed to 500 ppm VCM (Table 3). There was no significant effect of VC exposure on the sex ratio, or overall incidence of gross, soft tissue or skeletal anomalies. The incidence of unfused sternebrae, and delayed ossification in skull and sternebrae increased in animals exposed to 500 ppm VCM.

In general, effects were augmented in animals exposed to VCM and ethanol.

Table 1
Maternal weight gain, liver weights and feed consumption in mice exposed to VCM

	ppm VCM		
Parameters	0	50	50^
Number of dams	21	20	16
Weight gain days 6-21	16±4	17±6	11±7**
Relative liver weight, mg/g	59.5±8.7	57.8±4.5	56.6±7.3
Feed consumption days 6-15	6±1	6±1	4±2**

	ppm VCM		
Parameters	0	500	500^
Number of dams	26	19	7
Weight gain days 6-21	20±3	17±4*	10±7**
Relative liver weight, mg/g	55.5±5.5	54.4±4.2	45.8±5.1**
Feed consumption days 6-15	6±1	5±1*	3±1**

^ also treated with 15% ethanol in drinking water
* p<0.05 from control; ** p<0.05 from VCM alone

Table 2
Observations made during C-section of mice exposed to VCM

	ppm VCM		
Parameters	0	50	50^
Number of dams	21	20	16
implantation sites/dam	12±2	12±4	11±4
live fetuses	10+4	11+4	10+4
Fetal body weight, g	1.00±0.11	1.02±0.10	0.84±0.14**
Fetal crown-rump length, mm	23.0±1.9	24.2±0.8*	22.4±1.5**

	ppm VCM		
Parameters	0	50	50^
Number of dams	26	19	7
implantation sites/dam	14±2	13±2	10±6**
live fetuses	12±2	11±2*	8±6**
Fetal body weight, g	1.07±0.06	0.99±0.11*	0.78±0.15**
Fetal crown-rump	23.7±1.2	23.6±1.0	21.2±1.5**

^ also treated with 15% ethanol in drinking water
* p<0.05 from control; ** p<0.05 from VCM alone

Table 3
Incidence of malformations of mice exposed to VCM

	ppm VCM		
Parameters	0	50	50^
Number examined, fetuses (litters)			
gross	221 (20)	220 (20)	153 (14)
soft tissue	74 (20)	75 (20)	50 (14)
skeletals	221 (20)	220 (20)	153 (14)
fetuses affected (%) (litters affected, %)			
gross anomalies			
cleft palate	1 (10)	1 (10)	2 (21)
soft tissue			
small thymus	0	0	4 (7)

skeletal tissue			
sternebrae			
unfused	3 (20)	3 (25)	13 (57)**
delayed ossification	7 (50)	4 (35)	44 (100)**
No. 5 sternebra missing	0	0	3 (21)
ribs			
extra	4 (30)	5 (30)	0.6 (7)
spurs	4 (35)	5 (40)	2 (21)
vertebrae			
forked atlas	0.4 (5)	1 (10)	4 (36)**
delayed ossification of cervical arches	0	0	1 (14)
skull			
delayed ossification	9 (35)	8 (37)	40 (100)**
unfused occipital	0	0.7 (5)	24 (50)**

	ppm VCM		
Parameters	0	50	50^
Number examined, fetuses (litters)			
gross	325 (26)	215 (19)	56 (5)
soft tissue	107 (26)	73 (19)	19 (5)
skeletals	325 (26)	215 (19)	56 (5)
fetuses affected (%) (litters affected, %)			
gross anomalies			
exencephaly	1 (8)	1 (10)	2 (20)
anopthalmia	0	0	2 (20)
cleft palate	0	1 (5)	4 (40)
soft tissue			
small thymus	0	0	0
skeletal tissue			
sternebrae			
unfused	2 (19)	9 (42)*	34 (80)**
delayed ossification	1 (12)	6 (42)*	43 (100)**
No. 5 sternebra missing	0	1 (10)	7 (40)**
ribs			
extra	3 (31)	3 (32)	14 (60)**
spurs	4 (31)	3 (21)	14 (80)**
vertebrae			
forked atlas	0	0	4 (20)
missing cervical centra	0	1 (10)	38 (60)**
delayed ossification of cervical arches	0	0	5 (40)**
skull			
delayed ossification	13 (54)	30 (58)*	70 (100)**
unfused occipital	1 (12)	5 (21)	11 (20)

^ also treated with 15% ethanol in drinking water
* p<0.05 from control; ** p<0.05 from VCM alone

Source :

PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Test condition :

Test Organisms: Twenty one animals (controls) exposed to air, 20 animals exposed to 50 ppm vinyl chloride (VC) by inhalation, and 16 animals exposed to VC by inhalation plus 15% ethanol in drinking water were used in the first experiment. Twenty six animals (controls) exposed to air, 19 animals exposed to 500 ppm VC by inhalation, and 7 animals exposed to 500 ppm VC by inhalation plus 15% ethanol in drinking water were used in

the second experiment. Mice weighed approximately 25-30 g at study initiation.

Test Conditions: Exposure was conducted in 3.5 cubic meter chambers. The atmosphere was generated by diluting gaseous vinyl chloride with filtered room air. The actual exposure concentration was measured with an infrared spectrophotometer. The day on which a vaginal plug or sperm was seen in a vaginal smear was considered to be Day 0 of pregnancy. Animals were sacrificed on day 18 of gestation.

Parameters Assessed During Study: Food consumption (every 3 days), maternal body weight (Days 6,12,15 and 18), number and position of live, dead and resorbed fetuses, sex, weight and length (crown-rump) and external and skeletal condition of fetuses were determined. Soft tissues of one-third of each litter were examined microscopically.

Statistical Methods: The Fishers exact probability test was used to evaluate the incidence of resorption among litters.
Body weights, body measurements and maternal liver weights were analyzed using ANOVA and a Dunnett's test. The incidence of fetal anomalies was analyzed using a Wilcoxon test

Test substance :

Inhibited vinyl chloride monomer from Matheson Gas Products, Joliet, IL

Conclusion : Mice are more sensitive to toxic effects of vinyl chloride than rats or rabbits.
Reliability : (2) valid with restrictions
15.05.2002 (220)

Species : rabbit
Sex : female
Strain : New Zealand white
Route of admin. : inhalation
Exposure period : Day 6-18 of gestation
Frequency of treatment : 7 hr/d
Duration of test : Day 29 of gestation
Doses : 500 ppm, 2500 ppm w/wout 15 % ethanol
Control group : yes, concurrent no treatment
NOAEL Maternalt. : < 500 ppm
NOAEL Teratogen : = 2500 ppm
Method : other
Year : 1977
GLP : no data
Test substance : other TS
Remark : Fetal effects seen at 500 ppm were not considered to be of significance since they were not observed at 2500 ppm. Since the decrease in litter size at 500 ppm VC was associated with a decrease in corpora lutea (which was established prior to day 6 of gestation), this effect is probably not due to exposure to vinyl chloride
Result :

NOAEL (NOEL), LOAEL (LOEL): NOEL for developmental toxicity was 2500 ppm vinyl chloride (VCM). NOEL for maternal toxicity was 2500 ppm.

Maternal Toxic Effects by Dose Level: Decreased feed consumption occurred in animals exposed to 500 pm VCM (compared to control) but was unaffected in the 2500 ppm VCM exposure group (Table 1).

Reproductive Indices: Decreased numbers of corpora lutea/dam and implantation sites/dam were seen in animals exposed to 500 ppm VCM but

not 2500 ppm VCM (Table 2).

Fetal Data: A decreased number of live fetuses/litter was seen in animals exposed to 500 ppm VC but not 2500 ppm VCM (Table 3). No significant effect of exposure on overall incidence of gross, soft tissue or skeletal anomalies was noted. A significant increase in the incidence of delayed ossification of 5th sternebra and an increase in crown-rump length in animals exposed to 500 ppm VCM but not 2500 ppm VCM was observed.

In general, effects were augmented in animals exposed to VCM and ethanol.

Table 1
Maternal weight gain, liver weights and feed consumption in rabbits exposed to VCM

	ppm VCM	
Parameters	0	500
Number of dams	18	20
Weight gain days 6-21	0.05±0.19	0.01±0.19
Relative liver weight, mg/g	24.6±3.6	23.2±2.9
Feed consumption days 6-15	98±30	76±29*

	ppm VCM		
Parameters	0	2500	2500^
Number of dams	11	5	16
Weight gain days 6-21	0.06±0.27	0.01±0.13	-0.14±0.42
Relative liver weight, mg/g	24.7 +2.7	27.7 +5.9	30.0 +6.3
Feed consumption days 6-15	91±36	89±26	15±9**

^ also treated with 15% ethanol in drinking water
* p<0.05 from control; ** p<0.05 from VCM alone

Table 2
Observations made during C-section of rabbits exposed to VCM

	ppm VCM	
Parameters	0	500
Number of dams	18	19
Corpora lutea/dam	9±1	8±1*
Implantation sites/dam	9±1	8±1*
Live fetuses/litter	8±1	7±2*
Fetal body weight, g	35.23±4.82	34.13±4.17
Fetal crown-rump length, mm	91.0±4.2	92.6±5.0

	ppm VCM		
Parameters	0	2500	2500^
Number of dams	11	5	16
Corpora lutea/dam	10±2	10±7	10±2
Implantation sites/dam	8±2	8±4	9±2
Live fetuses/litter	6 +3	6+4	4+4
Fetal body weight, g	36.46±4.82	33.77±4.48	32.48±5.88
Fetal crown-rump length, mm	92.6±4.7	87.1±5.2	87.7±6.3

^ also treated with 15% ethanol in drinking water
* p<0.05 from control; ** p<0.05 from VCM alone

Table 3
Incidence of skeletal malformations of rabbits exposed to VCM

Parameters	ppm VCM 0	500
Number examined, fetuses (litters)		
gross	152 (18)	136 (18)
soft tissue	50 (18)	47 (18)
skeletals	152 (18)	136 (18)
fetuses affected (%) (litters affected, %)		
gross anomalies		
cleft palate	0	0
soft tissue		
dilated renal pelvis	0	0
dilated cerebral ventricle	0	0
enlarged right atrium of heart	0	0
skeletal tissue		
sternebrae		
delayed ossification #5	28 (77)	38 (94)*

Parameters	ppm VCM 0	2500	2500^
Number examined, fetuses (litters)			
gross	69 (9)	32 (4)	70 (9)
soft tissue	24 (9)	10 (4)	25 (9)
skeletals	69 (9)	32 (4)	70 (9)
fetuses affected (%) (litters affected, %)			
gross anomalies			
cleft palate	0	0	1 (11)
soft tissue			
dilated renal pelvis	0	0	8 (11)
dilated cerebral ventricle	0	10 (25)	0
enlarged right atrium of heart	0	0	8 (11)
skeletal tissue			
sternebrae			
delayed ossification #5	20 (44)	16 (75)	24 (67)

^ also treated with 15% ethanol in drinking water
* p<0.05 from control; ** p<0.05 from VCM alone

Source :

PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Test condition :

Test Organisms: Eighteen animals (controls) were exposed to air and 20 animals were exposed to 500 ppm vinyl chloride (VC) by inhalation in the first experiment. Eleven animals (controls) were exposed to air, 5 animals were exposed to 2500 ppm VC by inhalation, and 16 animals were exposed to 2500 ppm VC by inhalation plus 15% ethanol in drinking water in the second experiment. Rabbits weighed approximately 3.5-4.5 kg at study initiation.

Test Conditions: The exposure was conducted in 3.5 cubic meter chambers. The atmosphere was generated by diluting gaseous vinyl chloride with filtered room air. The actual exposure concentration was measured with an infrared spectrophotometer. Day of mating was considered to be Day 0 of pregnancy. Animals were sacrificed on day 29 of

gestation.

Parameters Assessed During Study: Food consumption (every 2 days), body weight (Days 6,12,18, 22 and 29), number and position of live, dead and resorbed fetuses, sex (based on examination of external genitalia), weight and length (crown-rump) and external and skeletal condition of fetuses were measured. Soft tissues of one-third of each litter were examined microscopically.

Statistical Methods: The Fishers exact probability test was used to evaluate incidence of resorption among litters. Body weights, body measurements and maternal liver weights were analyzed using ANOVA and a Dunnett's test. The incidence of fetal anomalies was analyzed using a Wilcoxon test

Test substance :

Inhibited vinyl chloride monomer from Matheson Gas Products, Joliet, I

Conclusion :

Rabbits are less sensitive to toxic effects of vinyl chloride than mic

Reliability : (2) valid with restrictions
21.05.2002 (220)

Species	:	Rat
Sex	:	Female
Strain	:	Other
Route of admin.	:	inhalation
Exposure period	:	6 - 9 days during 1., 2., or 3. trimester of gestation
Frequency of treatment	:	24 h/d
Duration of test	:	21 d
Doses	:	4,000 mg/m3 (1,500 ppm)
Control group	:	yes, concurrent no treatment
Method	:	other
Year	:	1978
GLP	:	no data
Test substance	:	no data
Remark	:	Strain: CFY rats Test design: pregnant rats (13 to 28 per group) were exposed to air, VC, air + Trypan Blue s.c. (2 times), VC + Trypan Blue s.c. (2 times) during day 1-9, 8-14, and 14-21 of gestation, respectively. On day 21 of gestation, animals were sacrificed.
Result	:	Maternal weight gain was decreased in females exposed on days 14-21 of gestation. Relative liver weight values were increased increased in dams exposed on days 1-9 or 8-14. The number of resorbed fetuses as well as fetal loss were significantly increased in the group exposed to VCM during day 1-9 of gestation. Fetal weight was almost normal in all groups. None of the fetal malformations or skeletal anomalies could be attributed to VCM.

Table 1

Litter size and fetal loss following exposure to VCM

	ppm VCM	
Parameter	0	1500
exposure days 1-9		
litter size	13.15±0.64	11.68±0.38
fetal loss (%)	1.7	5.5*
exposure days 8-14		
litter size	11.29±0.61	13.36±0.37

fetal loss (%)	3.18	4.54
exposure days 14-21		
litter size	11.78±0.94	11.18±0.74
fetal loss (%)	5.8	5.4

* p<0.05

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
22.05.2002 (221)

Species : rat
Sex : female
Strain : Wistar
Route of admin. : inhalation
Exposure period : 4 hrs/day
Frequency of treatment : Until day 20 of pregnancy
Duration of test : Up to 6 months after birth
Doses : 4.8 and 35.5 mg/m3
Control group : yes
Method :
Year : 1980
GLP : no data
Test substance :
Remark : Reference consulted was an English translation of a foreign-language document.
The results of this study are inconsistent with results of a recent GLP two generation study which was conducted at much higher concentrations.
Result : NOAEL for Maternal toxicity - unknown.
NOAEL for teratogenicity - <4.8 mg/m3.

Fetuses from rats treated with 4.8 mg/m3 showed evidence of hemorrhage, blood and urinary abnormalities and altered organ weight. Fetuses from rats treated with 35.5 mg/m3 had similar changes as those given 4.8 mg/m3 plus intumescence and abnormalities in nervous system function (at 6 months).
Test substance : Purity of vinyl chloride was not noted.
Reliability : (3) invalid
Maternal toxicity was not monitored.
20.05.2002 (222)

Species : rat
Sex : female
Strain : Wistar
Route of admin. : inhalation
Exposure period : not stated
Frequency of treatment : not stated
Duration of test : Day 21 of gestation
Doses : 6.15 mg/m3/day
Control group : yes
Method :
Year : 1978
GLP : no data
Test substance :
Remark : Reference consulted was an English translation of a foreign-language document.
The results of this study are inconsistent with results of a recent GLP

teratology study which was conducted at much higher concentrations.

Result : Embryonal mortality, early postimplantation lethality, abnormalities in brain, liver, skeleton, reduced fetal weight reported.

Test substance : Purity of vinyl chloride was not noted.

Reliability : (3) invalid
Maternal toxicity was not monitored.

22.05.2002 (223)

5.10 OTHER RELEVANT INFORMATION

Type : other: dermal absorption

Method : Male rhesus monkeys (Macaca mulatta) weighing 4-5 kg were used. Prior to exposure 30 mg/kg sodium pentobarbital was administered iv. An endotracheal catheter with an inflatable collar was inserted into the trachea and connected to a Harvard respiratory pump adjusted to deliver a volume of 20 ml of air at a rate of 28-38 cycles/min. Monkeys were exposed (whole body, excluding the head) to atmospheres containing 7000 and 800 ppm 14C-vinyl chloride for 2.0 and 2.5 hours, respectively. To ensure an adequate seal around the neck, the hair was removed and the membrane was fitted to the neck and secured to the skin with tape.

To trap VC from the expired air, a polyethylene tube filled with 0.5 g of activated charcoal was placed in the exhaust port of the respiratory pump. A similar tube placed on the intake port of the respirator filtered any vinyl chloride from the artificially inspired air. The expired air traps were changed at 0.5 or 1 hr intervals while the intake traps were changed every 2 hours. Vinyl chloride was eluted from the charcoal with carbon disulfide in a dry ice bath and analyzed by gas chromatography. At the end of the study, the animals were sacrificed and selected tissues were weighed and samples obtained for analysis. In addition urine and bile were collected and analyzed.

Chamber concentrations of vinyl chloride were measured by infrared specrophotometry.

Result : After a 2-2.5 hour exposure of rhesus monkeys to 800 and 7000 ppm, dermal absorption was estimated to be 0.031% and 0.023% of total bioavailable vinyl chloride, respectively.

Reliability : (2) valid with restrictions

22.05.2002 (226)

Type : Toxicokinetics

Remark : Method: Rats were exposed in vivo to VC at concentrations ranging from 51 ppm to 1167 ppm (0.13 to 2.99 mg/l) for 52.5 to 356.3 min. The time dependent decline of VC concentration was monitored.
Pretreatment of rats with pyrazole.
Determination of non-protein sulfhydryl content of the liver of rats exposed to VC concentrations ranging from 50 to 15,000 ppm for 7 h/d for 5 d, 3 w (7 h/d, 5 d/w), or 7 w.

Strain: Sprague-Dawley rats (Spartan strain), male, adult.

Results: Upon exposure to 50 to 105 ppm, the rate constant (apparent 1. order) of the metabolic removal of VC from the system was k = - 8.04 * E-3 +- 3.4 * E-3 /min (t1/2 = 86 min).
Upon exposure to 220 to 1167 ppm, the rate constant of metabolism was (mean value) k = - 2.65 * E-3 +- 1.35 * E-3/min (t1/2 = 261 min).
Pretreatment with pyrazole reduced the rate of metabolism. The non-

protein sulfhydryl content of the liver (glutathione and cysteine) is reduced without relationship to dose when animals are exposed to VC in vivo. The rate of depression decreased with continued exposure suggesting a compensatory mechanism.
Metabolic products excreted with the urine are S-(2-hydroxyethyl)cysteine and S-(2-carboxymethyl)cysteine, the respective N-acetyl derivatives, and chloroacetic acid.
Primary metabolic pathway presumably sequential oxidation to chloroethanol, chloroacetaldhyde, and chloroacetic acid. VC metabolising enzymes are saturated by exposure to concentrations exceeding 220 ppm. At higher concentrations, metabolism occurs via a secondary pathway, presumably epoxidation and/or peroxidation.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
20.05.2002 (227) (228)

Type : Toxicokinetics
Remark : Method: Determination of kinetic data for the uptake, metabolism, and clearance of VC in a closed spirometer system with defined initial concentration.

Species: rat, rabbit, mouse, desert mouse.
Results:
Uptake: rat: t1/2 = 3.2 min; K = 2.86
rabbit: t1/2 = 3.4 min; K = 0.91
Metabolism:
rat: t1/2 = 76.8 min; k = 0.61 /h
rabbit: t1/2 = 277 min; k = 0.15 /h
mouse: t1/2 = 44 min; k = 0.945 /h
des.mouse: t1/2 = 143 min; k = 0.29 /h
Clearance:
rat: 8.4 l/h*kg
rat (Wistar): 11.0 l/h*kg (ca. 6.9 mg/h*kg b.w.)
rabbit: 2.74 l/h*kg
mouse: 25.6 l/h*kg
gerbil: 12.5 l/h*kg
Rhesus: 3.55 l/h*kg (ca. 3.2 mg/h*kg b.w.)
Rhesus pretreated with disulfiram: 0.35 l/h*kg
Man 2.02 l/h*kg

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test substance : VC, purity: 99.995 %.
Reliability : (2) valid with restrictions
20.05.2002 (229) (230)

Type : Metabolism
Result : At low concentrations, vinyl chloride is oxidized sequentially to 2-chloroethanol, 2-chloroacetaldehyde and 2-chloroacetic acid by alcohol dehydrogenase.
Reliability : (2) valid with restrictions
22.05.2002 (84)

Type : Metabolism
Method : Human liver microsome assays of cytochrome P-450 IIE1 were used to examine the effects in the oxidation of vinyl chloride. Several studies were conducted, including 1) selective inhibition of catalytic activity in human liver microsomes by diethyldithiocarbamate, 2) correlation of rates of

different catalytic activities with each other, 3) demonstration of catalytic activity in reconstituted systems containing purified human P-450 IIE1 and 4) immunoinhibition of catalytic activity in human liver microsomes with rabbit anti-human P-450 IIE1.

Result : P-450 IIE1 is a major catalyst in the oxidation of vinyl chloride.
Reliability : (2) valid with restrictions
22.05.2002 (231)

Type : Metabolism
Result : Chloroacetaldehyde is formed during metabolism of vinyl chloride.
Reliability : (2) valid with restrictions
22.05.2002 (232)

Type : Metabolism
Method : Preweanling rats were exposed to 600 ppm for 4 hrs/day for 5 days. DNA adducts in liver, lung and kidney were determined 3, 7 and 14 days post-exposure.
Result : Both 2-chloroethylene oxide and 2-chloroacetaldehyde have been shown to produce DNA adducts, which are thought to play a role in vinyl chloride toxicity.

7-(2'-Oxoethyl)guanine (7OEG) was the major DNA adduct detected, representing ~98% of all adducts. N2,3-Ethenoguanine (eG) and 3,N4-etheno-2'-deoxycytidine (edC) were present at ~1% of the 7OEG concentration, while 1,N6-etheno-2'-deoxyadenosine (edA) was present in even lower concentrations.

Liver had 3-8-fold higher amounts of the DNA adducts than lung and kidney. Whereas 7OEG had a half life of ~62 hrs, all three etheno adducts were highly persistant. After accounting for dilution due to growth-related cell proliferation, eG had a half life of approximately 30 days, while edC and edA were not repaired.
Reliability : (2) valid with restrictions
22.05.2002 (233) (234) (151)

Type : Biochemical or cellular interactions
Method : Principal alkylation products after incubation of RNA with 14C-vinyl chloride in a rat liver microsomal system were identified.

Rats were exposed to 14C-vinyl chloride and the RNA adducts found in rat liver were identified.
Remark : Review of the alkylation of nucleotides by VC metabolites and its implications for VC -induced carcinogenesis.
Result : 7-(2-oxoethyl)guanine is by far the major DNA alkylation product of VC.

The roles of the different base adducts in the mechanism of VC -induced carcinogenesis have not yet been clearly defined.
Reliability : (2) valid with restrictions
20.05.2002 (171)

Type : Excretion
Result : At low exposure levels, the majority is excreted into the urine
Reliability : (2) valid with restrictions
22.05.2002 (235)

Type : Excretion
Method : A group consisting of 8 rats was exposed to 5000 ppm of nonlabeled vinyl chloride (VC) 6 hrs/day, 5 days/week for 7 weeks. On the last day of repeated exposure 14C-labeled VC was used. The fate of 14C -labeled VC

was compared with a group of 5 naive rats.

After the exposure 14C-labeled VC, three of the eight exposed repeatedly and two of the five exposed once were placed in glass Roth-type metabolism cages for collection of urine, feces and expired air. Samples were obtained for up to 72 hours after exposure to vinyl chloride.

The remaining rats wre sacrificed immediately following exposure. A liver sample was obtained from each animal to measure aniline hydroxylase and p-nitroanisole O-demethylase activity and macromolecular binding to hepatic tissue.

Result : The percentage of 14C activity excreted by each route as well as the total milligram equivalents of VC recovered were essentially identical for the singly and repeatedly exposed groups. The majority of 14C activity eliminated was expired as VC per se.

While the binding of reactive metabolites of VC to hepatic macromolecules was enhanced following repeated exposure, no differences were observed in the activity of hepatic microsomal enzymes to the substrates aniline or p-nitroanisole in any of the treatment groups when compared to nonexposed control rats.

Percentage 14C activity eliminated within 72 hours following exposure to 5000 ppm vinyl chloride

	Single exposure	Repeated exposure
Expired		
as VC	54.5 ±3.5	53.7 ±2.1
as CO2	8.0 +1.4	9.6+1.6
Urine	27.1 ±2.1	25.7 ±1.4
Feces	3.2 ±2.5	1.4±0.4
Carcass and tissues	7.3±2.5	9.7 ±1.6

Reliability : (2) valid with restrictions
12.02.2003 (236)

Type : Excretion
Method : Groups of 4 male Sprague-Dawley rats were exposed to 10 or 1,000 ppm 14C-VC for 6 hours. At the end of the exposure period, rats were placed individually into Roth-type metabolism cages to obtain respired air, urine and feces. After 72 hours, the animals were sacrificed and samples of tissue (fat, kidney, liver, lung, muscle and plasma) were obtained for analysis of 14C activity. The remaining carcass was also analyzed for 14C activity.

Remark : Results:

dose (ppm)	10 ppm	1,000 ppm
	(% of total 14C recovered)	
expired VC	1.61 %	12.26 %
expired CO2	12.09 %	12.30 %
urine	67.97 %	56.29 %
feces	4.45 %	4.21 %
carcass and tissue	13.84 %	14.48 %
pulmonary elimination:	t1/2 = 20.4 min	t1/2 = 22.4 min
urinary elimination:		
initial phase	t1/2 = 4.6 h	t1/2 = 4.1 h
late phase	variable	variable

After 72 h highest concentration of 14C-activity in liver and skin (may be

dose dependent).
In urine three major metabolites (by HPLC) roughly independent of dose; two of the metabolites have been identified as N-acetyl-S-(2-hydroxyethyl)cysteine and thiodiglycolic acid.

Test substance : 1,2-14C-VC
Reliability : (2) valid with restrictions
13.02.2003 (237)

Type : Biochemical or cellular interactions
Remark : Method: chemical synthesis, spectroscopical and chemical analysis.
Results: Hydroxyethanoguanine is formed by reaction of deoxyguanosine with chloroethylene oxide.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (238)

Type : Biochemical or cellular interactions
Remark : Results: Synthesis of the nucleoside and 5'''''''-diphosphate of ethenoguanine and copolymerization with CDP. The deoxypolynucleotide complement synthesized by AMV reverse transcriptase contained in addition to dG, dC and dT. While dC is neither lethal nor mutagenic, dT incorporation represents a mutagenic event that occurs with ca. 20 % frequency and may have a high probability of causing transitions which could initiate malignant transformation.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (239)

Type : Biochemical or cellular interactions
Remark : Method: Reaktion of poly(deoxyguanylate-deoxycytidylate) with chloroethylene oxide; evaluation of the reaction product as template in a replication fidelity assay.
Results: Misincorporation rates of dA and dT were found to increase with the level of template modification. 80% of the mispairing events were located opposite of minor cytidine lesions. 7-(2-oxoethyl)guanine, the major adduct identified, did not miscode for either thymidine or adenine. Thus 7-(2-oxoethyl)guanine may contribute only slightly to the induction of mutations by chloroethylene oxide or VC.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (167)

Type : Biochemical or cellular interactions
Remark : Method: Analysis of covalent binding to hepatic nucleic acids (RNA, DNA) and macromolecules after inhalative exposure to 14C-VC for 6 h in male rats (strain: Sprague-Dawley).
Dose: 1, 10, 25, 50, 100, 250, 500, 1,000, 5,000 ppm
Results:
A disproportionate decrease in macromolecular binding was observed as the concentration of VC increased. The covalent binding to hepatic macromolecules was related to the amount of VC metabolized.
There was no detectable binding of radioactivity to either DNA or RNA in the liver. Hepatic glutathione content was significantly depressed only at exposure concentrations greater than 100 ppm. Metabolism of VC was not increased in rats exposed to 100 ppm of VC after pretreatment with phenobarbital. Macromolecular binding, however, was increased markedly

when compared to non-pretreated animals.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (240)

Type : Excretion
Method : Groups of five male Sprague Dawley rats received a single oral dose of 0.05, 1.0, 100 mg/kg of 14C-VC in corn oil.
Immediately after dosing, rats were placed in glass Roth-type metabolism cages for collection of urine, feces and expired air. Samples were assayed for 14C activity following sample preparation. Urinary metabolites of VC were isolated by HPLC for identification and routine quantitation.

Remark : Results:

dose	0.05 mg/kg	1.0 mg/kg	100 mg/kg
	(percentage of dose excreted over 72 h)		
expired VC	1.43 %	2.13 %	66.64 %
expired CO2	8.96 %	13.26 %	2.52 %
urine	68.34 %	59.30 %	10.84 %
feces	2.39 %	2.20 %	0.47 %
carcass and tissue	10.13 %	11.10 %	1.83 %

pulm. elimination monophasic biphasic
t1/2 = 53.3 min t1/2 = 14.4 min
t1/2 = 40.8 min
urin. elimination biphasic at all dose levels
t1/2 = 4.6 h
t1/2 = highly variable
Three major metabolites in urine (by HPLC), two of which were identified: N-acteyl-S-(2-hydroxyethyl)-cysteine and thiodiglycolic acid (GC-MS).
Proportions of metabolites not influenced by dose.
Metabolism of VC appears to be a saturable process.
After 72 h, highest concentration of 14C-activity in liver (3 - 5 fold higher than in muscle, lung or fat).

Test substance : 1,2-14C-VC
Reliability : (2) valid with restrictions
29.05.2002 (241)

Type : Metabolism
Remark : Method: investigation of urinary S-containing metabolites after intragastric application of 14C-VC (100 mg/kg).
Other substances tested: chloroacetaldhyde, S-(2-hydroxyethyl)-L-cysteine, S-(carboxymethyl)-L-cysteine.

Species: rat, Alderley Park strain (Wistar-derived), male, adult.
Results: N-acetyl-S-(2-hydroxyethyl)cysteine is the major VC metabolite in rats. N-acetyl-S-vinylcysteine is a second related metabolite. These metabolites are not mutagenic in Salmonella typhimurium.
Chloroacetaldehyde and S-(carboxymethyl)-cysteine, but not chloroacetic acid, lie on a pathway connecting VC with thiodiglycollic acid.
The observations are consistent with the formation of chloroacetaldhyde and with the reaction of chloroethylene oxide or chloroacetaldehyde with glutathione in the presence of glutathione S-epoxide transferase.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test substance : 14C-VC, radiochemical purity > 99.0 %.
Reliability : (2) valid with restrictions
29.05.2002 (242)

5. Toxicity **Id** 75-01-4
Date 18.06.2002

Type : Metabolism
Remark : Results: Metabolism of VC by rats to non-volatile metabolites proceeds by action of mixed-function-oxidases.
Blockade of this enzyme system results in blockade of the VC metabolism. If atmospheric concentrations exceeding 250 ppm are present, the oxidative metabolism is saturated.
Metabolites are mostly excreted via the urine and comprise S-containing compounds arising from conjugates of glutathione with metabolic intermediates of VC.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (166)

Type : Metabolism
Remark : Method: Incubation of rat liver microsomes and a NADPH-regenerating system with 1,2-14C-VC and analysis of the covalent VC binding.

Results: Uptake of VC by microsomes and alkylation of proteins are observed. Uptake and binding are reduced when mixed-function-oxidases are blocked by addition of an inhibitor. Addition of glutathione results in depression of the covalent binding to proteins while VC uptake is increased. The presence of cysteine containing proteins is essential for occurrence of the covalent protein binding. Enzymatic generation of O2-radicals from H2O2 also results in VC uptake.
The results indicate that chloroethylene oxide is the reactive VC metabolite.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (243) (244)

Type : Metabolism
Remark : Method: Exposure of rats to 1.4, 9.3, 24.7, 51, 109, 250, 511, 1020, and 4600 ppm, respectively, of 14C-VC for 6 h.
Analysis of total bound radioactivity.

Strain: Sprague-Dawley rats, male, adult.

Results: Metabolism of VC follows Michaelis-Menten kinetics.
Thus a KM-equivalent exposure concentration of 0.86 mg/l and a V max of 5.7 mg VC/h/kg b.w. (ca. 90 umol VC/h/kg b.w.) apply for a rat with a body weight of 250 g.
The results are related to the dose dependence of the incidence of angiosarcomas.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (245)

Type : Metabolism
Remark : Method: Incubation of (1) a reconstituted system containing cytochrome P-450 and cytochrome P-450 reductase or (2) a microsomal preparation without/with epoxide hydratase added with 14C-VC. Analysis of binding of radioactivity.

Results: Cytochrome P-450 activates VC. 2-chloroethylene oxide is formed from VC and may be used as a substrate by epoxide hydratase. 2-chloroacetaldehyde, a rearrangement product of chloroethylene oxide, is

the alkylating agent derived from VC. In microsomal membranes, cytochrome P-450 is effectively segregated from epoxide hydratase and highly nucleophilic groups.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (246)

Type : Metabolism
Remark : Method: Incubation of (1) rat liver microsomal preparations or (2) a reconstituted system of cytochrome P-450 and cytochrome P-450 reductase with 1,2-14C-VC or 36Cl-VC. (3) in vivo exposure of rats to 14C-VC. Analysis of covalent binding to protein, DNA, RNA, and lipids as well as total non-volatile metabolites.

Results: Pretreatment of rats with phenobarbital increases binding of 14C-VC metabolites to protein and RNA, but not to DNA and lipids at low dose (10 ppm) but not at high dose (250 ppm) treatment.
36Cl-VC is metabolized by microsomes resulting in formation of Cl- ions.
14C-VC metabolites are bound to all subcellular fractions of rat liver when animals are exposed to VC in vivo.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (246)

Type : Metabolism
Remark : Review of the metabolism of VC and related compounds.
Bioactivation leads to highly reactive alkylating chloroethylene oxide that spontaneously rearranges into chloroacetaldehyde which is further oxidized to form chloroacetic acid. Chloroacetic acid may be conjugated to glutathione to form S-(carboxymethyl)cysteine and finally by action of a desaminase and a decarboxylase thiodiacetic acid.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (247)

Type : Metabolism
Remark : Review of the metabolism of various symmetric and asymmetric polychlorinated aliphatic compounds. Asymmetrically halogenated ethylenes (such as VC, vinylidene chloride, trichloroethylene) form oxiranes that are far less stable than that of symmetrically halogenated ethylenes.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (248)

Type : Metabolism
Remark : Review of VC metabolism.
VC is metabolized by the liver mixed function oxidase system to chloroethylene oxide which rapidly rearranges to chloroacetaldehyde. Chloroethylene oxide and chloroacetaldehyde bind directly or enzymatically to glutathione to form S-formylmethylglutathione. Chloroacetaldhyde can also be enzymatically oxidized to chloroacetic acid that is either excreted or bound to glutathione to form S-carboxymethylglutathione. The latter compound can also be formed by enzymatic oxidation from S-formylmethylglutathione. Both conjugation

products then are hydrolysed to form the respective S-substituted cysteine derivative. S-carboxymethylcysteine is either deaminated and decarboxylated to form thiodiacetate/thiodiglycollate or N-acetylated and excreted. S-formylmethylcysteine is enzymatically reduced to S-(2-hydroxyethyl)cysteine that is N-acetylated and excreted.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (249)

Type : Metabolism
Remark : Discussion of the metabolic pathways leading to formation of the different S-substituted cysteine derivatives observed under various experimental conditions, their chemical interrealation and the interaction of intermediate products with purine and pyrimidine residues. Comparison with the biological fate of vinylidene chloride.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (250)

Type : Metabolism
Remark : Review of VC metabolism and pharmacokinetics, VC genotoxicity and embryotoxicity, experimental VC carcinogenicity, and epidemiological data.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (251)

Type : Metabolism
Remark : Review of the metabolism and pharmaco/toxicokinetics of VC.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (200)

Type : Metabolism
Remark : Method: Incubation of a mouse-liver microsomal system with a VC/O2 mixture. Chemical and spectroskopic identification of metabolites and adenosine adducts.

Results: In the system used, volatile alkylating metabolites are formed that, by their chemical reactivity were identified to contain chloroethylene oxide. Reaction of chloroethylene oxide with adenosine results in formation of 3-beta-ribofuranosyl-imidazo-[2,1-i]purine.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (167)

Type : Metabolism
Remark : Method: Incubation of a rat liver microsomal preparation with a VC/O2 mixture. Trapping of reactive metabolites with 3,4-dichloro-phenylthioacetaldehyde added to the reaction mixture.
Results: The observations are consistent with the formation of chloroethylene oxide or chloroacetaldehyde as a reactive VC metabolite. Chloroacetaldehyde is known to be formed by intramolecular rearrangement of chloroethylene oxide.
Source : Huels AG Marl

EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (252)

Type : Metabolism
Remark : Method: Analysis of thiodiglycolic acid (TdGA) in the urine of 15 workers employed in PVC producing plants.

Results: Concentrations observed: 0.94 - 20.4 ug/l.
Amount of TdGA excreted during 24 h was correlated to effective VC body concentrations calculated from exposure data. Correlation resembles a function of Michaelis-Menten type.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (253)

Type : Metabolism
Remark : Method: Rats were exposed for 48 h to 1,000 ppm of VC in air. Urine was collected during the exposure and analysed for thiodiacetic acid and S-(carboxymethyl)cysteine.

Strain: Rats, Wistar, AF/Han strain, male, adult.

Results: Thiodiacetic acid and S-(carboxymethyl)cysteine were identified in the urine of exposed animals by GC-MS.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Test substance : VC 99.99 % purity
Reliability : (2) valid with restrictions
29.05.2002 (254)

Type : Metabolism
Remark : Method: Analysis (GC-MS) of thiodiglycolic acid (TdGA) in the urine of 18 workers exposed to VC at their workplace and correlated to mean air concentration of VC.

Results: Mean air concentration of VC: 0.14 - 7.0 ppm.
Excretion of TdGA: 0.3 - 4.0 mg/l.
Significant increases of the metabolite occur even at VC concentrations below 5 ppm.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (255)

Type : Metabolism
Remark : Review of the toxic and cancerogenic properties of VC.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (256)

Type : Metabolism
Method : DNA obtained from salmon testes was incubated with chloroacetaldehyde (CAA) for 24 hours. HPLC analysis of the CAA-treated DNA sample was conducted and compared to standards of N2,3-ethenoguanine.
Result : The reaction of chloroacetaldehyde, a reactive metabolic of the carcinogen vinyl chloride, with DNA produces in addition to the hitherto known adducts,

1,N6-ethenoadenine and 3,N4-ethenocytosine, an ethenoguanine adduct, namely N2,3-ethenoguanine. This adduct is formed in the reaction of chloroacetaldehyde with the free base as well. After DNA hydrolysis followed by isolation of this new adduct by h.p.l.c., its mass spectrum and fluorescence spectrum are identical with those published in the literature for the chemically synthesized N2,3-ethenoguanine. The formation of only this guanine derivative out of several theoretically possible reaction products allows the formulation of a reaction scheme. The absence of 7-(2-oxoethyl)-guanine, another recently detected DNa adduct of vinyl chloride, in chloroacetaldehyde-treated DNA suggests its origin from the other reactive metabolic of vinyl chloride, chloroethylene oxide.

Reliability : (2) valid with restrictions
29.05.2002 (150)

Type : other
Remark : Review of physico-chemical properties, production, toxicity, pharmaco/toxicokinetics, metabolism, mutagenicity, and carcinogenicity of VC and PVC.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (257)

Type : other: Carcinogenicity of VC metabolites
Remark : Method: 32 s.c. injections of 0.1 mg (1.38 umol) chloroethylene oxide (CEO) in 20 ul Nujol over a period of 42 weeks in male and female XVIInc/Z mice.

Other substances tested: bis(chloromethyl)ether (BCME; 32 times 0.3 mg (2.6 umol) s.c. over 42 weeks); chloroacetaldehyde (CAA; 0.05, 0.1, 1.0, 2.5 mg in acetone).

Initiation-promotion experiments in shaved animals using TPA and croton oil as promoting agents.

Results: Induction of tumors (s.c. fibrosarcomas, papillomas, squamous cell carcinomas) at injection site by CEO and BCME with similar incidence. Incidence of distant tumors (pulmonary adenomas) not increased significantly.
CEO and BCME had tumor initiating activity.
CEO seems to be largely responsible for the known genetic changes caused by VC.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (258)

Type : other: Carcinogenicity of VC metabolites
Method : Groups of male Wistar rats were exposed to VC, bis(chloroethyl)ether (BCEE) or chloroethanol (CE).

Covalent protein binding in the liver, lung, spleen, kidney, small intestine and muscle was determined following each exposure. Alkylation of RNA and DNA in the liver was determined. Induction of ATPase-deficient liver foci were measured also following each exposure.
Result : A large portion of BCEE binds to liver proteins compared to lung, spleen, kidney, muscle or small intestine; there was no indication of formation of 7-N-(2-oxoethyl)guanine, 1,N6-ethenoadenine, or 3,N4-ethenocytosine after BCEE exposure. Development of preneoplastic hepatocellular ATPase-

deficient foci occurred only after application of VC.

When liver DNA from rats exposed to 14CVC was isolated and hydrolyzed to the nucleosides, one radioactive peak, 7-N-(2-oxoethyl)guanine, was observed.

It is concluded that 2-chloroethylene oxide (which is not formed during metabolism of BCEE and CE), but not chloroacetaldehyde is the ultimate carcinogenic principle in VC carcinogenicity.

Reliability : (2) valid with restrictions
13.02.2003 (259)

Type : other: Genetic toxicity of VC metabolites.
Remark : Test system: Ames test with Salmonella typhimurium TA 1535.

Activation system: Microsomal fraction (S9) from rat liver.

Metabolites tested: chloroethylene oxide, 2-chloroethanol, chloroacetaldehyde, chloroacetic acid.

Results: Chloroethylene oxide is 450 times more effective than chloroacetaldhyde and 10,000 to 15,000 times more effective than ethylene oxide.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (147)

Type : other: Genetic toxicity of VC metabolites.
Remark : Test system: Ames test with Salmonella typhimurium, strains TA 1530, TA 1535, G-46.

Metabolic activation: With/without metabolic activation; liver microsomal fractions (S9 and soluble) from rat, mouse, and human (rat and mouse with/without induction by phenobarbital).

Metabolites tested: chloroethylene oxide, 2-chloroethanol, chloroacetaldehyde, chloroacetic acid.

Results: VC is mutagenic per se. Metabolic activation increases mutagenicity.
Chloroacetic acid has only toxic effect.
Chloroacetaldehyde, chloroethanol and chloroethylene oxide cause a mutagenic response.
Chloroethylene oxide, presumed to be an intermediary metabolite, has a strongly alkylating activity.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (155)

Type : other: Genetic toxicity of VC metabolites.
Remark : Test system: Yeast gene mutation assay using Schistosaccharomyces pompe (strain P1) and Saccharomyces cerevisiae (strain D4) with/without metabolic activation.

Activation system: purified microsomes from mouse liver (sediment at 105 000g).

Method: Incubation for 1 h at 37 degree C.

Additionally host-mediated test with chloroacetaldehyde.

Metabolites tested: chloroethylene oxide, 2-chloroethanol, 2-chloroacetaldehyde.

Results: VC is mutagenic only with microsomal fraction added.
Chloroethylene oxide showed highest mutagenic activity of all substances tested (without microsomal fraction added).
Chloroacetaldehyde showed feeble mutagenicity (with/witout metabolic activation).
Chloroethanol had no mutagenic activity.
Chloroacetaldehyde had no mutagenic activity in the host-mediated test.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (145)

Type : other: Genetic toxicity of VC metabolites.
Remark : Test system: Chinese hamster V79 cells in vitro.
Incubation with concentrations of compounds to be tested for 3 h.

Metabolites tested: chloroethylene oxide, 2-chloroacetaldehyde, monochloroacetic acid, chloroethanol.

Results: The mutagenic response to chloroethylene oxide and chloroacetaldehyde increased as a function of concentration.
Chloroacetaldehyde was toxic at higher concentrations (>= 13 uM).
Chloroethanol and chloroacetic acid had no mutagenic activity below concentrations of 2.5 mM.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (260)

Type : other: Genetic toxicity of VC metabolites.
Remark : Results: Based on kinetic data, chloroacetaldehyde is expected to be several orders of magnitude more mutagenic than chloroethylene oxide. This may be due to a different mode of action (formation of imidazo derivatives of adenosine or cytidine with chloroacetaldehyde versus alkylation with chloroethylene oxide).

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (261)

Type : other: Genetic toxicity of VC metabolites.
Remark : Test methods:
1) Ames test with Salmonella typhimurium LT-2 tester strains: TA 1535, TA 100, TA 1537, TA 1538, TA 98.
2) Bacillus subtilis recombination assay with B. subtilis tester strains: 168 M, Hcr-9, FB-13, MC-1.

Metabolites tested: VC, chlorooxirane, chloroacetaldehyde, chloroacetaldehyde monomer hydrate, chloroacetaldehyde dimer hydrate, chloroacetaldehyde trimer, epichlorohydrin.
Results:
1) Of the metabolites tested neither chloroethanol nor chloroacetic acid had

any mutagenic effect at 1 mM concentration.
Chloroacetaldehyde and its monomer hydrate were more mutagenic than the dimer hydrate and the trimer, chloroacetaldehyde being the most active compound.
Strain TA 100 was very sensitive to chlorooxirane and epichlorohydrine.
2) Chloroacetaldhyde and its monomer hydrate inhibited growth of strain MC-1. Chloroacetaldehyde dimer hydrate and trimer inhibited all mutants, MC-1 being most sensitive (metabolic poisoning ?).
Chlorooxirane but not epichlorohydrine inhibited growth of strain MC-1.
From the data derived from both tests it is concluded that chlorooxirane and chloroacetaldehyde and its monomer hydrate are the ultimate carcinogenic metabolites of VC.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (142)

Type : other: Genetic toxicity of VC metabolites.
Remark : Test system:
1) Ames test with Salmonella typhimurium strains TA 1535, TA 100, TA 1537, TA 1538, TA 98.
2) Modified recombination assay with B. subtilis strains RUB 783, BR 151, BUL 709, BUL 714, Hcr-9, MC-1, FB-13, 168WT.

Metabolites tested: chloroacetaldehyde monomer hydrate, chloroacetaldehyde dimer hydrate, chloroacetaldehyde trimer, epichlorohydrin, chloroethylene oxide, chloroethanol, chloroacetic acid, VC, vinylidene chloride, acetaldehyde.

Results: Chloroethylene oxide and chloroacetaldehyde are the ultimate mutagens in this system.
Other chemical forms of chloroacetaldehyde are also mutagenic.
Acetaldehyde, chloroethanol, and chloroacetic acid did not show a significant level of mutagenicity.
Epichlorohydrine was mutagenic in S. typhimurium strain TA 100.
In vitro treatment of DNA with either of the compounds has little or no apparent effect on the biological activity of this DNA in transformation.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (262)

Type : other: Genetic toxicity of VC metabolites.
Remark : Test system: Ames test with Salmonella typhimurium TA 1530, TA 1535, G-46, TA 1538, TA 100.

Activation system: S9 supernatant or microsomal and soluble fractions from male BD-IV rat, OF-1 mouse, and human liver, rat and mouse lung, and rat and mouse kidney.

Metabolites tested: chloroethylene oxide, chloroacetaldehyde, chloroethanol, chloroacetic acid.
Comparison with VC and other halogenated olefins.

Results: chloroethylene oxide and chloroacetaldehyde are potent mutagenes, chloroethanol is only weakly mutagenic, chloroacetic acid is only toxic.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

5. Toxicity **Id** 75-01-4
Date 18.06.2002

Reliability : (2) valid with restrictions
29.05.2002 (263) (264) (265)

Type : other: Genetic toxicity of metabolites.
Remark : Test system: Ames test with Salmonella typhimurium TA 100.

Activation system: S9 mix or S9 mix + S9 from liver of phenobarbital- or Aroclor-induced rats.

Metabolites tested: chloroacetaldehyde, chloroethanol, chloroacetic acid, 1,2-dichloroethane. Cyclophosphamide as positive control.

Results: chloroacetaldehyde or chloroethylene oxide may be the active VC metabolites causing mutagenicity.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (146)

Remark : Method: Determination of the kinetics of uptake of VC in a closed system in male rats (strain: Wistar).
Results:
Uptake of VC by the rats from the system as measured by the decline of radioactivity is logarithmic (t1/2 = 1.13 h).
Inhibition of uptake by pretreatment with potent inhibitors of cytochrome-P-450-dependent drug metabolism. Uptake increased by pretreatment with DDT and clotrimazol. No stimulation after pretreatment with phenobarbital, 3-methylcholanthrene, rifampicin, or chronic ethanol treatment.
Immediately after exposure, highest radioactivity levels were observed in liver and kidney. 14C-VC metabolites were rapidly excreted by the kidneys (69 % or radioactivity within 24 h).

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test substance : 1,2-14C-VC (purity: 99.9 %).

Reliability : (2) valid with restrictions
29.05.2002 (191)

Remark : Method: Determination of distribution (autoradiography) and elimination kinetics and biotransformation of 14C-VC (250 ug or 450 mg) after oral (intragastric), i.v. or i.p. administration.
Additionally: after chronic administration of unlabelled compound (3, 30, 300 mg/kg/day) for 60 days.

Species: Wistar rat, male, adult.
Results:

dose	time (h)	14C-activity excreted (% of dose) exh. air VC	exh. air CO2	urine	faeces
intragastric:					
250 ug/kg	0-24	3.7	12.6	71.5	2.8
	24-48		0.9	3.3	1.6
	48-72			0.3	0.2
450 mg/kg	0-24	91.9	0.6	4.5	0.4
	24-48		0.1	0.8	0.3
	48-72			0.1	

intravenous:
250 ug/kg 0-24 99.0 0.1 0.5 0.1

intraperitoneal:
250 ug/kg 0-24 43.2 10.3 41.5 1.6
24-48 0.7 1.6 0.2
450 mg/kg 0-24 96.2 0.7 2.5 0.1
24-48 0.1

Elimination after oral application unchanged by chronic pretreatment.

Distribution of VC as revealed by whole-body autoradiography agrees with excretion data. Small localizations of 14C in Zymbal glands.

Biotransformation into chloroacetic acid, thiodiglycollic acid, glutamic acid, formaldehyde, CO2 and urea.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test substance : VC, purity not specified;
14C-VC, radiochemical purity 99.0 %

Reliability : (2) valid with restrictions
19.06.2002 (266)

5.11 EXPERIENCE WITH HUMAN EXPOSURE

Memo : Developmental toxicity

Remark : Analysis of numbers of congenital malformations in three communities in the northeast part of Ohio during 1970 -1973. The three communities have PVC production plants.
In the ATSDR review (1997) of vinyl chloride, their conclusion of the available data was "Although a statistically significant increase in congenital abnormalities has been observed in members of some communities near a vinyl chloride processing facility, reports have failed to establish a statistically significant association between developmental toxicity and either parental occupation or proximity to the facility."
Results:
The rate of malformations per 1,000 births for the three communities studied was significantly higher than that in control areas (Table 1). The greatest excess included malformations of the CNS, cleft lip and palate, club foot and genital organs (Table 2).

Table 1
Malformation rates per 1000 live births
in 3 selected communities

Area	Births	Malformations number Rate/1000	number observed	number expected
Entire state of Ohio	719,287	10.1	7295	--
Ashtabula	1,900	17.4	33*	19.3
Painesville	1,381	18.1	25*	14.0
Avon Lake	738	20.3	15*	7.5
Combined	4,019	18.2	73*	40.8

Table 2
Relative risk for specific congenical anomalies in three selected communities including N Ridgeville

Defects	Number of defects Observed	expected	risk ratio
All defects	109	56.0	1.95
Central nervous system	17	5.6	3.02
Cleft plate and lip	10	6.5	1.53
Genital organs	16	8.4	1.90
Clubfoot	23	8.2	2.79
all other defects	43	27.2	1.58

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (267) (268) (269)

Memo : Case report-cancer
Remark : First case report of a patient (helper and operator in a plant manufacturing PVC) that died due to a hemangiosarcoma of the liver in 1971.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
21.05.2002 (270)

Memo : Epidemiological Study
Remark :

Study Design: Mortality through December 31, 1995 was followed in a cohort of 10,109 men who had been occupationally exposed to vinyl chloride between 1942 and 1972 at any one of 37 facilities (17 companies) in the United States or Canada

Study Population: The data set included some or all of the following variables for each study subject: identification number, name, Social Security number (SSN), date of birth, date of hire, date of separation, date of first assignment to a vinyl chloride-exposed job, duration of exposure, facility, employment status as of Dec. 31, 1980, vital status as of Dec 31, 1995, and cause of death. Data sources lacked adequate information on potential confounders such as smoking, race (only known for 3,165 members, 96% white), or other occupational exposures or health-related risk factors. Of the 10,173 subjects initially included in the original cohort described by Wong (1991), 11 were excluded because they were women, 52 were excluded because they were already included (duplicates), and one was excluded because he terminated employment prior to Jan 1, 1942

Reference Rates: Reference mortality rates were compiled by NIOSH for 92 cause of death categories obtained for white male population of the United States using CDC-Wonder.
Rates were grouped according to 15 five-year age intervals (starting at age 15), and 7 five-year calendar periods (starting at 1960). Mortality rates for 4 years prior to 1960 were obtained directly from NIOSH. Mortality rates for white male populations were obtained for the 16 states where the 37 plants were located (California, Delaware, Florida, Illinois, Kentucky, Louisiana, Maryland, Massachusetts, Michigan, Mississippi, New Jersey, New York, Ohio, Pennsylvania, Texas and West Virginia). Michigan mortality rates were used for 45 subjects who worked in Ontario, near the Michigan-Canadian border. State rates for 1960-64 were used for 1940-59. National and state rates for 1990-94 were used for 199.5

Data analysis: Standardized mortality ratios (SMR's) and 95% confidence intervals (CI's) were calculated for 92 causes of death using ProSMR (ProQuest database system). SMRs were based on white male reference rates of the US population as a whole and the populations of the states with plants (state-weighted). Standardized mortality ratios were calculated for the cohort as a whole. Analyses were stratified according to length of exposure (total number of months worked in all exposed jobs), time since last exposure, age at first exposure, year of first exposure, and vinyl chloride production start data for the plant.
Selected exploratory analyses (using Kaplan-Meier estimation, log rank test and Cox proportional hazards modeling approaches) were conducted to investigate variations in death occurrence. Person-years for subjects began accruing one year after first exposure to vinyl chloride, or on Jan 1, 1942 (whichever was later). A reanalysis of data through 1982 was conducted to verify results reported in Wong (1991)

Results: Results of the re-analysis of mortality through 1982 were similar to those reported by Wong (1991). Through 1995, mortality from all causes of death of the cohort was 9% lower than the national rate and 17% lower than state mortality rates weighted according to person-years accumulated among employees in the states where plants were located. In contrast to the 2% increase in mortality from all cancers for 1982 cohort, the 1995 cohort showed a 4% deficit (as compared to state mortality rates). Cancers that showed meaningful excesses in the entire cohort included cancers of the digestive system, brain, and connective and soft tissues. For the 1995 cohort, increased mortality from cancers of the digestive system (17% or 18% compared to national or state reference population, respectively) was predominantly due to elevated mortality from cancer of the liver and biliary tract (N=80 vs. 22.3 for states; SMR = 359, 95% CI: 284-446). The SMR for liver and biliary tract cancer was 83, 215, 679, and 688 in those exposed from 1-4 years, 5-9 years, 10-19 years, and 20 years or more, respectively. Angiosarcoma of the liver was identified on the death certificates of 41% of those with liver/biliary tract cancer. Mortality from cancers of the brain also was higher in the 1995 cohort (N= 36 vs. 25.29 for states; SMR = 142, 95% CI :100-197), but was less than the 1982 cohort (N = 22 vs. 13.05 for states; SMR = 162, 95% CI: 101-245). SMRs for brain cancer in the 1995 cohort were elevated among those exposed 5-9 years (SMR = 193; 95% CI = 96-346) or 20 years or more (SMR = 290; 95% CI: 132-551). Age at employment of 35 years or older and duration of employment were associated with increased risk of mortality from brain cancer. Mortality from cancers of connective and soft tissues were also increased in the cohort (N = 12 vs. 4.44 for states; SMR = 270; 95 % CI = 139-472).
The underlying cause of death or these cancers was anigiosarcoma (4 deaths), liposarcoma (2 deaths), malignant fibrous histiocytoma (2 deaths), fibrosarcoma (2 deaths), leiomyosarcoma (1 death), and neurogenic sarcoma (1 death). Mortality due to lung cancers, cancers of lymphatic and hematapoetic tissue, emphysema or other lung diseases (including COPD) was not increased in the cohort

Source :

PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Conclusion :

This update confirmed a strong association between duration of employment in the vinyl chloride industry and cancers of the liver and biliary tract, predominantly due to a large excess of deaths due to angiosarcoma of the liver. The association between vinyl chloride and the excess in mortality due to brain cancer and connective and soft tissues is less clearly defined. Since 1982, no excess in brain cancer was observed

in the cohort. Many of the soft and connective tissue sarcomas found in the cohort may arise in a variety of different tissues, and may, in some instances, be ascribed to a particular organ instead of smooth muscle or connective tissue associated with it. Given the lack of any predominant histological type among the group of deaths due to connective and soft tissue sarcomas, and the typical histological specificity of most carcinogens, it is difficult to postulate that this variety of outcomes was due to vinyl chloride exposure

Reliability : (2) valid with restrictions
20.05.2002 (271) (272)

Memo : Epidemiological Study
Remark :

Study Design: Vital status from subjects who worked for at least one year in any of 19 different vinyl chloride and/or PVC production facilities in Italy, Norway, Sweden and the UK were updated from 1993 to 1997. The observation period began in 1955 for all factories except two in Italy (1972 and 1974) and one in Sweden (1961).

Study Population: Out of the original 14,351 subjects who contributed to the original database, 12,700 were included in this update. Twenty nine were deleted due to corrections in study files. Females (59) were exluded because they only came from two facilities in Sweden. 1513 (mainly from Sweden and Italy) were excluded because they did not have at least one year of employment. Other reasons for exclusion included unknown date of first employment (1), in more than one cohort (21), or having all of the period of employment outside of the observation period (28).

Reference Rates: Age- and calendar-specific (males only) national mortality rates for each country were used as the reference for the SMR analyses. These were computed using the WHO mortality database, in which only 3 digit ICD codes were stored consistently since 1955. As different ICD revisions were used over the followup period, some codes had to be converted. Liver cancer, which is coded as ICD in the 7th, 8th and 9th revisions of the ICD, may include either primary or secondary liver cancer in the 7th and 9th revisions.

Data: A search for the best evidence for diagnosis of liver cancers was conducted by reviewing all available documentation (e.g. death certificate, cancer registry, medical records, and a registry of angiosarcomas (UK)). Records of liver cancer cases from all countries were also matched to an angiosarcoma registry maintained by the Association of European Plastics Manufacturers. The diagnosis was based on consensus between IARC and national investigators. The incidence analysis used reference rates from national cancer registries.

Data Anayses: Person-years at risk were calculated using a modified life-table approach. Tabulation of person-years started at the beginning of the observation period or on day one of the second year of employment (if it began after the start of the observation period). Expected deaths or incident cases of cancer were computed by multiplying the person-years in each age- and five-year calendar period-specific stratum by the national reference rates. The Standardized Mortality Ratio (SMR) or Incidence Ratio (SIR) is the ratio of observed to expected deaths or cases, respectively. Cause of death was analyzed according to time since first employment, calendar period of hire, and age at hire. Exposure was further analyzed according to autoclave worker (ever/never), duration of employment, ranked level of exposure, and cumulative exposure. Calendar period-specific job exposure data from 13 of the 19 factories were also analyzed.

These data were validated by industrial hygienists. With the exception of two facilities, work histories from the orignal study (1941-1996) were used in the analysis. To examine the effects of the systematic bias (i.e. pssible underestimation of exposure), a 15-year lagged analysis was conducted. No separate analyses were performed in those who had been followed for over 15 years since onset of exposure.

Data were analyzed according to total combined cohort, country, process (vinyl chloride monomer (VCM), PVC or mixed VCM/PVC production or PVC processing), or factory. Stratified analyses for those employed in curing, filtering and packing jobs were also performed. Poisson regression analyses were perfomred to assess the significance of several variables simultaneously

The current study is an update of mortality and cancer incidence among individuals included in the European Multicentric Cohort Study of Workers in the Vinyl Chloride Industry described in Simonato L, L'Abbe KA, Andersen A, et al. 1991. A collaborative study of cancer incidence and mortality among vinyl chloride workers. Scan J Work Environ Health 17(3):159-169

Result :

Mortality: Mortality from all causes of death was less than expected (2664 deaths, SMR = 0.85, 95% CI = 0.82-0.88) and mortality for all malignant neoplasms was close to that expected (883 deaths, SMR = 0.99, 95% CI = 0.93-1.06). There were more than twice as many deaths from liver cancer (n = 53) in this study than in the previous study (n = 24). However, the SMR for liver cancer was less in this study than in the previous study (2.4 vs. 2.86, but was still significant (95% CI =1.8-3.14). Twenty six of the 53 deaths from liver cancer were known to be angiosarcomas.
Significant deficits in mortality due to bronchitis, emphysema and asthma, cancer of the prostate, diseases of the nervous, overall circulatory and genitourinary systems, and external causes were observed in the cohort (versus expected). There were no significant differences in cohort mortalities due to neoplasms of the trachea, bronchi and lungs, brain cancer, cirrhosis of the liver, malignant melanoma, soft tissue neoplasms, bladder cancer and non-Hodgkin's lymphoma. However, there was a significant excess in liver cirrhosis mortality in the high-exposure group, a significant trend towards an increase in liver cirrhosis mortality with cumulative exposure, and a significant increase in lung cancer in those who had only worked as packers and baggers.

Most of the deaths were in mixed production (1829/8485) and PVC production (512/2614). Workers in PVC production experienced higher mortality from all malignant neoplasms (168), cancer of the liver(9) and cirrhosis of the liver (10) than the total cohort. Overall mortality in the VCM production cohort (76/268) was similar to the total cohort. There was only one death from liver cancer in the VCM cohort. The SMR for lung cancer was higher in the VCM cohort than the total cohort (14 deaths, SMR = 1.47, 95% CI =0.80-2.47). There were no statistically significant elevations in any cause of death in PVC processing workers (247/1353).

Cancer Incidence: In the cancer incidence analysis, there were 760 observed cancers (versus 896 expected). Analyses of all incidence sources revealed 71 cases of liver cancer (of which 37 were angiosarcomas, 10 were hepatocellular carcinomas, 7 were other types, and 17 were unspecified). Six angiosarcomas occurred in workers with estimated cumulative exposures < 1000 ppm-years. The incidence of liver cancer was related to time since first exposure, duration of employment, cumulative exposure, and ranked level of exposure. If angiosarcoma

deaths were excluded, the resulting SMR for liver cancer was 1.27 (95% CI = 0.84-1.83). A separate analysis that included only hepatocellular carcinomas found significant trends between time since first exposure, duration of employment, and cumulative exposure. There were no deaths from liver cancer before 15 years since first exposure and no angiosarcoma deaths in workers hired after 1973. All countries except Norway had a significant excess of liver cancer. Liver cancer mortality was not in excess in VCM and PVC processing plants.

The results of the cancer incidence analyses revealed no association between vinyl chloride exposure and brain cancer, lung cancer, soft-tissue sarcoma(other than liver), Non-Hodgkin's lymphoma, malignant melanoma, bronchitis, emphysema or asthma. There were 6 incidences of thyroid cancer (SIR 1.94, 95% CI 0.71-4.22)

Source :

PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Conclusion :

A strong relationship was observed between vinyl chloride exposure and angiosarcoma. The finding that angiosarcomas were observed in those with cumulative exposures < 1000 ppm suggest that an increased risk of angiosarcoma may be present at cumulative VC exposures within an order of magnitude of those permitted by current standards. However, these data must be interpeted with caution due to the imprecision of the exposure estimates. A significant exposure-response trend was also present for hepatocellular carcinoma, suggesting that vinyl chloride exposure may be associated with these types of tumors. Exposure at moderate to high levels was associated with increased mortality from cirrhosis of the liver. The relationship between vinyl choride exposure and the increas ed incidence of thyroid cancer remains to be examined further

Reliability : (2) valid with restrictions
20.05.2002 (273)

Memo : Epidemiological Study

Remark :

Study Design: Mortality and vitality through 1996 was followed in a cohort of 2,526 individuals who had been occupationally exposed to vinyl chloride for at least one year between January 1, 1942 and January 1, 1973 at a chemical manufacturing facility in Louisville, Kentucky. An excess in brain cancer mortality at this facility had been identified in a previous studies, and the facility was included in the large sacle epidemiology study reported by Applied Epidemiology, Inc.

Data analysis: Standardized mortality ratios (SMR) for brain cancer (based on US white male reference rates) were calculated for the cohort. National rather than state rates were used because the rates in the county where the plant was located were more similar to national than state rates. Brain cancer cases with ICD9 codes of 191 and 192 (which included malignant neoplasm of the brain, spinal cord, and meninges) were used in the SMR analysis. Any brain cancer or cause of death that was listed as an ancillary cause was included in the case control analysis but not the SMR. No brain cancers listed on death certificates as non-primary were used as cases. Hospitals were contacted to validate diagnoses. Pathology records were used to determine if brain malignancies were primary or metastatic. Employees were stratified by intensity of exposure to vinyl chloride (low, medium, high) based on their CERM, time since first employment, age at first employment, length of employment, and year of first employment. For each of the 15 brain cancer cases in the analysis, matching controls (similar age, date of hire and length of employment) with no cancer were

selected. Cumulative exposure to vinyl chloride and latency for each control were determined using CERMs. For each of the two measures of exposure, the rank of each case within each stratum was obtained and divided by the number of controls plus one to obtain a case percentile rank. The Cuzick-van Elteren statistic was calculated as the weighted sum of the case percentile ranks. P-values for the test statistic were calculated using normal approximation. Conditional logistic regression analyses on cumulative exposure were also performed.

Reference Rates: US reference rates for frequencies of brain cancer for white males were calculated using raw counts of US brain cancer cases divided by appropriate US population-based counts. Data were stratified according to 5 year age periods (beginning at age 15) and 5 year time periods (from 1940 through 1992). The rate for 1992 was used for years 1993-1996.

Study Population: Subjects were included in the Applied Epidemiology Inc. study performed for the CMA in 1999. Mortality and vitality from 1942 through 1996 were determined using company records, transfer records, pension records, vehicle license registrations, death certificates, clones of the State of Kentucky Vital Statistics (KVS) and Social Security Administration databases, data from Applied Epidemiology Inc., attendance records to social clubs and/or personal phone records to last known addresses. The National Death Index (NDI) also was searched between January 1, 1979 and December 31, 1996. Death certificates were requested from states if cause of death was unknown. Each employee's work history was tracked and assigned a job-area code for each month the employee worked. All job area codes were given an exposure rank for vinyl chloride by knowledgeable people from each area of the plant. Work histories were linked with job-exposure ranks and monthly scores or rankings were totaled to give a Cumulated Exposure Rank Month (CERM) score. Data sources lacked adequate information on potential confounders such as smoking, race and gender (estimated to be 93% white males), or other occupational exposures or health-related risk factors

Results: The mortality rate of the cohort (37.6%, SMR=108, 95% CI =101-115) and mortality from brain cancer (14 cases, SMR = 221, 95% CI = 121-371) was significantly higher than the reference population. In the subcohort hired before 1950, the SMR was 349 (95% CI = 140-719). There was no brain cancer excess in employees hired after 1960. Brain cancer mortality was not related to exposure when the cohort was stratified by rank of exposure. Fifteen brain cancer controls were matched with controls. Results of both conditional logistic regression and rank-order analyses failed to show any relationship between cumulative vinyl chloride exposure and brain cancer

Source :

PCA Services, Inc
PCA Services, Inc. Kingsport, TN

Conclusion :

Excess brain cancer mortality at Louisville plant was not related to vinyl chloride exposure. The Applied Epidemiology Study and previous studies which have identified an increase in brain cancer mortality in those exposed to vinyl chloride included subjects from the Louisville plant

Reliability : (2) valid with restrictions
20.05.2002 (274)

Memo : Epidemiology study
Remark : Method: Historical prospective mortality study of 8,384 workers (from 33 plants) that had at least one year been occupationally exposed to VC.

Results: The overall mortality of the study population was ca. 75 % of what would have been expected in a comparable population of US males. No cause of death showed statistically significant excess over expected values. 6 cases of angiosarcoma of the liver; only two of them were diagnosed as such on the death certificate. Brain cancer is overrepresented in the study population.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
20.05.2002 (275)

Memo : Human exposure

Method : Three men (26, 35, 50 years; 86, 78, 71 kg) and three women (25, 40, 55 years; 64, 52 61 kg) were exposed twice each day (separated by a 6-hour interval) for 3 successive days to six different concentrations of vinyl chloride: 0.0, 0.4, 0.8, 1.2, 1.6 and 2.0% (at random) via a plastic breathing mask affixed over the face (covering the mouth and nose). The rate of air or air-gas mixture was sufficient (50 liters per min) to prevent any dilution effects from the atmosphere. Exposures were terminated after 5 minutes and the subjects were asked to compare their feelings before and after taking off the masks.

Result : One subject reported feeling dizzy after 0 % and 0.8% (same subject). No effects were noted at 0.4%. Two out of the 6 reported dizziness at 1.2%. Five out of 6 reported dizziness, lightheadedness, nausea, and dulling of visual and auditory cues at 1.6%, (which disappered after cessation of exposure). All subjects were intoxicated by 2.0%. The same symptoms were observed as those caused by 1.6%, although they appeared earlier in the exposure and were more intense. One subject reported a headache that persisted for 30 minutes.

According to the authors, the maximum concentration causing no effect in any subject lies between 0.8 and 1.2% (8000-12,000 ppm).

No additional information provided.

Reliability : (2) valid with restrictions
20.05.2002 (276)

Memo : Human exposure

Remark : Accidental exposure of three workers (VC polymerization plant) is reported. Results: Two of the workers were found dead on the plant (unrelated cases). Autopsy did not reveal any specific diagnostic features. One person recovered after experiencing symptoms of a narcotic effect.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
20.05.2002 (277)

Memo : Developmental toxicity

Remark : In a case control study, analysis of incidence rates of central nervous system malformations in infants born to residents of Kanawha County, West Virginia, USA, during 1970 - 1974 was studied. (This county contains a PVC production plant).
In the ATSDR review (1997) of vinyl chloride, their conclusion of the available data was "Although a statistically significant increase in congenital abnormalities has been observed in members of some communities near a vinyl chloride processing facility, reports have failed to establish a statistically significant association between developmental toxicity and either parental occupation or proximity to the facility."

Result : Incidence rates for CNS malformations for Kanawha County residents are

listed in Table 1. Although the rates of central nervous system defects in infants born to residents of Kanawha County were larger than in control areas, no relationship with parental occupation or residential exposure was found. The parents place of residence at time of infant's conception was determined and distances from the PVC plant were measured for each case and control. There was no significant difference between the two groups (p>0.4).

Table 1
CNS malformation rates for Kanawha County residents, 1970-1974

Defect	Cases	rate/10,000 births
anencephaly	23	14.1
Spina bifida	15	9.2
Hydrocephalus	7	4.3
Other CNS defects	2	1.2
Total CNS defects	47	28.8
Total white births	16,289	

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
20.05.2002 (278)

Memo : Developmental toxicity
Method : A case control study of all babies born with CNS effects in Burlington County, New Jersey was conducted. The relationship of the cases and controls with two vinyl chloride plants were examined. For each subject, the distance from the subjects residence and each plant was determined.
Remark : In the ATSDR review (1997) of vinyl chloride, their conclusion of the available data was "Although a statistically significant increase in congenital abnormalities has been observed in members of some communities near a vinyl chloride processing facility, reports have failed to establish a statistically significant association between developmental toxicity and either parental occupation or proximity to the facility."
Result : There was no relationship between proximity to the vinyl chloride plants and CNS or all birth defects combined.

Reliability : (2) valid with restrictions
20.05.2002 (279)

Memo : Developmental toxicity
Remark : Analysis of the incidence of birth defects in infants born to residents of Shawinigan, Canada during 1966 - 1979 with regard to relation to VC exposure was compared with three other communities, Drummondville, Baie-Comeau-Hauterive and Rimouski. A case-control study was also conducted.
In the ATSDR review (1997) of vinyl chloride, their conclusion of the available data was "Although a statistically significant increase in congenital abnormalities has been observed in members of some communities near a vinyl chloride processing facility, reports have failed to establish a statistically significant association between developmental toxicity and either parental occupation or proximity to the facility."
Result : Although some data from this study raised the hypothesis of an association between VC in the air and birth defects in the exposed community, such an association can not be substantiated within the sample size available (Table 1).

In the case-control phase of the study, tThe occupational and residential histories of parents who gave birth to malformed infants were compared with those of parents of normal infants. The two groups did not differ in

occupational exposure or closeness of residence to the VC polymerization plant.

Birth-defect rates did not differ between school districts with high and low VCM exposure, either for all birth defects or for CNS defects (Table 2). School districts adjacent to the plant did not differ from the other school districts in numbers of birth defects (total or CNS), nor did districts differ within and beyond a 1-mile radius of the plant.

Table 1
Number of malformed children observed in Shawinigan compared with three comparison communities

Parameter	expected based on Shawinigan	expected based on Baie-Comeau Drummondville	expected based on Hauterive	Rimouski
Total	159	102.68**	98.80**	124.08**
CNS	30	19.69*	18.18*	15.33**
Urogenital	30	19.15*	13.94**	13.14**

* p<0.05; ** p<0.01
Values only significant in all three comparison communities is presented.

Table 2
Birth defects between school districts with high and low VCM exposure

	high exposure	low exposure	total
births with defects	87	70	157
births without defects	2,285	2,125	4,410
births with CNS defects	16	13	29
births without CNS defects	2,356	2,182	4,538

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
20.05.2002 (280)

Memo : Developmental toxicity
Result : Results of both retrospective and prospective studies indicate that pregnancy outcomes of mothers occupationally exposed to vinyl chloride are not altered by exposure.
Reliability : (2) valid with restrictions
22.05.2002 (281)

Memo : Raynaud syndrome
Result : Vinyl chloride disease is characterized by acroosteolysis, a condition characterized by lytic lesions of bones (primarily of fingers), scleroderma of the connective tissue in the fingers with dermal thickening, and a Raynaud-like condition with reversible arteriole constriction causing numbness, pallor and cyanosis of the fingers. The attribution of acroosteolysis to vinyl chloride exposure is based almost entirely on case reports and has been estimated to affect <3% of workers involved in the polymerization of vinyl chloride
Reliability : (2) valid with restrictions
22.05.2002 (282) (283)

Memo : Chromosomal aberrations
Remark : Method:

Chromosomal analysis in cultured lymphocytes from 57 workers employed in plants manufacturing VC or PVC; 19 on-site controls, 5 off-site controls.
Results:
Types of anomalies observed: chromatid break or gap or chromosomal gap (B cells); larger chromosomal abnormalities (C cells).
There was a significant increase in chromosomal abnormalities in the exposed workers when compared to controls. The increase in chromosomal abnormalities correlated with the length of exposure and with a history of exposure to excursion levels of VC during the year before sampling. A positive correlation between smoking habits and total C cell abnormalities was observed.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (284) (285)

Memo : Chromosomal aberrations

Remark : Method:
Analysis of chromosomal abnormalities in cultured peripheral lymphocytes from men employed in a plant manufacturing VC and PVC.
Sampling: This is the same group of workers studied earlier by Purchase et al., 1975. After threshold limit values for VC and plant exposure levels had been reduced, two further samples were drawn at 18 months (21 VC workers, 6 off-site controls) and 42 months (23 workers, 8 on-site controls) after the initial sampling.
Results:
In the second sampling there was a tendency to an increase in chromosomal abnormalities except for those workers who had changed occupation.
By the third sampling there was a decrease by comparison with previous samplings and the levels of abnormalities had returned to values similar to those of controls.
Thus reduction in exposure to VC is accompanied by a reduction in the chromosomal abnormalities to levels indistinguishable from those of controls.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (286)

Memo : Chromosomal aberrations

Remark : Method: Analysis of chromosomal abnormalities and sister-chromatid exchange in cultured peripheral lymphocytes from 21 workers professionally exposed to VC and 6 controls (same as 2. sampling reported by Anderson et al., 1980).
Results:
The VC exposed workers showed levels of chromosomal aberrations elevated above those of controls.
Sister-chromatide exchange (per cell or per chromosome) was only slightly increased (n.s.) above normal.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (287)

Memo : Chromosomal aberrations

Remark : Method: Analysis of peripheral blood lymphocyte cultures from 11 VC polymerization workers and 10 controls for chromosomal aberrations (classification according to Buckton et al. and Hirschhorn and Cohen,

respectively).
Results: Significantly higher incidence of chromosomal aberrations in exposed population. Most excess damage was of the unstable variety and involved the grossest kind of these changes (e.g. fragments or rearrangements). The incidence of breaking events was significantly increased in the workers.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (288)

Memo : Chromosomal aberrations
Remark : Method: Analysis of chromosomal aberrations in cultered peripheral blood lymphocytes from 7 male occupationally exposed workers and 3 non-exposed control subjects from the same factory (workers had been exposed for 9 - 29 years). None of the exposed subjects exhibited signs of VC disease.
Results: The frequency of abnormal cells in the group exposed to VC was significantly increased above control values. This was also true for chromatid and isochromatid breaks, but not for the remaining types of aberrations.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (289)

Memo : Chromosomal aberrations
Remark : Method: Analysis of chromosomal aberrations in cultured peripheral blood lymphocytes from 45 PVC workers exposed to VC for 0.5 to 12 years. 44 industrial controls (other chemical plants, but not exposed to VC, and only indirectly exposed to other chemicals) and 49 normal controls (no occupational exposure to chemicals).
Results: The rate of numerical chromosome aberrations did not differ significantly between PVC workers and normal controls. The frequency of chromatide-type aberrations and unstable chromosome-type aberrations was significantly higher in PVC workers than in the two control groups.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (290)

Memo : Chromosomal aberrations
Remark : Method: Analysis of chromosomal aberrations and sister-chromatid exchange in cultures of peripheral blood lymphocytes from 9 workers occupationally exposed to VC for 10 - 27 years (mean annual dose ca. 20 -150 ppm in air). 8 healthy persons (matched for age and sex; not exposed to known mutagens during 3 months befor time of blood sampling) as controls.
Results: Frequency of chromosomal aberrations unstable and non-homogenious over a period of two years (repeated sampling).
Mostly chromatid and chromosome breaks detected, only sporadically chromatid and chromosome exchanges.
The frequency of SCEs was significantly higher in cells of VC workers in comparison with controls.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (291)

5. Toxicity **Id** 75-01-4
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Memo : Chromosomal aberrations
Remark : Method: Cytogenetic studies in cultured peripheral blood lymphocytes from 39 workers from a PVC plant. 16 healthy men without any connection to the plant as controls. Studies were repeated for 37 of the workers 2 - 2.5 years later (during this time interval workers had only minimal exposure to VC). For repeat study: 32 matched controls from office employees in the factory.
Results: The mean frequency of chromosome-breakage was significantly higher for the workers than for controls in the 1. investigation. In the repeat study, no differences were observed between the workers and their matched controls. No differences were observed when the control groups of the two studies were compared. Sister-chromatid exchange was studied for 16 workers with matched controls in the repeat study. No differences were observed between workers and controls. During the 1. investigation, bone-marrow samples were studied from 4 workers. The mean frequency of chromosome-breakages was higher in the bm of workers than reported for normal bm and higher than for the corresponding lymphocyte cultures.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (292)

Memo : Chromosomal aberrations
Remark : An increased rate of chromosomal aberrations compared to a control group was observed in lymphocyte cultures taken from 20 VC exposed workers showing signs of VC illness (acroosteolysis, Raynaud syndrome, thrombocytopenia, liver function disturbances etc.). No increased rate was observed in VC exposed workers (10) without signs of VC illness.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (293) (181)

Memo : Chromosomal aberrations
Remark : The chromosomal aberration rate of 5 workers at a PVC production site was 0-5% (no exposure concentration reported).
No increased chromosomal aberration rate was observed in 4 workers of a PVC manufacturing plant. The VC concentration was reported to be < 1 ppm to 26 ppm.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (294)

Memo : Chromosomal aberrations
Method : Workers exposed to vinyl chloride were divided into groups based on type of work.
Result : workers had higher incidences of chromosomal aberrations than control groups. The highest incidences of abnormalities were found in autoclave operators and maintenance workers (as cited in a review by Giri et al., 1995).
Reliability : (2) valid with restrictions
29.05.2002 (295) (296)

Memo : Chromosomal aberrations
Result : Increased frequencies of chromatid and chromosome aberrations were found in lymphocytes of 35 males occupationally exposed to vinyl chloride and other chemicals in the rubber industry (as cites in a review by Giri et al., 1995).

5. Toxicity **Id** 75-01-4
Date 18.06.2002

Reliability : (2) valid with restrictions
29.05.2002 (295) (297)

Memo : Chromosomal aberrations
Result : Increased frequencies of chromosome aberrations were found in lymphocytes of workers exposed to vinyl chloride (as cited in a review by Giri et al., 1995).
Reliability : (2) valid with restrictions
29.05.2002 (298) (295)

Memo : Chromosomal aberrations
Result : Increased frequencies of chromosomal aberrations were found in lymphocytes of 43 workers exposed to vinyl chloride as compared to 22 subjects from the same locality (controls). The average duration of exposure was 11.2 years. There was no difference in results between nonsmokers and smokers (as cited in a review by Giri et al., 1995).
Reliability : (2) valid with restrictions
29.05.2002 (295) (299)

Memo : Chromosomal aberrations
Result : Increased cytogenicity was not found in lymphocytes from 121 workers occupationally exposed to vinyl chloride and vinylidene chloride (as compared to 75 controls selected from pre-employment records)(as cited in a review by Giri et al., 1995).
Reliability : (2) valid with restrictions
29.05.2002 (295) (300)

Memo : Chromosomal aberrations
Result : Increased cytogenicity was not found in lymphocytes from 209 workers occupationally exposed to vinyl chloride as compared to 295 other employees. The duration of exposure ranged from 1 to 332 months (average 43.3 months) (as cited in a review by Giri et al., 1995).
Reliability : (2) valid with restrictions
29.05.2002 (295) (301)

Memo : Chromosomal aberrations
Result : Increased cytogenicity was not found in lymphocytes from 31 male workers occupationally exposed to vinyl chloride as compared to 295 other employees. The number of chromatid and chromosome breaks and exchanges, but not the number of gaps were included in the calculations (as cited in a review by Giri et al., 1995).
Reliability : (2) valid with restrictions
29.05.2002 (295) (302)

Memo : Chromosomal aberrations
Result : An increase in cytogenicity was not noted in workers exposed to vinyl chloride. It was noted that at the time the study was carried out (1988), the allowable level of vinyl chloride exposure at the facility had been reduced to 1 ppm (as cited in a review by Giri et al., 1995).
Reliability : (2) valid with restrictions
29.05.2002 (303) (295)

Memo : Corneal burns
Remark : Chemical burns of the cornea after spray accident with liquid VC (presumably due to hypothermal effect). Treatment with denuding technique. Prompt healing within 48 h.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions

29.05.2002 (304)

Memo : Frostbite
Remark : Liquid VC accidentally sprayed on the skin caused second degree frostbite due to its hypothermal effect.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (277)

Memo : Human exposure
Method : Five young adult male volunteers were exposed to 2.9, 5.1, 11.7 or 23.5 ppm for 6 hours through gas masks. Retention was estimated by measuring the difference between inhaled and exhaled concentrations via gas chromatography. Samples of exhaled air were also collected for 90 minutes after cessation of exposure to determine the rate of elimination of VC from the lung.
Result : Although variation was observed between the 5 humans, over the concentration range samples approximately 42% of inhaled vinyl chloride was absorbed.
Reliability : (2) valid with restrictions
22.05.2002 (305)

Memo : Raynaud syndrome
Remark : Clinical symptoms of two workers from a PVC production plant (autoclave workers).
Results:
Acroosteolysis o
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
22.05.2002 (306)

Memo : Raynaud syndrome
Remark : Clinical symptoms in seven workers of a PVC polymerisation plant (i.e. autoclave workers).
Results:
Raynaud syndrome in 5 patients, clubbing of fingers, increased sensitivity to cold, aching and dyssensation of fingers, acroosteolysis in 5 patients, impaired hepatic function in 2 patients, obstruction of arteries of the arms in 2 patients, skin biopsies in 3 patients revealed indications of sclerodermia.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (4) not assignable
4d
22.05.2002 (307)

Memo : Raynaud syndrome
Remark : Clinical observations in 13 workers employed in PVC producing plants for 1 3/4 - 18 years.
Results:
Sclerodermia with alterations of the collagenous tissue of the skin (8 patients), clubbing of the fingers (7 patients), circulatory impairment (11 patients), Raynaud syndrome (4 patients), acroosteolysis of fingers (6 patients), thromcytopenia (all patients), splenomegaly (12 patients), impaired liver function (11 patients), periportal liver fibrosis (5 patients), varices of the oesophagus (4 patients).
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
22.05.2002 (308)

Memo : Raynaud syndrome
Remark : Clinical observations in 5 out of 103 workers employed in PVC producing plants (autoclave cleaning). In the same group of patients, 9 other cases of Raynaud syndrome without bone lesions and 14 other cases with increased sensitivity to cold were discovered.
Results:
Raynaud syndrome of hands and/or feet, clubbing of the fingers, acroosteolysis, no scleroderma, border line hepatic tests.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
21.05.2002 (309)

Memo : Raynaud syndrome
Remark : Radiologic observations in 2 patients employed as autoclave cleaners in PVC producing plants.
Results:
Ligamentous acroosteolysis of terminal finger phalanges, scleroderma-like lesions; the lesion is reversible upon removal from the intoxication.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
21.05.2002 (310)

Memo : Raynaud syndrome
Remark : Clinical symptoms in 22 workers from a PVC producing plant (autoclave cleaners).
Results:
Increased sensitivity to cold, circulatory impairment of fingers; acrocyanosis, swelling of fingers or hands; acroosteolysis of fingers.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
21.05.2002 (311)

Memo : Sister chromatid exchange
Remark : Method: Study of sister-chromatide exchange in cultured peripheral lymphocytes exposed in vitro to VC (doses: 10, 25, 50, 75, 100 % VC in air) for 3 hours with and without addition of S 9 mix.
Results: Little or no sister-chromatid exchange without metabolic activation. Marked increase in sister-chromatid exchange with metabolic activation.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (287)

Memo : Sister chromatid exchange
Method : Sister chromatid exchange (SCE), micronuclei (MN) and proliferation were measured in peripheral blood lymphocytes from 93 individuals (of whom 52 were exposed to vinyl chloride occupationally). An increase in SCE and MN as well as in cell kinetics was observed in lymphocytes from workers (as cited in a review by Giri et al., 1995).
Result : An increase in SCE and MN as well as in cell kinetics was observed in lymphocytes from workers (as cited in a review by Giri et al., 1995).
Reliability : (2) valid with restrictions
29.05.2002 (295) (312)

Memo : Sister chromatid exchange

Result : Lymphocytes from 19 males exposed occupationally to vinyl chloride had a greater incidence of chromosomal abnormalities and micronuclei than cells from 20 controls (as cited in a review by Giri et al., 1995).
Reliability : (2) valid with restrictions
29.05.2002 (313) (295)

Memo : Sister chromatid exchange
Result : The distribution of breaks along chromosomes in lymphocytes from 67 males exposed occupationally to vinyl chloride was examined. Breaks induced by vinyl chloride were not random (as expected in an unexposed population), but were more apt to be located at chromosome A2, chromosomes from groups B and C, and the terminal segments of chromosome A1 (as cited in a review by Giri et al., 1995).
Reliability : (2) valid with restrictions
29.05.2002 (314) (295)

Remark : Chromosomal investigations of 20 VC exposed persons with indications of a VC illness (Acroosteolysis, Raynaud syndrome, thrombocytopenia, liver function disturbance) showed an aberration rate increased significant in relation to a control group. With 10 VC exposed persons without indications of a VC illness, no increased Chromosomal aberration rate could be determined.
Source : BASF AG Ludwigshafen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
12.07.1996 (315) (316)

Remark : Chromosome investigations with 6 coworkers of PVC production pointed an aberration rate between 0-5 %. details data to the exposition are not presented. With 4 coworkers of the PVC subsequent treatment none was observed in relation to a control's group increased Chromsome aberration rate. The VC concentration in the room air lay between < 1 ppm to 26 ppm.
Source : BASF AG Ludwigshafen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
12.07.1996 (317)

Remark : The peripheral blood picture from a control individual with those of a vinyl chloride exposed individual was no different.
Source : BASF AG Ludwigshafen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
12.07.1996 (318)

Remark : A mortality investigation with a cohort of 1618 VC/PVC exposed individuals resulted in a significant increase of the following illnesses: Lungentuberkulose, karzinome of the stomach and the large intestine as well as Prostate ahypertrophy. Angiosarcoma was not registered. The duration of the VC exposure did not effect mortality rate.
Source : BASF AG Ludwigshafen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
12.07.1996 (319) (320)

Remark : An increased chromsomal aberration rate was observed with one VC exposed person employed with an angiosarkom of the liver. The VC concentrations were indicated as 35-150 ppm, length of employment as 13 years.
Source : BASF AG Ludwigshafen
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
12.07.1996 (315) (321)

Remark : Two experimenters were exposed to a VC concentration of 2.5 % for three

minutes.
Results: reversible dizziness, slight disorientation, burning sensation of the feet. Immediate recovery upon leaving the chamber. Slight headache for about 30 minutes.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (123)

Remark : Medical examination of workers employed in plants working with PVC resins and plasticised resins.
Symptomes observed:
Irritation of the mucous membranes of the upper respiratory tract; chronic bronchitis. Cutaneous affections such as acne etc. Chronic gastritis, chronic colitis. More or less pronounced hepatitis and enlargement of the liver.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (322)

Remark : Medical examinations in 168 workers from 2 PVC producing plants.
Results:
First symptoms are due to effects on the nervous system: euphorisation, headache, insomnia, weakness, blunting of the memory. These are followed by unspecific symptomes of the digestive tract; increased liver size in 30 %, in late stages chronic hepatitis, accompanied by abnormalities of serum protein pattern (e.g. increased a2-globulin, serum aldolase). RAYNAUD-syndrome in 6 %: vaso-motoric dysregulation. Contact dermatitis 4.4 %, sclerodermia 3.6 %, impaired thyroid function. Early effects are reversible upon removal from the intoxicating environment.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (323)

Remark : Summary of clinical signs, radiologic signs, hematologic signs, vascular signs, and histopathology in workers employed in PVC producing plants (autoclave cleaners). Discussion of the pathogenesis and of therapeutic and preventive measures.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (324)

Remark : Method: Determination of kinetic data for the VC metabolism in two human volunteers in (a) a closed spirometer system or (b) an open system.
Results: Closed system: VC concentration 0.026 mg/l for 30 min. Average clearance rate 2 l/h kg b.w.. The equilibrium is reached fast (t1/2 of invasion of VC into the organism 1.5 - 2 min). Upon termination of the exposure, VC is exhaled fast. t1/2 for metabolism 18 to 20 min. Elimination constant 2.0 to 2.3 /h.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Test substance : VC, purity: 99.995 %.

Reliability : (2) valid with restrictions
29.05.2002 (229)

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Remark : Method: Exposure of 6 volunteers to 48 ppm, 4 volunteers to 248 ppm, and 4 volunteers to 459 ppm of VC for a total of 7.5 h. The concentration of VC in the exhaled air was measured every hour for 20 h after cessation of exposure.
Results: Generation of decay curves. Comparison of the exhaled air concentration after 1 h and the exposure concentration provide evidence for saturation of the metabolic pathways. Exposure concentration at which the metabolic conversion rate is half maximal is 435 ppm (deduced by ECETOC from Baretta""s data)
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (325) (200)

Remark : Report on 118 cases of VC related hemangiosarcoma of the liver recorded in a register of the Association of Plastic Manufacturers in Europe.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (326)

Remark : Method: Analysis of the VC metabolite thiodiglycolic acid (TdGA) in the urine of 15 workers employed in a PVC producing plant.

Results: Urinary concentration 0.94 - 20.4 ug/l.
The amount of TdGA excreted during 24 h was correlated with the effective VC body concentrations calculated from the exposure data. The correlation resembles a function of the Michaelis-Menten type. VC body concentrations do not normally reach steady state values.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (253)

Remark : Method: Analysis of thiodiglycolic (TdGA) acid in urine from 18 workers that were exposed to VC at the workplace.

Results: Mean air concentration at the workplace: 0.14 - 7.0 ppm.
Excretion of TdGA 0.3 - 4.0 mg/l of urine. A significant increase of the metabolite occurs even at VC concentrations below 5 ppm.
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (255)

Remark : Workplace concentrations of VC dropped from values of several 100 ppm (259 mg/m3) measured prior to the seventies, including maximum values of several 1,000 ppm (2590 mg/m3), to current levels of around 1 ppm (2.59 mg/m3).
Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
Reliability : (2) valid with restrictions
29.05.2002 (327) (328)

Remark : A significant increase of lung tuberculosis, carcinomas of the stomach and colon, and hypertrophy of the prostate was observed in a cohort of 1618 persons, formerly exposed to VC/PVC. No angiosarcomas were observed. The duration of VC exposure did not influence mortality rate.
Source : Huels AG Marl

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EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (329)

Remark : A chromosomal analysis on a 43-year old man with an angiosarcoma of the liver revealed an increased aberration rate. The man was occupied in a PVC manufacturing area for 13 years.

Source : Huels AG Marl
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

Reliability : (2) valid with restrictions
29.05.2002 (293) (181)

Result : Point mutations of c-ras genes were located in human angiosarcomas of the liver associated with occupational exposure to vinyl chloride (as cited in a review by Giri et al., 1995).

Reliability : (2) valid with restrictions
29.05.2002 (295) (330)

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7.1 END POINT SUMMARY

7.2 HAZARD SUMMARY

7.3 RISK ASSESSMENT