# CHEMICAL REVIEW: VINYL CHLORIDE

**CAS RN 75-01-4**
**NIOSH # KU 9625000**
**SAX # VNP000**
**DOT # 1086**
**SIC CODE 2813**

See N.I. Sax. 1988. *Dangerous Properties of Industrial Materials*, 7th ed. New York: Van Nostrand Reinhold, p. 3473.

**SYNS** Chlorethylene, chloroethene; chlorethene; chloroethylene; chlorure de vinyle (French); cloruro di vinile (Italian); ethyl ne monochloride; Exon 470; monochloroethene; monochloroethylene; Trovidur; vinile (cloruro di) (Italian); vinyl chloride monomer; vinyl chloride, inhibited; vinyl chloride, monomer; vinyl C monomer; vinylchlorid (German); vinylchloride; vinyle(chlorure de) (French); VC; VCM; winylu chlorek (Polish).

MF $C_2H_3Cl$

MW 62.50

**SPECIES IN MIXTURE** 99.42% pure.

**COMMON USES** Approximately 96% is used in production of vinyle chloride homopolymer and copolymer resins. It is also used in production of methyl chloroform and as a comonomer with vinylidene chloride in the production of resins. Polyvinyl chloride resins are used in production of plastic piping and conduit. Other uses are in floor covering, consumer goods, electrical applications, and transport applications. Vinyl chloride has been used as refrigerant, an extraction solvent, and as aerosol propellant. (R-63)

## STORAGE AND HANDLING

**TRANSPORT, RAIL (%)** 90.0.

**TRANSPORT, BARGE (%)** 2.0.

**TRANSPORT, PIPE (%)** 8.0.

**CONTAINERS** Pressure cylinders, tank cars, tank barges.

**GENERAL STORAGE PROCEDURE** Protect against physical damage. Outside or detached storage is preferable. Inside storage should be in a fire resistive storage room, provided with adequate ventilation and free of sources of ignition and heat.

**GENERAL HANDLING PROCEDURE** Guard against all sources of ignition.

**PRODUCERS** Allied Chemical Corp., Moundsville, WV; American Chemical Corp., Watson, CA; Cumberland Chemical Corp., Calvert City, KY, Charleston, WV; Dow Chemical Co., Oyster Creek Division, P.O. Box BB, Freeport, TX 77541; Dow Chemical Co., P.O. Box 150, Plaquemine, LA 70764; Ethyl Corp., Gulf States Rd., P.O. Box 341, Baton Rouge, LA 70821; U.S. Tire and Rubber Co., Ashtabula, OH; U.S. Rubber Co., Painesville, OH; Goodyear Tire and Rubber Co., Niagara Falls, NY; Monochem, Inc., Highway 73, Geismar, LA, 70734; Monsanto Co., Texas City, TX; Tenneco Chemical Co., Houston, TX; Union Carbide Corp., Chemicals Div., Texas City, TX; U.S. Rubber Co., Painesville, OH; Goodrich Chemical Co., Louisville, KY, Niagara Falls, NY; Stauffer Chemical Company, Plastics Div., 2112 East 223 St., Carson, CA 90745; Ethyl Corp., La Porte Rd., Pasadena, TX 77501; PPG Industries, Inc., Attn: J.R. Farst, P.O. Box 1000, Lake Charles, LA 70601; PPG Industries, Inc., Attn: K.R. Mesloh, P.O. Box 7572, Ponce, PR 00731; Allied Chemical Corp., Gulf States Rd., Baton Rouge, LA 70821; Independence Plant, P.O. Box 150, Attn: E.R. Henderson, Deer Park, TX 77536; Union Carbide Corp., Highway 1765, P.O. Box 471, Texas City, TX 77590; BF Goodrich, Chemical Div., Attn: R.K. Hinderer, Highway 1523, Calvert City, KY 42029; Borden Petrochemical, Geismar, LA 70734; Shell Oil Company, P.O. Box 100, Deer Park, TX 77536; Shell Chemical Co., Norco Manufacturing Complex, P.O. Box 10, Norco, LA 70079; Continental Oil Co., Lake Charles VCM Plant, Box 605, Westlake, LA 70669. (R-47, R-63, R-70)

**ADDITIVE (%)** Phenol.

**STANDARD CODES** NFPA 2,4t,1; ICC Flammable Gas, Red Gas label, 300 lb in an outside container; USCG

Liquefied Nonflammable Gas; IATA (Inhibited) Flammable Gas, Red label, not acceptable passenger, 140 kg cargo.

**HAZARDS** Flammable gas. (R-1) Severe explosion risk at 30,000 ppm. (R-7) When heated to decomposition, it emits highly toxic fumes of phosgene; can react vigorously with oxidizing materials. (R-9)

**WATER: AGENCY RESTRICTIONS, STANDARDS, OR CRITERIA** EPA recommends an ambient water concentration of zero for maximum protection of human health from potential carcinogenic effects due to exposure to vinyl chloride through ingestion of contaminated water and contaminated aquatic organisms. The levels which may result in incremental increase of cancer risk over the lifetime are estimated at $1 \times 10^{-5}$, $1 \times 10^{-6}$ and $1 \times 10^{-7}$. The corresponding recommended criteria are 20 μg/L, 2.0 μg/L, and 0.2 μg/L. (R-11)

**AIR: AGENCY RESTRICTIONS, STANDARDS, OR CRITERIA** M.E.C. = 150 mg/m³ if emission > 3 kg/H. (R-6) Clean Air Act designates the concentration of vinyl chloride in all exhaust gases discharged to the atmoshpere during ethylene dichloride purification shall not exceed 10 ppm except as provided for in 40 CFR 61.65(a). (R-107) Clean Air Act emission standards for vinyl chloride producing plants are specified. (R-108)

**FOOD: AGENCY RESTRICTIONS, STANDARDS, OR CRITERIA** U.S. Treasury Dept. has banned the use of vinyl chloride polymers in packaging of alcoholic beverages. (R-63)

**TRANSPORTATION: AGENCY RESTRICTIONS, STANDARDS, OR CRITERIA** HMTA designates vinyl chloride as a hazardous material for the purpose of transportation in commerce. Hazard class is Flammable Gas. A Flammable Gas label is required. Material is forbidden for transport on passenger-carrying aircraft or railcar. Maximum net quantity permitted in one package is 300 lb for cargo-only aircraft and package must bear a Cargo Aircraft Only label. Material may be stowed on or below deck and away from living quarters on cargo vessels. For passenger vessels, the material is limited to quantities specified in 49 CFR 173.304 (charging of cylinders with liquefied compressed gas), 49 CFR 173.314 (requirements for compressed gases in tank cars), and 49 CFR 173.315 (compressed gases in cargo tanks and portable tank containers), and is also subject to the same stowage requirements as for a cargo vessel for the same material. (R-101) CERCLA designates vinyl chloride waste and heavy ends from the distillation of vinyl chloride in vinyl chloride monomer production as hazardous materials under HMTA. (R-101) CWA sections 307(a) and 112 designate vinyl chloride as hazardous material under HMTA. (R-101) HMTA also designates inhibited vinyl chloride as an optional hazardous material for international shipment. IMCO code is Flammable Gases and DOT class is Flammable Gas. A Flammable Gas label is required. Material may be stowed on or below deck and away from living quarters on cargo vessels, but must be stowed on deck and away from living quarters for passenger vessels. (R-102)

**OCCUPATIONAL EXPOSURE: AGENCY RESTRICTIONS, STANDARDS, OR CRITERIA** OSHA standard for vinyl chloride is 1 ppm averaged over an 8-H period, with a short-term ceiling exposure level of 5 ppm averaged over any period of time not to exceed 15 min. No employees may be exposed to vinyl chloride by direct contact with liquid vinyl chloride. (R-109) ACGIH recommends a TLV of 5 ppm. (R-106) The NIOSH recommendation for occupational health standard environmental exposure limit is the minimum detectable level averaged over a 10-H work period, with a short-term ceiling exposure of 1 ppm averaged over any period of time not to exceed 15 min. (R-110) Regulated by OSHA as a recognized carcinogen, Appendix Ala. (R-111)

**DISPOSAL: AGENCY RESTRICTIONS, STANDARDS, OR CRITERIA** RCRA 3001-3004 subjects the heavy ends from the distillation of vinyl dichloride in vinyl chloride monomer production to handling and report/recordkeeping requirements. (R-103) The Act also subjects the waste product, off-specification batches, and spill residues in excess of 1000 kg to handling and report/recordkeeping requirements. (R-104) The Act also designates vinyl chloride as an Appendix VIII chemical. (R-105)

**OTHER AGENCY RESTRICTIONS, STANDARDS, OR CRITERIA** OSHA prohibits the use of vinyl chloride in aerosol sprays. (R-7)

**FLAMMABILITY** Very flammable. Extreme hazard. Do not enter.

**FLAMMABILITY LIMIT (%), LOWER** 3.6.

**FLAMMABILITY LIMIT (%), UPPER** 33.

**TOXIC COMBUSTION PRODUCTS** HCl, phosgene, CO. Hazardous. Use self-contained breathing apparatus.

**EXTINGUISHING METHOD** Stop flow of gas. Use water

to keep containers cool. Do not extinguish unless necessary to effect an immediate shutoff of flow. Dry chemical and carbon dioxide can be used to extinguish vinyl chloride fires.

**FLASH POINT (C)** −78.

**AUTOIGNITION POINT (C)** 472. (R-7) 472.22.

**MELTING CHARACTERISTICS** −153.8C (caution, flash point −78C). (MERCK* 83/WIN)

**BOILING CHARACTERISTICS** −13.37 C; ignites, flash point −78 C. (MERCK* 83/WIN)

**SOLUBILITY CHARACTERISTICS** Slightly soluble.

**SPECIFIC GRAVITY** 0.9106.

**VAPOR PRESSURE TEXT** 400 mm Hg @ −28 C.

**STATE** Gas. (R-63)

**COLOR** Colorless. (R-6)

**ODOR** Mild, sweetish. (R-6)

**EXPLOSION LIMITS (%)** Lower = 4%; upper = 22%. (R-47)

**EXPLOSIVENESS** Reactive at high temperature or pressure. Polymerizes by evolution of heat, in the presence of air, oxygen, sunlight, or heat.

**SPECIFIC GRAVITY** 20 4 D = 0.9106. (R-63) 250/25 D = 0.908. (R-71)

**SOLUBILITY: OTHER SOLVENTS** Soluble in ethanol; very soluble in ether, carbon tetrachloride, and benzene. (R-63)

**CONVERSION FACTOR** 1 ppm in air = 2.6 mg/m$^3$ (R-63) 1 mg/L = 391 ppm. (R-112)

**ODOR THRESHOLD: AIR** Air = 25,000 ppm; slight odor at 4,000 ppm. Odor index at 20 C = 100. (R-6)

**OTHER PHYSICAL-CHEMICAL PROPERTIES** Polymerizes in light or in presence of catalyst; on combustion it degrades to HCl, CO, $CO_2$ with traces of phosgene; on treatment with strong alkalis at high temperatures it releases HCl. (R-63) Vapor density = 2.2 (air = 1). (R-63) Vinyl chloride is an inert gas which has no

## ■ AQUEOUS SOLUBILITY

| *Solubility (ppm)* | *Temp (C)* | *Meas/Est* | *Method* | *Ref* |
|---|---|---|---|---|
| 60 | 10 | | | R-118 |
| TEST CONDITIONS No method or test conditions reported. | | | | |
| 1.1 | 25 | | | R-119 |
| TEST CONDITIONS No method or test conditions reported. | | | | |

## ■ VAPOR PRESSURE

| *Vapor Pressure (mm Hg)* | *Temp (C)* | *Meas/Est* | *Method* | *Ref* |
|---|---|---|---|---|
| 2530 | 20 | | | R-63 |
| TEST CONDITIONS No method or test conditions reported. | | | | |
| 2320 | 20 | | | R-118 |
| TEST CONDITIONS No method or test conditions reported. | | | | |
| 2660 | 25 | | | R-120 |
| TEST CONDITIONS No method or test conditions reported. | | | | |
| 2320.0 | 20 | | | R-121 |
| TEST CONDITIONS No method or test conditions reported. | | | | |

## ■ N-OCTANOL/WATER COEFFICIENT

| *Kow* | *Log Kow* | *Meas/Est* | *Method* | *Ref* |
|---|---|---|---|---|
| | 1.38 | E | Substituent constant estimation | R-11 |

tendency to escape. When the gas escapes, high concentrations may accumulate and become very dangerous. (R-114)

**CHEMICAL SYNTHESIS METHODS** Direct chlorination of ethylene to form ethylene dichloride (EDC) and subsequent purification. Vinyl chloride is produced by thermal cracking of EDC. (R-70) Vinyl chloride gas and vapor is produced during the production of polyvinyl chloride. (R-113)

**PERSISTENCE** Polymerizes in presence of air, oxygen, sunlight, or heat. Volatilizes from water quickly.

## TOXICITY

**CARCINOGENICITY** Studies indicate positive development from occupational exposure.

**CARCINOGENICITY: IARC DETERMINATION** Vinyl chloride is a human carcinogen. Vinyl chloride is carcinogenic in mice, rats, and hamsters by oral and inhalation exposure. (R-63)

**CARCINOGENICITY: POSITIVE REFERENCES** R-12, R-31, R-41, R-63, R-85, R-86, R-89, R-90, R-93, R-97.

### ■ CARCINOGENICITY: ANIMAL STUDIES

| *Species* | *Route* | *Doses* | *Dosing Schedule* | *Ref* |
|---|---|---|---|---|
| Rat | Ihl | 0, 5000 ppm | 7 H/D, 5 D/W for 52 W | R-31 |

TEST CONDITIONS After exposure to 0 ppm (control) or 5000 ppm, 2 male and 62 female Wistar rats were sacrificed (at 4, 13, 26, and 52 W) and subjected to extensive examinations. Morphological changes were observed in respiratory tract, ceruminous glands, brain, kidney, heart, and spleen.

RESULTS Primary tumors were found in the brain (ependymona), lungs (papillary adenoma and mesenchymal types of tumors), ceruminous glands (mainly keratinized squamous cell tumors), and nasal cavity (carcinomas of the olfactory epithelium, carcino-sarcoma, esthesioneuroepithelioma).

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|---|---|---|---|---|
| Mus | Ihl | 50, 250, or 1000 ppm | 6 H/D, 5 D/W | R-41<br>R-86 |

TEST CONDITIONS Two-month-old albino CD-1 mice were divided into 4 groups, each consisting of 36 males and 36 females. Each group received 0, 50, 250, or 1000 ppm VC. Four animals of each sex and exposure level were terminated for various laboratory tests and gross and histopathologic examinations at the end of 1, 2, 3, 6, and 9 mos. Surviving animals were terminated at the end of 12 mos.

RESULTS Exposure to VC caused a high incidence of bronchioalveolar adenomas, liver hemangiosarcomas, and mammary gland tumors. The incidence of bronchiolar adenomas was: control group, 1/26 males and 0/36 females; 50 ppm group, 8/20 males and 4/34 females; 250 ppm group, 10/29 males and 12/34 females; 1000 ppm group, 22/33 males and 26/36 females. The incidence of liver hemangiosarcomas was: control group, 0/26 males and 0/36 females; 50 ppm group, 3/29 males and 0/34 females; 250 ppm group, 7/29 males ($p < 0.05$) and 16/34 females ($p < 0.05$); 1000 ppm group, 13/33 males ($p < 0.05$) and 18/36 females ($p < 0.05$). Mammary gland tumors consisted of adenocarcinomas and squamous and anaplastic cell carcinomas. There were a total of 0/36, 9/34, 3/34, and 13/36 mammary gland tumors in females exposed to 0, 50, 250 and 1000 ppm, respectively. Metastases in the lung occurred in 0/36, 2/34, 2/34, and 8/36 females in the 0, 50, 250, and 1000 ppm groups, respectively.

## ■ CARCINOGENICITY: ANIMAL STUDIES *(Continued)*

| *Species* | *Route* | *Doses* | *Dosing Schedule* | *Ref* |
|---|---|---|---|---|
| Rat | Ihl | 0, 50, 250, or 1000 ppm | 6 H/D, 5 D/W for 1, 2, 3, 6, or 12 mos | R-41, R-86 |

TEST CONDITIONS Two-month-old CD rats were divided into 4 groups each consisting of 36 males and 36 females. Each group received 0, 50, 250, or 1000 ppm VC. Four animals of each sex and exposure level were terminated at the end of 1, 2, 3, 6, and 9 mos; the surviving animals were terminated at the end of 12 mos.

RESULTS The incidence of liver and lung hemangiosarcomas was significantly increased in female rats. An increased incidence of these tumors was also seen in male rats, but this was not significantly ($p < 0.05$) increased. None of the male (0/35) or female (0/35) controls, and none of the 50 ppm dose group (0/36 males, 0/36 females) developed either liver or lung hemangiosarcomas. The incidence of these tumors in the medium- and high-dose groups were as follows: 2/36 males and 10/36 females ($p < 0.05$) from the 250 ppm group developed hemangiosarcomas in the livers; 0/36 males and 3/34 females from the same group developed hemangiosarcomas in the lungs. A total of 6/34 males and 15/36 females ($p < 0.05$) from the 1000 ppm group developed hemangiosarcomas in the liver; 4/34 males and 9/36 females ($p < 0.05$) developed hemangiosarcomas in the lungs. VC did not cause any other type of tumor in rats.

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| Rat | Ihl | 30,000 ppm | 4 H/D, 5 D/W for 52 W | R-89 |

TEST CONDITIONS Thirty male and 30 female 17-W-old Sprague-Dawley rats were exposed to 30,000 ppm VC for 1 Y. The animals were then kept under observation until spontaneous death.

RESULTS A total of 31/60 animals had Zymbal gland carcinomas and 17/60 had liver angiosarcomas. No mention of control animals was made.

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|---|---|---|---|---|
| Rat | Ihl | 50 ppm | 4 H/D, 5 D/W for 1 Y | R-89 |

TEST CONDITIONS A total of 300 male and female Sprague-Dawley rats (11 W old) were exposed to 50 ppm VC for 1 Y (4 H/D, 5 D/W). A control group consisted of 100 untreated rats. The animals were then kept under observation until spontaneous death.

RESULTS After 100 W there were 55 survivors in the treated group and 28 in the control group. At this time the following results were observed: Out of 300 animals in the treatment group, 6 had Zymbal gland carcinomas (0/100 controls), 1/100 had a nephroblastoma (1/100 control), 6/300 had liver angiosarcomas (0/100 controls), 7/300 had angiosarcomas at other sites (0/100 controls), 43/300 had mammary carcinomas (3/100 controls), 2/300 had mammary carcinosarcomas (2/100 controls), 45/300 had mammary fibroadenomas (3/100 controls) and 28/300 had other types of tumors (and/or sites) (7/100 controls).

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|---|---|---|---|---|
| Rat | Ihl | 1, 5, 10, and 25 ppm | 4 H/D, 5 D/W for 1 Y | R-89 |

TEST CONDITIONS Groups of 120 (males and females combined) Sprague-Dawley rats, age 13 W, were exposed to 0, 1, 5, 10, or 25 ppm VC for 4 H/D, 5 D/W for 1 Y. The animals were then observed until spontaneous death.

RESULTS After 87 W there were 49, 49, 62, 51, and 45 survivors for the 0, 1, 5, 10, and 25 ppm dose groups, respectively. The numbers of animals with tumors (excluding survivors) at this time were as follows: within the 25 ppm group, 3 rats had Zymbal gland carcinomas, 3 had liver angiosarcomas, 10 had mammary carcinomas, and 7 had other type and/or site tumors; within the 10 ppm group, 1 had Zymbal gland carcinoma, 11 had mammary carcinomas, and 5 had other type and/or site tumors; within the 1 ppm group, 8 had mammary carcinomas and 4 had other type and/or site tumors; in the control group, 2 had mammary carcinomas and 4 had other type and/or site tumors.

## ■ CARCINOGENICITY: ANIMAL STUDIES *(Continued)*

| *Species* | *Route* | *Doses* | *Dosing Schedule* | *Ref* |
|---|---|---|---|---|
| Rat | Ihl | 6,000 or 10,000 ppm | 4 H/D, 7 D | R-89 |

TEST CONDITIONS A group of 110 pregnant Sprague-Dawley rats was exposed to 6,000 or 10,000 ppm VC for 4 H/D for 7 D, from the 12th to the 18th D of pregnancy. Offspring were examined for tumors to see if VC was transported transplacentally. The animals were examined 143 W posttreatment. Four groups were used: Group I consisted of 30 dams who received 10,000 ppm VC; Group II of 30 dams who received 6,000 ppm VC; Group III of 54 offspring whose mothers received 10,000 ppm VC; Group IV of 32 offspring whose mothers received 6,000 ppm VC. No controls were used.

RESULTS Group I: 1 animal had a Zymbal gland carcinoma, 1 an intraabdominal angiosarcoma, 1 a liver fibroangioma, and 1 a liver angioma. Group II: No tumors were found. Group III: 3 animals had Zymbal gland carcinomas, 1 a nephroblastoma, 1 a liver fibroangioma, 1 a liver angioma, 1 a Zymbal gland fibrosarcoma, and 1 an ovarian leiomyosarcoma. Group IV: 1 animal had a Zymbal gland carcinoma, 1 a subcutaneous angiosarcoma, 1 an intraabdominal angiosarcoma, 1 a Zymbal gland adenoma, 1 a skin carcinoma, 1 a subcutaneous fibroangioma, and 1 a mammary carcinoma.

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|---|---|---|---|---|
| Rat | Ihl | 6,000 or 10,000 ppm | 4 H/D, 5 D/W for 5 W | R-89 |

TEST CONDITIONS A group of 45 female and 44 male Sprague-Dawley rats began treatment at 1 D of age. Animals received 6,000 or 10,000 ppm VC 4 H/D, 5 D/W for 5 W. The animals were then observed until spontaneous death.

RESULTS Of the 46 animals receiving 10,000 ppm VC, there were 10 angiosarcomas and 15 hepatomas (total of 19 rats with tumors). Exposure to 6,000 ppm VC to 43 rats resulted in 10 angiosarcomas and 13 hepatomas (total of 17 rats with liver tumors). At W 104 (from start of treatment) there were 5 and 8 survivors in the 6,000 and 10,000 ppm exposure groups, respectively.

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|---|---|---|---|---|
| Ham | Ihl | 50, 250, 500, 2,500, 6,000 or 10,000 ppm | 4 H/D, 5 D/W for 30 W | R-89 |

TEST CONDITIONS A total of 268 male Golden hamsters were exposed to 0, 50, 250, 500, 2,500, 6,000 or 10,000 ppm VC, 4 H/D, 5 D/W for 30 W. After treatment animals were observed until spontaneous death. Surviving animals were examined after 109 W of treatment.

RESULTS Group I (10,000 ppm): 6/35 had skin trichoepitheliomas and basaliomas: 4/35 had forestomach epithelial tumors, 1 subcutaneous angioma, and 1 gall bladder adenocarcinoma: Group II (6,000 ppm): 1/32 had a liver angiosarcoma, 2/32 skin trichoepitheliomas and basaliomas, 2/32 melanomas, 7/32 forestomach epithelial tumors, 2/32 hepatomas, 2/32 livr fibroangiomas, 2/32 liver angiomas, and 1/32 a biliducts adenocarcinoma. Group III (2,500 ppm): out of 33 hamsters, 1 had skin trichoepitheliomas and basaliomas, 1 had melanomas, 1 had lymphomas, 11 had forestomach epithelial tumors, 1 had hepatoma, 1 had a liver fibroangioma, and 1 had a liver angioma. Group IV (500 ppm): out of 33 hamsters, 2 had liver angiosarcomas, 4 had skin trichoepitheliomas and basaliomas, some had lymphomas, 7 had forestomach epithelial tumors, 1 had a subcutaneous angioma, and 1 had a bronchial carcinoma. Group V (250 ppm): out of 32 hamsters, 3 had skin trichoepitheliomas and basaliomas, 1 had lymphomas, and 2 had forestomach epithelial tumors. Group VI (50 ppm): out of 33 hamsters, 6 had skin trichoepitheliomas and basaliomas, 1 had a melanoma, 1 had lymphoma, and 4 had forestomach epithelial tumors. Group VII (0 ppm): out of 70 animals, 2 had skin trichoepitheliomas and basaliomas, 2 had lymphomas, and 2 had forestomach epithelial tumors.

## ■ CARCINOGENICITY: ANIMAL STUDIES *(Continued)*

| *Species* | *Route* | *Doses* | *Dosing Schedule* | *Ref* |
|---|---|---|---|---|
| Rat | Ihl | 50, 250, 500, 2,500, 6,000 or 10,000 ppm | 4 H/D, 5 D/W for 52 W | R-89 |

TEST CONDITIONS Groups of 64–74 Sprague-Dawley rats (male and female combined), age 13 Weeks, were exposed to the above VC concentrations for 52 W. Controls consisted of 68 untreated rats. After exposure the animals were observed until spontaneous death.

RESULTS After 135 weeks (end of experiment) increased incidences of liver angiosarcomas, Zymbal gland carcinomas, and nephroblastomas were observed in the treated rats. The following incidences of these tumors were observed in rats that survived until at least 26 W, when the first tumor was observed (for the controls, 50, 250, 500, 2,500, 6,000, and 10,000 ppm dose groups, respectively): liver angiosarcoma, 0/58, 1/59, 4/59, 7/59, 13/59, 13/60, and 9/61; Zymbal gland carcinoma, 0/58, 0/59, 0/59, 4/59, 2/59, 7/60, and 16/61; nephroblastoma, 0/58, 1/59, 6/59, 4/59, 6/59, 4/60, and 5/61.

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|---|---|---|---|---|
| Rat | Ihl | 100, 150, and 200 ppm | 4 H/D, 5 D/W for 52 W | R-89 |

TEST CONDITIONS Groups of 120 (male and female combined) Sprague-Dawley rats, age 13 W, were exposed to the above VC concentrations for 52 W. Controls consisted of 185 untreated rats. After exposure the animals were observed until spontaneous death.

RESULTS The results after 143 W (end of experiment) were given. Liver angiosarcomas and nephroblastomas were observed in the treated but not control animals. The following number of animals with these tumors for the control, low-, medium-, and high-dose groups, respectively, were observed: liver angiosarcoma, 0, 1, 5, and 12; nephroblastomas, 0, 10, 7, and 3.

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|---|---|---|---|---|
| Rat | Ihl | 50, 250, 500, 2,500, 6,000, and 10,000 ppm | 4 H/D, 5 D/W for 17 W | R-89 |

TEST CONDITIONS Groups of 60 (male and female combined) Sprague-Dawley rats, age 17 W, were exposed to the above concentrations of VC. Controls consisted of 190 untreated rats. After exposure the animals were observed until spontaneous death.

RESULTS The results after 155 W (end of experiment) were given. The incidence of Zymbal gland carcinomas and brain euroblastomas were increased in the treated rats. The number of animals with these tumors for the control 50, 250, 500, 2,500, 6,000, and 10,000 ppm dose groups, respectively, were as follows: Zymbal gland carcinoma, 1, 0, 1, 3, 6, and 7; brain neuroblastoma, 0, 0, 0, 0, 2, 2, and 6. Nephroblastomas and liver angiosarcomas were observed in 0–2 animals per each exposed group, but none were seen in the control animals.

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|---|---|---|---|---|
| Mus | Ihl | 50, 250, 500, 2,500, 6,000 and 10,000 ppm | 4 H/D, 5 D/W for 30 W | R-89 |

TEST CONDITIONS Groups of 30 male and 30 female Swiss mice, age 11 W, were exposed to the above VC concentrations for 30 W. Controls consisted of 80 untreated males and 70 untreated females. After exposure the animals were observed until their spontaneous death.

RESULTS The experiment was terminated after 81 W. Lung tumors, mammary carcinomas, liver angiosarcomas, and epithelial tumors of the skin were increased in the treated mice. The following incidences (males and females combined) of these tumors were noted in animals alive after 16 W, when the first tumor was observed (the control group, followed by lowest through highest dose group): lung tumors, 8/141, 2/57, 33/58, 38/58, 30/53, 8/54, and 35/50; mammary carcinomas, 0/141, 12/57, 11/58, 7/58, 9/53, 8/54, and 13/50; liver angiosarcomas, 0/141, 1/57, 11/58, 1/58, 11/53, 5/54, and 8/50; and skin epithelial tumors, 0/141, 0/57, 2/58, 1/58, 3/53, 6/54, and 3/50.

## ■ CARCINOGENICITY: ANIMAL STUDIES *(Continued)*

| *Species* | *Route* | *Doses* | *Dosing Schedule* | *Ref* |
|---|---|---|---|---|
| Rat | Ihl | 50, 250, 500, 2,500, 6,000, and 10,000 ppm | 4 H/D, 5 D/W for 52 W | R-89 |

TEST CONDITIONS Groups of 30 Wistar rats (males and females combined) were exposed to VC by inhalation for 52 W. Controls consisted of 40 untreated rats. After treatment the animals were observed until spontaneous death.

RESULTS After 136 W there were 3 animals still alive in the control group and none in the treated groups. Treatment with VC caused an increased incidence of liver angiosarcomas. The numbers of rats with this tumor were 0, 0, 1, 4, 3, 2, and 8 for the controls, 50, 250, 500, 2,500, 6,000 and 10,000 ppm dose groups, respectively.

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|---|---|---|---|---|
| Rat | Orl | 3.33, 16.65, and 50 mg/kg | 4–5 D/W for 52 W | R-89 |

TEST CONDITIONS Groups of 80 Sprague-Dawley rats were administered VC by gavage, 4–5 D/W for 52 W. A control group of rats received the olive oil vehicle only. After treatment the animals were observed until spontaneous death.

RESULTS After 120 W there were 4, 4, 2, and 2 animals still alive in the control, low-, medium-, and high-dose groups, respectively. Treatment with VC was associated with an increased incidence of liver angiosarcomas. The numbers of animals with this tumor at 120 W were 0, 0, 9, and 16 for the control, low-, medium-, and high-dose groups, respectively.

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| Rat | Orl | 0.03, 0.3, and 1 mg/kg | 4–5 D/W for 104 W | R-89 |

TEST CONDITIONS Groups of 158–163 Sprague-Dawley rats were to be given VC by gavage for 104 W. This experiment was still underway at the time of the report. The control group received the olive oil vehicle only.

RESULTS Since this experiment was still underway, conclusions were not made. However, the tumors found in animals that died at the time of the report (57 W) are given in the report.

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|---|---|---|---|---|
| Mus | Ihl | 50 ppm<br>500 ppm | 6 H/D, 5 D/W for 52 W<br>6 H/D, 5 D/W for 26 W | R-90 |

TEST CONDITIONS Albino NMRI mice, 12 W old, were used. Twelve male and 12 females were exposed to 50 ppm VC for 6 H/D, 5 D/W for 52 W. The same number of rats were exposed at the same schedule for 26 W to 500 ppm VC. Each experimental group had a control series that ran parallel to it. Four animals of each sex from all groups were sacrificed and examined for pathology 26 W after start of exposure. Additionally, 4 control animals were sacrificed 1 Y after the start of the experiment. Remaining animals were allowed to live until spontaneous death, or were sacrificed when moribund.

RESULTS Results of the control animals were pooled since no difference between the 2 groups was found. Out of a total of 48 control animals, 3 were found with tumors (1 mammary adenocarcinoma, 1 ovarian disgerminoma, and 1 reticulum cell sarcoma). In the 50 ppm group, 18/24 animals developed tumors. Alveologenic adenomas were observed in 13/24 animals. Subperitoneal hemangiosarcomas were found in 14/24 animals, and subcutaneous hemangiosarcomas in 5/24 animals. In the 500 ppm group exposure was stopped at 26 W due to the bad condition of most of the animals. All (24/24) exposed animals in this group developed alveologenic adenomas. Subperitoneal hemangiosarcomas were found in 8/24 animals, and mammary carcinomas were observed in 4/24 animals. The primary subcutaneous and subperitoneal hemangiosarcomas found in both the 50 and 500 ppm groups were all located in fat tissue.

## ■ CARCINOGENICITY: ANIMAL STUDIES *(Continued)*

| *Species* | *Route* | *Doses* | *Dosing Schedule* | *Ref* |
|---|---|---|---|---|
| Mus | Ihl | 50, 200, or 2,500 ppm | 7 H/D, 5 D/W for 9 mos | R-63 |
| | TEST CONDITIONS Groups of 100 male and 100 female CDI Swiss ChR mice (age NG) were exposed to 50, 200, or 2,500 ppm VC in air for 7 H/D, 5 D/W for 9 mos and were observed for an additional 9 mos. | | RESULTS After 8 mos of exposure, 49 treated animals died with tumors. A total of 42 pulmonary adenomas, 41 liver angiosarcomas, and 11 mammary gland adenocarcinomas were observed. Distribution of these tumors were as follows: pulmonary adenomas, 2 in the 50 ppm group, 12 in the 200 ppm group, 28 in the 2500 ppm group, and 0 in the control group; liver angiosarcomas, 3 in the 50 ppm group, 11 in the 200 ppm group, 28 in the high-dose group, and 0 in the controls; and mammary adenocarcinomas, 2 in the low-dose group, 3 in the mid-dose group, 6 in the high-dose group, and 0 in the controls. | |
| Rat | Ihl | 30,000 ppm | 4 H/D, 5 D/W for 12 mos | R-12, R-85 |
| | TEST CONDITIONS Male Wistar rats, 3 mos old, were exposed to 30,000 ppm VC (99% purity) vapors for 4 H/D, 5 D/W for 12 mos. There were 25 rats in the control group. At the end of treatment surviving animals were sacrificed at 20 D intervals. | | RESULTS Of 26 treated rats, 17 developed skin carcinomas (predominately epidermoid carcinomas). No tumors were found in the control animals. Treated animals with lesions of the lungs: 1 adenocanthoma, 3 adenocarcinomas, 1 squamous cell carcinoma, and 1 mucous producing adenocarcinoma. Treated animals with lesions of the bone: 5 osteochondromas. | |
| Rat | Ihl | 600 ppm or 600 ppm plus 5% ethanol in drinking water | 4 H/D, 5 D/W for 1 Y | R-40 |
| | TEST CONDITIONS Groups of 80 Sprague-Dawley male rats were used. One group was exposed to 600 ppm VC vapors; a second group received 5% ethanol in the drinking water *ad libitum* 4 W before the beginning of VC inhalation and continued to receive ethanol-water until death; the control group received only the ethanol-treated drinking water; and a fourth group received no treatment. | | RESULTS At the time of this preliminary report, 17% of the animals had been autopsied. Histological evidence showed the latent period for angiosarcoma of the liver to appear was 53 W in rats exposed to vinyl chloride alone and 38 W in rats exposed to VC and 5% ethanol. Preliminary results of this long-term study indicated synergism between inhaled VC and ingested ethanol in the induction of tumors. | |
| Rat | Ihl | 50, 500, 2,000, 5,000, 10,000, and 20,000 ppm | 4 H/D, 5 D/W for 12 mos | R-98 |
| | TEST CONDITIONS Groups of 150–200 male and female Wistar Ar/IRE rats, 3 mos old, were exposed to the above VC concentrations for 12 mos. Controls consisted of 200 rats not exposed to VC and kept under the same conditions for 13 mos. | | RESULTS Exposure to VC was associated with an increased incidence of liver angiosarcomas, skin squamous cell carcinomas, and lung adenocarcinomas. The following incidence of these tumors were observed in the control group, followed by lowest- to highest-dose groups, respectively: liver angiosarcoma, 0/200, 0/200, 4/150, 10/200, 12/200, 16/200, and 18/150; skin squamous cell carcinoma, 0/200, 0/200, 3/150, 0/200 (6/200 skin cecanlhomas, however, at 2000 ppm), 20/200, 34/200, and 67/150; and lung adenocarcinomas, 0/200, 0/200, 0/150, 8/200, 4/200, 14/200, and 21/150. | |
| Rbt | Ihl | 10,000 ppm | NG | R-98 |
| | TEST CONDITIONS Forty rabbits were exposed to 10,000 ppm VC. Controls consisted of 20 rabbits not exposed to VC and kept under similar conditions for 15 mos. | | RESULTS Skin acanthomas were observed in 12/40 exposed rabbits and 0/20 controls. Lung adenocarcinomas were observed in 6/40 exposed rabbits and 0/20 controls. | |

## ■ CARCINOGENICITY: HUMANS

| *Route* | *Dose* | *Dosing Schedule* | *Ref* |
|---|---|---|---|
| NG | NG | Occupational exposure | R-93 |

TEST CONDITIONS A retrospective cohort study of workers at 4 VC facilities (that had been engaged in the polymerization of VC for at least 15 Y and had a sizable work force) was conducted. Employment records initially were obtained of every individual who had ever worked at any of the 4 VC plants. Individuals for study were selected from the records of individuals having 5 or more Y of employment and 10 Y since initial employment. A modified life-table technique was used to obtain the 12,720 person-years at risk of dying, according to 5 Y age group, 5 Y calendar period, years of work experience, and time since onset of exposure to VC. Comparison was made between the observed number of deaths among the study cohort members and that expected on the basis of the U.S. white male death rates specific for age and calendar year and cause.

RESULTS A total of 136 deaths occurred among workers exposed to VC as contrasted with 126.3 deaths expected. Only 2 causes of death were in excess among workers exposed to VC: nonmalignant respiratory disease, and all malignant neoplasms (6 observed vs 3.4 expected and 35 observed vs 23.5 expected, respectively). The latter excess was statistically significant at $p < 0.05$. When cancer mortality was analyzed by site, excesses were found for 4 organ systems: brain and central nervous system (3 observed vs 0.9 expected), respiratory system (12 vs 7.7 expected), hepatic system (7 vs 0.6 expected, $p < 0.01$), and lymphatic and hematopoietic systems (4 vs 2.5 expected). Of the 14 histologically confirmed cases of biliary and liver cancer, 11 cases of angiosarcoma of the liver were diagnosed (this includes 4 cases still alive at the time of the report).

| | | | |
|---|---|---|---|
| NG | NG | Occupational exposure | R-95 |

TEST CONDITIONS Identification particulars were obtained for over 7,000 men who were at some time between 1940 and 1974 exposed to VC monomer in the manufacture of PVC in Great Britain. Approximately 99% of these men have been traced and their mortality experience studied. The number of deaths observed was compared to that expected using sex and age standardized death rates for England and Wales.

RESULTS The overall standardized mortality ratio, 75.4, shows a significant reduction compared with the national rates. Four cases of liver cancer were found. Two of these have been confirmed by a panel of liver pathologists as angiosarcoma and 2 as not angiosarcoma. There is no evidence to support the hypothesis that cancers other than those of the liver are associated with exposure to VC monomer. The 2 cases of angiosarcoma were found in men who had been exposed to high concentrations of the monomer although the 2nd man died only 8 Y after first exposure.

| | | | |
|---|---|---|---|
| NG | 5–240 ppm TWA | Occupational exposure | R-97 |

TEST CONDITIONS A retrospective cohort study of the mortality experience of individuals occupationally exposed to VC between 1942 and 1960 was conducted. Employees were grouped into 4 exposure categories according to the highest levels of VC exposure experiences for at least 1 mo. Departmental census lists were reviewed over the specified years (1942 and 1960) for 5 production units: unit I, copolymer plant, 1942–1960; unit II, PVC and copolymer plant, 1953–1960; unit III, VC monomer plant, 1947–1954; unit IV, copolymer semiplant, 1946–1955; and unit V, vinyl latexes and polymer plant, 1946–1960. Exposure measurements were available of units I and II but not for the 3 smaller units. To investigate dose-response relationships with respect to VC, industrial hygiene data were reviewed for each job classification and each job was assayed on exposure level of low, intermediate, or high. The 3 categories primarily were based on estimated TWA concentrations for an 8 H day. The low level was defined as TWA concentrations below 25 ppm VC, the intermediate level as 25–200 ppm, and the high level as 200 plus ppm VC. A subjective evaluation of the other 3 units by industrial hygienists indicated that exposures were in the low to intermediate range, with occasional excursions to high levels. The observed mortality of the study population was compared to that of the U.S. white male population.

RESULTS The distribution of the malignant neoplasms with respect to exposure category suggests a possible dose-response relationship. Although the numbers of deaths were small, 9 of the 13 malignancies were observed in the high-exposure group. An approximate statistical evaluation of the difference between observed and expected malignancy deaths in the high-exposure group compared with all other exposure groups combined was performed, based on the conditional distribution of independent Poisson random variables. A Chi-square value of 6.1 ($p < 0.025$) was obtained after adjusting the total expected deaths to the observed number of deaths (high exposure 9 vs 4.64 expected; all other groups 5 vs 9.36 expected). Mortality experienced 15 or more Y after initial exposure was examined. Eight of the 9 malignancies occurred in the high-exposure groups. Again, the Chi-square comparison of the distribution of malignancy deaths between the high- and all other exposure groups was significant ($p < 0.01$). A comparison within the high-exposure group between those individuals with less than 1 Y of high exposure versus those with more than 1 Y of high exposure was not significant.

## ■ CARCINOGENICITY: HUMANS *(Continued)*

| *Route* | *Dose* | *Dosing Schedule* | *Ref* |
|---|---|---|---|
| NG | NG | Occupational exposure | R-96 |

TEST CONDITIONS A retrospective mortality study was conducted of 8,384 men from 33 plants who had worked for at least 1 Y in a job involving exposure to VC before December 31, 1972. The observed mortality was compared to that of the U.S. male population. Vital status could not be determined for 15% of the study population. Analysis was restricted to the 7,128 workers on whom follow-up was complete.

RESULTS No specific cause of death (cancer or otherwise) was (statistically) significantly greater than expected in the total group. When the group was analyzed according to duration or level of exposure, again no significant increases in cancer mortality were observed. However, some cancer mortality increased, although not significantly, and may have been related to exposure. According to the authors, mortality from digestive cancer, respiratory cancer, cancer of other unspecified sites, and lymphomas appeared to be related to exposure.

**CARCINOGENICITY: OTHER STUDIES** ■This study investigated the possibility that changes in nuclear size of HeLa S3 cells, exposed *in vitro*, might be used as an index of the carcinogenicity of compounds. VC, along with other tested carcinogens, caused an increased nuclear size in exposed cells. These effects were not seen with noncarcinogens. (R-4) ■In this study, 1,047 workers exposed to VC monomer from 3 different VC/PVC plants and 289 workers from a polyvinylchloride (PVC) extrusion plant manufacturing a PVC textile product (exposed to much lower concentrations of VC) were examined. Carcinoembryonic antigen (CEA) titers were determined. The investigation demonstrated that occupational exposure in VC/PVC plants can cause elevations in the CEA titers of otherwise healthy individuals. (R-35)

**MUTAGENICITY: GENE MUTATION–POSITIVE REFERENCES** R-2, R-20, R-22, R-27, R-58, R-59.

**MUTAGENICITY: GENE MUTATION–NEGATIVE REFERENCES** R-56.

## ■ MUTAGENICITY: GENE MUTATION STUDIES

| *Assay Type* | *Species/Cell Type* | *Route* | *Doses* | *Ref* |
|---|---|---|---|---|
| Bacterial mutation assay | *Escherichia coli* K12 | | 10.6 mM | R-100 |

TEST CONDITIONS Mutagenicity of VC was evaluated in *E. coli* K12 at 4 different loci, consisting of three back mutation systems (gal+, arg+, and nad+) and one forward mutation (MTR). The test was performed using liver microsomes from male mice pretreated for 10 D with 0.1% phenobarbital in the drinking water. VC gas (> 99.9% purity) was bubbled through the liquid medium to give a concentration of 10.6 mM.

RESULTS Mutagenicity was expressed as number of colony forming units (cfu) on selective media per number of cfu on complete media. VC was mutagenic in the presence of a metabolic activation system. The percentages of spontaneous mutation rate at the different loci were as follows: gal+ 231%; arg+ 663%; MTR 172%; and nad+ 148%.

| | | | | |
|---|---|---|---|---|
| Yeast mutation assay | *Schizosaccharomyces pombe* | | 16 or 48 mM | R-20 |

TEST CONDITIONS This haploid strain of *S. pombe* contains a missense mutation in the ade6 locus. Treatment with a mutagen causes forward mutation at 5 genetic loci for the biosynthesis of adenine. These mutations produce a change in the phenotype of the colonies, which can be scored. VC was bubbled through liquid cell suspensions, producing concentrations of 16 and 48 mM.

RESULTS Mutagenic activity was found in *S. pombe* only when microsomal preparations (105,000 g) from mouse liver were included with the treatment solution. A dose-effect relationship was linear with mMolar concentrations in treatments of 30 min. The vinyl chloride monomer (VCM) treatment did not produce any detectable decrease in the survival of cells.

| | | | | |
|---|---|---|---|---|
| Host-mediated microbial mutation | mus-*Schizosaccharomyces pombe* | Orl | 700 mg/kg | R-20 |

TEST CONDITIONS Swiss albino mice weighing 25 g each were treated orally with 1.85% vinyl chloride monomer (VCM) in 1 mL of olive oil (700 mg/kg body weight). Yeast cells of *S. pombe* (P. strain) were injected into the peritoneum and incubated for various times to measure the forward mutation frequency.

RESULTS VCM was found active at a dose of 700 mg/kg during 12 H of treatment. Data from regression analysis were significant at the 1% level. This demonstrated VCM was genetically active, *in vivo*.

## ■ MUTAGENICITY: GENE MUTATION STUDIES *(Continued)*

| *Assay Type* | *Species/Cell Type* | *Route* | *Doses* | *Ref* |
|---|---|---|---|---|
| Ames assay | *Salmonella typhimurium* TA1530, TA1535, G46 | | 0.2, 2, or 20% | R-22 |

RESULTS Exposure of *S. typhimurium* strains to VC increased the number of His+ revertants/plate, 16, 12, or 5 times over the spontaneous mutation rate. After 6 H of exposure to 20% vinyl chloride monomer (VCM) in air, the mutagenic response for TA1530 strain was enhanced 7-, 4-, or 5-fold when fortified postmitochondrial liver fractions from humans, rats, or mice were added. VC enzyme-mediated mutagenicity was dependent on an NADPH generating system. Highest mutagenic response was seen with TA1530. Exposure of this strain to 20% VC in air, in the absence of any metabolic activation system caused a linear increasing mutagenic response as a function of incubation time, which was 20 times the spontaneous rate, at 48 H. Phenobarbitone pretreatment of rats and mice increased the mutagenic response by up to 15–40% as compared to untreated controls.

| | | | | |
|---|---|---|---|---|
| Sex-linked recessive lethal | *Drosophila melanogaster* | Ihl | 10,000, 100,000, 200,000 ppm | R-27 |

TEST CONDITIONS Male *D. malanogaster*, wild type strain Karsnas 60, 0 to 2 D old, were used for treatment with VC. Males were mated individually with 2–3 Muller 5 females for D 6–12 after treatment without any brooding. Heterozygous daughters were individually mated to 2–3 Muller 5 males and the progeny was tested for recessive lethals. In induction experiments, males were treated with sodium phenobarbiturate and/or VC (1% solution sodium phenobarbiturate dissolved in sucrose water for 24 H).

RESULTS VC increased mutagenicity at the lowest exposure tested. There was no indication of an increased effect with higher concentrations. Experiments with sodium phenobarbiturate (one with 1% VC and one with 10% VC) produced a pronounced effect. The total number of recessive lethals (when 1% VC was used) with sodium phenobarbiturate pretreatment was different from control at 0.1% significance level (using Chi-square and Yates Correction).

| | | | | |
|---|---|---|---|---|
| Mammalian spot test | Mus | Ihl | 4,600 ppm | R-56 |

TEST CONDITIONS Female mice of inbred C57BL/6J Han (a/a; wild type) were mated to Han rotated-bred males of T-stock strain. On the 10th D of gestation females were exposed to 12,000 mg/m³ (4,600 ppm) of VCM in air for 5 H. F1 offspring were examined at 3–5 W of age for mosaic coat colors. An experiment using cyclophosphamide to test the ability to induce colored spots in the F1 hybrids served as a positive control. Statistical evaluations of the data were done by Chi-square test.

RESULTS The mammalian spot test did not provide evidence that VC induces somatic gene mutations in mammals *in vivo*. No offspring with abnormal morphology were found in the vinyl chloride monomer (VCM) exposure group. Treatment with 10 mg (scu) CP/kg produced significant differences in the number of white and colored spots in the offspring in comparison with the control or VCM-treated group.

| | | | | |
|---|---|---|---|---|
| Ames assay | *Salmonella typhimurium* TA1530 | | 20% | R-58 |

TEST CONDITIONS Liver S-9 fractions from adult female BD-V1 rats and from human patients were used as metabolic activation systems.

RESULTS VC was mutagenic in the presence of both rat and human liver S-9 fractions. The number of his – revertants in *S. typhimurium* mediated by human and rodent liver S-9 exposed to 20% VC (v/v) in air for 4 H and incubated for 48 H at 37 C was 85 and 100 revertants/plate, respectively. The number of revertants/plate after exposure to VC in the absence of cofactors NADP-, G 6-P) was subtracted.

## ■ MUTAGENICITY: GENE MUTATION STUDIES *(Continued)*

| *Assay Type* | *Species/Cell Type* | *Route* | *Doses* | *Ref* |
|---|---|---|---|---|
| Na/K ATPase assay | Chinese ham-V79 | | 5, 10, 20, and 30% | R-2 |

TEST CONDITIONS The mutagenicity of VC was tested in V79 Chinese hamster cells in the presence and absence of a S-15 liver fraction from phenobarbitone-pretreated rats. The cells were exposed to a vapor concentration of 5–30% (v/v) for 5 H. Mutagenicity was measured by the induction of 8-azaguanine and oubain resistance.

RESULTS VC induced both 8-azaguanine and oubain resistant dose-related mutants at 5–30% VC in air in the presence of the S-15 fraction. At a concentration of 30%, mutation frequencies were 10–20 times those of spontaneous reversions. At this concentration there were 51 azaguanine and 4 oubain resistant colonies per 100,000 survivors. Neither toxicity nor mutation was induced in the absence of the metabolic activation system.

| | | | | |
|---|---|---|---|---|
| Ames assay | *Salmonella typhimurium* TA1530 | | 2, 7, 12, and 20% | R-59 |

TEST CONDITIONS The mutagenicity of VC in *S. typhimurium* TA1530 without metabolic activation at the above concentrations was evaluated. In tests to evaluate the effect of a metabolic activation system, a 2% VC concentration was used. The metabolic activation system consisted of S-9 liver fraction from adult male NMRI mice either left untreated or treated with Aroclor 1254.

RESULTS In the absence of a metabolic activation system, VC increased the number of his− revertants in a dose-related manner. At the highest concentration (20%) there were 101 revertants in the treated plate compound to 10 in the controls. The addition of the S-9 fraction enhanced the mutagenicity of VC. This effect was even more pronounced when liver S-9 from pretreated mice was used.

## ■ MUTAGENICITY: CHROMOSOMAL EFFECTS STUDIES

| *Assay Type* | *Species/Cell Type* | *Route* | *Doses* | *Ref* |
|---|---|---|---|---|
| *In vivo* cytogenetics | Chinese hamster-bone marrow | Ihl, ipr | 2,500 or 5,000 ppm by ihl followed by 600 and 300 mg/kg ipr | R-3 |
| | Human lymphocytes | Ihl | NG | |

TEST CONDITIONS Bone marrow cells from Chinese hamsters treated with VC in the above doses and routes were studied to determine whether chromosomal aberrations in the bone marrow cells were significantly higher in comparison to control groups. A similar analysis of workers from a PVC plant was undertaken, using lymphocytes from 20 workers with symptoms of VC illness, from 10 workers with no symptoms of VC illness, and from 10 controls matched according to age. A total of 100 cells per individual were scored for gaps, breaks, fragments, dicentrics, rings, chromatid and chromosome translocations, and deletions.

RESULTS In humans, only the group consisting of workers with VC illness showed a significant increase in the rate of aberrations in comparison to the control group (statistical information and exact data not given). In the hamsters, chromosomal aberrations were also significantly higher in the treated animals as compared to controls.

| | | | | |
|---|---|---|---|---|
| Dominant lethal | CD-1 mus | Ihl | 3,000, 10,000, 30,000 ppm | R-55 |

RESULTS No mutagenic effects were seen on any maturation stage of spermatogenesis in male CD-1 mice exposed by inhalation to 7.8, 26, or 78 g/m³ VC in air for 6 H/D for 5 D as compared to controls.

| | | | | |
|---|---|---|---|---|
| *In vivo* cytogenetics | Hmn-peripheral blood lymphocytes | Ihl | 20–30 ppm | R-28 |

TEST CONDITIONS Seven occupationally exposed male workers and 3 nonexposed control subjects, all employed in the same PVC factory, were studied for chromosomal effects of VC exposure. In weeks prior to blood sample collection, air concentration was approximately 20–30 ppm. Workers who were studied had been exposed to VC for periods ranging from 9 to 29 Y.

RESULTS Investigators found that the average frequency of chromosomal aberrations in this group (9.52%) was significantly ($p < 0.001$) greater than in the controls (1.94%). This was true for chromatid and isochromatid breaks.

## ■ MUTAGENICITY: CHROMOSOMAL EFFECTS STUDIES *(Continued)*

| *Assay Type* | *Species/Cell Type* | *Route* | *Doses* | *Ref* |
|---|---|---|---|---|
| *In vivo* cytogenetics | Chinese hamster-bone marrow | Ihl | 2.5% or 5.0% | R-49 |
| TEST CONDITIONS Groups of 4 adult (10–15 W old) Chinese hamsters, weighing 30 g, were exposed to 2.5% VC in air for 6, 12, or 24 H. The male-female ratio was 1:1. Another group of 10 hamsters was exposed to 5% VC for 24 H only. Hamsters received intraperitoneal injection of 8 mg colchicine/kg body weight 24 H after beginning VC exposure. Bone marrow chromosomes were analyzed for gaps, breaks, fragments, deletions, and exchanges 2 H later. | | | RESULTS The frequency of chromosome aberrations depended on dose and exposure time. After 6 and 12 H of exposure at the 2.5% level, aberrations (breaks and fragments) were induced in 0.8% of the metaphase. After 24 H the frequency of induced breaks and fragments increased to 4.5%. In 1,400 metaphases of 14 control hamsters only 1 break (0.1%) was found. Gaps included chromosome aberrations increased from 0.6% in controls to 7.3% in group exposed 24 H to 2.5% VC. The highest measured effect was 25.7% metaphases with aberrations when hamsters were exposed to 5% VC for 24 H ($p < 0.02$). Significance of differences in the number of metaphases with aberrations was verified using the Chi-square test. | | |
| Micronucleus test | CBA mus | Ihl | 5% | R-64 |
| TEST CONDITION Three CBA male mice were exposed to 5% VC for 4 H. Controls consisted of 3 untreated mice. | | | RESULTS Exposure to VC caused a significant increase in the number of polychromatic micronucleated cells as compared to controls. Statistical evaluation was performed with t-tests and combined probability analysis according to Fisher. | |
| *In vivo* cytogenetics | Hmn-peripheral blood lymphocyte | Occupational | NG | R-60, R-94 |
| TEST CONDITIONS The 11 subjects were male workers who had received repeated exposure to VC in an upstate NY polyvinyl chloride polymerization plant. Duration of recurrent occupational exposure in the 11 men ranged from 4 to 28 Y, with an average of 15 Y. Of the 10 healthy male controls, 4 were from within the same factory population without known VC exposure; 6 controls were also selected from outside the factory environment. The chromosome studies were performed on cultures of peripheral blood lymphocytes. Fifty metaphases from each individual were evaluated. | | | RESULTS Exposure to VC increased the frequency of chromosomal aberrations. Much of this increased damage was due to cells with unstable chromosome changes such as fragments, dicentrics, and rings. | |
| *In vivo* cytogenetics | Hmn-lymphocytes | Ihl | 20–150 ppm | R-66 |
| TEST CONDITIONS Lymphocytes from humans who were exposed occupationally to VC for periods ranging from 10 to 27 Y to concentrations most frequently between 20 and 150 ppm were examined. | | | RESULTS Of the examined lymphocytes from exposed workers, 5.2% had chromosomal aberrations as compared with 1.8% in the control workers. The aberrations included chromatid and chromatin breaks; chromatid and chromosome exchanges were frequent. | |

**MUTAGENICITY: CHROMOSOMAL EFFECTS – POSITIVE REFERENCES** R-3, R-28, R-49, R-60, R-64.

**MUTAGENICITY: CHROMOSOMAL EFFECTS – NEGATIVE REFERENCES** R-55.

**MUTAGENICITY: DNA DAMAGE/REPAIR – POSITIVE REFERENCES** R-20, R-49.

## ■ MUTAGENICITY: DNA DAMAGE/REPAIR STUDIES

| Assay Type | Species/Cell Type | Route | Doses | Ref |
|---|---|---|---|---|
| SCE | Chinese ham | Ihl | 1.25 or 2.5% | R-49 |

TEST CONDITIONS Groups of 4 adult chinese hamsters (10–15 W old) were used in a 1:1 male to female ratio. Hamsters were exposed to VC 6, 12, and 24 H at concentrations of 1.25 or 2.5% (v/v). The Brd-U-tablet method was used to obtain *in vivo* induced sister chromatid exchanges (SCE).

RESULTS The number of *in vivo* induced SCEs depended on dose and length of exposure to VC. Data were analyzed statistically using the t-test. The 6 H exposure of the low dose doubled the SCE frequency with 4.41 SCEs/cell in controls, and 8.72 in the experimental group. Lengthening of exposure time increased frequency of SCE. After 12 H, 17.51 SCEs/cell were found and 22.33/cell were found after 24 H exposure. SCE frequency increased in all exposure-time-groups after exposure to 2.5% as compared to the lower dose: 12.66 (6 H), 19.80 (12 H). The highest measured effects were 33.25 SCEs/cell after a 24 H exposure to 2.5% VC.

| | | | | |
|---|---|---|---|---|
| SCE | Hmn-lymphocytes | Ihl | 20–150 ppm | R-66 |

TEST CONDITIONS Lymphocytes from humans who were exposed occupationally to VC for periods of 10–27 Y (to concentrations most frequently between 20 and 150 ppm) were examined.

RESULTS The number of sister chromatid exchanges was increased from 9.41 to 13.80 per lymphocyte.

| | | | | |
|---|---|---|---|---|
| Mitotic gene conversion | *Saccharomyces cerevisiae* | | 16 and 48 mM | R-20 |

TEST CONDITIONS VC was bubbled through a liquid cell suspension to give concentrations of 16 and 48 mM. The assay was performed in the presence and absence of purified mouse liver microsomes. Induction of gene conversion was measured at the ade 2 and trp 5 loci of this strain of yeast.

RESULTS Both gene conversion systems (ade 2 and trp 5) showed a positive response which was dependent on the presence of purified mouse liver microsomes.

**MUTAGENICITY: OTHER STUDIES** A prophage lambda induction test was conducted using 0.1 mL of 20% VC in DMSO/plate. The test used activated microsomal enzymes (S-9) from livers of rats induced with Aroclor. Results were negative (no other data or statistical analysis given). (R-21)

**TERATOGENICITY: MAMMALS–NEGATIVE REFERENCES** R-15, R-26.

## ■ TERATOGENICITY: MAMMALIAN STUDIES

| Species | Route | Doses | Dosing Schedule | Ref |
|---|---|---|---|---|
| Rat | ihl | 2,000, 7,000, 12,000 ppm | 2.5 H on D 18 | R-26 |

TEST CONDITIONS Groups of 3 pregnant CFY rats were exposed to VC at 2,000, 7,000 or 12,000 ppm in air for 2.5 H on the 18th D of pregnancy.

RESULTS VC was shown to be present in the fetal and maternal blood as well as in the amniotic fluid, indicating the permeability of the placenta to the agent.

## ■ TERATOGENICITY: MAMMALIAN STUDIES *(Continued)*

| *Species* | *Route* | *Doses* | *Dosing Schedule* | *Ref* |
|---|---|---|---|---|
| Rat | Ihl | 1,500 ppm | 24 H/D | R-26 |

TEST CONDITIONS Pregnant (first trimester) CFY rats (13–28/group) were allocated to experimental groups as follows: Groups IA, IC, IIA, and IIIA inhaled air in an inhalation chamber for 24 H/D on days of pregnancy 1–9, 8–14, 8–14, and 14–21, respectively; Groups IB, ID, IIB, and IIIB were exposed to VC (4,000 mg/m³) or approximately 1,500 ppm, for the same length of time during the same periods of gestation as their respective controls. The rats in groups IC and ID were given, subcutaneously, 2 injections (50 mg/kg bw) of trypan blue (1% solution) on the 7th and 8th D of gestation. Group IV was another control. On the 21st D of gestation, the position of fetuses living, dead, or resorbed was noted. Fetuses and placentae were excised and weighed, and macroscopic examination was carried out. The t-test was used for statistical comparison of means. The Mann-Whitney U-test was used to compare number affected/total fetuses ratio.

RESULTS The maternal liver weight and liver weight/body weight ratio increased in response to trypan blue as well as to VC applied in the 1st or 2nd W of pregnancy ($p < 0.01$ and $p < 0.05$). The number of resorbed fetuses as well as fetal loss (% total implants) was significantly increased in the group exposed to VC during the first 9 D of pregnancy ($p \leq 0.05$). Author concluded that VC in itself has no teratogenic effect on CFY rats, but an embryotoxic effect during the early stages of pregnancy (at 1,500 ppm). Fetal losses and induction of central nervous system malformations due to trypan blue administration were not potentiated by a combined exposure of pregnant rats to VC and the dye.

| | | | | |
|---|---|---|---|---|
| Mus | Ihl | 50, 500 ppm | 7 H/D | R-15 |
| Rat | Ihl | 500, 2,500 ppm | 7 H/D, D 6–15 of gestation | |
| Rbt | Ihl | 500, 2,500 ppm | 7 H/D, D 6–18 of gestation | |

TEST CONDITIONS: Three groups of each species (CF-1 mice, Sprague-Dawley rats, New Zealand rabbits) were tested: control, inhalation of VC only, and inhalation of vinyl chloride and ethanol (15%) in drinking water (ethanol blocks metabolism).

RESULTS While maternal toxicity was observed, VC alone did not produce any significant anomalies when compared to controls ($p > 0.05$). There were significant increases in the number of fetal anomalies in the group that was given 15% ethanol in their drinking water, while receiving 500 ppm VC (mice). Also among mice exposed to VC in combination with 15% ethanol, several skeletal anomalies occurred at an incidence significantly greater than among mice exposed to VC alone (modified Wilcoxon test, $p < 0.05$). Authors concluded that exposure of pregnant mice, rats, and rabbits to VC (ihl) at concentrations high enough to cause maternal toxicity was not teratogenic in any of the 3 species. Exposure of VC alone was not consistently embryotoxic in the 3 species studied. Among mice, at 2,500 ppm, the incidence of resorptions was significantly higher (13%) than among the concurrent controls (7%). Ingestion of 15% ethanol in the drinking water enhanced the toxic effects of the inhaled VC. Maternal toxicity was enhanced to an extent greater than embryotoxicity.

## ■ TERATOGENICITY: HUMAN STUDIES

| *Route* | *Doses* | *Dosing Schedule* | *Ref* |
|---|---|---|---|
| Environmental exposure | NG | NG | R-92 |

TEST CONDITIONS Three Ohio communities that had polyvinyl production facilities were studied. Since 1968, information for specific congenital malformations in Ohio residents has been recorded on birth certificates. Any information recorded under the congenital anomalies section of the certificate was analyzed. Data for deaths resulting from cancer of the central nervous system, leukemia, and lymphomas in the adult population aged 45 Y and older were also analyzed.

RESULTS The findings suggest that mothers living in communities with PVC production facilities gave birth to an excess number of children with congenital malformations as compared to the expected number based on the state average or based on experience in the balance of counties in which these cities are located. With regard to specific malformations, anomalies of the central nervous system appear to be of the greatest concern. Deaths from central nervous system tumors in adult male residents of 2 of the cities were also significantly greater than expected. On a community basis, excess deaths from other cancers were not apparent.

**PLACENTAL TRANSFER: POSITIVE REFERENCE** R-26.

**MAJOR SPECIES THREATENED** Terrestrial life.

**INHALATION LIMIT (Value)** 300.

**INHALATION LIMIT (Text)** *Regulations*: OSHA carcinogen (29CFR* 1910); OSHA PEL (TWA) 1 ppm (29CFR* 1910); OSHA peak 5 ppm/15 min (29CFR* 1910). *Recommendations*: NIOSH ceiling 2.55 mg/m$^3$/15 min; 1 ppm/15 min (CRSOE* PB-246619/NIOSH); ACGIH human carcinogen (TLVADM 83/ACGIH); ACGIH TLV (TWA) 10 mg/m$^3$; 5 ppm (TLVADM 83/ACGIH).

**DIRECT CONTACT** Acts as refrigerant under prolonged contact and as such can cause skin burns.

**GENERAL SENSATION** Sweet-smelling gas. Proposed limits are 1 ppm for 8 H working day, 5 ppm for 15 min average; may be anesthetic above 500 ppm. Handling of uninhibited material has caused circulatory and bone changes. (30ZNA5 0001)

**PERSONAL SAFETY PRECAUTIONS** Gas-tight goggles and breathing apparatus are required in fire areas or where closed environment or poor ventilation causes high vapor concentration. Eye goggles and impervious outerwear are recommended for areas where liquid vinyl chloride may be encountered.

**ACUTE HAZARD LEVEL** Irritant. Moderately toxic when inhaled. Should cause no problem in water. Emits toxic vapors when heated to decomposition.

**CHRONIC HAZARD LEVEL** Chronic exposure has shown liver injury in rats and rabbits. Chronic irritant.

**DEGREE OF HAZARD TO PUBLIC HEALTH** Irritant. Moderately toxic with inhalation. Emits highly toxic vapors when heated to decomposition.

**CARCINOGENICITY INDICATOR** Positive.

## ■ ANIMAL TOXICITY

| *Value (mg/kg)* | *Time* | *Species* | *Param* | *Route* | *Ref* |
|---|---|---|---|---|---|
| 20 ppm | | Hmn | TCLo | Ihl | JWPFA5 0017 |
| 500 | | Rat | $LD_{50}$ | Orl | TXAPA9 0031 |

## ■ CARCINOGENICITY RESULTS

| *Species* | *Strain* | *Sex* | *Route of Admin* | *Tumor Site* | *Lesion Type* | *Ref* |
|---|---|---|---|---|---|---|
| Ham | Golden | | Inh | Liver | | IMEMDT 79190377 |
| Hmn | | | Inh | Liver | | IMEMDT 74070291, IMEMDT 79190377 |
| Hmn | | | Inh | Brain | | IMEMDT 79190377 |
| Hmn | | | Inh | Lung | | IMEMDT 79190377 |
| Mus | Swiss | | Inh | Liver | | IMEMDT 79190377 |
| Mus | Swiss | | Inh | Lung | | IMEMDT 79190377 |
| Mus | Swiss | | Inh | Mammary glands | | IMEMDT 79190377 |
| Rat | Sprague-Dawley | | PO | Liver | | IMEMDT 79190377 |
| Rat | | | Inh | Liver | | IMEMDT 74070291, IMEMDT 79190377 |
| Rat | | | Inh | Lung | | IMEMDT 79190377 |
| Rat | | | Inh | Kidney | | IMEMDT 79190377 |
| Rat | | | Inh | Ear (Zymbal gland) | | IMEMDT 79190377 |

## ■ MUTAGENICITY TESTING RESULTS

| *Strain* | *Indicator* | *Met Act* | *Method* | *Test System* | *Ref* |
|---|---|---|---|---|---|
| G-46 | | R, L, S-9, PB | Desiccator | Ames *Salmonella typhimurium* | IJCNAW 75150429, BBRCA9 75630363 |
| TA100 | | R, L, S-9, PB, A | Desiccator | Ames *S. typhimurium* | PNASA6 75725135, DTESD7 77020249 |
| TA1530 | | R, L, S-9, PB | Desiccator | Ames *S. typhimurium* | BBRCA9 75630363, IJCNAW 75150429 |
| TA1535 | | R, L, S-9, PB | Desiccator | Ames *S. typhimurium* | IJCNAW 75150429, BBRCA9 75630363, PNASA6 75725135 |
| TA98 | | R, L, S-9, PB | Desiccator | Ames *S. typhimurium* | PNASA6 75725135 |

## ■ GENE MUTATION RESULTS*

| *Assay Code* | *Assay* | *Species* | *Endpoint Code* | *Result Code* |
|---|---|---|---|---|
| CY8 | In vivo cytogenic lymphocyte/leucocyte | Human | C | Positive |
| DLT | Dominant lethal test | Rodents | C; G | Negative |
| MST | Mouse spot test | Mouse | M | Negative |
| PGM | Plant gene mutation | All tests | M | Positive, D |
| RE2 | DNA repair-deficient bacteria | *E. coli* polA (&3110-P3478)-all test with S-9 | N | Positive |
| SRL | Sex-linked recessive lethal test | *Drosophilia melanogaster* | M | Positive |
| YEC | Gene conversion test | *Saccharomyces cervisiae* | C | Positive;M |
| YEH | Recombination or gene conversion | *S. cervisiae* | C | Negative |
| YEY | Forward mutation | *Schizosaccharomyces pombe* | M | Positive;M |
| DHT | Heritable (reciprocal) translocation test | *D. melanogaster* | C | Negative |
| CCG | Gene-Tox Carcinogenicity Panel's list of chemicals | NR | I | Positive |
| SAL | Histidine reversion test | *Salmonella typhimurium* | G | Positive |

*Parameter type: health effects; genetic mutation studies
Chemical type: test

## ■ SUMMARY TABLE

| *Endpoint Code* | *Endpoint* | *Findings* |
|---|---|---|
| C | Chromosomal effect | 2 Positive; 3 negative; 1 MA (6) |
| M | Gene or point mutations | 3 Positive; 1 negative; 1 MA; 1 D |
| N | DNA-related effects | 1 Positive (1) |
| G | General group; may include several endpoints | 1 Positive; 1 negative (2) |
| I | Unidentified assays | 1 Positive (1) |

MA = a metabolic activation system used as part of the experimental protocol for the given in vitro test.
D = a dose effect when paired with a positive response.

## GASTROINTESTINAL ABSORPTION AND TOXICITY

■ **CHEMICAL TYPE** Test.

**PURITY** Not reported.

**CHEMICAL CHARACTERISTICS** $^{14}C$ labeled.

**OTHER CHEMICALS PRESENT** No.

**STUDY PURPOSE** Absorption (administration route involves the gastrointestinal tract), distribution (blood and tissues), metabolism (analyses are made up for the unchanged drug or metabolites), excretion (urine, feces, bile, or other excretory products are analyzed for presence of the drug, metabolites, or radiolabel).

**ORGANISM CLASS** Rodent.

**SPECIES NAME** Rat.

**STRAIN** Sprague-Dawley.

**TEST DURATION** 72 H.

**ROUTE/METHOD** Oral.

**REFERENCE** Watanabe, P.G., G.R. McGowan, ar P.J. Gehring. 1976. Fate of $^{14}C$-vinyl chloride aft single oral administration in rats. *Toxicol Appl Pha macol* 36(2): 339–352.

■ **CHEMICAL TYPE** Test.

**PURITY** 95% or greater purity.

**CHEMICAL CHARACTERISTICS** Solution, 99.9% pur

**OTHER CHEMICALS PRESENT** No.

**STUDY PURPOSE** Distribution (blood only)

**ORGANISM CLASS** Rodent.

**SPECIES NAME** Rat.

**STRAIN** Wistar.

**TEST DURATION** 150 min.

**ROUTE/METHOD** Intravenous.

**REFERENCE** Withey, J.R. 1976. Pharmacodyna ics and uptake of vinyl chloride monomer admi

tered by various routes to rats. *J Toxicol Environ Health* 1(3):381–394.

■ **CHEMICAL TYPE** Test.

**PURITY** 95% or greater purity.

**CHEMICAL CHARACTERISTICS** Solution, 99.9% pure.

**OTHER CHEMICALS PRESENT** No.

**STUDY PURPOSE** Absorption (administration route involves the gastrointestinal tract), distribution (blood only).

**ORGANISM CLASS** Rodent.

**SPECIES NAME** Rat.

**STRAIN** Wistar.

**TEST DURATION** 6 H.

**ROUTE/METHOD** Oral, gavage.

**REFERENCE** Withey, J.R. 1976. Pharmacodynamics and uptake of vinyl chloride monomer administered by various routes to rats. *J Toxicol Environ Health* 1(3):381–394.

## AQUATIC TOXICITY

■ **PARAMETER TYPE** Environmental studies; bioconcentration factor data.

**CHEMICAL TYPE** Test.

**CHEMICAL CHARACTERISTICS** $^{14}C$ label, > 99%.

**STUDY PURPOSE** Bioconcentration factor data.

**STUDY RELIABILITY** 3. Studies assigned a reliability code of 3 do not meet the criteria for quality testing and are generally characterized by: (1) control mortality unsatisfactory (e.g., greater than 10% and not accounted for statistically); (2) methods section shows weakness in experimental procedures or insufficient description to judge quality of experimental design; (3) static test with unmeasured concentration conducted improperly (e.g., in the presence of precipitate or some undisolved chemical, or in an unacceptable container).

**ORGANISM CLASS** Crustacean.

**SPECIES NAME** *Daphnia magna*; water flea.

**AGE/LIFE STAGE** Not reported.

**ROUTE/METHOD** Static.

**EXPOSURE REGIMEN** 72 D.

**CONTROLS** Indeterminate (source document does not provide enough information regarding controls).

**GENERAL TEST CONDITIONS** Freshwater; laboratory study.

**TEMPERATURE (C)** 26.7.

**HARDNESS** Not reported.

**ALKALINITY** Not reported.

**DISSOLVED $O_2$** Not reported.

**pH** Not reported.

**EFFECT ENDPOINT TYPE** Bioconcentration factor data (Calc).

**EFFECT ENDPOINT VALUE** 0.19.

**OTHER ENDPOINT DATA** Partition coefficient, metabolism, photolysis, sediment.

**MEASURED/UNMEASURED** Measured.

**REMARKS** Closed aquatic model ecosystem with mixed species. Nominal conc reported.

**REFERENCE** Lu, P.Y., R.L. Metcalf, N. Plummer, and D. Mandel. 1977. The environmental fate of three carcinogens: Benzo-(alpha)-pyrene, benzidine, and vinyl chloride evaluated in laboratory model ecosystems. *Arch Environ Contam Toxicol* 6(2–3):129–142.

■ **PARAMETER TYPE** Environmental studies; aquatic toxicity or effects data.

**CHEMICAL TYPE** Test.

**CHEMICAL CHARACTERISTICS** Not reported.

**STUDY PURPOSE** Other.

**STUDY RELIABILITY** 4. Studies assigned a reliability code of 4 are either an abstract or a foreign paper, or they have not been reviewed prior to their inclusion.

**ORGANISM CLASS** Algae; cyanaphyta.

**SPECIES NAME** *Anacystis aeruginosa*; blue-gree alga.

**AGE/LIFE STAGE** Not reported.

**ROUTE/METHOD** Static.

**EXPOSURE REGIMEN** Not reported.

**CONTROLS** Indeterminate (source document does not provide enough information regarding controls).

**GENERAL TEST CONDITIONS** Not reported; laboratory study.

**TEMPERATURE (C)** 27.

**HARDNESS** Not reported.

**ALKALINITY** Not reported.

**DISSOLVED $O_2$** Not reported.

**pH** 7.0.

**EFFECT ENDPOINT TYPE** Mortality.

**EFFECT ENDPOINT VALUE** 105,000 µg/L.

**OTHER ENDPOINT DATA** Not reported.

**MEASURED/UNMEASURED** Unmeasured.

**REMARKS** Toxicity threshold.

**REFERENCE** Bringmann, G., and R. Kuhn. 1978. Grenzwerte der Schadwirkung Wassergefahrdender Stoffe Gegen Blaualgen (*Microcystis aeruginosa*) und Grunalgen (*Scenedesmus quadricuada*) Im. . .*Vom Wasser* 50:45–60.

■ **PARAMETER TYPE** Environmental studies; aquatic toxicity, or effects data.

**CHEMICAL TYPE** Test.

**CHEMICAL CHARACTERISTICS** Not reported.

**STUDY PURPOSE** Other.

**STUDY RELIABILITY** 4. Studies assigned a reliability code of 4 are either an abstract or a foreign paper, or they have not been reviewed prior to their inclusion.

**ORGANISM CLASS** Algae.

**SPECIES NAME** *Chilomonas paramecium*; cryptomonad flagellate.

**AGE/LIFE STAGE** Not reported.

**ROUTE/METHOD** Other.

**EXPOSURE REGIMEN** 48 H.

**CONTROLS** Indeterminate (source document does not provide enough information regarding controls).

**GENERAL TEST CONDITIONS** Not reported; labatory study.

**TEMPERATURE (C)** 20.

**HARDNESS** Not reported.

**ALKALINITY** Not reported.

**DISSOLVED $O_2$** Not reported.

**pH** 6.9.

**EFFECT ENDPOINT TYPE** Population growth, 5% decreased cell count.

**EFFECT ENDPOINT VALUE** 943,000 µg/L.

**OTHER ENDPOINT DATA** Not reported.

**MEASURED/UNMEASURED** Unmeasured.

**REMARKS** Composition described.

**REFERENCE** Bringmann, G., R. Kuhn, and A. Winter. 1980. Bestimmung der Biologischen Schadwirkung Wasserge-Fahrdender Stoffe Gegen Protozoen III. Saprozoische Flagellaten. *Z Wasser Abwasser Forsch* 13(5):170–173.

## DERMAL ABSORPTION AND TOXICITY

■ **PARAMETER TYPE** Health effects; absorption, distribution, metabolism, excretion.

**CHEMICAL TYPE** Test.

**PURITY** 95% or greater purity.

**CHEMICAL CHARACTERISTICS** 99.9% pure $^{14}C$ labeled vapor.

OTHER CHEMICALS PRESENT No.

STUDY PURPOSE Absorption, distribution, excretion.

ORGANISM CLASS Primate.

SPECIES NAME Monkey.

STRAIN Rhesus.

AGE/LIFE STAGE Not reported.

WEIGHT 4–5 kg.

GROUP INFORMATION One group of one member.

SEX Male.

TEST DURATION 2 H.

ROUTE/METHOD Dermal, topical-vapor, isolated, restrained.

EXPOSURE REGIMEN 1 × for 2 H.

SITE/AREA Whole body.

CONTROLS Not reported.

CONCENTRATION/DOSE RANGE 3,423 mg.

REMARKS Exposure regimen: 2.5 H.

REFERENCES Hefner, R.E. Jr., P.G. Watanabe, and P.J. Gehring. 1975. Percutaneous absorption of vinyl chloride. *Toxicol Appl Pharmacol* 34:529–532.

■ PARAMETER TYPE Health effects; absorption, distribution, metabolism, excretion.

CHEMICAL TYPE Test.

PURITY 95% or greater purity.

CHEMICAL CHARACTERISTICS 99.9% pure $^{14}C$ labeled vapor.

OTHER CHEMICALS PRESENT No.

STUDY PURPOSE Absorption, distribution, excretion.

ORGANISM CLASS Primate.

SPECIES NAME Monkey.

STRAIN Rhesus.

AGE/LIFE STAGE Not reported.

WEIGHT 4–5 kg.

GROUP INFORMATION One group of one member.

SEX Male.

TEST DURATION 2.5 H.

ROUTE/METHOD Dermal, topical-vapor, isolated, restrained.

EXPOSURE REGIMEN Once for 2.5 H.

SITE/AREA Whole body.

CONTROLS Not reported.

CONCENTRATION/DOSE RANGE 391 mg.

REMARKS Exposure regimen: 2 H.

REFERENCE Hefner, R.E. Jr., P.G. Watanabe, and P.J. Gehring. 1975. Percutaneous absorption of vinyl chloride. *Toxicol Appl Pharmacol* 34:529–532.

## ■ ACUTE TOXICITY: TERRESTRIAL LIFE—INHALATION $LC_{50}$

| *Species* | *$LC_{50}$ (mg/m³)* | *Duration (H)* | *Ref* |
|---|---|---|---|
| Mus | 305,500 | 2 | R-11 |
| Mus | 68,550 | 2 | R-114 |

TEST CONDITIONS A total of 536 white mice were tested in Pravdin-type gas chambers. Ten concentrations were used.

RESULTS The $LC_{50}$, found using the Behren's method was 27,419 ppm (1 ppm = 2.5 mg/m³ under test conditions). The $LC_{10}$ was 139,975 ppm.

■ **ACUTE TOXICITY: TERRESTRIAL LIFE – INHALATION $LC_{50}$** *(Continued)*

| *Species* | *$LC_{50}$ (mg/m³)* | *Duration (H)* | *Ref* |
|---|---|---|---|
| Rat | 119,100 | 2 | R-114 |
| | TEST CONDITIONS A total of 70 rats were tested at 5 concentrations of VC in a Pravdin-type gas chamber. | RESULTS The $LC_{50}$, determined using Behren's method, was 47640 ppm (1 ppm = 2.5 mg/m³ under test conditions). The $LC_{100}$ was 208,425 ppm. | |
| Gpg | 590,000 | 2 | R-114 |
| | TEST CONDITIONS A total of 30 guinea pigs were tested at 5 concentrations of VC in a Pravdin-type gas chamber. | RESULTS The $LC_{50}$, determined using Behren's method, ws 236,215 ppm (1 ppm = 2.5 mg/m³ under test conditions). The $LC_{100}$ was 277,900 ppm. | |
| Rbt | 590,000 | 2 | R-114 |
| | TEST CONDITIONS A total of 20 rabbits were tested at 5 concentrations of VC in Pravdin-type gas chambers. | RESULTS The $LC_{50}$, determined using Behren's method, was 236,215 ppm (1 ppm = 2.5 mg/m³ under test conditions). The $LC_{10}$ was 277,900 ppm. | |
| Mus | 293,750 | 2 | R-117 |
| Rat | 390,000 | 2 | |
| Gpg | 595,000 | 2 | |
| Rbt | 595,000 | 2 | |
| | TEST CONDITIONS Experiments were carried out in a 580 L chamber of the Pravdin type. The animals were exposed to various concentrations of VC for 2 H. After animals were placed in the chamber, gas was introduced at the beginning at the lower part of the chamber without any ventilation. Gas was measured volumetrically. A total of 536 mice, 70 rats, 30 guinea pigs, and 20 rabbits were used. $LD_{50}$ values were calculated according to the Behrens method. | | |

**ACUTE TOXICITY: TERRESTRIAL LIFE – OTHER STUDIES** ■ For mice, the smallest concentration fatal in 10 min is 10–12 mmole/L (about 25–30% volume). The smallest narcotic concentration is about 3.5–5 mmole/L (8–12% volume). Death occurs due to respiratory paralysis with resultant heart arrest. At a concentration of 7 mmols in air, vinyl chloride anesthetizes rabbits and dogs within a minute. Recovery is rapid with no apparent adverse effects, even after prolonged anesthetization. (R-115) ■ Single exposure of guinea pigs to vinyl chloride gas at 250 mg/L in air resulted in narcosis and death within 30–60 min. Lower concentrations resulted in ataxia and narcosis. Pathology examination revealed congestion and edema of lungs and hyperimia of kidneys and liver. (R-11) ■ Vinyl chloride was considered for use as an anesthetic because of its narcotic properties and low acute inhalation toxicity. However, studies with dogs found that vinyl chloride caused cardiac irregularities at anesthetic concentrations. (R-106) ■ EEG's in rats were altered following oral administration of vinyl chloride, and the alteration varied with sex. Vinyl chloride at 45 and 135 mg/kg altered learning ability. The compound at 12 mg/kg had immunosuppressant activity in rabbits. (R-36) ■ Guinea pigs exposed to 5–7% concentration of vinyl chloride lived only 1 H following exposure; exposure to 2.5% resulted in an 8 H survival time following exposure. Exposure to 1.5% for 1 H or to 0.5% for 8 H had no effect. (R-114) ■ Five mice, 5 rats, and 5 guinea pigs were exposed to concentrations at 10, 20, and 30% for 30 min. At 10% concentrations, the animals became agitated, then had unconscious movements, and some fell in a state of narcosis. At 20%, the animal's symptoms were salivary secretion, narcosis, and respiratory failure. At 30%, all these symptoms occurred faster. Dead animals showed lung, hepatic, and renal congestion, lung edema, and hepatic degeneration.

(R-114) ■ Mice, rats, guinea pigs, and rabbits were tested to determine acute toxicity levels, symptoms of toxicity, and pathologic effect on the organs. Exposure was for 2 H in a gas chamber. Animals exposed to vinyl chloride gas without homogenization (no ventilation) died at concentrations 3 times lower than when the gas was stirred up continuously. The most common symptom in all animals was a state of narcosis, usually attained during the first hour. Narcosis proceeded from excitment to tranquility to falling down. These symptoms included muscular contractions, tanico-clonic convulsions, respitory disturbances, bradypnea, Cheyne-Stokes type respiration, and finally death by respiratory failure. Circulatory disturbances were noted also. Animals that survived 2 H exposure rapidly regained a normal appearance. Autopsy revealed congestion of the lungs, liver, kidneys, brain, and spleen. Some animals also showed pulmonar edema, marmorated liver, and slight tumefaction of the kidneys.(R-114)

**ACUTE TOXICITY: HUMAN STUDIES** ■ Two Canadian workers died following acute exposure to vinyl chloride gas; autopsies discovered congestion of the liver, spleen, and kidneys. (R-11) ■ Workers exposed to vinyl chloride reported symptoms of euphoria and intoxication. Irritation of the respiratory tract, chronic bronchitis, headache, irritability, poor memory, and weight loss were also noted. (R-11) ■ A 3-min exposure to 2.5% vinyl chloride produced a dizziness and disorientation in humans. (R-113)

## ■ ACUTE TOXICITY: AQUATIC LIFE—OTHER FRESHWATER STUDIES

| *Species* | *Duration (H)* | *Effect Level (mg/L)* | *Ref* |
|---|---|---|---|
| Northern pike (*Esox lucius*) | 240 | 388 | R-67 |

RESULTS The 10 D $LD_{100}$ Northern Pike (*Esox lucius*) was 388 ppm. Fifteen fish were exposed to 388 ppm in 15–20 gallon tanks. Within 10 D all had died. First indication of toxicity was loss of scales. This phenomenon was followed by appearance of a gray white ulcerated area surrounded by indurated borders. A lack of neutrophilic response also was noted. Twenty fish from uncontaminated Illinois Benedictine Lake were used as controls. After 120 D, 1 fish died due to mechanical injury. (R-67)

## ■ SUBACUTE–CHRONIC EFFECTS: TERRESTRIAL LIFE

| *Species* | *Route* | *Doses* | *Dosing Schedule* | *Ref* |
|---|---|---|---|---|
| Rat | Ihl | 30,000 ppm | 4 H/D, 5 D/W for 12 mos | R-12 |

TEST CONDITIONS Twenty-five rats were sacrificed in lots at 20 D intervals after 12 mos of exposure.

RESULTS After 10 mos, some animals showed decrease in weight, aggressiveness to outside stimuli, and disturbed equilibrium. Thirteen animals died from cardiorespiratory complications. Two animals died from hematoperitoneum. Most exposed animals showed pathological degeneration of the brain, liver, kidneys, and thyroid. Six rats showed histopathological alterations of the skeleton. Degeneration of skeleton and connective tissue was similar to that observed in human acroosteolysis of the hands.

## ■ SUBACUTE–CHRONIC EFFECTS: TERRESTRIAL LIFE *(Continued)*

| *Species* | *Route* | *Doses* | *Dosing Schedule* | *Re* |
|---|---|---|---|---|
| Rbt | Ihl | 9–10 mg/L | 4 H/D for 5.5 mos | R- |

RESULTS After 5.5 mos exposure to VC, altered beta-waves (frequency > 80 Hz) appeared on the electroencephalogram from the anterior hypothalmic nuclei, and potentials of the anterior and posterior nuclei increased by 18–30% and 70–85%, respectively, over control values. Concommitant changes in the cardiovascular system (bradycardia, arrhythmia, decreased voltage of electrocardiogram peaks or whole complexes, decreased duration of systole, increased arterial pressure, and retarded blood flow) also occurred. Functional changes in the anterior and posterior hypothalmic nuclei may have a role in pathogenesis of toxic angioneurosis due to VC.

| | | | | |
|---|---|---|---|---|
| Rat | Ihl | 0.03–0.04 mg/L | 5 mos | R- |

RESULTS Chronic exposure of rats to VC disrupted cardiac work rhythm, induced bradycardia and arrhythmia, and reduced the relative duration of I-II and T-II sound intervals. The relative duration of the Q-T complex did not change significantly. Within 15 D after termination of exposure, the rat cardiac activity rhythm returned to normal, but the duration of I-II and T-II sound intervals remained below the initial levels for another 15 D. The author concluded that the maximal permissible concentration of VC is significantly less than 0.03 mg/L.

| | | | | |
|---|---|---|---|---|
| Rat | Ihl | 5,000 ppm | 7 H/D, 5 D/W for 52 W | I |

TEST CONDITIONS Eighty male and female Wistar rats were used. A control group also was used.

RESULTS After 4, 13, 26, and 52 W, 10 rats/sex/group were sacrificed and subjected to extensive examinations as to growth, mortality, hematology, clinical chemistry, and organ weights. Slight growth retardation throughout the experimental period and high mortality in the second half of the study were observed in the VC-exposed animals. Some of the hematological parameters and biochemical blood parameters were influenced by VC after an experimental period of 52 W only. Blood clotting time was shorter in rats exposed to vinyl chloride monomer (VCM) than in the controls. There were minor indications of increase potassium contents of the blood serum in VCM-exposed animals during the first half of the experimental period. The kidneys were adversely affected by VCM as indicated by increased blood urea nitrogen levels and relative kidney weights. After 52 W, increased weights of heart and spleen and slight signs of anemia were noticed in VCM-exposed rats.

| | | | | |
|---|---|---|---|---|
| Mus | NG | NG | Up to 6 mos *in vitro* | |

RESULTS Electron microscopic studies of mouse liver exposed to vinyl chloride monomer for up to 6 mos revealed changes mainly in and around sinusoids and in sinusoidal lining cells, particularly with only mild alteration of hepatocytes. The angiosarcomas which developed in some mice arose from the sinusoidal lining cells.

## ■ SUBACUTE–CHRONIC EFFECTS: TERRESTRIAL LIFE *(Continued)*

| *Species* | *Route* | *Doses* | *Dosing Schedule* | *Ref* |
|---|---|---|---|---|
| Rat | Ihl | 5,000 ppm | 7 H/D, 5 D/W for 52 W | R-3. |

TEST CONDITIONS After exposure to 0 ppm (control) or 5,000 ppm, 62 male and 62 female Wistar rats were sacrificed (at 4, 13, 26, and 52 W) and subjected to extensive examinations. Descriptions of morphological changes observed in respiratory tract, ceruminous glands, brain, kidney, heart, and spleen were noted.

RESULTS The VC effects included increased degree of tubular nephrosis, mild focal [illegible] of the myocardia, and increased haemo[illegible] activity in the spleen.

| | | | | |
|---|---|---|---|---|
| Mus, rat | Ihl | 50, 250, 10,000 ppm | 6 H/D, 6 D/W for up to 1 Y | R-4! |

RESULTS Exposure of albino [illegible] mice (50 of each sex), 2 mos old, to 1,000 ppm of VC [illegible], were acute deaths with toxic hepatitis and marked tubular necrosis of the renal cortex. Starting with the 1st mo, mice exposed to 50 or 250 ppm VC became lethargic, lost weight quickly, and died. Only a few mice exposed to 50 ppm survived for 12 mos. Pulmonary macrophage [illegible] was elevated in some mice. In rats (groups of 50 male and 36 female CD), exposure to 1,000 ppm VC resulted in slightly depressed body weight of the females. Exposures of 250 or 1,000 ppm caused a number of deaths.

| | | | | |
|---|---|---|---|---|
| Rat | Ihl | 50, 500, 20,000 ppm | 10 mos | R-45 |

TEST CONDITIONS The activity of microsomal cytochrome P-450 monooxygenase and ultrastructure of the liver were studied in rats exposed dynamically to 50, 500, and 20,000 ppm VC over 10 mos.

RESULTS After 1 and 3 mos of exposure to 50 and 20,000 ppm VC, the level of cytochrome P-450 was slightly lower than in the control animals. After termination of exposure, it was restored to the control level, accompanied by a slight increase of activity of [illegible]peroxisome. Liver enlargement, developed at the onset of exposure, was accompanied by ultrastructural alterations beginning in the 3rd mo of exposure to all concentrations of VC. Development of hepatic steatosis, hypertrophy of smooth and rough endoplasmic reticulum, swelling of mitochondria, accumulation of lipid droplets, focal cytoplasmic degradation) also occurred.

| | | | | |
|---|---|---|---|---|
| Rat | Ihl | 50, 500, 20,000 ppm | 5 H/D, 5 D/W for 10 mos | R-48 |

TEST CONDITIONS A total of 340 male Wistar rats, 180–220 g, were exposed to VC at concentrations of 50, 500, and 20,000 ppm, 5 H/D, 5 D/W for 10 mos.

RESULTS Morphological lesions in liver and testes, detected by light and electron microscopy, intensified with duration of exposure. After 1 mo of treatment, difference from controls was statistically significant ($p < 0.05$) at all levels of VC exposure. Absolute and relative weights of spleen, liver, kidneys, heart, and testes were elevated significantly in some groups of treated animals, the difference being most pronounced in spleen and dose-related for both liver and kidneys. The no-effect level of VC could not be established. The lowest concentration of VC (50 ppm) still caused adverse effects in rats, including slight hematological and biochemical changes and fluctuations, as well as ultrastructural changes in hepatocytes and a tendency for increased incidence of histological liver alterations. Statistical analysis employed the Students' t-test.

## ■ SUBACUTE–CHRONIC EFFECTS: TERRESTRIAL LIFE *(Continued)*

| *Species* | *Route* | *Doses* | *Dosing Schedule* | *Ref* |
|---|---|---|---|---|
| Dog | Ihl | 10%, 20% volume in air | 7 X/3 W, for 3 H each exposure | R-11 |
| | | | RESULTS At 10% volume, dogs showed no considerable changes in liver and kidneys. At 20% volume, there was respiratory paralysis and strong flow of saliva; after necrosis, vomiting occurred. | |

## ■ SUBACUTE–CHRONIC EFFECTS: HUMAN STUDIES

| *Route* | *Doses* | *Dosing Schedule* | *Ref* |
|---|---|---|---|
| NG | NG | Occupational | R-5 |
| | TEST CONDITIONS An epidemiological study was performed covering 5,011 employees with 21,510 man-years experience in various phases of VC and PVC manufacturing in 32 plants throughout the U.S. and Canada. | RESULTS The total number of definitive cases of acroosteolysis (AOL) was 25; 16 other individuals were under suspicion. This condition is clearly associated with the hand cleaning of polymerizers. Workers engaged in other phases of VC or PVC manufacturing do not appear to be at risk for developing AOL. AOL appears to be a systemic rather than local disease. At present neither the etiological agent nor its portal of entry is known. | |
| NG | NG | Occupational | R-6 |
| | | RESULTS Two cases of acroosteolysis occurring in men engaged in the polymerization of VC are described. The bones affected were the terminal phalanges of the fingers and the sacroiliac joints, but in one case the patella and in the other the phalanges of the feet were involved. The condition was accompanied by Raynaud's phenomenon and skin lesions. | |
| NG | NG | Occupational | R-9 |
| | TEST CONDITIONS The cohort of workers employed in a Swedish VC/PVC plant since its start in the early 1940s has been followed for mortality and cancer morbidity patterns. Only 21 of the 771 persons could not be traced. Difficulties in establishing exposure levels at different work ares in the past makes an evaluation of dose-effect relationships impossible. | RESULTS A four- to five-fold excess of pancreas/liver tumors was found, including 2 cases later classified as angiosarcomas of the liver. The numbers of brain tumors and suicides do not deviate significantly from expected. Cardiovascular and cerebrovascular diseases, on the other hand, differ significantly from the expected. | |
| Ihl, dermal | NG | NG | R-8 |
| | | RESULTS VC is a skin irritant, and contact with liquid may cause frostbite upon evaporation. VC gas depresses the central nervous system. Lightheadedness, some nausea, and dulling of visual and auditory responses may develop in acute exposures. Chronic exposure of workers may result in acro-osteolysis, Raynaud's phenomenon, and sclerodermatus skin changes. Chronic exposure also may cause hepatic damage. | |

## ● SUBACUTE–CHRONIC EFFECTS: HUMAN STUDIES *(Continued)*

| | *Doses* | *Dosing Schedule* | *Ref* |
|---|---|---|---|
| NG | NG | Occupational | R-11 |

RESULTS There are numerous clinical indications that chronic exposure to VC is toxic to humans. Hepatitis-like liver changes, angioneurosis of a spastic character, Raynaud's syndrome, scleroderma-like skin changes, lytic lesions of the terminal phalanges in hands and feet, and pseudoclubbing of the fingers have been reported in many workers in the U.S. and Europe. The latter conditions have been termed occupational acro-osteolysis. Other long-term effects include functional disturbances of the CNS with adrenergic sensory polyneuritis, thrombocytopenia, splenomegaly, liver malfunction with marked fibrosis in the portal areas, and pulmonary insufficiency with restrictive changes in the lungs.

| | | | |
|---|---|---|---|
| NG | NG | Occupational for 1 Y | R-11 |

RESULTS Workers exposed to VC for 1 Y showed a decreae of peroxidase, indophenoloxidase, and glutathione levels. Serum levels of gammaglutamic transpeptidase in exposed workers appear to be the best clinical parameter for detecting abnormalities. Alkaline phosphatase, serum glutamic pyruvic transaminase, serum glutamic oxaloacetic transaminase, lactic dehydrogenase, and bilirubin levels also were increased in many cases. Other data suggest that VC disease is an immune-complex disorder. Immunological and immuno-chemical investigations of workers with the syndrome showed presence of circulating immune complexes in 19 of 28 patients

| | | | |
|---|---|---|---|
| NJ | NG | NG | R-43 |

RESULTS Liver function tests showed no difference between exposed workers and controls not exposed to VC, and no cases of angiosarcoma or florid-vinyl chloride induced liver disease. However, of 422 exposed workers, 4 had enlarged spleens, compared with none for 202 controls. Liver biopsies of selected cases showed no significant pathological changes, although there was a minimal increase in portal tract and sinusoidal fibrosis in exposed workers.

| | | | |
|---|---|---|---|
| NG | NG | Occupational | R-44 |

RESULTS Capillary microscopy study showed that 10% or more of workers exposed to VC have capillary abnormalities which were not found in workers without exposure to VC.

| | | | |
|---|---|---|---|
| NJ | NG | NG | R-61 |

RESULTS A cytological examination of the sputa of nearly 4,000 Italian workers in the VC/PVC industry has shown a high incidence of changes in bronchial epithelia, among which squamous dysplasia and atypical adenomatious proliferation were observed.

**PHARMACOKINETICS/METABOLISM** ■ In rats inhaling 20,000 ppm $^{14}C$ vinyl chloride for 5 min $^{14}C$ was found in the liver, bile duct, digestive lumen, and kidneys 10 min from the beginning of the inhalation exposure. The amount of vinyl chloride and its metabolites increased up to 3 H postexposure. Additional deposition sites showing $^{14}C$ activity included urinary tract, salivary glands, lacrimal glands, skin, and thymus. (R-11) ■ The tissue deposition of $^{14}C$ vinyl chloride has been studied. Immediately after exposure by inhalation of 50 ppm vinyl chloride for 5 H in a closed system, the percentage incorporated as $^{14}C$ radioactivity per gram tissue was highest for kidney (2.13%), liver (1.86%), and spleen (0.73%). Labeled material could still be found in these tissues 48 H after the beginning of exposure. (R-11) ■ Present data indicate that VC is metabolized to an activated carcinogen electrophile which is capable of covalently reacting with nucleophilic groups or cellular macromolecules. There is also ample evidence that the mixed function oxidase (MFO) system may be involved in the metabolism of vinyl chloride. Rat liver microsomes catalyze the covalent binding of vinyl chloride metabolites to protein and nucleic acids. Chloroethylene oxide is thought to be the primary microsomal metabolite capable of alkylating these cellular macromolecules. (R-11) ■ The metabolism of vinyl chloride may be inhibited by administering to rats, 320 mg/kg of pyrazole, 1 H prior to inhalation of the gas. Pyrazole is an inhibitor of alcohol dehydrogenase and xanthine oxidase. Pretreatment of rats with ethanol, 5 mg/kg, 95%, also inhibited vinyl chloride metabolism. (R-11) ■ When a mixture of vinyl chloride/oxygen (1:1 v/v) was passed through a medium consisting of liver microsomes from phenobarbitone-pretreated mice, and an NADPH-generating system, a volatile metabolite was formed; this was trapped by its reaction with 4-(4-nitrobenzyl)pyridine, in ethylene glycol. (R-13) ■ Radioactivity from $^{14}C$-labeled vinyl chloride was covalently bound to protein and nucleic acids *in vivo* and *in vitro*, in the presence of rat liver microsomal fractions of highly purified cytochrome P-450 and NADPH-cytochrome P-450 reductase preparations. The ratio of bound to total nonvolatile metabolites increased from the *in vivo* to the microsomal to the purified system. *In vivo*, the total metabolism of $^{14}C$-labeled vinyl chloride was not induced by phenobarbitol pretreatment (0.1% in drinking water for 5 days) in rats exposed to either 10 ppm or 250 ppm of the $^{14}C$ vinyl chloride. However, binding to protein and RNA was enhanced but only at the lower exposure level. *In vitro*, phenobarbitol pretreatment increased microsomal conversion of $^{14}C$ vinyl chloride to both total and bound metabolites. The metabolites of $^{14}C$ vinyl chloride metabolism in an *in vitro* liver microsomal fraction were distributed among many microsomal proteins and not localized to cytochrome P-450. (R-25) ■ $^{14}C$-labeled vinyl chloride was studied in rats. Rats exposed to 10 ppm VC for 6 H eliminated 68% of the absorbed radioactivity in their urine and 2% (as VC) in the expired air over 72 H. Six hour exposures to 1,000 ppm resulted in 56% of the dose appearing in the urine with 12% in the expired air as VC. The pulmonary excretion of VC followed first order kinetics with similar half lives at both treatment levels: 20.4 min at 10 ppm and 22.4 min at 1000 ppm. (R-29) ■ The mechanisms responsible for and protecting against metabolic activation of vinyl chloride were investigated in male Sprague-Dawley rats. They inhaled 5% VC for 18 H. When $^{14}C$ vinyl chloride was incubated with hepatic microsomes, a $^{14}C$-labeled material became irreversibly bound to microsomal proteins. Binding required NADPH, was decreased by CO, SKF-525A (2-diethylaminoethyl 2,2-diphenylvalerate hydrochloride, 75 mg/kg, ipr), or glutathione, and was increased by 1,1,1-trichloropropene-2,3-oxide (TCPO). Inhalation of a 5% vinyl chloride atmosphere decreased hepatic cytochrome P-450 and glutathione. Pretreatment of the animals with DDT or phenobarbital had the following effects: increased *in vitro* irreversible binding to microsomal proteins measured in the presence but not in the absence of TCPO; increased *in vivo* loss of cytochrome P-450 during inhalation of the vinyl chloride; decreased *in vitro* irreversible binding to 10,000 g supernatant proteins; and *in vitro* loss of glutathione during inhalation of vinyl chloride. (R-32) ■ In rats exposed to 400 ppm vinyl chloride for 6 H and then treated ipr with 20 mg 3,4-dichlorobenzenethiol, and again exposed to 400 ppm VC for 12 H S-2-(3,4-dichlorothiophenyl)acetic acid was detected in the urine. Authors concluded that the formation of nucleophilic carcinogens from nonelectrophilic precursors can be proven by the use of nucleophilic reagents *in vitro* as well as *in vivo*. (R-33) ■ Rats were exposed to 5,000 ppm of vinyl chloride, via inhalation, 6 H/D, 5 D/W for 7 W. This VC was nonlabeled. On the last day of repeated exposure, $^{14}C$ VC was used. The fate of the $^{14}C$ VC was compared in a group of rats exposed repeatedly, to a group exposed simultaneously for a single 6 H period to 5,000 ppm of $^{14}C$ VC. The routes and rates of excretion of $^{14}C$ activity were the same for the two experimental groups. The activity of microsomal enzymes, as reflected by aniline hydroxylase and p-nitroanisole-o-demethylase derived from 9,000 g liver supernatants was essentially the same in rats exposed repeatedly or in nonexposed control rats. Covalent binding to hepatic macromolecules was greater in rats repeatedly exposed as compared to those subjected to a single exposure. Thus

repeated exposure to VC does not induce its biotransformation. However, the increase in hepatic macromolecular binding indicates that repeated exposure augments the reaction of electrophilic metabolites with macromolecules, and this may be expected to enhance potential toxicity including carcinogenicity. (R-37) ■ After a 5 H inhalation exposure, rats metabolized $^{14}C$-labeled vinyl chloride much faster than carbon tetrachloride ($CCl_4$). The half life was found to be 1.1 H. The $^{14}C$ vinyl chloride bound covalently to tissue proteins, particularly in the liver. In kidney, small intestine, and other organs much less radioactivity was observed. (R-39) ■ Vinyl chloride uptake rate and proportion metabolized by isolated perfused rat livers remained constant for VC concentrations of 50–25,000 ppm. The overall VC conversion was 14.6% of the offered concentration. ETOH, pyrazole, and 6-bromobenzothiazole inhibits VC metabolism by 12.7, 31.6, and 48.9%, respectively. Phenobarbital and fasting increases VC metabolism by 20.9 and 31. , respectively. VC has no effect on marker enzymes, but slight liver damage occurs after increased metabolic VC transformation. Mixed function oxygenation is apparently involved in VC metabolism. (R-42) ■ The metabolic elimination of vinyl chloride in Rhesus monkeys is a dose-dependent, saturable process, as in rats. Below 200–300 ppm of VC in atm, elimination obeys a 1st-order law. Clearance rate is much closer to that found in man than that for rats, mice, or gerbils. Maximal velocity of metabolic elimination of VC at high concentrations in Rhesus monkeys is only about half that of rats when related to kg body weight. Thus Rhesus monkeys mimic quantitative aspects of VC metabolism better than do rats or mice. (R-46) ■ In the presence of hepatic microsomes, vinyl chloride produced a type I difference spectrum and stimulated coinhibitable NADPH consumption. A comparison of the binding and Michaelis parameters for the interaction of VC with uninduced phenobarbitol-, and 3-methylcholanthrene-induced microsomes, indicates that the binding and metabolism of VC was catalyzed by > 1 type P-450 cytochrome, but predominately by cytochrome P-450. Metabolites of VC from this enzyme system decreased the levels of cytochrome P-450 and microsomal heme, but not cytochrome b5 or NADPH-cytochrome c reductase, *in vitro*. (R-51) ■ Thiodiacetic acid and S-(carboxy-methyl) cysteine were found in the urine of rats after a 48 H exposure to 1000 ppm vinyl chloride. The structures of both compounds were clarified by means of gas-chromatography mass spectroscopy. Chloroethylene oxide, chloroacetaldehyde, and chloroacetic acid are assumed to be intermediates in VC metabolism. Compounds which can be transformed to one of these alkylating agents *in vivo* may also lead to renal excretion of thiodiacetic acid and S-(carboxymethyl)cysteine. (R-54) ■ Strong evidence has been obtained that the biotransformation of vinyl chloride involves microsomal mixed-function oxidase; i.e., the metabolic activation of VC by a liver microsomal system from rats, mice, or humans, depends on the presence of necessary cofactors for a NADPH-generating system and oxygen. Chloroethylene oxide rearranges to 2-chloroacetaldehyde spontaneously. In aqueous solution at pH 7.4 and 37 C, the epoxy compound has a half life of 1.6 min. Chloroethylene oxide is capable of reacting with glutathione and with nucleophilic groups of macromolecules. N-acetyl-S-(2-hydroxyethyl)cysteine (a major metabolite), S-(carboxymethyl)cysteine and N-acetyl-S-vinyl cysteine are metabolites of VC after inhalation or oral administration in rats. Chloroethylene oxide and chloroacetaldehyde alkylate to 4-(4-nitrobenzyl)pyridine and adenosine. Rat liver microsomes catalyze covalent binding of $^{14}C$ vinyl chloride to proteins and nucleic acids. (R-57) ■ Ethylene and its analogues (i.e., vinyl chloride, vinyl bromide) are converted to the corresponding ethylene oxides by cell-free preparations from mature cotyledons of the broad bean (*Vicia faba*). Vinyl chloride acts as a competitive inhibitor in the first order oxidation of ethylene. The measured $K_i$ where $K_i$ (gas) = $3.19 \times 10^{-6}$ M; $K_i$ (liquid) = $1.5 \times 10^{-6}$ M. (R-73) ■ Post-mitochondrial supernatants of liver, kidney, and lung tissue from rats and mice that had been exposed to 20% VCM were assayed for their capacity to generate VCM metabolites mutagenic for *Salmonella typhimurium* TA1530. Data indicate that the liver tissue efficiently converted VCM into mutagenic metabolites. (R-60)

**PHYTOTOXICITY: TERRESTRIAL PLANTS** Research was designed to study the effect of vinyl chloride on the rate of production of excess hydrogen peroxide ($H_2O_2$), which is toxic to germinating oat seeds. The effect of the increased $H_2O_2$ by VC on the sulfhydryl content in germinating seeds and in potatos was studied also. No apparent increase in the $H_2O_2$ level was found when germinated seeds were exposed to 50, 100, or 200 ppm VC gas. Results showed that the amount of $H_2O_2$ gradually increased from 0.35–0.45, 0.65, 0.92, and 1.15 μg $H_2O_2$/g seed when VC gas was successively increased to 300, 400, 500, and 1,000 ppm. The 2,000 ppm VC response was very similar to 1,000 ppm. There was a 10-fold increase in the sulfhydryl content of the seeds after 72 H germination without exposure to VC. The sulfhydryl content was decreased gradually by 5.5, 15.2, 21.7, and 30.4% when VC gas was successively increased to 300, 400, 500, and 1000 ppm. The increased production of $H_2O_2$ in the germinating seeds exposed to VC gas de-

creased their sulfhydryl content and thereby produced adverse effects and caused abnormalities in growth. The conclusion was that threshold levels of VC are > 200 ppm and that saturation level is 1,000 ppm. (R-34)

**OTHER ADVERSE EFFECTS** ■ Male CD-1 mice were exposed to 10, 100, or 1000 ppm vinyl chloride for 2–8 W at 6 H/D, 5 D/W. A slight increase in the spleen weight of mice was noted at the highest level. Spleens were obtained from these animals (4 mice/group after 2, 4, and 8 W exposure) and their lymphocytes cultured *in vitro* with or without the presence of phytomitogens, phytohemagglutinin (PHA), and pokeweed mitogen (PWM). Relative blast formation and the DNA synthesis was measured by the incorporation of $^{3}$H-thymidine in the cultured cells. The response of splenic lymphocytes to the phytomitogens was increased several fold by vinyl chloride exposure. The effects were apparent at 1000 ppm VC after 2 W of exposure and at all levels of VC exposure after 4–8 W. The effects were generally more pronounced at 100 ppm VC exposure than those at 1,000 ppm. *In vitro* culture of splenic lymphocytes from control or VC-exposed mice in the VC atmosphere did not show enhancement of blast formation. Alteration of VC metabolism during the VC exposure *in vivo* yielded results indicating that metabolites of VC may be responsible for the stimulation of lymphocyte transformation observed in splenic cultures. (R-50) ■ Male, but not female, rats were susceptible to the acute hepatotoxic effects of inhaled vinyl chloride. In phenobarbital-pretreated male rats, pyrazole and SKF-525A, inhibitors of ethanol metabolism and mixed function oxidase system (MFO) activity, protected against toxicity. When disulfiram and ethanol were given acutely, a slightly increased toxic effect of vinyl chloride was observed. Ethanol given in drinking water (10% for 7 D or an equivalent dose of 10 ml/kg/D) did not, by itself, enhance vinyl chloride hepatotoxicity in male rats, even though this dose regimen did slightly increase mixed function oxidase system activity. Apparently, inhibition of either liver alcohol dehydrogenase or microsomal oxidase protects rats from acute hepatotoxicity of vinyl chloride. Since pyrazole has some inhibitory action on microsomal oxidases, it also is possible that inhibition of reactions catalyzed by the mixed function oxidase system alone could account for protection against vinyl chloride. (R-52) ■ Single exposure to vinyl chloride induced acute liver injury in rats whose mixed function oxidase system was stimulated by pretreatment with Aroclor 1254 or phenobarbital. The endoplasmic reticulum was involved in the primary morphological injury, with denaturation of the smooth membranes. The increased hepatotoxicity of vinyl chloride may involve their metabolic activation via free radical or epoxide intermediates. (R-53) ■ Male rats were pretreated by gavage with the PCB mixture Aroclor 1254 (300 μmol of PCB/kg) for 3 consecutive days. On D 4, these rats were exposed by inhalation (4 H) to 24,000 ppm vinyl chloride. Animals were sacrificed 24 H later and acute hepatic responses were estimated by measurement of serum-alamine alpha-ketoglutarate transaminase (SAKT) and by light microscopy. Vinyl chloride caused significant elevations of (SAKT) and produced severe degeneration and necrosis of the liver. SAKT elevations (mg pyruvate/mL serum/H) were: untreated controls, 0.17 ± 0.01; PCB pre-treated, not exposed, 0.19 ± 0.02; PCB plus vinyl chloride, 2.58 ± 1.25. (R-5) ■ Absorption through the skin is minor. Calculations based on the percutaneous absorption of vinyl chloride by Rhesus monkeys indicate that a 6 ft, 90 kg man exposed to 7,000 ppm (dermal) for 2 H would absorb the equivalent of a 0.2 ppm, 8 H inhalation exposure. (R-11) ■ Vinyl chloride reacted to a greater extent with denatured than with native herring sperm DNA, *in vitro*, in aqueous solution. However, vinyl chloride failed to react with previously acylated calf thymus DNA *in vitro* in citrate buffer. (R-38) ■ Vinyl chloride may be anaesthetic above 500 ppm. Handling of material has caused circulatory and bone changes. (R-47) ■ $^{14}$C vinyl chloride, 0.5 mmole/kg in 0.5 mL/kg methanol, was given ipr for 1–6 D to male Sprague-Dawley rats. After administration of the vinyl chloride, hepatic P-450 was not significantly decreased after 1 dose, but progressively decreased after repeated doses. Hepatic glutathione and SGPT activity were unchanged and histologic examination of liver specimens obtained after 1, 3, or 6 doses showed no liver necrosis. The amount of $^{14}$C material irreversibly bound to proteins increased in various tissues during administration of the first 3 doses but then tended to decrease in the liver and in the kidney. (R-68)

## ENVIRONMENTAL IMPACT

**AIR POLLUTION** High.

**ACTION LEVELS** Evacuate area. Enter from upwind after gas levels have subsided. Notify fire and air authority. Remove ignition sources.

***IN SITU* AMELIORATION** Use carbon or peat on dissolved portion. Seek professional environmental engineering assistance through EPA's Environmental Response Team (ERT), Edison, NJ, 24-Hour No. (201) 321-6660.

**AVAILABILITY OF COUNTERMEASURE MATERIAL** Carbon: water treatment plants, sugar refineries. Peat: nurseries, floral shops.

**DISPOSAL METHOD** Dilute to 1% solution and remove phenol inhibitor as sodium. (1) Pour onto vermiculite, sodium bicarbonate or a sand-soda ash mixture (90/10). (Add slaked lime if fluoride is present.) Mix in paper boxes, place in incinerator, cover with scrap wood and paper, ignite with excelsior train. Stay upwind. Or, dump in closed incinerator with afterburner. (2) Dissolve in flammalbe solvent and spray in incinerator firebox equipped with afterburner and alkali scrubber.

**DISPOSAL NOTIFICATION** Local air authority.

**MAJOR WATER USE THREATENED** Recreational.

**PROBABLE LOCATION AND STATE OF MATERIAL** Colorless gas. Heavy vapors will cling near ground. Some will dissolve. Polymerizes readily in air or sunlight.

**WATER CHEMISTRY** Subject to polymerization.

**COLOR IN WATER** Colorless.

**ACCIDENT DESCRIPTIONS** ■ Discharge of a spray of vapor and liquid under pressure from a cylinder into a fume hood generated static and ignited the vapor. ■ Vinyl chloride tends to self-polymerize explosively if peroxidation occurs, and several industrial explosions have been recorded. ■ Accidental exposure of the recovered monomer to atmospheric oxygen for a long period caused formation of an unstable polyperoxide which initiated an explosion. ■ An explosion in a valve in a liquid monomer line was ascribed to traces of oxides of nitrogen remaining after the valve had been passivated by treatment with nitric acid. (Bretherick, L. 1985. *Handbook of Reactive Chemical Hazards*, 3rd ed. Butterworth, London, p. 239.)

**ENVIRONMENTAL FATE: TRANSPORT PROCESSES – SORPTION** Sorption measurements of vinyl chloride by 4 basic food constituents (water, corn oil, casein, and sucrose) were conducted. For water, oil/water emulsions, and casein, it was found that the partition coefficient values (defined as the equilibrium concentration of VCM sorbed over the equilibrium VCM in headspace) were fairly constant within the sorbate (VCM) concentrations studied. At 24 C, the partition coefficient values for oil, casein and water were $23.7 \times 10^3$, $11.7 \times 10^3$, and $2.1 \times 10^3$, respectively. Sucrose did not sorb detectable amounts of VCM under the experimental conditions employed. (R-75)

**ENVIRONMENTAL FATE: MICROBIAL EFFECTS** Serum bottles (125 mL) were used in the anaerobic toxicity assay (ATA). This allowed gas production to be measured periodically with a syringe, and analyzed. The bottles were purged with 70% $N_2$ and 30% $CO_2$, and then the following were added: 30 mL of a nutrient and buffer solution ($NaHCO_3$, 5.7 g/L, and $FeCl_2$, 0.37 g/L), 20 mL of sludge from a laboratory digester to serve as a "seed" of anaerobic microorganisms, and 0.100 mL of ethanol to serve as substrate. VC was added to ethanol in various concentrations prior to its addition. The bottles were incubated at 35 C, and a reduction in the rate or extent of gas production in chemical-containing samples in comparison with controls indicated inhibition. Inhibition was quantified approximately by determining the concentration of VC that causes a 50% reduction in total gas production over a fixed period of time (50% inhibition). Semicontinuous bioassays were conducted using continuously stirred, 1.5 L digesters, operated at a 15 D detention time, and a temperature of 35 C ± 1 C. The digesters were initially seeded with digested municipal sludge. Primary sludge was used as feed. Each day 100 mL of digested sludge was removed, and an equal amount of feed sludge was added; 4, 16, or 64 mg/L of VC were added to ethanol and 0.1 mL of the mixture was added each day prior to feeding. Digester performance was evaluated from daily gas production and routine analysis of COD, total and volatile solids, volatile acids, pH, alkalinity, and gas composition. Batch results for VC indicate that 5.4 mg/L was marginally inhibitory and 32 mg/L was strongly inhibitory, although some acclimation did occur. A concentration of approximately 40 mg/L was required for 50% inhibition lasting 3.5 D. Semicontinuous digestion with VC did not result in adverse digester performance, even at the highest concentration of 64 mg/L. Volatile acids were slightly higher with VC at 16 and 64 mg/L than in the controls, but no significant signs of stress were apparent. (R-99)

**ENVIRONMENTAL FATE: OTHER PROCESSES** The level of vinyl chloride found in potable water as a result of polyvinyl chloride piping is directly proportional to the level of residual vinyl chloride in the pipe. Pipe containing < 1.0 ppm residual showed no vinyl chloride in the water with a test sensitive to 2 ppb.

## CHEMICAL HAZARD RESPONSE INFORMATION

**NAME ASSESSMENT CODE** VCM.

**DESCRIPTION** Gas. Colorless. Sweet odor. Liquid floats and boils on water. Flammable, irritating visible vapor cloud is produced.

**ACTIONS IN CASE OF EMERGENCY** Stop discharge if possible. Keep people away. Shut off ignition sources and call fire department. Stay upwind and use water

spray to "knock down" vapor. Evacuate area in case of large discharge. Avoid contact with liquid and vapor. Notify local health and pollution control agencies.

FIRE *Flammable. Poisonous gas is produced in fire.* Flashbacks along vapor trail may occur. May explode if ignited in an enclosed area. Wear self-contained breathing apparatus. Cool exposed containers and protect personnel effecting shutoff with water. Stop flow of gas if possible. Let fire burn. Extinguish small fires with dry chemical.

EXPOSURE *Call for medical aid.*

VAPOR Irritating to eyes, nose, and throat. If inhaled, will cause dizziness or difficult breathing. Move to fresh air. If breathing has stopped, give artificial respiration. If breathing is difficult, give oxygen.

LIQUID Will cause frostbite. Flush affected areas with plenty of water. *Do not rub affected areas.*

WATER POLLUTION Not harmful to aquatic life.

RESPONSE TO DISCHARGE Issue warning: High Flammability. Evacuate area.

LABEL CATEGORY Flammable gas.

LABEL CLASS 2.

CG COMPATIBILITY CLASS Vinyl halides.

IMO UN DESIGNATION 2.0/1086.

DOT ID NUMBER 1086.

PHYSICAL STATE (As Shipped) Liquefied compressed gas.

COLOR Colorless.

ODOR Pleasant, sweet.

PERSONAL PROTECTIVE EQUIPMENT Rubber gloves and shoes; gas-tight goggles; organic vapor canister or self-contained breathing apparatus.

SYMPTOMS FOLLOWING EXPOSURE *Inhalation*: High concentrations cause dizziness, anesthesia, lung irritation. *Skin*: May cause frostbite; phenol inhibitor may be absorbed through skin if large amounts of liquid evaporate.

TREATMENT OF EXPOSURE *Inhalation*: Remove patient to fresh air and keep him or her quiet and warm; call a doctor; give artificial respiration if breathing sto
*Eyes and skin*: Flush with plenty of water for at le
15 min; for eyes, get medical attention; remove c
taminated clothing.

THRESHOLD LIMIT VALUE 5 (ppm).

SHORT-TERM INHALATION LIMIT 500 ppm for 5 mi

LATE TOXICITY Chronic exposure may cause li
damage.

VAPOR (Gas) IRRITANT CHARACTERISTICS Vapors ca
moderate irritation such that personnel will find hi
concentrations unpleasant. The effect is tempora

LIQUID OR SOLID IRRITANT CHARACTERISTICS Minim
hazard. If spilled on clothing and allowed to rema
may cause smarting and reddening of skin. May ca
frostbite.

ODOR THRESHOLD 260 ppm.

FLASH POINT – 110 F (OC).

FLAMMABLE LIMITS IN AIR 4–26 %.

FIRE-EXTINGUISHING AGENTS For small fires use
chemical or carbon dioxide. For large fires stop f
of gas. Cool exposed containers with water.

SPECIAL HAZARDS OF COMBUSTION PRODUCTS Fo
highly toxic combustion products such as hydro
chloride, phosgenic, and carbon monoxide.

BEHAVIOR IN FIRE Container may explode in f
Gas is heavier than air and may travel consider
distance to a source of ignition and flash back.

IGNITION TEMPERATURE 882 F.

ELECTRICAL HAZARD Class I, Group D.

BURNING RATE 4.3 mm/min.

STOICHIOMETRIC AIR TO FUEL RATIO 5.490 (est.).

REACTIVITY WITH WATER No reaction.

REACTIVITY WITH COMMON MATERIALS No reaction

STABILITY DURING TRANSPORT Stable.

POLYMERIZATION Polymerizes in presence of
sunlight, or heat unless stabilized by inhibitors.

**INHIBITOR OF POLYMERIZATION** Not normally used except when high temperatures are expected. Then, 40–100 ppm of phenol used.

**REACTIVITY GROUP** 35.

**WATERFOWL TOXICITY** None.

**BIOLOGICAL OXYGEN DEMAND (BOD)** None.

**FOOD CHAIN CONCENTRATION POTENTIAL** None.

**GRADES OR PURITY** Commercial or technical 99+%.

**STORAGE TEMPERATURE** Under pressure; ambient At atm. pressure; low.

**INERT ATMOSPHERE** No requirement.

**VENTING** Under pressure; safety relief At atm. pressure; pressure-vacuum.

**HAZDARD ASSESSMENT CODE** A-B-C-D-E-F-G-Z.

**CODE OF FEDERAL REGULATIONS** Flammable gas.

**PHYSICAL STATE @ 1 C AND 1 ATMOSPHERE** Gas.

**BOILING POINT AT 1 ATMOSPHERE** 13.8 C = 259.4 K = 7.2 F.

**FREEZING POINT** −153.8 C = −119.4 K = −244.8 F.

**CRITICAL TEMPERATURE** 158.4 C = 431.6 K = 317.1 F.

**CRITICAL PRESSURE** 52.7 (atm) = 5.34 $MN/m^2$ = 774 psia.

**SPECIFIC GRAVITY** 0.969 @ −13 C, liquid.

**LIQUID SURFACE TENSION** 16.0 dynes/cm = 0.0160 N/m @ 25 C.

**LIQUID WATER INTERFACIAL TENSION** 30 est., dynes/cm = 0.03 N/m @ 20 C.

**VAPOR (GAS) SPECIFIC GRAVITY** 2.2.

**RATIO OF SPECIFIC HEATS OF VAPOR (GAS)** 1.186.

## ■ NAS HAZARD RATING FOR BULK WATER TRANSPORTATION

| *Category* | *Rating* | *Comments* |
|---|---|---|
| Fire | 4 | Flash point < 100 F (CC); boiling point < 100 F |
| Health | | |
| Vapor Irritant | 2 | Moderate irritation; temporary effect |
| Liquid or Solid Irritant | 1 | Causes skin smarting |
| Poisons | 2 | Intermediate toxicity |
| Water Pollution | | |
| Human Toxicity | 0 | Nontoxic; $LD_{50}$ > 15 g/kg |
| Aquatic Toxicity | 0 | Acute threshold limits > 10,000 ppm |
| Aesthetic Effect | 0 | No significant pollution; gases and odorless liquids |
| Reactivity | | |
| Other Chemicals | 2 | React with material rated 3 or 4 |
| Water | 0 | No reaction |
| Self-Reaction | 2 | Will undergo self-reaction if contaminated; does not require stabilizer |

## ■ NFPA HAZARD CLASSIFICATION

| *Category* | *Rating* | *Comment* |
|---|---|---|
| Health Hazard (Blue) | 2 | Materials that on intense or continued exposure could cause temporary incapacitation or possible residual injury unless prompt medical treatment is given |
| Flammability (Red) | 4 | Materials that will rapidly or completely vaporize at atmospheric pressure and normal ambient temperature, or that are readily dispersed in air and that will burn readily |
| Reactivity (Yellow) | 1 | Materials that in themselves are normally stable, but that can become unstable at elevated temperatures and pressures or that may react with water with some release of energy but not violently |

**LATENT HEAT OF VAPORIZATION** 88 cal/g = $3.7 \times 10^5$ J/kg = 160 Btu/lb.

**HEAT OF COMBUSTION** $-4520$ cal/g = $-189.1 \times 10^5$ J/kg = $-8.136$ Btu/lb.

**HEAT OF POLYMERIZATION** $-405$ cal/g = $16.9 \times 10^5$ J/kg = $-729$ Btu/lb.

**HEAT OF FUSION** 18.14 cal/g.

**REID VAPOR PRESSURE** 75 psia.

## EPA CHEMICAL ACTIVITY STATUS REPORT

■ **AUTHORITY** Safety Drinking Water Act of the Public Health Service Act.

**TYPE** EPA.

**ACTIVITY** RPAR or ANPR: includes all stages of Rebuttable Presumption Against Registration under FIFRA; with any other statutory authority, will reflect an Advance Notice of Proposed Rulemaking.

**STATUS** Completed/published; 03/04/82; 47FR P9350.

**REASON** General health effects; general environmental effects; environmental levels.

**EXPOSURE** Potential.

**CONTACT** DW/CS/Craig Vogt.

■ **AUTHORITY** Toxic Substances Control Act.

**TYPE** EPA.

**ACTIVITY** Other; FYI-submission.

**STATUS** Referred to; OTS/ECAD/CSB.

**REASON** General health effects; general environmental effects.

**EXPOSURE** Potential.

**CONTACT** TS/ECA/Terry O'Bryan.

■ **AUTHORITY** Consumer Product Safety Act.

**TYPE** Non-EPA.

**ACTIVITY** Other; status tracking.

**STATUS** Completed/published; 09/81; repo available.

**REASON** Member of class of concern; aerosol pr pellants.

**EXPOSURE** Potential.

**CONTACT** CPSC/DHS/Bill Menza.

## INDUSTRY FILE INDEX

■ **SUBMISSION NUMBER** 87.

**REGULATING AUTHORITY** Clean Water Act.

**SECTION** 301; 304; 306; 307; 501.

**REGULATION STATUS** Proposed.

**PRECISION QUANTIFICATION** Estimated and empir cal.

**MEDIA** Surface water.

**TYPE OF TECHNOLOGY** Best practical technology, be available technology, pretreatment standards for e isting sources, pretreatment standards for new sourc new source performance standards.

**REGULATION TITLE** Effluent Limitations and Guid lines for the Paint Formulating Point Source Cat gory.

**INDUSTRY CODE AND NAME** 44; Pigment Base Indu try.

**CHEMICAL STATUS** Implicitly regulated.

**DESCRIPTOR** Toxic pollutant (CWA) of toxic was (RCRA).

**USE INFORMATION** Use code, O; use name, othe use, resin constituent; reference, R189:105.

■ **SUBMISSION NUMBER** 114.

**REGULATING AUTHORITY** Clean Water Act.

**SECTION** 301; 304; 306; 307; 308; 501.

**REGULATION STATUS** Proposed.

**PRECISION QUANTIFICATION** Empirical.

**MEDIA** Surface Water.

**TYPE OF TECHNOLOGY** Best practical technology, best available technology, pretreatment standards for new sources, pretreatment standards for existing sources, new source performance standards.

**REGULATION TITLE** Inorganic Chemicals Manufacturing Point Source Category; Effluent Limitations Guidelines, Pretreatment Standards, and New Source Performance Standards.

**INDUSTRY CODE AND NAME** 26; Inorganic Chemicals.

**CHEMICAL STATUS** None.

**DESCRIPTOR** Toxic pollutant (CWA) of toxic waste (RCRA); not treatable by current methods (48FR49408).

**USE INFORMATION** Unknown.

■ **SUBMISSION NUMBER** 115.

**REGULATING AUTHORITY** Clean Water Act.

**SECTION** 301; 304; 306; 307; 501.

**REGULATION STATUS** Proposed.

**PRECISION QUANTIFICATION** Emperical.

**MEDIA** Surface water.

**TYPE OF TECHNOLOGY** Best practical technology, best available technology, best conventional technology, new source performance standards, pretreatment standards for existing sources, pretreatment standards for new sources.

**REGULATION TITLE** Organic Chemicals and Plastics and Synthetic Fibers Category Effluent Limitations Guidelines, Pretreatment Standards; and New Source Performance Standards.

**INDUSTRY CODE AND NAME** 38; Organic Chemicals and Plastics; Synthetic Fibers.

**CHEMICAL STATUS** Explicitly regulated.

**DESCRIPTOR** Toxic pollutant (CWA) of toxic waste (RCRA).

**USE INFORMATION** Use code, P; use name, product; reference, R216:15.

## CLINICAL TOXICOLOGY OF COMMERCIAL PRODUCTS

**PRIMARY TRADE NAME** Pliovic.

**MANUFACTURER'S APPROVED USE** Vinyl chloride type resins.

**USE CODE** Chloride/Resins/Vinyl.

**PRODUCER** Goodyear.

**ACTIVITY OF PRODUCT** July 1979.

**CURRENT STATUS OF PRODUCT** Replaced.

| *Ingredient Name* | *CAS RN* | *Loc. #* | *Amount* |
|---|---|---|---|
| Vinyl chloride | 75-01-4 | 6570 | 95% |

## TOXICOLOGICAL DATA

| MUTAGEN DATA | CODEN |
|---|---|
| mmo-sat 2000 ppm/48H | BBRCA9 63,363,75 |
| mma-sat 1 pph | CBTOE2 1,159,85 |
| mma-esc 10600 μmol/L | BCPCA6 24,2013,75 |
| dnr-esc 100 μg/plate | MUREAV 54,101,78 |
| sln-dmg-ihl 1 pph | MUREAV 57,307,78 |
| mrc-smc 48 mmol/L/3H | MUREAV 40,85,76 |
| mma-ssp 16 mmol/L/30M | MUREAV 40,85,76 |
| cyt-hmn:hla 10 mmol/L | TXCYAC 9,21,78 |
| otr-rat-ihl 2000 ppm/14W-I | ARTODN 47,71,81 |
| dnd-rat-orl 18 gm/kg/2Y-C | CBINA8 22,211,78 |
| oms-rat:lvr 1 nmol | NATUAS 257,134,75 |
| dnd-rat-ihl 205 ppm/5H | CBINA8 37,219,81 |
| dns-rat:lvr 2100 μmol/L | CRNGDP 5,1629,84 |
| dni-rat-ivn 9500 μg/kg | CBINA8 17,239,77 |
| cyt-rat-ihl 150 μg/m³/14W-C | GISAAA 43(7),111,78 |
| hma-rat/smc 1 pph/24H-C | MUREAV 91,381,81 |
| mnt-mus-ihl 5 pph/4H | MUREAV 75,191,80 |
| otr-mus:emb 75 mg/L | CALEDQ 28,85,85 |
| hma-mus/ssp 700 mg/kg | MUREAV 40,85,76 |
| hma-mus/smc 700 mg/kg | TOERD9 3,131,81 |
| mma-ham:lng 20 pph/5H | MUREAV 67,173,79 |
| cyt-ham-ihl 12500 ppm/6H | ARTODN 45,1,80 |
| cyt-ham-mul 600 mg/kg | MUREAV 53,187,78 |
| sce-ham-ihl 12500 ppm/6H | ARTODN 45,1,80 |
| msc-ham:ovr 10 pph | EVSRBT 25,91,82 |

| TERATOGENIC DATA | CODEN |
|---|---|
| ihl-man TCLo:30 mg/m³ (5Y male) | GTPZAB 24(5),28,80 |
| ihl-rat TCLo:1000 ppm/6H (55D male) | JTEHD6 3,965,77 |
| ihl-rat TCLo:1500 ppm/24H (1-9D preg) | TXCYAC 11,45,78 |
| ihl-rat TCLo:500 ppm/7H (6-15D preg) | EVHPAZ 41,171,81 |
| ihl-rat TCLo:2500 ppm/7H (6-15D preg) | EVHPAZ 41,171,81 |
| ihl-rat TCLo:250 ppm/6H (55D preg) | JTEHD6 3,965,77 |
| ihl-mus TCLo:30000 ppm/6H (5D male) | EVHPAZ 21,71,77 |
| ihl-mus TCLo:500 ppm/7H (6-15D preg) | EVHPAZ 41,171,81 |
| ihl-rbt TCLo:500 ppm/7H (6-15D preg) | EVHPAZ 41,171,81 |

| TUMORIGENIC DATA | CODEN |
|---|---|
| ihl-man TCLo:200 ppm/14Y-I | VAPHDQ 372,195,76 |
| orl-rat TDLo:3463 mg/kg/52W-I | EVHPAZ 41,3,81 |
| ihl-rat TCLo:1 ppm/4H/52W-I | EVHPAZ 41,3,81 |
| ihl-rat TCLo:10000 ppm/4H (12-18D preg) | CSHCAL 4,119,77 |
| ipr-rat TDLo:21 mg/kg/65W-I | APDCDT 3,216,76 |
| scu-rat TDLo:21 mg/kg/67W-I | APDCDT 3,216,76 |
| ihl-mus TCLo:50 ppm/30W-I | ANYAA9 271,431,76 |
| ihl-ham TCLo:50 ppm/4H/30W-I | APDCDT 3,216,76 |
| ihl-rat TC :50 ppm/7H/26W-C | TXAPA9 68,120,83 |
| ihl-rat TC :100 ppm/7H/26W-C | TXAPA9 68,120,83 |
| ihl-mus TC :50 ppm/47W-I | JTEHD6 4,15,78 |
| orl-rat TD :34 gm/kg/3Y-I | EVHPAZ 21,1,77 |
| ihl-mus TC :50 ppm/6H/4W-I | JTEJD6 7,909,81 |
| ihl-mus TC :50 ppm/4H/30W-I | CSHCAL 4,119,77 |
| ihl-rat TC :250 ppm/2Y-I | AANLAW 56,1,74 |
| ihl-hmn TC :300 mg/m³/W-C | GTPZAB 26(1),28,82 |
| ihl-rat TC :5 ppm/4H/52W-I | EVHPAZ 41,3,81 |
| ihl-rat TC :50 ppm/6H/43W-I | JTEHD6 7,909,81 |

| TOXICITY DATA | CODEN |
|---|---|
| orl-rat $LD_{50}$:500 mg/kg | DOWCC* |

| DATA REFERENCES | CODEN |
|---|---|
| Classification: Agricultural Chemical, Tumorigen, Mutagen, Teratogen | |
| ACGIH TLV-Human Carcinogen | 85INA8 5,623,86 |
| ACHGIH TLV-TWA 5 ppm | 85INA8 5,623,86 |
| IARC Cancer Review: Human Sufficient Evidence | IMEMDT 19,377,79 |
| IARC Cancer Review: Animal Sufficent Evidence | IMEMDT 7,291,74 |
| IARC Cancer Review: Human Limited Evidence | IMEMDT 7,291,74 |
| IARC Cancer Review: Animal Sufficient Evidence | IMEMDT 19,377 |
| IARC Cancer Review: Group 1 | IMSUDL 4,260,8. |
| Toxicology Review | FAZMAE 18,365. |
| Toxicology Review | JTEHD6 1(1),47. |
| Toxicology Review | CMTVAS 10(3),49,73 |
| Toxicology Review | CHWEAP 70,5,7 |
| Toxicology Review | CANCAR 39,1792,77 |
| Toxicology Review | MUREAV 32(2),93,76 |
| Toxicology Review | ZHPMAT 166,113,78 |
| Toxicology Review | BNYMAM 54,413,78 |
| Toxicology Review | ABMHAM 35,585,77 |
| Toxicology Review | CBINA8 22,117. |
| Toxicology Review | GTPZAB 20(4),46,76 |
| Toxicology Review | VHTODE 22,31. |
| Toxicology Review | MUREAV 41,131,76 |
| DOT-Hazard: Flammable Gas; Label: Flammable Gas | CFRGBR 49,172.101,86 |
| MSHA Standard-air:TWA 200 ppm (510 mg/m³) | DTLWS* 3,31,7 |
| OSHA STANDARD-Air: TWA 1 ppm; CL 5 ppm/15M | FEREAC 40,23073,75 |
| OSHA-Cancer Suspect Agent | CFRGBR 29,1910.1017.8 |
| NIOSH REL to Vinyl Chloride-Air: Lowest Detectable Level | MMWR** 34(1S),30S,85 |
| EPA Genetox Program 1986, Positive: Carcinogenicity-Mouse/Rat | |
| EPA Genetox Program 1986, Positive: *In vivo* Cytogenetics-Human Lymphocyte; *E. coli* polA with S9 | |
| EPA Genetox Program 1986, Positive: Histidine Reversion-Ames Test | |
| EPA Genetox Program 1986, Positive: *D. melanogaster* Sex-Linked Lethal | |
| EPA Genetox Program 1986, Positive: *S. cerevisiae* Gene Conversion; *S. Pombe*-Forward Mutation | |
| EPA Genetox Program 1986, Negative: *D. melanogaster*-Reciprocal Translocation | |
| EPA Genetox Program 1986, Negative: Rodent Dominant Lethal; Mouse Spot Test | |
| EPA Genetox Program 1986, Negative: *S. cerevisiae*-homozygosis | |

EPA TSCA Chemical Inventory, 1986
EPA TSCA Section 8(e) Status Report 8EHQ-0680-0345;8EHQ-0382-0457;8EHQ-0378-0104
EPA TSCA Section 8(e) Status Report 8EHQ-0986-0629
EPA TSCA Test Submission (TSCATS) Database, June 1987
NIOSH Current Intelligence Bulletin 28, 1978
NIOSH Analytical Methods: see Vinyl Chloride, 1007
NTP Fourth Annual Report on Carcinogens, 1984
Meets Criteria for Proposed OSHA Medical Records Rule — FEREAC 47,30420,82

**FEDERAL REGISTER CITATIONS**

**CITATION NUMBER** 47.169.549 (47FR38462ff, 8-31-82)

**PROPOSED RULE** Revision of 40CFR413, add 40CFR433, Environmental Protection Agency, Clean Water Act; electroplating and metal finishing point source category; effluent limitation guideline, pretreatment standard, New Stationary Source Performance Standard; comments solicited by 11-1-82.

**CITATION NUMBER** 47.173.4 (47FR39168, 9-7-82)

**FINAL RULE** Revision of 40CFR61, Environmental Protection Agency, Clean Air Act; Revision of Test Methods, Quality Assurance Procedures; National Emission Standard For Hazardous Air Pollutants; effective date 9-7-82. (45FR26682, 45FR76346, 46FR1318)

**CITATION NUMBER** 47.174.4 (47FR39485, 9-8-82)

**FINAL RULE** Revision of 40CFR61, Environmental Protection Agency, Clean Air Act; revision of Test Method 107A; effective date 9-8-82. (46FR12188)

**CITATION NUMBER** 47.190.249 (47FR43055ff, 9-30;82)

**NOTICE OF DELEGATION** Revision of 40CFR60.4, 61.04, Environmental Protection Agency, Clean Air Act; New Source Performance Standards and National Emission Standard for Hazardous Air Pollutants, California, Arizona, Nevada and Guam; effective date 9-27-82.

**CITATION NUMBER** 48.102.783 (48FR23552ff, 5-25-83)

**PROPOSED RULE** Add 40CFR302, Environmental Protection Agency, Comp. Env. Response, Compensation, and Liability Act; Hazardous Substances, Reportable Quantities; comments solicited by 7-25-83; Resource Conservation and Recovery Act Hazardous Waste No. U043.

**NOTICE** P88-1245, Mitsubishi Chemical for substituted vinyl chloride as automobile equipment; source: 53, 102, page 19031, May 26, 1988

**NOTICE** Civil Action No. 85-C-1193G, re asbestos emission violations (90-5-2-1-784), in U.S. vs Georgia Pacific Corp, 84-457-B & 85-136-B, requiring NESHAP compliance for vinyl chloride emissions from Plaquemine, LA facilities (90-5-2-1-657), p. 47290. Source: 50, 221, page 47289, November 15, 1985.

**NOTICE** Dainichiseika Color & Chemicals America, P87-674, substituted vinyl chloride/ethylene polymer as paper saturant. Source: 52, 44, page 7019, March 6, 1987.

**NOTICE** EPA receives TSCA premanufacture notices with a comment deadline of June 21, 1984: PMN84-633, BASF System Corp, polymer of vinyl chloride, dimethyl esters as site limited consumer binder in magnetic media coating. Source: 49, 88, page 19110, May 4, 1984.

**NOTICE** EPA delegates authority to Georgia Dept. of Natural Resources' Environmental Protection Division to implement NSPS for ferroalloy production facilities and NESHAPS for vinyl chloride. Effective Dec 22, 1977. Source: 42, 246, page 64145, December 22, 1977.

**PROPOSED** 40 CFR Part 61, EPA extends comment deadline until Aug. 19, 1977 on proposed national emission standards for vinyl chloride, published in FR of June 2 1977 (42FR 28154). Makes reference to The Society of Plastics Industry Inc request for extension of comment period. Source: 42, 154, page 40452, August 10, 1977.

**MEETING** EPA and Society of Plastics Industry Inc will meet July 19 at the Society's request to discuss amendments to Natl Emission Standard for vinyl chloride as proposed in Clean Air Act Amendments of 1977. Meeting begins at 10 am, Crystal Mall, Bldg 2, Rm 1112, 1921 Jefferson Davis Hwy, Arlington, VA, 22202; Doc. No. FRL 755-3. Source: 42, 129, page 34532, July 6, 1977.

**RULE** 40 CFR Part 61, EPA corrects typographical errors and provides for clarification in certain parts with respect to the vinyl chloride standards; ef-

fective June 7, 1977. Source: 42, 109, page 29005, June 7, 1977.

**PROPOSED** 40 CFR Part 61, EPA proposes National Emission Standards for ethylene dichloride, vinyl chloride and polyvinyl chloride plants. Makes reference to court case involving the Environmental Defense Fund and Society of the Plastics Industry, Inc., Goodyear Tire, Air Products & Chemicals, Inc. EPA proposes amendments which would require sources presently subject to a 10 ppm emission limit to reduce emissions to 5 ppm within 3 years. Amendments would require more efficient use of existing control technology at existing plants without banning vinyl chloride; describes the more stringent standards for new sources p. 28155; text of regulation p. 28157; comment deadline Aug. 1, 1977. Source: 42, 106, page 28154, June 2, 1977.

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CIS SOURCES OF INFORMATION
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EPA/CIS, OHM/TADS: 7216947
CIS, Merck Index: 9796
NIOSH/CIS, RTECS: KU 9625000
USCG, CHRIS (Chemical Hazards Response Info System): VCM
CIS, TSCAPP (TSCA Plant and Production)
CIS, TSCATS (TSCA Test Submissions)
CIS, WMSSS (Wiley Mass Spectral Database)
CIS, CTCP, Toxicity Statement Information
CIS/NCI, CCRIS (Carcinogenicity Studies)
CIS, THERMO: NBS TN-270 Series
CIS, FRSS (Federal Register Search System)
CIS, CESARS (Chemical Monographs)
CIS, GIABS (Gastro-Intestinal Absorptivity)
CIS, IFIS (EPA Industry Specific Regulations)
CIS, CASR (EPA Chemical Activities)
CIS, GENETOX (Genetic Assay Studies)
CIS, ISHOW (Physical Properties)
CIS, ENVIROFATE (Environmental Fate)
EPA, CIS, AQUIRE (Aquatic Toxicity)
CIS, DERMAL (Dermal Absorption)

NON-CIS REFERENCES
EPA, TSCA Inventory List
EPA, Chemical Spills
EPA, AEROS SOTDAT: 3860
EPA, Pesticides—Register Inert Ingredients
NBS/NIH, Ionization Potential
NFPA, Hazardous Chemicals: 49300
U.S. International Trade Commission P&I Statistics: PROD/T15-77, PROD/T 15-79
European Economic Community Inventory: 9019
EPA, Effluent Guidelines Priority Pollutants
EPA, Organic Chemical Producers: 3520
IPC, Chemical Product: 8612867576445
IPC, Chemical Plant: 867576445
NSF, Hazardous Chemicals List: A4, 65
EROICA, Organic Properties
PHS-149 Carcinogenic Activity: G129, J45
NIOSH, NOHS: 76445
ORNL, EMIC
ORNL, ETIC
Japan, Chem. Sub. Control Law, Existing Chem. Sub.: 2-117
EPA/IERL, Non-Criteria Pollutant Emissions
EPA, Chemical Indicators, Industrial Contamination
EPA, Selected Organic Air Pollutants
Clean Air Act—Section 112
EPA, Carcinogen Assessment Group List of Chemicals
CIS, CTCP, Product Formulation Information
API/TRC, Thermodynamics and Spectroscopy
NTP, Annual Report on Carcinogens: 1:69
EPA/NCTR, Industrial Carcinogen and Mutagen Study
EPA, Environmental Carcinogen Assessment Program
DHEW/NIH, Laboratory Chemicals Monographs
ITII, Toxic and Hazard Indust. Chem Safety Manual
EPA/NSF, Econ. & Tox. Data—Selected Comm. Chem.
IARC, Monographs (Carcinogenicity Reviews): 7:291, 19:377
EPA, Expanded Potential Industrial Car. & Mut.
NLM, Tox Tips: 9:9, 1:10, 1:13, 1:8, 1:3, 5:5, 16:45, 1:6
NLM, CHEMLINE: TOXLINE, TDB, TOXBACK

IARC, Bulletin on Chemicals Tested for Carcin.
Biomedical Aspects of Biorefractories in Water: 4,8,12
NCI, Environmental Determinants of Cancer
EPA, Quality Criteria for Water: PB81-117889
OSHA, Air Contaminants: .1017
NFPA #491M, Manual of Hazardous Chemical Reactions: 491M-440
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Japan, Priority List for Assessment in Environment: 1017
Dictionary of Organic Compounds (DOC5): V-00199
Water Quality Characteristics of Haz. Materials
NTP, Annual Plan: 10961-H
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