The following information was generated from the Hazardous Substances Data Bank (HSDB), a database of the National Library of Medicine’s TOXNET system (http://toxnet.nlm.nih.gov) on January 3, 2005.

Query: The chemical name vinyl chloride was identified. The following terms were added from ChemIDplus:
chloroethylene
vinylchlorek
vinylchlorid
monochloroethylene
monochloroethene
ethylene monochloride
chloroethene
CAS Registry Number: 75-01-4

NAME: VINYL CHLORIDE
HSN: 169
RN: 75-01-4

HUMAN HEALTH EFFECTS:

EVIDENCE FOR CARCINOGENICITY:


WEIGHT-OF-EVIDENCE CHARACTERIZATION: On the basis of sufficient evidence for carcinogenicity in human epidemiology studies, vinyl chloride is considered to best fit the weight-of-evidence characterization Category A, according to current EPA Risk Assessment Guidelines (USEPA, 1986). Agents classified into this category are considered known human carcinogens. This classification is supported by positive evidence for carcinogenicity in animal bioassays including several species and strains, and strong evidence for genotoxicity. Under the Proposed Guidelines for Carcinogen Risk Assessment (USEPA, 1996), it is concluded that vinyl chloride is a known human carcinogen by the inhalation route of exposure, based on human epidemiological data, and by analogy the oral route because of positive animal bioassay data as well as pharmacokinetic data allowing dose extrapolation across routes. Vinyl chloride is also considered highly likely to be carcinogenic by the dermal route because it is well absorbed and acts systemically. The weight of evidence for human carcinogenicity is
based on 1) consistent epidemiologic evidence of a causal association between occupational exposure to vinyl chloride via inhalation and the development of angiosarcoma, an extremely rare tumor; 2) consistent evidence of carcinogenicity in rats, mice, and hamsters by both the oral and inhalation routes; 3) mutagenicity and DNA adduct formation by vinyl chloride and its metabolites in numerous in vivo and in vitro test systems; and 4) efficient vinyl chloride absorption via all routes of exposure tested, followed by rapid distribution throughout the body. In light of the very high percentage of angiosarcoma worldwide that are associated with vinyl chloride exposure, the evidence for /its/ carcinogenicity is considered strong. The International Agency for Research on Cancer (IARC) has also concluded that sufficient evidence for carcinogenicity in humans exists and has placed vinyl chloride in carcinogenicity category 1, that is, carcinogenic to humans. Vinyl chloride carcinogenicity occurs via a genotoxic pathway and is understood in some detail. Vinyl chloride is metabolized to a reactive metabolite, probably chloroethylene oxide, which is believed to be the ultimate carcinogenic metabolite of vinyl chloride. The reactive metabolite then binds to DNA, forming DNA adducts that, if not repaired, ultimately lead to mutations and tumor formation. Therefore, a linear extrapolation was used in the dose-response assessment. Because of uncertainty regarding exposure levels in the occupationally exposed cohorts, recommended potency estimates are based on animal bioassay data. HUMAN CARCINOGENICITY DATA: Sufficient. ANIMAL CARCINOGENICITY DATA: Sufficient. [U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS) on Vinyl Chloride (75-01-4) Available from: http://www.epa.gov/iris on the Substance File List as of August 8, 2000]**PEER REVIEWED**

**HUMAN TOXICITY EXCERPTS:**

...VINYL CHLORIDE DOES NOT EXERT CLEARLY PERCEPTIBLE ACUTE EFFECTS BELOW 1,000 PPM. AT THAT DOSE HUMANS EXHIBIT SLIGHT ANESTHESIA, DROWSINESS, SLIGHT VISUAL DISTURBANCES, FALTERING GAIT, NUMBNESS, & TINGLING OF EXTREMITIES. [Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968.82]**PEER REVIEWED**

THERE WAS SIGNIFICANT INCR IN CHROMOSOMAL ABNORMALITIES IN CULTURED PERIPHERAL LYMPHOCYTES FROM 57 MALE WORKERS WHEN COMPARED WITH CONTROLS. GREATEST STATISTICAL INCR OCCURRED IN AUTOCLAVE OPERATORS. [PURCHASE I HF ET AL; MUTAT RES 57 (3): 325 (1978)]**PEER REVIEWED**

THE HEALTH STATUS OF 13 WORKERS EMPLOYED FOR 1.75-18 YR IN A POLYVINYL CHLORIDE FACTORY WAS STUDIED. 8 OF THEM HAD SCLERODERMA-LIKE SKIN CHANGES CHARACTERIZED HISTOlGICALLY BY THICKENING & RAREFRACTION OF THE ELASTIC FIBERS. IN 7 PATIENTS, THICKENING OF TERMINAL FINGER PHALANGES RESEMBLING CLUBBING WAS NOTED; 11 PATIENTS HAD CIRCULATORY DISTURBANCES OF THE EXTREMITIES (4 HAD RAYNAUD'S SYNDROME) & 6 PATIENTS HAD BAND-LIKE OSTEOlySES OF TERMINAL FINGER PHALANGES. THROMBOCYTOPENIA WAS OBSERVED IN ALL PATIENTS, SPLENOMEGALY IN 12 PATIENTS, & MALFUNCTION OF THE LIVER IN 11 PATIENTS. LONG TERM EXPOSURE TO VAPORS MAY CAUSE OCCUPATIONAL ACROOSTEOLYSIS. [LANGE CE ET AL; INT ARCH ARBEITSMED 32 (1-2): 1 (1974)]**PEER REVIEWED**

An unusual distribution in the cell type of brain cancer was noted in vinyl chloride exposed workers. Of 10 brain cancer deaths identified, 9 had a histologic diagnosis of glioblastoma multiforme. The other case did not have histological confirmation. [Waxweiler RJ et al; Ann NY Acad Sci 271: 40-8 (1976)]**PEER REVIEWED**
A population of 10,173 men employed in 37 plants, identified as having worked for at least one yr in jobs involving probable exposure to vinyl chloride monomer (VCM). Of the 9677 men whose vital status was determined, 707 were known to have died. For 699, death certificates were obtained. ... The only type of malignancy found in significant excess was ... malignant neoplasms of the brain and other parts of the nervous system. ... There were slight but inconclusive upward trends for malignancies of the respiratory tract, digestive tract, and central nervous system associated with reported levels of maximum exposure to vinyl chloride. [Cooper WC; Environ Health Perspect 41: 101-6 (1981)]**PEER REVIEWED**

Hepatic angiosarcoma in man was first associated with exposure to vinyl chloride in Louisville, Kentucky where it was identified in 10 persons from a single vinyl chloride polymerization plant. ... Clinical manifestations ... /were/ ... nonspecific hepatic injury with mildly abnormal ... liver test results. Carcinoembryonic antigen and alpha-fetoprotein /were/ undetectable. ... A definite diagnosis was made only by open liver biopsy. ... Average survival from diagnosis is about 12 months. Overt liver failure usually occurs only as a preterminal event and was the major cause of death. [Dannaher CL et al; Am J Med 70 (2): 279-87 (1981)]**PEER REVIEWED**

The livers from five vinyl chloride workers /showed/ angioformative and hepatocellular growth disturbance in varying proportions: angiosarcoma in four cases, liver cell hyperplasia in all cases, hyperplastic nodules in three cases, and hepatocellular carcinoma in two cases. [Evans DM et al; Histopath 7 (3): 377-88 (1983)]**PEER REVIEWED**

The results of angiography of the hand in workers in the vinyl chloride industry were described. Among 93 patients, there were 19 on whom angiograms of the hand were performed because of Raynaud-like changes, pain, or other pathological findings. All patients examined by angiography showed abnormalities of the vessels in the hands and fingers of varying severity. Vascular occlusions (17 patients), stenoses (9 patients), and thread-like narrowing of the digital arteries (6 patients) with the development of a collateral circulation were prominent findings ... There was elongation and tortuosity of the digital arteries (14 patients) which were regarded as crisoid aneurysms. [Koischwitz D et al; Roefo 132 (1): 62-8 (1980)]**PEER REVIEWED**

Of a group of 155 males and 45 females employed for 1 to 25 yr (mean 14 yr) in a facility producing vinyl chloride, 58 (29%) were free of complaints and nervous disturbances. An astheno-autonomic syndrome was found in 54 (27%) and in 88 (44%) in combination with positive neurological findings, ie pyramidal syndrome in 52, cerebellar disturbances in 38, trigeminal neuropathy in 24, and extrapyramidal symptoms in 3, ... pyramidal + cerebellar in 12, trigeminal + pyramidal in 7, trigeminal + cerebellar in 5. Headaches (48%), nervousness (26%), decr in physical strength (16%), loss of memory (14%), sleeping disturbances and somnolence were the most frequent complaints. Scleroderma-like skin changes were found in 10 subjects, but only 6 of them had any neurological disturbances. ... Frequency of the arterial hypertension were the same in both groups, whereas acroparesthesias, Raynaud's syndrome, and increased gamma guanosine triphosphate serum activity were significantly more frequent in workers with neurological disturbances. 62% of the
neurologically pos group and only 24% of the neg group reported euphoric or narcotic states after exposure. This probably indicates episodic exposures to high concn of vinyl chloride. This difference points to a possibility that neurological disturbances may be related to short exposures to peak concn. The neurological injury may be both a direct neurotoxic effect of vinyl chloride and secondary to vascular disorders. [Langauer-Lewowicka H; Int Arch Occup Envir Health 52 (2): 151-7 (1983)]**PEER REVIEWED**

... The nervous system and bioelectric functioning of the brain (EEG) were evaluated in 114 workers aged 20-62, employed in significant exposed to vinyl chloride for 1-28 yr on avg 7.5 + or - 4.0 years. Clinical symptoms of the nervous system occurred in the form of peripheral-vegetative syndrome with accompanying vasomotor disturbances of Raynaud syndrome type. EEG yielded 39 (34.2%) correct and 75 (65.8%) incorrect records. Among incorrect records most frequent (32.5%) were low-voltage and flat records; those with fast spindled activity and frequent changes typical for reduced wakefulness. The nature of clinical symptoms and EEG disturbances may point to the contribution of the hypothalamus in the pathomechanism of changes in those chronically exposed to vinyl chloride. [Si'nczuk-Walczak H, Gluszcz M; Med Pr 33 (5-6): 349-54 (1982)]**PEER REVIEWED**

... The mortality in a cohort of 451 workers exposed to vinyl chloride monomer for more than 5 yr was compared with that of 870 workers from the same company ... not exposed to vinyl chloride. The relative risk for digestive cancer was significantly higher than 1 (6.25, confidence interval 2.69-14.52) in the exposed group. The standardized mortality ratio for digestive cancer was also higher (standardized mortality ratio 259.26 p < 0.01) than that of the general population. No other cancer was in excess. Since the exposed workers are known to have had a cigarette smoking experience similar to that of those who were not exposed, it is concluded that the association between lung cancer and vinyl chloride monomer exposure ... is ... rather small. [Th'eriault G, Allard P; J Occup Med 23 (10): 671-6 (1981)]**PEER REVIEWED**

The incidence of birth defects in infants born to residents of Shawinigan, Canada in 1966-1979 were significantly higher than in three comparison communities. Since there has been a vinyl chloride polymerization plant in this town since 1943 from which ten cases of /liver/ angiosarcoma have been identified, this study explored the possible association between exposure to vinyl chloride monomer in ambient air and the occurrence of birth defects in the community. The excess of birth defects fluctuated seasonally in a way that corresponded to changes in vinyl chloride monomer concn in the environment. ... There /was/ no excess of still births in Shawinigan. The excess in birth defects involved most organ systems, and variation in birth-defect rates among school districts could not be accounted for by estimates of vinyl chloride monomer in the atmosphere. The occupational and residential histories of parents who gave birth to malformed infants were compared with those of normal infants. The two groups did not differ in occupational exposure or closeness to the vinyl chloride polymerization plant. [Theriault G et al; Teratol 27 (3): 359-70 (1983)]**PEER REVIEWED**

... RESULTS OF MASSIVE & APPARENTLY REPEATED EXPOSURES > 10,000-20,000 PPM VOL/VOL ... EUPHORIA ... FOLLOWED BY STATE OF INEBRIATION SIMILAR TO THAT OF ALCOHOL INTOXICATION, ... EPIGASTRIC PAIN,

... MORTALITY STUDY OF 8384 MEN ... /WITH/ @ LEAST 1 YR ... EXPOSURE ... BEFORE DEC 31, 1972, DEMONSTRATED THAT CANCERS OF DIGESTIVE SYSTEM (PRIMARILY ANGIOSARCOMA), RESP SYSTEM, BRAIN, & CANCERS OF UNKNOWN SITE, AS WELL AS LIMPHOMAS OCCURRED MORE OFTEN THAN EXPECTED IN ... STUDY POPULATION WITH GREATEST ESTIMATED EXPOSURE. [American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH: American Conference of Governmental Industrial Hygienists, 1986.625]**PEER REVIEWED**


Pathologic porphyrinuria, especially secondary coproporphyrinuria with transition to subclinical chronic hepatic porphyria, is a consistent pathobiochemical parameter for the recognition of vinyl chloride hepatic lesions. ... Erythrocyte uroporphyrinogen decarboxylase activity studied in 6 cases with initial chronic hepatic porphyria was normal, suggesting that vinyl chloride affects this enzyme only in the liver. [Doss M et al; Klin Wochenshr 62 (4): 175-258 (1984)]**PEER REVIEWED**

Nine retrospective mortality studies of workers exposed to vinyl chloride were reviewed to determine whether differences in their hypothesis testing results might be due to differences in statistical power. Where possible, the power of each study was calculated for cancer of the lung, brain and liver. When power was taken into consideration, the results for liver and brain cancer were consistent with an etiologic role for vinyl chloride. For lung cancer, the data were not consistent with an etiologic role, in that 2 studies with very high power yielded negative results. [Beaumont JJ, Breslow NE; Am J Epidemiol 114 (5): 725-34 (1981)]**PEER REVIEWED**

A case of angiosarcoma of the penis associated with 2 hepatic angiomata in a 61 year old man is presented. The patient had worked in a polycvinyl chloride factory as an accountant for 10 yr. The relationship of this low vinyl chloride exposure to the development of the vascular lesions is discussed with a review of the experimental and epidemiologic data on this subject. [Ghandur-Mnaymneh L, Gonzalez MS; Cancer 47 (6): 1310-24 (1981)]**PEER REVIEWED**

This /study/ briefly reviews suspected causes of malignant melanoma.
Industrial chemicals that have been suggested include arsenic, polychlorinated biphenyls, alcohol and alpha-chloroacetophenone. Recent studies of an increased incidence at plants producing polyvinyl chloride and asbestos products are reported. The question of the mechanism of action is discussed: inhaled vinyl chloride monomer migrates to the subcutaneous layers of the skin after a short time. Transcutaneous penetration of asbestos fibers is a possibility. [Hilt B et al; Scand J Work Environ Health 9 (1): 52-3 (1983)]**PEER REVIEWED**

The carcinogenicity of vinyl chloride and polyvinyl chloride is reviewed with specific attention to the gaps in knowledge for risk estimation and epidemiological presentation of the available data. Although experimental studies have demonstrated the carcinogenicity and mutagenicity of vinyl chloride/polyvinyl chloride in general, the epidemiologic studies available for review do not include an assessment of carcinogenic risk among humans exposed to these chemicals. This conclusion is based on the observation that the majority of cohort studies reviewed lacked sufficient statistical power because of small sample sizes. Further, in epidemiological studies, individuals were not followed over an adequate period of time during which cancer could become clinically manifest. [Kalmaz EE, Kalmaz GD; Regul Toxicol Pharmacol 4 (1): 13-27 (1984)]**PEER REVIEWED**

Epidemiological evidence of an occupational risk of brain cancer has been reported in four industries where chemical exposures are likely, most recently in a series of prospective studies in the petrochemical industry. However, only in the case of vinyl chloride exposure has an occupational central nervous system carcinogen been identified. This report reviews the convergence of epidemiological and laboratory evidence that established the occupational carcinogenicity of vinyl chloride, and discusses in detail the current evidence for an occupational risk of brain tumors in the petrochemical industry. [Moss AR; J Toxicol Environ Health 16 (5): 703-11 (1985)]**PEER REVIEWED**

In 1974, vinyl chloride (VC) was first reported in the open scientific literature to induce angiosarcoma of the liver both in humans and in animals. Additional research has now demonstrated the carcinogenicity of VC to other organs and at lower concentrations. The target organs for VC now clearly include the liver, brain and the lung, and probably the lymphohematopoietic system. The evidence for a carcinogenic risk has been extended to jobs associated with poly (vinyl chloride) exposure. Cases of liver angiosarcoma have been reported among individuals employed in polyvinyl chloride fabrication facilities and an epidemiological study has demonstrated a significant association between exposure to polyvinyl chloride dust and the risk of lung cancer mortality. Cases of angiosarcoma of the liver also have been reported among individuals living in near proximity to vinyl chloride-poly vinyl chloride plants. An association between polyvinyl chloride dust and pneumoconiosis also has been demonstrated. On the basis of findings, prudent control of polyvinyl chloride dust in the industrial setting is indicated. [Wagoner JK; Environ Health Perspect 52: 61-6 (1983)]**PEER REVIEWED**

A standardized mortality ratio of 1.49 for respiratory system cancer (42 observed deaths versus 28.2 expected, p < 0.01) was observed among a cohort of 4806 males employed at a synthetic chemicals plant since its startup in 1942. Upon review of pathologic material, the excess was found to be limited to adenocarcinoma and large cell undifferentiated lung
Many of the workers had been exposed to vinyl chloride, as well as to chlorinated solvents, polyvinyl chloride (PVC) dust, acrylates and acrylonitrile. To evaluate the association between lung cancer and occupational chemical exposures, detailed work histories for each cohort member were combined with exposure ratings for each of 19 chemicals for each job for each calendar year since 1942. A serially additive expected dose model was then constructed which compared the doses of the chemicals observed for the lung cancer cases to the doses expected based on subcohorts without lung cancer individually matched to the cases. Poly vinyl chloride dust appeared to be the most likely etiologic agent (p = 0.037). Time trends of poly vinyl chloride dust exposure indicated a potential latent period of 5-16 years before death. [Waxweiler RJ et al; Environ Health Perspect 41: 159-65 (1981)]**PEER REVIEWED**

A method generally used for chromosomal analysis is presented, and the main morphological abnormalities that may appear spontaneously are summarized. In a survey of 109 persons not exposed to chemicals, abnormalities, mainly of the "gap" or "break" type, were present in 76.1% of the cases. A brief review of the literature, giving results of studies of workers exposed to /the/ vinyl chloride monomer ... showed that these substances induce increased chromosome changes. [Siou G et al; Cahiers de Notes Documentaires - S'écrit’è et Hygi’ene du Travail 2nd quarter No 107, Note No 1379-107-82 p.269-76 (1982)]**PEER REVIEWED**


A retrospective mortality study of 454 male workers exposed to chloroethene during its production and polymerization to polyvinyl chloride was conducted. The cohort consisted of men working for at least 1 year during 1950-1969 and the group was followed during 1953-1979. A total of 23 cancer deaths were observed (20.2 expected) with 1 case of liver angiosarcoma, 5 lung cancers (2.8 expected), 3 colon cancers (1.4 expected), 2 thyroid cancers (0.16 expected) and 4 malignant melanomas of the skin (0.8 expected) ... "the increased incidence of cancer is accounted for almost entirely by the high exposure group" ... The high level of malignant melanoma among this group of workers is unique and warrants further attention. [Heldaas SS et al; Br J Ind Med 41 (1): 25-30 (1984) as cited in USEPA; Health and Environmental Effects Profile for Chloroethene; p.59 (1985) ECAO-CIN-P155]**PEER REVIEWED**


Vinyl chloride is an asphyxiant at high concentrations. [Environment Canada; Tech Info for Problem Spills: Vinyl Chloride (Draft) p.1 (1980)]**PEER REVIEWED**

It appears that metabolism of vinyl chloride is necessary before many of its toxic effects occur. [Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc.,
Russian studies examined sexual function and hormone levels in men and sexual function and gynecological health in women occupationally exposed to vinyl chloride and in unexposed control groups. An exposure and duration related decline in sexual function was reported in exposed men and women. Ovarian dysfunction, benign uterine growths, and prolapsed genital organs were reported in 77% of exposed women. [Makarov IA et al; Gig Tr Prof Zabol 3: 22-7 (1984)]**PEER REVIEWED**

Vinyl chloride causes hepatic damage by interfering with essential metabolic pathways, which leads to cytotoxic (necrosis or steatosis) and/or cholestatic (biliary stasis) injury patterns. [Ellenhorn, M.J. and D.G. Barceloux. Medical Toxicology - Diagnosis and Treatment of Human Poisoning. New York, NY: Elsevier Science Publishing Co., Inc. 1988.36]**PEER REVIEWED**

TO DATE, 48 CASES OF HEPATIC ANGIOSARcoma ... DIAGNOSED IN INDUST ... WORKERS AROUND WORLD. ALL AUTHENTICATED CASES ... FOUND IN WORKERS ENGAGED IN CLOSED-IN PLANTS HANDLING VERY LARGE QUANTITIES OF LIQUEFIED VINYL CHLORIDE UNDER PRESSURE ... EXPOSURE CONCn WERE HIGH, PROBABLY RANGING FROM 1,000 PPM TO SEVERAL THOUSAND PPM. [National Research Council. Drinking Water & Health Volume 1. Washington, DC: National Academy Press, 1977.784]**PEER REVIEWED**


5037 of the workers in Japan who are exposed to vinyl chloride receive regular medical examinations. 8 cases of liver damage due to occupational exposure to vinyl chloride have been confirmed; 3 of them involved hepatic haemangiosarcoma. All 3 of the latter cases were fatal. The major initial complaints were anorexia, general malaise, abdominal distention or gingival bleeding. Liver dysfunction at the outset was slight. [Fujisawa K; Japanese Journal of Traumatology and Occupational Medicine 36 (5): 366-73 (1968)]**PEER REVIEWED**

The results of a mortality study of British vinyl chloride monomer workers between the years 1940 and 1974 were described. The data included the
personnel records of nine chemical plants that manufactured or polymerized vinyl chloride. Individuals included in the study had been employed in a job involving vinyl chloride monomer exposure for 25 percent of the work week for a minimum of 1 year. Deaths were followed from 1940 through 1984 and coded according to the categories defined in the International Classification of Diseases. A total of 5,498 male workers were included in the cohort, and 780 deaths were identified. The exposed workers showed significantly fewer deaths from circulatory disease, diseases of the digestive tract, peptic ulcer, diseases of the genitourinary system, and pulmonary disorders relative to the general male population. A significant increase in mortality due to nonsecondary liver cancer was noted. Mortality from malignant diseases where an association with exposure to vinyl chloride monomer was previously suggested included malignant neoplasms of the liver, lymphosarcoma, and reticulocyte sarcoma. Autoclave workers experienced the greatest exposure to vinyl chloride monomer and showed the highest mortality rate due to liver cancer with a latency period ranging from 8 to 33 years. No significant increase in respiratory disease was determined for baggers and driers exposed to increased amounts of polyvinyl chloride dust. [Jones RD et al; Scandinavian Journal of Work, Environment, and Health 14 (3): 153-60 (1988)]**PEER REVIEWED**

A study of central nervous system birth defects in persons living near two polyvinyl chloride production facilities in New Jersey was conducted. Delivery room logs at all hospitals in counties adjoining the PVC production factories were reviewed for birth defects and CNS birth defects occurring in children born between 1977 and 1980. Information on the residence of the mother was obtained from birth certificates. The cases were matched to three offspring each born without defects according to race, sex of the child, month and year of birth, and age of the mother. The distances of the residences of the subjects from the facilities were calculated. Odds ratios for all and CNS birth defects were computed as a function of distance from the facilities. No data on ambient air concentrations of vinyl chloride were available; however, the factories reported stack and fugitive vinyl chloride emissions of 1,910,493 (factory-A) and 216,800 pounds per year (factory-B). Twenty children were born with CNS defects during the study period. The odds ratios for CNS birth defects were nonsignificantly increased for offspring whose mothers lived within 5 km of the factories. The odds ratios were higher for those living near factory A. The odds ratios decreased with increasing distance from the factories. No trend was found for total birth defects. It was concluded that the increase in CNS defects is probably associated with vinyl chloride emissions. [Rosenman KD et al; Archives of Environmental Health 44 (5): 279-82 (1989)]**PEER REVIEWED**

A review was undertaken of the deaths of 253 workers in seven facilities in Italy manufacturing vinyl chloride monomer and polyvinyl chloride and at one facility for extruding polyvinyl chloride. Thirty nine of the deaths resulted from liver disease, 14 of which were primary liver cancers. Of these 14, seven were angiosarcoma (primary liver cancer-A), and two were hepatocellular carcinoma. Histological data were not available for the other five, but clinical data would suggest angiosarcoma of the liver. Mean age at death was 48 years for primary liver cancer-A, 53 years for primary nonangiosarcoma liver cancer (primary liver cancer-non-A) and 60 years for liver cirrhosis and other chronic liver diseases. Mean duration of exposure was 16 years for primary liver cancer-A, 18 years for primary liver cancer-non-A, and 12 years for other pathological entities. Mean latency was 19, 20, and 20 years,
respectively. The list of longest held jobs for the afflicted individuals included PVC loader, dryer operator, and maintenance worker for primary liver cancer-A and primary liver cancer-non-A. It was concluded that vinyl chloride may have a broader carcinogenicity spectrum on the liver than known before and that exposure lower than that occurring in autoclave cleaning can cause primary liver cancers. [Pirastu R et al; American Journal of Industrial Medicine 17 (2): 155-61 (1990)]**PEER REVIEWED**

Cytogenetic analysis of peripheral blood lymphocytes was used to examine 43 workers, average age 34.4 years, having an average of 11.2 yr exposure to vinyl chloride monomer and 22 referent subjects, average age 40.3 yr, not exposed to vinyl chloride monomer or other known mutagenic agents. At least 100 metaphases with 46 centromeres were analyzed per person for the presence of chromosomal aberrations, specifically, chromatid breaks, chromosome breaks, chromatid exchanges, and gaps. All aberration types were increased in the exposed group as compared to the referent group, with the differences highly significant for chromatid breaks, percentage of aberrant cells, and breaks per cell. In both groups of subjects, there was no difference between smokers and nonsmokers in respect to percentage of aberrant cells; however, there was a highly significant difference in this percentage between nonsmokers in the two groups, as well as a significant difference between smokers in the two groups. It was concluded that the main reason for the increased aberration frequencies is the exposure to vinyl chloride monomer. [Hrivnak L et al; Mutation Research 240 (2) 83-85 (1990)]**PEER REVIEWED**

A group of 67 workers occupationally exposed for an average of 15 years to vinyl chloride monomer were examined for the presence of chromosome aberrations and their distribution along the chromosomal length. The procedure made use of lymphocyte cultures from blood samples. Measurements of 2000 cells per person were scored for chromatid and bichromatid chromosomal breaks. The estimation of the number and locations of breaks involved the division of each chromosome into five and six segments. A total of 626 breaks were counted in chromosomes A1, A2, and A3, and chromosome group-B, group-C, and group-D. The distribution of breaks along the chromosome arms of the lymphocytes of the vinyl chloride monomer exposed workers was not identical to the expected random distribution of breaks in the lymphocytes of an unexposed normal population. A statistically larger number of breaks compared with that expected was observed on the first and second segment of chromosome A1, the fifth and sixth segment of chromosome A2, and the third, fourth, and fifth segment of chromosomes in group-B and group-C. However, a statistically smaller number of breaks was observed on the first segment of chromosome A2, the first and third segment of chromosome A3, the first and second segment of chromosomes from group-B and group-C, and the first and fourth segment of chromosome from group-D. The results indicated the existence of chromosome locations highly sensitive and highly resistant to the actions of vinyl chloride monomer. [Fucic A et al; Mutation Research 243 (2) 95-9 (1990)]**PEER REVIEWED**

An investigation was made of 13 workers at a vinyl chloride monomer polymerization facility in Singapore, who showed persistent abnormalities in liver function tests. All subjects were males aged 19 to 55 years at time of first exposure. All began employment between 1971 and 1982, when environmental monomer levels ranged from 1 to 21 ppm. After 1983, environmental levels were controlled to a geometric mean of 1.5ppm. Exposure duration was 1 to 13 years, with a mean of 5.1 years. Only one
worker consumed more than a very low level of alcohol. Subjects were identified during screening of serum bilirubin, alkaline phosphatase, gamma-glutamyl-transpeptidase, glutamic oxaloacetic transaminase and glutamic pyruvic transaminase. Six workers complained of nausea, dizziness, loss of weight and/or loss of appetite. Two workers with hyperbilirubinemia only were confirmed to have Gilbert's syndrome, and elevated bilirubin persisted after removal from exposure. One worker with elevated glutamic pyruvic transaminase only showed a decrease on removal from exposure and an increase with resumption of exposure. Two workers had two abnormalities and eight had three or more. Increased glutamic pyruvic transaminase was generally the earliest abnormality noted. Removal from exposure produced improvement in liver function parameters in 83.3% of workers within 6 mo to 2 yr. One worker had probable alcoholic liver cirrhosis rather than monomer induced liver dysfunction. Of the remaining 12, eight who returned to work showed return of abnormal liver function within 3 mo to 1 yr. Hepatomegaly, hepatosplenomegaly, and splenomegaly were noted in four, four, and two workers, respectively. Nine workers underwent biopsies, which revealed mild to moderate nonspecific fatty changes. Six workers each were determined to have probable or possible vinyl chloride monomer induced liver dysfunction. The authors conclude that continual vigilance with environmental monitoring and medical surveillance is necessary with vinyl chloride monomer exposure. [Ho SF et al; Journal of the Society of Occupational Medicine 41 (1): 10-6 (1991)]**PEER REVIEWED**

A mortality and cancer morbidity study was conducted to investigate whether there was an increased risk for cancer among employees in the polyvinyl chloride processing industry and whether such risks could be associated with special chemical exposures, including exposure to vinyl chloride monomer. The main products manufactured at the company included thick film floor sheeting, floor tiles, homogenous mats, thin film, and extruded pipes. The group of workers studied included 2031 male workers employed at this facility for at least 3 mo from 1945 through 1980. Total mortality was almost significantly increased, and deaths by violence or intoxication were significantly increased. Deaths from ischemic heart disease were not significantly increased. There was a significant increase in total cancer morbidity, and respiratory cancers. Liver hemangiosarcoma was not observed. No significant dose response associations were found associated with exposure to vinyl chloride monomer, asbestos, or plasticizers. [Hagmar L et al; American Journal of Industrial Medicine 17 (5): 553-565 (1990)]**PEER REVIEWED**

The effects of exposure to vinyl chloride monomer on lymphocyte chromosomes were investigated using the chromosome aberration assay, the micronucleus assay, and the sister chromatid exchange method. The influence of smoking on the mutagenic activity of vinyl chloride monomer was also studied. Nineteen workers who had been employed at a polyvinyl-chloride facility for an average of 15 yr were chosen for cytogenetic examination. Workers had been exposed to a vinyl chloride monomer concentration of 50 ppm, with periodic excursions to 2000 ppm. Twenty male subjects from the general population were used as comparisons. The values for chromosome aberrations, micronuclei and sister chromatid exchange frequencies in workers exposed to vinyl chloride monomer show statistically significant increases over comparisons. The mean group value for micronuclei was 12.2% with a range of 2.1 to 26.9%. With increasing numbers of micronuclei per binucleated cell the number of cells with more than one micronucleus increased. The mean group value for chromosome
aberration was 8.5%. Chromatid breaks were the predominant type of aberration and represented 61.2% of all breaks. Chromosome breaks, dicentric chromosomes and acentric fragments were also present. The results of the micronucleus and chromosome aberration assays were comparable. Increasing numbers of micronuclei per binucleated cell and increased numbers of cells with more than one micronucleus were followed by a higher percentage of chromosome aberrations or more severe chromosomal damages. Sister chromatid exchange frequencies were also increased, with a mean group value of 9.2 per cell. Individual range of sister chromatid exchange frequencies was 4 to 27 per cell. [Fucic A et al; Mutation Research 242 (4): 265-70 (1990)]**PEER REVIEWED**

The methods and results of a collaborative study, coordinated by the International Agency for Research on Cancer and conducted in many research centers in Europe, were examined. The study examined the cancer incidence and mortality among vinyl chloride workers. A total of 14,351 subjects were contributed to the combined data base. The results indicated that vinyl chloride is associated with an increase in liver cancer incidence. An exposure response relationship was noted for both ranked and estimated cumulative exposure. The relationship was even more evident when only liver angiosarcoma was analyzed. No significant excess of mortality was observed for the other sites suspected a-priori to be affected by vinyl chloride exposure. While the incidence of lung cancer was slightly increased, neither it nor lung cancer mortality appeared to be associated with any of the exposure variables. Brain cancer and lymphosarcoma mortality, while demonstrating slight increases, did not appear to be consistently associated with exposure, although the small numbers prohibited firm conclusions. An increased risk of bladder cancer and melanoma of the skin was detected which did not appear to be related to exposure in that the association with employment in the vinyl chloride industry was confined to one country only. No increased mortality was observed for the other main causes of death. [Simonato L et al; Scandinavian Journal of Work, Environment and Health 17 (3): 159-69 (1991)]**PEER REVIEWED**

Sister chromatid exchanges and micronuclei frequency in workers exposed to vinyl chloride monomer were measured to determine which of the two endpoints was the most selective in this occupational setting. Blood samples were obtained from 93 human males, all of whom were nonsmokers. The occupationally exposed group, 52 workers, was divided into two subgroups based on workplace and the vinyl chloride monomer concentration in the air during the 4 weeks prior to sampling. One subgroup, exposed to concentrations of 1.3 to 16.69 ppm, consisted of 31 workers aged 24 to 54 yr at a manufacturing facility. The other subgroup contained 21 workers who were exposed to concentrations of 0.3 to 7.3 ppm on the polymerization control lines. The comparison group included 41 unexposed men. Both sister chromatid exchange and micronuclei were increased among exposed workers. The sister chromatid exchange frequency was increased 61.8% above comparisons. It was possible to discriminate between the high exposure and low exposure subgroups using sister chromatid exchanges. A significant increase in micronuclei frequency was seen in the exposed group; there was a significant difference between the high exposure and low exposure subgroups, but not between the comparison group and the low exposure subgroup. Sister chromatid exchange was the more sensitive endpoint for indicating a biological response. However, the authors point out that methods for restricting the micromuclei analysis to only cells at risk were not used. [Sinues B et al; Toxicology and Applied Pharmacology 108
The immunobiochemical studies were conducted in a group of 98 production workers engaged in polyvinyl chloride manufacture from ethylene (group A workers) and in a group of 59 vinyl chloride workers from a chemical plant employing classic production technology from acetylene (group B workers). Both groups of workers were matched by age (group A workers: 37.7 ± or - 8.66 years; group B workers: 34.9 ± or - 11.2 years) and average exposure length (group A workers: 8.6 ± or - 3.0 years; group B workers: 10.7 ± or - 8.4 years). All workers were examined for the serum concentrations of immunoglobulins IgG, IgA and IgM and acute reactants lysozyme, transferrin, ceruloplasmin, alpha-1-antitrypsin, alpha-2-macroglobulin and orosomucoid. The statistical analysis included calculations of means, standard deviations and 95% confidence intervals. Differences in means were evaluated by t-test, differences in the distribution pattern of values by F-test. Abnormality of values was assessed by comparisons to normal values valid in Czechoslovakia. Group A worked in conditions meeting the MAC 10 mg VC/cu m comparing with group B workers had elevated levels of IgG (p < 0.005), IgA and IgM (p < 0.001 both). Group B workers differed from group A workers by exhibiting significantly elevated levels of alpha-1-antitrypsin, and ceruloplasmin (p < 0.001). The differences in the frequency of abnormal values between group A and group B worked in substantially less favourable hygienic conditions were significant for immunoglobulins elevated in group A and for orosomucoid (p < 0.01) and ceruloplasmin (p < 0.001) elevated in group B. The possible relationship of these immunobiochemical findings with the degree of vinyl chloride exposure are critically analyzed. [Bencko V et al; J Hyg Epidemiol Microbiol Immunol 32 (4): 375-84 (1990)]**PEER REVIEWED**

In acute vinyl chloride intoxication, patients complain of vertigo, nausea and headache. At higher concentrations, vinyl chloride exerts a narcotic effect. In patients with chronic occupational exposure, neurological disturbances include sensory-motor polyneuropathy, trigeminal sensory neuropathy, slight pyramidal signs and cerebellar and extrapyramidal motor disorders. Psychiatric disturbances present as neurasthenic or depressive syndromes. Sleep disorders and disorders of sexual functions are frequently encountered. Pathological EEG alterations can be found in a high proportion of patients. The long term course and prognosis of the neurological and psychiatric disorders in vinyl chloride disease are obscure. In an one case, a slight sensory polyneuropathy, bilateral hyposmia, a marked neurasthenic syndrome, typical EEG changes and computed tomography signs of cerebral atrophy were found in a 56 years old patient as late as 16 years after the exposure to vinyl chloride. [Podoll K et al; Fortschr Neurol Psychiatr 58 (11): 439-43 (1990)]**PEER REVIEWED**

We report the case of a 45 year old man with asymptomatic hepatic angiosarcoma after professional exposure to vinyl chloride. Diagnosis was made with annual ultrasound examination during a medical surveillance program. Two years after surgical resection and adjuvant chemotherapy, hepatic recurrence was treated with radiation therapy and chemoembolization. A complete response was observed. Peliosis hepatis, confirmed by liver biopsy, occurred secondarily. Eight years after initial diagnosis, the patient was asymptomatic without recurrence of angiosarcoma. The difficulty of diagnosis of angiosarcoma at an early stage, therapy modalities, and the relation between peliosis, fibrosis, and angiosarcoma are discussed. [Paliard P et al; Gastroenterol Clin Biol 15 (5): 445-8 (1991)]**PEER REVIEWED**
To present the first case of vinyl chloride related hepatic angiosarcoma in Australia. A 51 year old male caucasian former polyvinyl chloride autoclave cleaner in an Australian chemical plant developed hepatic angiosarcoma, presenting 15 years after his last exposure to vinyl chloride monomer. He developed encephalopathy and died in oliguric renal failure 21 days after admission to hospital. Hepatic angiosarcoma may develop in other workers similarly exposed. [Riordan SM et al; Med J Aust 155 (2): 125-8 (1991)]**PEER REVIEWED**

The cohort consisted of 10,173 men who had worked for at least one year in jobs involving exposure to vinyl chloride prior to 1 January 1973. These men were employed at 37 plants in the U.S., belonging to 17 companies. Observation of the mortality experience of the cohort was updated from 31 December 1972 to 31 December 1982 (the study now covering 1942-1982). A total of 1,536 cohort members were identified as having died. The observed mortality, by cause, was compared with the expected based on U.S. mortality rates, standardized for age, race, and calendar time. Analyses by length of exposure, latency, age at first exposure, calendar year of first exposure, and type of products were performed. The study confirmed that the vinyl chloride workers experience a significant mortality excesses in angiosarcoma (15 deaths), cancer of the liver and biliary tract (SMR = 641), and cancer of the brain and other CNS (SMR = 180). In addition, the study also found a significant mortality excess in emphysema/chronic obstructive pulmonary disease (SMR = 179). On the other hand, the study did not find any excess in either respiratory cancer or lymphatic and hematopoietic cancer. This study also found an increase in biliary tract cancers, independent from liver cancer. [Wong O et al; Am J Ind Med 20 (3): 317-34 (1991)]**PEER REVIEWED**

Increased levels of chromosomal abnormalities, compared to control populations, were found in workers exposed to high levels of vinyl chloride but not in workers exposed to less than 13 mg/cu m (5 ppm). [WHO; Environmental Health Criteria 215: Vinyl Chloride p. 223 (1999)]**PEER REVIEWED**

An investigation into reproductive function in 2736 workers exposed to vinyl chloride in 13 PVC factories and 3442 workers in other factories not exposed to vinyl chloride showed no significant differences in reproductive outcome. However, in the female exposed group, the incidence of pregnancy complication was significantly higher than that of the control group, suggesting that vinyl chloride may effect the pregnancy process in female workers. [WHO; Environmental Health Criteria 215: Vinyl Chloride p. 199 (1999)]**PEER REVIEWED**

In patients with chronic occupational exposure, neurological disturbances include sensory-motor polyneuropathy, trigeminal sensory neuropathy, slight pyramidal signs and cerebellar and extrapyramidal motor disorders. Psychiatric disturbances included neurasthenic or depressive syndromes. Sleeplessness and loss of sexual functions were frequently encountered. Pathological EEG alterations were found in a high proportion of patients. [WHO; Environmental Health Criteria 215: Vinyl Chloride p. 196 (1999)]**PEER REVIEWED**

DNA damage & the formation of stable carcinogen-DNA adducts are considered critical events in the initiation of the carcinogenic process. This study was carried out to assess whether exposure of plastics industry
workers to the vinyl chloride monomer (VCM) for different periods of time would cause DNA damage, using the single-cell gel electrophoresis (SCGE) technique. Levels of DNA damage was assessed by both extent of DNA migration & numbers of DNA damaged spots in the peripheral blood lymphocytes from 32 plastics workers with different periods of exposure to VCM; they were evaluated by comparison with a group of non-exposed individuals. It was found that plastics workers who were exposed to VCM for different periods of time showed significantly increased levels of DNA damage compared with the non-exposed subjects. There was a significant correlation between the severity of DNA damage & duration of exposure. However, no significant correlation was found between the age of all subjects & DNA damage. Concns of VCM in the air inside the factory were found to be significantly higher than values in non-exposed areas, despite being lower than the threshold limit value (TLV). Our results encourage the application of SCGE as a sensitive, simple, fast & useful technique in the regular health screening of workers occupationally exposed to VCM (even at concns below the TLV) to assess the possibility of any DNA damage. [Awara WM et al; Toxicology 128 (1): 9-16 (1998)]**PEER REVIEWED**

N-acetyl-S-(2-hydroxyethyl)-L-cysteine (2-hydroxyethyl mercapturic acid, HEMA) is a urinary metabolite of several hazardous chemicals, including vinyl chloride (VC), ethylene oxide (EO), & ethylene dibromide (EDB). Information about the levels of HEMA in the general population is useful for assessing human exposures to HEMA parent cmpds, including VC, EO, & EDB. To establish reference range concns for HEMA, we analyzed urine samples from 412 adult participants in the Third National Health & Nutrition Examination Survey (NHANES II) by using isotope-dilution high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS). HEMA was detected in 71% of the samples examined. Creatinine-corrected concns ranged from < 0.68 ug/g creatinine to 58.7 microg/g creatinine; the 95th percentile concn was 11.2 ug/g creatinine; & the geometric mean & median creatinine-corrected concns were both 1.6 ug/g creatinine. We observed a statistically significant difference (P=0.0001) in the creatinine-corrected geometric mean concn values of HEMA between smokers (2.8 ug/g creatinine) & nonsmokers (1.1 ug/g creatinine). The high levels of HEMA seen among smokers likely originated from HEMA-producing chemicals known to be present in tobacco smoke. [Calafat AM et al; J Expo Anal Environ Epidemiol 9 (4): 336-342 (1999)]**PEER REVIEWED**

The authors investigated whether exposure to ethylene dichloride (EDC) & vinyl chloride monomer (VCM) resulted in increased risk of liver damage. Epidemiological information, including occupational, medical, smoking, & drinking history, was obtained by interview from 251 male workers. Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), & gamma-glutamyltransferase (GGT) were used as indicators of liver damage. Exposure to moderate or low levels of EDC & VCM resulted in a higher risk of developing abnormal ALT levels than did exposure to lower levels of the chemicals. Results were similar for AST. GGT was not associated with EDC or VCM exposure. Combined exposure to EDC & VCM showed a dose-response relationship in association with abnormal ALT levels. ... Relatively low concns of VCM & EDC cause liver damage. [Cheng TJ et al; J Occup Environ Med 41 (12): 1128-1133 (1999)]**PEER REVIEWED**

OBJECTIVES: To determine if there is an increased risk of admission to
hospital for various diseases among vinyl chloride monomer (VCM) workers. METHODS: 2224 workers with occupational exposure to VCM were identified for occurrence of disease based on a search of hospital computer files on labour insurance. These data were compared with those of workers manufacturing optical equipment & motorcycles from 1 Jan 1985 to 31 March 1994. Cardiovascular & cerebrovascular diseases were used as reference diseases, & the age adjusted morbidity odds ratio (MOR) was calculated. RESULTS: A significantly increased risk of admission to hospital among VCM workers due to primary liver cancer (MOR 4.5-6.5), cirrhosis of the liver (MOR 1.7-2.1), & other chronic diseases (MOR 1.5-2.0) was found. There were 8 cases of primary liver cancer, all with heavy previous exposure to VCM. Another 4 cases of hepatoma in polyvinyl chloride (PVC) workers were found in the death registry. 10 of 11 cases of hepatoma, with detailed medical information, were carriers of hepatitis B virus. The average latent period (20 yr) was not different from other studies. Alternative agents of primary liver cancer were largely ruled out, suggesting that the combination of hepatitis B & VCM may lead to primary liver cancer. CONCLUSION: There is an increased risk of primary liver cancer in workers exposed to VCM...

On the first of June, 1996 an environmental accident occurred in Schonebeck, Germany in which free vinyl chloride was evaporated into the atmosphere. Thereby, the human population living in this area was exposed to vinyl chloride & its byproducts. Chromosomal aberrations were measured in peripheral blood lymphocytes from 29 potentially exposed & 29 non-exposed (control) individuals. Both groups were matched regarding age, gender & smoking habits. 200 metaphases were analysed for chromosomal aberrations/ each individual. The exposed group showed a statistically significant incr in the mean frequency of aberrant cells (1.47% versus 1.07% in the control group). Chromosomal aberrations in peripheral lymphocytes have been shown to be a very sensitive biomarker of genotoxic effects not only for occupational exposure to vinyl chloride... , but also for an accidental environmental exposure. [Huttner E et al; Toxicol Lett 96-97: 143-148 (1998)]**PEER REVIEWED**

Based on results from two previous studies where an excess of melanomas was found in a cohort of workers exposed to vinyl chloride (VCM), a follow up of the incidence of cancer in the same cohort of 428 workers was carried out to scrutinize whether or not the excess could be confirmed by new cases. The total number of deaths in the study group from 1953 to the end of 1993 was 132 v 141 expected, & the total number of incident cancer cases was 56 v 57 expected. There were 11 cases of lung cancer v eight expected, seven cases of melanomas v 2.07 expected, & 2 cases of thyroid cancer v 0.34 expected. 5 of the 7 melanoma cases had occurred in the group that had been most heavily exposed to VCM v 0.7 expected. In the present follow up we also found 5 cases of the spinocellular cancer of the skin v 1.7 expected. Out of these 5 cases 4 were diagnosed after 1984. 2 of the 5 cases v 0.7 expected had occurred in the most heavily exposed group. The total number of skin cancers (melanomas & spinocellular cancers) were 12 v 3.7 expected. There was 1 new case of melanoma between 1985 & 1993 v 0.7 expected. Hence, the strength of the relation between the observed & expected number of cases was reduced compared with the last follow up, & does not strengthen the previously indicated causal relation between exposure to VCM & development of malignant melanoma. There was no excess of testicular cancers in this study. The present results may indicate that occurrence of spinocellular
Skin cancer could bear some relation to work in the manufacture of polyvinyl chloride. [Langard S et al; Occup Environ Med 57 (1): 65-68 (2000)]**PEER REVIEWED**

The production of mutations in cellular oncogenes such as ras is involved in the development of many human cancers. These mutations result in the expression of mutant forms of the encoded p21 protein which can potentially serve as a biomarker for this carcinogenic process. Workers exposed to vinyl chloride (VC) who are at risk for the development of the sentinel neoplasm angiosarcoma of the liver (ASL) represent a model population for the study of such a mutant p21ras biomarker, since VC is known to cause a specific ras mutation in ASL. To determine the relationship between VC exposure & this biomarker, serum samples from a cohort of 225 French VC workers & 111 age-sex-race-smoking-drinking matched unexposed controls were examined for the presence of mutant p21ras by immunoblotting with a mouse monoclonal antibody specific for the mutant protein. Stratifying the exposed workers by degree of VC exposure in estimated ppm-years by quartiles yielded a statistically significant trend for increasing odds ratio for sero-positivity of the p21ras biomarker with increasing exposure. These results suggest that this serum biomarker is related to VC exposure and may be an early indicator of carcinogenic risk in exposed individuals. [Li Y et al; BIOMARKERS 3 (6): 433-439 (1998)]**PEER REVIEWED**

Vinyl chloride (VC) workers are known to be at risk for development of angiosarcoma of the liver (ASL), a rare tumor. Previously, a study of p53 gene mutations in tumors of VC-exposed workers found that 50% of liver angiosarcomas contained such mutations. Mutant p53 oncoprotein & anti-p53 antibodies can also be found in the sera of ASL patients & VC-exposed workers without cancer. ... In this study, we used enzyme-linked immunosorbent assays to detect mutant p53 protein & anti-p53 antibodies in the plasma of VC-exposed workers in Taiwan. Thirty-three of 251 (13.2%) VC-workers tested positive for the p53 overexpression (10% with positive mutant p53 protein & 3.6% with positive anti-p53) in their plasma, but only 2 of 36 controls (5.6%) tested positive (2.8% with positive mutant p53 protein & 2.8% with positive anti-p53). There was a significant association between cumulative VC exposure concn & positive p53 expression ... among VC workers after we adjusted for age, hepatitis, drinking, & smoking status. In summary, P53 overexpression (mutant p53 protein or anti-p53 antibody) can be found in the plasma of VC workers in Taiwan, & a significant dose-response relationship exists between plasma p53 overexpression & VC cumulative exposure concn. [Luo JC et al; J Occup Environ Med 41 (6): 521-526 (1999)]**PEER REVIEWED**

Vinyl chloride (VC) workers are known to be at risk for development of liver angiosarcoma, a rare tumor. Previously, more than 80% of VC workers with liver angiosarcoma have been found to have an Asp-13 c-Ki-ras oncogene mutation, & more than 50% of VC-exposed workers without liver tumors were found to have Asp13-Ki-ras oncoprotein in their plasma. ... In this study, we used enhanced chemiluminescence Western blotting to detect Asp13-p21-Ki-ras in the sera of VC-exposed workers in Taiwan. There were 14 of 113 (12.4%) VC workers positive for the Asp13-Ki-ras oncoprotein in plasma, but 0 of 18 controls were positive. There were 10 of 69 (14.5%) plasma-positives among the more highly exposed ( > 1000 ppm-months) workers & 4 of 48 (9.1%) plasma-positives among the lesser exposed ( < or = 1000 ppm-months). Compared with the unexposed controls, the
odds ratios (95% confidence intervals [CI]) for plasma-positivity were 4.11 ... in the lower-exposed workers & 6.53 ... in the higher-exposed workers, & there was a linear trend between exposure & plasma-positivity ... . After adjusting for age & drinking status, the odds ratios (95% CIs) were 1.64 ... , & 2.65 ... , respectively, & there was a significant linear trend between exposure & plasma-positivity ... . In summary, Asp13-Ki-ras oncoprotein can be found in the plasma of VC workers ... , & a significant dose-response relationship exists between plasma oncoprotein expression & VC exposure.[Luo JC et al; J Occup Environ Med 40 (12): 1053-1058 (1998)]**PEER REVIEWED**

Gap junctional intercellular communication is often impaired in cancers, & the genes which encode the connexin gap junction proteins are considered to be tumor-suppressor genes. In this study, we analyzed the presence of mutations in the connexin 37 (Cx37) gene in 22 human hepatic angiosarcomas, 6 & 4 of which were associated with exposure to vinyl chloride & Thorotrast, respectively. The other 12 samples were from patients with no history of exposure to these 2 agents. In 9 samples, a proline (ACC) to serine (ACT) amino acid change in codon 319 was detected. However, DNA from non-tumorigenic tissue of the same patients also showed this amino acid change, suggesting that this is a polymorphism rather than a mutation. Subsequent analysis of 84 DNA samples from normal donors revealed the frequencies of Pro/Pro, Pro/Ser & Ser/Ser alleles to be 65.5%, 23.8% & 10.7%, respectively, while among the group of angiosarcoma patients the corresponding figures were 59.1%, 31.8% and 9.1%, respectively. Thus, there was no correlation between the polymorphism at codon 319 & hepatic angiosarcoma occurrence. However, among the 6 cases of vinyl chloride-associated angiosarcoma, the percentages of the polymorphic alleles were 33.3%, 66.7% & 0%, respectively. While the number of samples was too small to allow us to conclude that the Ser319 allele in Cx37 predisposes to this rare type of human cancer, it may be noted that codon 319 is located at the cytoplasmic tail of Cx37, where most regulatory sequences reside, and that it could be a site of phosphorylation for some protein kinases, which may in turn affect the function of Cx37, including intercellular communication. [Saito T et al; Int J Cancer 86 (1): 67-70 (2000)]**PEER REVIEWED**

Two human carcinogens that have been extensively studied are vinyl chloride & benzene. The active metabolites used in this study are chloroacetaldehyde (CAA) & para-benzoquinone (pBQ). Each forms exocyclic adducts between the N1 & N6 of A, the N3 & N4 of C & the N1 & N2 of G. Only CAA has been found to form the N2,3 adduct of G. CAA & pBQ adducts differ structurally in size & in the number of added rings, pBQ adding 2 rings to the base, while etheno bases have a single 5-membered ring. The mechanism of repair of these 2 types of adducts by human enzymes has been studied in our laboratory with defined oligodeoxynucleotides & a site-specific adduct. The etheno derivatives are repaired by DNA glycosylase activity; two mammalian glycosylases are responsible: alkylpurine-DNA-N-glycosylase (APNG) & mismatch-specific thymine-DNA glycosylase. The former repairs 1,N6-ethenoA (epsilon A) as rapidly as the original substrate, 3-methyladenine, while the latter repairs 3,N4-ethenoC (epsilon C) more efficiently than the G/T mismatch. Our finding that there are separate enzymes for epsilon A & epsilon C has been confirmed by the use of tissue extracts from an APNG knockout mouse. ... Furthermore, the pBQ adduct-containing oligomers are cleaved, to various extents by a different class of enzyme: human & bacterial
N-5'-alkylpurine (AP) endonucleases. The enzyme incises such oligomers 5' to the adduct & generates 3'-hydroxyl & 5'-phosphoryl termini but leaves the modified base on the 5'-terminus of the 3' cleavage fragment ('dangling base'). Using active-site mutants of the human AP endonuclease, we found that the active site for the primary substrate, abasic (AP) site, is the same as that for the bulky pBQ adducts. There appears to be no clear rationale for the widely differing recognition & repair mechanisms for these exocyclic adducts, as shown for the repair of the same types of modification on different bases (e.g. epsilon A & pBQ adducts). Another important variable that affects the rate & extent of repair is the effect of neighbouring bases. In the case of epsilon A, this sequence-dependent repair correlates with the extent of double-strandedness of the substrate, as demonstrated by thermal stability studies. [Singer B et al; IARC Sci Publ 150: 233-247 (1999)]**PEER REVIEWED**

The production of mutations in cellular tumor suppressor genes such as p53 is involved in the development of many human cancers. These mutations result in the expression of mutant forms of the encoded p53 protein which can potentially serve as a biomarker for this carcinogenic process. Workers exposed to vinyl chloride who are at risk for the development of the sentinel neoplasm angiosarcoma of the liver represent a model population for the study of such a mutant p53 biomarker, since vinyl chloride is known to cause specific p53 mutations in persons with angiosarcoma of the liver. To determine the relation between vinyl chloride exposure & this p53 biomarker, the authors examined serum samples collected between 1987 & 1992 from a cohort of 225 French vinyl chloride workers & 111 unexposed controls (matched according to age, sex, race, smoking, & alcohol drinking) for the presence of mutant p53 protein, using an enzyme-linked immunosorbent assay. Stratification of the exposed workers by quartile of vinyl chloride exposure (in estimated ppm-yr) yielded a statistically significant trend of increasing odds ratios for p53 biomarker seropositivity with increasing exposure. These results suggest that this serum biomarker for mutant p53 protein is related to vinyl chloride exposure & may be an early indicator of carcinogenic risk in exposed individuals. [Smith SJ et al; Am J Epidemiol 147 (3): 302-308 (1998)]**PEER REVIEWED**

Vinyl chloride (VC) is a known animal & human carcinogen that is associated with liver angiosarcoma & most likely also with hepatocellular carcinoma (HCC) in humans. The authors examined the presence of p53 gene mutations in 18 HCC specimens from patients with known exposure to VC (median, 8883 ppm-yr; median duration, 245 months). In all cases, other risk factors for the development of HCC (hepatitis B virus & hepatitis C virus infections, alcohol consumption, & metabolic or autoimmune disorders) were excluded. Three patients had concomitant cirrhosis. The p53 gene was examined by direct sequencing of exons 5-9. Mutations of the p53 gene were found in 11 of 18 HCCs examined. The point mutations detected were comprised of five transversions & five transitions. Five of 11 mutations (codons 175, 245, 248, 273, & 282) occurred at CpG sites. Histopathologic liver alterations (mild sinusoidal dilatation, [portal] fibrosis, & centrilobular siderosis) in tumor surrounding nonneoplastic liver confirmed exposure to VC. The results of the current study indicated a relation between VC exposure & the development of HCC. The mutation pattern of p53 with a nearly equal rate of incidence of transitions & transversions & a high
rate of incidence of mutations at CpG sites may reflect endogenous mechanisms (e.g., deamination of 5-methylcytosine) rather than exogenous carcinogens. [Weihrauch M et al; Cancer 88 (5): 1030-1036 (2000)]**PEER REVIEWED**

Vinyl chloride monomer (VCM) is a human carcinogen. However, the exact mechanism of carcinogenesis remains unclear. VCM may be metabolized by cytochrome P450 2E1 (CYP2E1), aldehyde dehydrogenase 2 (ALDH2) & glutathione S-transferases (GSTs). Thus workers with inherited variant metabolic enzyme activities may have an altered risk of genotoxicity. This study was designed to investigate which risk factors might affect sister chromatid exchange (SCE) frequency in polyvinyl chloride (PVC) workers. Study subjects were 44 male workers from three PVC factories. ... SCE frequency in peripheral lymphocytes was determined using a standardized method, & CYP2E1, GSTM1, GSTT1 & ALDH2 genotypes were identified by the polymerase chain reaction (PCR). Analysis revealed that smoking status & exposure to VCM were significantly associated with increased SCE frequency. The presence of ALDH2 1-2/2-2 genotypes was also significantly associated with an elevation of SCE frequency (9.5 vs. 8.1, p < 0.01). However, CYP2E1, GSTM1 or GSTT1 genotypes were not significantly associated with SCE frequency. When various genotypes were considered together, combination of CYP2E1 clc2/c2c2 with ALDH2 1-2/2-2 showed an additive effect on SCE frequency. Similar results were also found for the combination of smoking with CYP2E1, or smoking with ALDH2. These results suggest that VCM workers with ALDH2 1-2/2-2 genotypes, who also smoke, may have increased risk of DNA damage. [Wong RH et al; Mutat Res 420 (1-3): 99-107 (1998)]**PEER REVIEWED**

SKIN, EYE AND RESPIRATORY IRRITATIONS: ... Primary irritant for skin ... [Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968.82]**PEER REVIEWED**

MEDICAL SURVEILLANCE: 
Exam by wide field capillary microscopy of the hands of polyvinyl chloride workers demonstrated capillary abnormalities in a high percentage of exposed men. This /non-invasive/ technique may be useful as a mass screening procedure in the early detection of vinyl chloride induced disease. [Mariq HR et al; JAMA 236: 1368 (1976) as cited in USEPA; Ambient Water Quality Criteria Doc: Vinyl Chloride p.C-19 (1980) EPA 440/5-80-678]**PEER REVIEWED**


PRECAUTIONS FOR "CARCINOGENS": ... In relation specifically to cancer hazards, there are at present no health monitoring methods that may ensure the early detection of preneoplastic lesions or lesions which may preclude them. Whenever medical surveillance is indicated, in particular when exposure to a carcinogen has occurred, ad hoc decisions should be taken concerning additional tests that might become useful or mandatory. /Chemical Carcinogens/ [Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International
The assessment of vinyl chloride exposure can be accomplished through measurement of thiodiglycolic acid, which has been found to correlate well with environmental levels of vinyl chloride. However, other compounds such as 1,2-dichloroethane also produce thiodiglycolic acid in the urine, and may confound the assessment of vinyl chloride exposure. Urine Reference Ranges: Normal - none detected; Exposed - Thiodiglycolic acid levels of 0.3 to 4.0 mg/l have been associated with exposure to air levels of vinyl chloride of 0.14 to 7.0 ppm. ... Toxic - not established. [Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997.2279]**PEER REVIEWED**

Chest Radiography: This test is widely used for assessing pulmonary disease. Chest radiographs have been found to be useful for detection of early lung cancer in asymptomatic people, especially for detection of peripheral tumors such as adenocarcinomas. However, even though OSHA mandates this test for exposure to some toxicants such as asbestos, there are conflicting views on its efficacy in detection of pulmonary disease. [Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997.2282]**PEER REVIEWED**

Pulmonary Function Tests: The tests that have been found to be practical for population monitoring include: Spirometry and expiratory flow-volume curves; Determination of lung volumes; Diffusing capacity for carbon monoxide; Single-breath nitrogen washout; Inhalation challenge tests; Serial measurements of peak expiratory flow; Exercise testing. [Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997.2282]**PEER REVIEWED**

Liver Function Tests: The earliest parameter found for assessing vinyl chloride associated liver disease is elevation in serum glutamic pyruvic transaminase, followed by elevation in serum GGT, both of which can remain elevated for up to 2 years post-exposure. ... Biochemical tests - Enzymes that reflect cholestasis: alkaline phosphatase (AP), 5'-nucleotidase (5'-NT) /and/ leucine aminopeptidase (LAP); ... Enzymes that detect direct hepatic damage: aspartate aminotransferase (AST) /and/ alanine aminotransferase (ALT). ... Clearance tests - indocyanine green ... antipyrene test ... /and/ serum bile acids. [Ryan, R.P., C.E. Terry (eds.). Toxicology Desk Reference 4th ed. Volumes 1-3. Taylor & Francis, washington, D.C. 1997.2280]**PEER REVIEWED**

POPULATIONS AT SPECIAL RISK:
Older individuals, females, newborns, and alcohol consumers may be particularly sensitive to the effects of vinyl chloride. [USEPA, Office of Drinking Water; Criteria Document (Draft): Vinyl Chloride p.IX-3 (1983)]**PEER REVIEWED**


PROBABLE ROUTES OF HUMAN EXPOSURE:
The incidence of hepatic angiosarcoma caused by occupational exposure to vinyl chloride is highest in "reactor cleaners". [Haddad, L.M., Clinical Management of Poisoning and Drug Overdose. 2nd ed. Philadelphia,
Inhalation is the major route of exposure for nearby residents and workers (1). Exposure is also possible by ingestion of contaminated foods, drinking water and absorption through skin from cosmetics (1). [(1) USEPA; Ambient Water Quality Criteria for Vinyl Chloride. p.C-2 USEPA-440/5-80-078 (1980)]**PEER REVIEWED**

NIOSH (NOES Survey 1981-1983) has statistically estimated that 21,018 workers (8,840 of these are female) are potentially exposed to vinyl chloride in the US (1). Occupational exposure to vinyl chloride may occur through inhalation and dermal contact with this compound at workplaces where vinyl chloride is produced or used (SRC). The mean TWA concentrations of vinyl chloride in various jobs of polyvinyl chloride factories were given as follows: tank supplier, 659.67 mg/cu m; PVC reliever, 153.07 mg/cu m; tank cleaner, 95.57 mg/cu m; vinyl chloride unloader, 12.56 mg/cu m; safety and health specialist, 12.04 mg/cu m; foreman, 9.04 mg/cu m; stripper operator, 4.51 mg/cu m; vinyl chloride recovery operator, 4.38 mg/cu m; control room operator, 4.01 mg/cu m; field supervisor, 3.42 mg/cu m; office personnel, 3.34 mg/cu m; maintenance, 2.69 mg/cu m; dryer, 1.84 mg/cu m; bagger and trucker, 0.93 mg/cu m; gatekeeper, 0.93 mg/cu m (2). The general population may be exposed to vinyl chloride via inhalation of ambient air, ingestion of food and drinking water (SRC). [(1) NIOSH; National Occupational Exposure Survey (NOES) (1983) (2) Du CL et al; Bull Environ Contam Toxicol 56: 534-42 (1996)]**PEER REVIEWED**

BODY BURDEN:
A STRONG CORRELATION WAS FOUND BETWEEN VINYL CHLORIDE (VC) CONCN AT WORKING PLACES AND THE INCR EXCRETION OF THIODIGLYCOLIC ACID OF 18 EXPOSED WORKERS. THE VALUES OBTAINED WERE IN THE RANGE OF 0.14-7.00 PPM. THE EXCRETION OF THIODIGLYCOLIC ACID, MEASURED BY GAS CHROMATOGRAPHY-MASS SPECTROMETRY ANALYSIS, AMOUNTED TO 0.3-4.0 MG/L. [MUELLER G ET AL; INT ARCH OCCUP ENVIRON HEALTH 41 (3): 199 (1978)]**PEER REVIEWED**

EMERGENCY MEDICAL TREATMENT:

EMERGENCY MEDICAL TREATMENT:
LIFE SUPPORT:
  o This overview assumes that basic life support measures have been instituted.

CLINICAL EFFECTS:

0.2.1 SUMMARY OF EXPOSURE

0.2.1.1 ACUTE EXPOSURE

A) GENERAL - In acute exposure, deaths are most often due to CNS and respiratory depression. The primary toxic hazard is exposure to vinyl chloride monomer (VCM) gas rather than to PVC products (except during pyrolysis). There may be a long latent period between exposure and symptom onset.

B) ACUTE - The nervous system is the primary target of acute vinyl chloride exposure. Signs and symptoms include nausea; abdominal pain; GI bleeding; weakness; ataxia; inebriation; headache; fatigue; numbness; tingling and pallor or cyanosis of the extremities; visual disturbances; cardiac dysrhythmias; narcosis and death. Vinyl chloride is a severe irritant of the eyes, skin, and mucous membranes.

C) CHRONIC - Enhanced collagen deposition and thickening of the subepidermal layer of the skin, Raynaud's phenomenon, hepatomegaly, hepatic fibrosis, splenomegaly, thrombocytopenia, sensory-motor polyneuropathy, trigeminal sensory neuropathy, minor pyramidal signs, cerebellar and extrapyramidal motor disorders, degenerative bone changes, and acro-osteolysis may occur with chronic exposure to vinyl chloride. Vinyl chloride is a known human carcinogen and has caused angiosarcoma of the liver in heavily exposed workers.

D) DERMAL - Direct contact with liquid vinyl chloride or escaping gas can cause frostbite injury.

E) INHALATION - Inhalation may cause CNS and respiratory depression and seizures.

0.2.1.2 CHRONIC EXPOSURE

A) CHRONIC/SUBACUTE - Target organ is the liver. Direct hepatotoxicity, hepatomegaly, and hepatic cancers, including angiosarcoma, have been reported. Vinyl chloride is a human carcinogen and causes cancer of the hepatic, hematopoietic, central nervous, respiratory, and digestive systems.

B) VINYL CHLORIDE DISEASE is characterized by a scleroderma-like condition of the connective tissue of the fingers, Raynaud's phenomenon followed by acro-osteolysis, liver damage, and sometimes hematologic changes and pulmonary effects. It develops after exposures from 1 month to 3 years and is reversible after cessation of exposure.

0.2.4 HEENT

0.2.4.1 ACUTE EXPOSURE

A) Contact with escaping, compressed gas may cause mechanical injury and frostbite. The vapor is irritating to the eyes.

0.2.5 CARDIOVASCULAR

0.2.5.1 ACUTE EXPOSURE

A) VCM sensitizes animal hearts to epinephrine-induced
dysrhythmias. Ventricular fibrillation may be a cause of sudden death.

0.2.6 RESPIRATORY
0.2.6.1 ACUTE EXPOSURE
A) Various pulmonary abnormalities have occurred including dyspnea, asthma and pneumoconiosis.
B) A chronic interstitial pulmonary change is thought to be caused by vinyl chloride monomer; this change is distinct from a pneumoconiosis.

0.2.7 NEUROLOGIC
0.2.7.1 ACUTE EXPOSURE
A) VCM may cause CNS depression characterized by fatigue, headache, vertigo, ataxia, euphoria, visual disturbances, numbness and tingling in the extremities, narcosis, loss of consciousness, and death from respiratory failure.

0.2.8 GASTROINTESTINAL
0.2.8.1 ACUTE EXPOSURE
A) Nausea, vomiting, diarrhea, and severe epigastric pain can result from ingestion of the liquid.

0.2.9 HEPATIC
0.2.9.1 ACUTE EXPOSURE
A) In chronic/subacute exposures, the target organ is the liver. Direct hepatotoxicity, hepatomegaly, and hepatic cancers, including angiosarcoma, have been reported.
B) Portal hypertension can result from liver injury.

0.2.10 GENITOURINARY
0.2.10.1 ACUTE EXPOSURE
A) Decreased libido and sperm count have occurred following chronic exposures in men.

0.2.13 HEMATOLOGIC
0.2.13.1 ACUTE EXPOSURE
A) Thrombocytopenia, porphyrinuria, and capillary abnormalities have also been reported.

0.2.14 DERMATOLOGIC
0.2.14.1 ACUTE EXPOSURE
A) Scleroderma, frostbite, irritation and cyanosis have been reported. Vinyl chloride may be absorbed through the skin.
B) Contact dermatitis has been associated with VCM or its plasticizers or additives.

0.2.15 MUSCULOSKELETAL
0.2.15.1 ACUTE EXPOSURE
A) Acro-osteolysis, arthralgias, and cold extremities have been reported in workers exposed to VCM.

0.2.20 REPRODUCTIVE HAZARDS
A) Fetotoxicity and congenital malformations have been seen in animals. Human birth defects have not been substantiated.

0.2.21 CARCINOGENICITY
0.2.21.1 IARC CATEGORY
A) IARC Carcinogenicity Ratings for CAS75-01-4 (IARC, 2004):
   1) IARC Classification
      a) Listed as: Vinyl chloride
      b) Carcinogen Rating: 1
      1) The agent (mixture) is carcinogenic to humans. The
exposure circumstance entails exposures that are carcinogenic to humans. This category is used when there is sufficient evidence of carcinogenicity in humans. Exceptionally, an agent (mixture) may be placed in this category when evidence of carcinogenicity in humans is less than sufficient but there is sufficient evidence of carcinogenicity in experimental animals and strong evidence in exposed humans that the agent (mixture) acts through a relevant mechanism of carcinogenicity.

0.2.21.2 HUMAN OVERVIEW
A) Vinyl chloride is a HUMAN CARCINOGEN inducing hepatic angiosarcoma, a rare form of liver cancer. Cancers of the brain, lungs, blood and digestive systems, and melanoma have also been associated with vinyl chloride monomer (VCM) exposure.

0.2.21.3 ANIMAL OVERVIEW
A) Vinyl chloride has produced gastrointestinal, liver (including angiosarcoma), and kidney tumors and skin and appendage tumors in rats; respiratory system, liver, vascular and/or skin/appendage tumors in mice; and lymphomas and skin/appendage tumors in hamsters.

0.2.22 GENOTOXICITY
A) Chromosomal aberrations have been found in workers exposed to vinyl chloride. It has induced DNA damage, unscheduled DNA synthesis, DNA inhibition, mutations, chromosome aberrations, sister chromatid exchanges, micronuclei, and oncogenic transformation in a variety of in vivo and in vitro assays.
B) A specific ras mutation was found to be linked with occupational vinyl chloride exposure.

LABORATORY:
A) No toxic serum or blood level has been established.

TREATMENT OVERVIEW:
0.4.3 INHALATION EXPOSURE
A) Monitor for CNS and respiratory depression after acute exposure.
B) VCM and PVC dust may cause various respiratory abnormalities and respiratory cancers. Workers exposed to dust should have periodic chest x-rays.
C) There is no specific test to detect VCM hepatic toxicity. Periodic monitoring of liver function tests in exposed workers is recommended, although there is disagreement about its utility.

0.4.4 EYE EXPOSURE
A) DECONTAMINATION: Irrigate exposed eyes with copious amounts of room temperature water for at least 15 minutes. If irritation, pain, swelling, lacrimation, or photophobia persist, the patient should be seen in a health care facility.

0.4.5 DERMAL EXPOSURE
A) OVERVIEW
1) DECONTAMINATION: Remove contaminated clothing and wash exposed area thoroughly with soap and water. A physician may need to examine the area if irritation or pain persists.
A) Airborne vinyl chloride may be narcotic in concentrations as low as 7 to 10 percent. Twelve percent may be dangerous. Concentrations greater than 10,000 ppm to 20,000 ppm may cause significant symptoms.

ANTIDOTE AND EMERGENCY TREATMENT:
Basic treatment: Establish a patent airway. Suction if necessary. Watch for signs of respiratory insufficiency and assist ventilations if necessary. Administer oxygen by nonrebreather mask at 10 to 15 L/min. Monitor for pulmonary edema and treat if necessary. Monitor for shock and treat if necessary. Anticipate seizures and treat if necessary. For eye contamination, flush eyes immediately with water. Irrigate each eye continuously with normal saline during transport. Do not use emetics. For ingestion, rinse mouth and administer 5 ml/kg up to 200 ml of water for dilution if the patient can swallow, has a strong gag reflex, and does not drool. Administer activated charcoal. Cover skin burns with sterile dressings after decontamination. /Carbon tetrachloride and related compounds/ (Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994.194-5)**PEER REVIEWED**

Advanced treatment: Consider orotracheal or nasotracheal intubation for airway control in the patient who is unconscious. Positive pressure ventilation techniques with a bag valve mask device may be beneficial. Monitor cardiac rhythm and treat arrhythmias if necessary. Start an IV with D5W/SRP: "To keep open", minimal flow rate/. Use lactated Ringer's if signs of hypovolemia are present. Watch for signs of fluid overload. Consider drug therapy for pulmonary edema. For hypotension with signs of hypovolemia, administer fluid cautiously. Consider vasopressors if patient is hypotensive with a normal fluid volume. Watch for signs of myocardial irritability and fluid overload. Treat seizures with diazepam (Valium). Use proparacaine hydrochloride to assist eye irrigation. /Carbon tetrachloride and related compounds/ (Bronstein, A.C., P.L. Currance; Emergency Care for Hazardous Materials Exposure. 2nd ed. St. Louis, MO. Mosby Lifeline. 1994.195)**PEER REVIEWED**

ANIMAL TOXICITY STUDIES:

EVIDENCE FOR CARCINOGENICITY:


WEIGHT-OF-EVIDENCE CHARACTERIZATION: On the basis of sufficient evidence
for carcinogenicity in human epidemiology studies, vinyl chloride is considered to best fit the weight-of-evidence characterization Category A, according to current EPA Risk Assessment Guidelines (USEPA, 1986). Agents classified into this category are considered known human carcinogens. This classification is supported by positive evidence for carcinogenicity in animal bioassays including several species and strains, and strong evidence for genotoxicity. Under the Proposed Guidelines for Carcinogen Risk Assessment (USEPA, 1996), it is concluded that vinyl chloride is a known human carcinogen by the inhalation route of exposure, based on human epidemiological data, and by analogy the oral route because of positive animal bioassay data as well as pharmacokinetic data allowing dose extrapolation across routes. Vinyl chloride is also considered highly likely to be carcinogenic by the dermal route because it is well absorbed and acts systemically. The weight of evidence for human carcinogenicity is based on 1) consistent epidemiologic evidence of a causal association between occupational exposure to vinyl chloride via inhalation and the development of angiosarcoma, an extremely rare tumor; 2) consistent evidence of carcinogenicity in rats, mice, and hamsters by both the oral and inhalation routes; 3) mutagenicity and DNA adduct formation by vinyl chloride and its metabolites in numerous in vivo and in vitro test systems; and 4) efficient vinyl chloride absorption via all routes of exposure tested, followed by rapid distribution throughout the body. In light of the very high percentage of angiosarcoma worldwide that are associated with vinyl chloride exposure, the evidence for /its/ carcinogenicity is considered strong. The International Agency for Research on Cancer (IARC) has also concluded that sufficient evidence for carcinogenicity in humans exists and has placed vinyl chloride in carcinogenicity category 1, that is, carcinogenic to humans. Vinyl chloride carcinogenicity occurs via a genotoxic pathway and is understood in some detail. Vinyl chloride is metabolized to a reactive metabolite, probably chloroethylene oxide, which is believed to be the ultimate carcinogenic metabolite of vinyl chloride. The reactive metabolite then binds to DNA, forming DNA adducts that, if not repaired, ultimately lead to mutations and tumor formation. Therefore, a linear extrapolation was used in the dose-response assessment. Because of uncertainty regarding exposure levels in the occupationally exposed cohorts, recommended potency estimates are based on animal bioassay data. HUMAN CARCINOGENICITY DATA: Sufficient. ANIMAL CARCINOGENICITY DATA: Sufficient. [U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS) on Vinyl Chloride (75-01-4) Available from: http://www.epa.gov/ngispgm3/iris on the Substance File List as of August 8, 2000]**PEER REVIEWED**

NON-HUMAN TOXICITY EXCERPTS:

... 26 MALE AR/IRE WISTAR RATS ... EXPOSED TO ... 3% VOL/VOL ... COMMERCIAL-GRADE VINYL CHLORIDE MONOMER ... (99% PURE) 4 HR/DAY ON 5 DAY/WK FOR 12 MO. ... SKIN TUMORS DEVELOPED IN SUBMAXILLARY PAROTID REGION ... (14 EPIDERMOID CARCINOMAS, 2 MUCOEPIDERMOID CARCINOMAS, 1 PAPILLOMA) ... LUNG TUMORS DEVELOPED IN 7 RATS AND OSTEOCHONDROMAS IN 5. NO TUMORS ... IN 25 UNTREATED CONTROLS ... /SKIN TUMORS WERE ZYMBA GLAND TUMORS AND LUNG TUMORS WERE METASTASIS FROM THESE/. [IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work).V19 386 (1979)]**PEER REVIEWED**

GROUPS OF MALE AND FEMALE 11 WEEK OLD SWISS MICE WERE EXPOSED TO CONCENTRATIONS OF 50 TO 10,000 PPM VINYL CHLORIDE IN AIR FOR 4 HOURS/DAY ON 5 DAYS/WEEK FOR 30 WEEKS. AT 81 WEEKS, 70% (OF THE 10,000 PPM GROUP)
HAD ADENOMAS AND/OR ADENOCARCINOMAS OF THE LUNG, 47% HAD MAMMARY
ADENOCARCINOMAS AND 16% HAD ANGIOSARCOMAS OF THE LIVER. IN 80 MALE AND 70
FEMALE UNTREATED CONTROLS, 8 PULMONARY TUMORS AND 3 LYMPHOMAS WERE
OBSERVED. [IARC. Monographs on the Evaluation of the Carcinogenic Risk of
for Research on Cancer, 1972-PRESENT. (Multivolume work).V19 384
(1979)]**PEER REVIEWED**

VINYL CHLORIDE WAS ADMIN FOR 7 HR/DAY ON DAYS 6-18 OF GESTATION IN MICE,
RATS, & RABBITS. IT WAS CONCLUDED THAT ALTHOUGH MATERNAL TOXICITY ...
OBSERVED, VINYL CHLORIDE ALONE DID NOT CAUSE SIGNIFICANT EMBRYONAL OR
FETAL TOXICITY & WAS NOT TERATOGENIC IN ANY OF THE SPECIES @ CONCN

... EXPOSURE OF SALMONELLA TYPHIMURIUM STRAINS TA1530, TA1535, & G-46
... INCR NUMBER OF HIS+ REVERTANTS/PLATE 16, 12 OR 5 TIMES OVER
SPONTANEOUS MUTATION RATE. MUTAGENIC RESPONSE FOR TA1530 STRAIN ... INCR
WHEN S9 LIVER FRACTIONS FROM HUMANS, RATS, OR MICE ... ADDED. [National
Research Council. Drinking Water & Health Volume 1. Washington, DC:
National Academy Press, 1977.784]**PEER REVIEWED**

... INHALATION ... /OF/ VINYL CHLORIDE ... SHOWN TO PRODUCE LUNG
CONGESTION & SOME HEMORRHAGING, BLOOD-CLOTTING DIFFICULTIES, &;
CONGESTION OF LIVER & KIDNEYS IN LAB ANIMALS. [National Research
Academy Press, 1977.784]**PEER REVIEWED**

AFTER 2 HR @ 5% VINYL CHLORIDE, RATS SHOWED MODERATE INTOXICATION; 2 HR @
15% PROVOKED RESP FAILURE. [National Research Council. Drinking Water

... DEGENERATION OF BONE & CONNECTIVE TISSUE IN MALE WISTAR RATS
EXPOSED TO CONCN OF 30,000 PPM ... 4 HR/DAY ON 5 DAYS/WK FOR UP TO 12 MO.
DEGENERATIVE CHANGES WERE OBSERVED IN LIVER (INTERSTITIAL HEPATITIS,
NECROSIS, PROLIFERATION OF KUPFER CELLS AND FIBROSIS), KIDNEY (TUBULAR
NEPHROSIS & INTERSTITIAL NEPHRITIS), BRAIN (NEURONAL AND GLIAL CELL
DEGENERATION). [IARC. Monographs on the Evaluation of the Carcinogenic
Agency for Research on Cancer, 1972-PRESENT. (Multivolume work).V7 302
(1979)]**PEER REVIEWED**

CONTINUOUS EXPOSURE OF CFY RATS TO VINYL CHLORIDE (4000 MG/CU M IN AIR)
DURING PREGNANCY CAUSED INCR IN FETAL DEATHS & EMBRYOTOXIC EFFECTS.
[UNGVARY G ET AL; TOXICOLOGY 11 (1): 45 (1978)]**PEER REVIEWED**

DOMINANT LETHAL STUDIES OF MALE CD-1 MICE THAT HAD BEEN EXPOSED TO 3000,
10,000, & 30,000 PPM FOR 5 DAYS SHOWED NO MUTAGENIC EFFECT. [ANDERSON
D ET AL; ENVIRON HEALTH PERSPECT (21): 71 (1977)]**PEER REVIEWED**

SPRAGUE-DAWLEY RATS WERE EXPOSED TO 10,000 PPM VINYL CHLORIDE IN AIR FOR 4
HOURS/DAY ON 5 DAYS/WEEK FOR 5 WEEKS, STARTING AT THE AGE OF 13 WEEKS (120
RATS PER GROUP) OR 1 DAY (43 AND 46 RATS). ANIMALS WERE OBSERVED FOR 135
WEEKS. ONE HEPATOMA WAS REPORTED IN THE OLDER RATS ... IN NEWBORN RATS, 10
ANGIOSARCOMAS AND 15 HEPATOMAS WERE FOUND. NO LIVER TUMORS WERE REPORTED
IN 249 CONTROLS. [IARC. Monographs on the Evaluation of the Carcinogenic


Rats and mice were exposed in an inhalation chamber to single 1 hr /concentration/ of vinyl chloride ranging from 50-50,000 ppm. A second group was given 10 1 hr exposures to 500 ppm or 100 1 hr exposures to 50 ppm of the same chemical. All animals were then observed for the remainder of their lives, generally 18-24 months. Moribund animals were euthanized, and survivors were sacrificed on schedule and their tissues examined for pathological changes. Specifically, the oncogenic study demonstrated dose related effects for single 1 hr exposure of vinyl chloride monomer, at high levels, ie 5000 and 50,000 ppm. The concn increased the incidence of pulmonary adenomas and carcinomas in mice. Repeated exposure of A/J mice ... at 500 ppm x 10 1 hr exposures also increased the incidence of pulmonary adenomas and carcinomas. ... Rats exposed to identical concn of vinyl chloride monomer failed to elicit a tumorigenic response. [Hehir RM et al; Environ Health Perspect 41: 63-72 (1981)]**PEER REVIEWED**

Wistar rats were exposed to atmospheres containing 0 (control) or 5000 ppm vinyl chloride monomer, 7 hr/day, 5 day/wk, for 52 wk. ... 10 rats/sex per group were killed. ... Growth, mortality, hematology, clinical chemistry, and organ weights were studied. Slight growth retardation throughout the experimental period and high mortality in the second half of the study were observed in vinyl chloride monomer exposed animals. ... Blood clotting time was ... shorter in vinyl chloride monomer exposed rats than controls. There were minor /incr in/ potassium content in the blood serum in vinyl chloride monomer exposed animals during the first half of the test period. Increased blood urea nitrogen levels and relative kidney weights were evidence that the kidneys were adversely affected by vinyl chloride monomer. After 52 wk increased weights of heart and spleen, and slight signs of an anemia were noted in vinyl chloride monomer-exposed rats. ... [Feron VJ et al; Toxicol 13 (1): 25-8 (1979)]**PEER REVIEWED**

Rats exposed to vinyl chloride (in air at 2500 ppm, 4-7 hr/day, 5 days/wk) from day 12 of embryonic life for 57 wk had a 63.1% incidence of liver angiosarcoma with a latency period of 49.9 wk and a 41.4% incidence of lung metastasis. The experimental tumors were similar to those of humans with respect to gross pathology, histopathology, and metastatic behavior.
... The mutagenicity of vinyl chloride ... was tested in V79 Chinese hamster cells in the presence of a 15,000 g supernatant from phenobarbitone pretreated rats and mice. Mutations ... of 8-azoguanine and ouabain resistance were induced in a dose related fashion by exposure to vapor of vinyl chloride in the presence of liver supernatant from phenobarbital-pretreated rats. [Drevon C, Kuroki T; Mutat Res 67 (2): 173-82 (1979)]**PEER REVIEWED**

... ZYMBAL GLAND CARCINOMAS, NEPHROBLASTOMAS, & ANGIOSARCOMAS OF LIVER & OF OTHER LOCATIONS /INDUCED/ IN RATS FOLLOWING 52 WK OF EXPOSURE FOR 20 HR EACH WK. CONCN ... 10,000 PPM ... 6000 PPM ... 2500 PPM ... 50 PPM, WITH ANGIOSARCOMAS IN 7, 13, 14, 7, 4, & 1 RATS, RESPECTIVELY (AIR CONTROLS WERE NEGATIVE). [Searle, C. E. (ed.). Chemical Carcinogens. ACS Monograph 173. Washington, DC: American Chemical Society, 1976.333]**PEER REVIEWED**

... Repeated exposures of animals for 7 hr/day, 5 days/week at 500 ppm, rats showed increased liver weight and histopathology. At 200 and 100 ppm, rats showed increased liver weight, but no changes were observed in dogs or guinea pigs. All species tolerated 50 ppm for 6 months with no adverse effects. [Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley & Sons Inc., 1993-1994.4170]**PEER REVIEWED**


The carcinogenicity of vinyl chloride for experimental animals when administered transplacentally is reviewed in comparison with known transplacental carcinogens, including those that, like vinyl chloride, are dependent on enzyme mediated metabolic conversion to a reactive intermediate in maternal or fetal tissues. Vinyl chloride is converted by mixed function oxidases to the reactive metabolite chlorooxirane, the carcinogenicity of which is also reviewed. Vinyl chloride is unequivocally a transplacental carcinogen for the rat. No evidence exists, however, to support the hypothesis that exposure of male rats to vinyl chloride or any other carcinogen confers an increased risk of tumor development on their progeny. Many structural analogs of vinyl chloride, ie, substituted ethylenes, are also carcinogenic for adult animals, and can with confidence likewise be predicted to be effective transplacental carcinogens. [Rice JM; Environ Health Perspect 41: 179-88 (1981)]**PEER REVIEWED**

Inhaled vinyl chloride (VC) was carcinogenic in rats. Four groups of 2 month old CRL:CD rats of both sexes exposed to filtered air (control), 50, 250, or 1000 ppm VC for 6 hours/day, 5 days/week for 1, 3, 6, or 10 mo. Animals were autopsied when moribund; all others were autopsied at 12 mo. There were no differences in the survival rate of control, 1, or 3 month exposure groups; however, the mortality incidence increased in the 6 and 10 month exposure groups in proportion to the VC concentration. Tumors were examined microscopically. The tumor incidence in the 1 and 3 month
exposure groups did not differ from controls. The cumulative tumor incidence in rats exposed for 6 and 10 months was: liver neoplasms (including neoplastic nodules, hepatocellular carcinoma, and hemangiosarcoma) 1 of 72 (controls), 0 of 66 (50 ppm VC), 17 of 68 (250 ppm VC), and 23 of 72 (1000 ppm VC); lung tumors (bronchioloalveolar and hemangiosarcoma) 0 of 72 (controls), 0 of 66 (50 ppm VC), 4 of 68 (250 ppm VC), and 11 of 72 (1000 ppm VC); mammary gland tumors (females only; includes fibroadenoma, adenocarcinoma, and carcinoma) 6 of 36 (controls), 15 of 36 (50 ppm VC), 10 of 32 (250 ppm VC), and 5 of 36 (1000 ppm VC); malignant lymphoma 0 of 72 (controls), 0 of 66 (50 ppm VC), 1 of 68 (250 ppm VC), and 4 of 72 (1000 ppm VC). [Hong CB et al; J Toxicol Environ Health 7: 909-24 (1981)]**PEER REVIEWED**

Few data on the responses of freshwater and marine organisms to chloroethene ... reported complete mortality of northern pike (Esox lucius) after a 10 day exposure at 388 ppm chloroethene. [Brown et al; Chemical Pollutants in Relation to Diseases in Fish 298: 535-46 (1977)]**PEER REVIEWED**

Recent inhalation studies with albino CD-1 mice and CD rats ... confirmed the carcinogenicity of vinyl chloride at concentrations as low as 50 ppm ... liver angiosarcomas as well as other forms of cancer were found in both species. (USEPA; Drinking Water Criteria Document for Vinyl Chloride p.iv-5 (1986)]**PEER REVIEWED**

Recent results of the long term carcinogenicity bioassay in which vinyl chloride was administered prenatally and postnatally to Sprague-Dawley rats were presented. The animals were exposed to 2500 parts per million through inhalation over 4 to 7 hours a day, 5 days a week, or through the transplacental route (by exposure of the parents) and then by inhalation. The parental rats and some offspring were exposed for 104 weeks; the remainder of the offspring were exposed for 15 weeks. Mortality was higher in exposed rats; in rats exposed both transplacentally and by inhalation, mortality was related to the length of exposure. The percentage of rats bearing benign or malignant tumors was found to be increased in rats exposed for 15 or 104 wk. Benign mammary tumors, leukemias, pheochromocytomas, and pheochromoblastomas were found at a lower rate in exposed rats, possibly due to the early death of these animals. Vinyl chloride monomer produced unexpectedly high numbers of liver angiosarcomas, hepatocarcinomas and brain neuroblastomas in exposed rats. The onset of neuroblastoma was affected by the length of treatment. The onset of hepatocarcinoma was affected by the age at the start of treatment. The onset of angiosarcoma was affected by both the treatment and age. [Maltoni C, Cotti G; Annals of the New York Academy of Sciences 534: 145-59 (1988)]**PEER REVIEWED**

Long-term feeding studies in male and female rats showed increased mortality in males at doses = or > 5,0 mg/kg body weight per day and in females at doses of = or > 1.3 mg/kg body weight per day. At 14.1 mg/kg body weight per day, blood clotting time was decreased and alpha-fetoprotein levels in blood serum were increased. Skin fibrosis was observed at 30 mg/kg body weight per day administration by gavage. (WHO; Environmental Health Criteria 215: Vinyl Chloride p. 138 (1999)]**PEER REVIEWED**

Vinyl chloride is also carcinogenic in animals after oral application. The spectrum of tumors is similar to that observed after inhalation exposure.
The lowest observed dose producing a carcinogenic effect (ASL) in rats was 1.3 mg/kg body weight per day. [WHO; Environmental Health Criteria 215: Vinyl Chloride p. 145 (1999)]**PEER REVIEWED**

Vinyl chloride causes a wide spectrum of tumors in animals and this spectrum is similar in a number of different species. ... In rats, the following tumors have been described after vinyl chloride inhalation exposure: liver and other angiosarcomas, other liver tumors, mammary gland carcinoma, nephroblastoma, neuroblastoma, stomach tumors and Zymbal gland tumors. The lowest dose at which an increase in tumor incidences was observed when rats were exposed by inhalation was 130 mg/cu m for liver angiosarcoma (ASL) and 13 mg/cu m for mammary tumors. There is evidence that animals are more susceptible to tumor induction early in life. There is also evidence that liver tumors are induced in female rats at lower doses than in males. [WHO; Environmental Health Criteria 215: Vinyl Chloride p. 145 (1999)]**PEER REVIEWED**

The effect of age on the susceptibility to induction of ASL in Sprague Dawley rats was studied ... Rats aged 6, 18, 32 or 52 weeks were exposed to vinyl chloride at the same dose level and exposure period. ... The results in this demonstrated that the older the rats were at the start of the exposure period, the greater was the tumor incidence. The maximum incidence was observed in male rats 52 weeks old at first exposure and in females 32 weeks old at first exposure (significantly increased compared to 6- or 18-week old females). For males the effect of age was statistically significant. [WHO; Environmental Health Criteria 215: Vinyl Chloride p. 167 (1999)]**PEER REVIEWED**

Vinyl chloride, a hepatocarcinogen in humans & rodents, can form promutagenic etheno bases in DNA after metabolic activation. The formation of 1,N6-ethenoadenine (epsilon A) & 3,N4-ethenocytosine (epsilon C) was measured in adult Sprague Dawley rats by immunoaffinity purification & (32)P-postlabelling. A highly variable background was found in all tissues from untreated animals: the mean molar ratios of epsilon A:A & epsilon C:C in DNA ranged from 0.043 x 10(-8) to 31.2 x 10(-8) & from 0.062 x 10(-8) to 20.4 x 10(-8), respectively. After exposure to 500 ppm vinyl chloride by inhalation (4 hr/day, 5 days/wk for 8 wk), increased levels of epsilon A were found in the liver, lung, circulating lymphocytes & testis, the mean (+/- SD) of induced levels (treated-control values) being (4.1 +/- 1.5) x 10(-8) for these tissues. No incr in the epsilon A:A ratio was observed in kidney, brain or spleen. The levels of epsilon C increased in all the tissues examined except the brain. The mean value of the induced epsilon C:C ratios was (7.8 +/- 1.2) x 10(-8) for the liver, kidney, lymphocytes & spleen, & these ratios were higher in the lung (28 x 10(-8)) & testis (19 x 10(-8)). The results suggest a variable repair capacity for epsilon A or epsilon C in different tissues. The results are discussed in relation to published studies on the accumulation & persistence of etheno bases in the liver during & after exposure to vinyl chloride & on mutation spectra in the ras & p53 genes in liver tumours induced by vinyl chloride. In addn, studies show that the linear relationship established for monofunctional alkylating agents between their carcinogenic potency in rodents & their covalent binding index for promutagenic bases in hepatic DNA holds for vinyl chloride. It is concluded that etheno bases are critical lesions in hepatocarcinogenesis induced by vinyl chloride. Further work is needed on the role of DNA repair pathways & of endogenous lipid peroxidation products in the formation & persistence of etheno bases
Ethenobases are exocyclic adducts formed with DNA by some environmental carcinogens such as vinyl chloride or urethane. Increased levels of DNA etheno adducts have been measured in target tissues from rodents exposed to vinyl chloride or urethane. Hepatic tumours caused by exposure to vinyl chloride in humans and in rats and lung tumours induced by urethane in mice exhibit base pair substitution mutations in the ras and p53 genes which seem to be exposure-specific and consistent with the promutagenic properties of ethenobases. Background levels of etheno adducts have been detected in DNA from non-exposed humans or animals, pointing to an alternative, endogenous pathway of formation. This background may be affected by dietary factors. It could arise from the reaction of trans-4-hydroxy-2-nonenal (or its epoxide 2,3-epoxy-4-hydroxynonanal), a lipid peroxidation product, with nucleic acid bases. Elevated levels of etheno adducts are found in hepatic DNA from humans and rodents with genetic predisposition to oxidative stress and lipid peroxidation in the liver, and with an associated increased risk of liver cancer. These data suggest that DNA ethenobases could serve as new biomarkers of oxidative stress/lipid peroxidation.

Previous studies have shown that a high proportion (5/6) of human liver angiosarcomas (ASL) associated with exposure to vinyl chloride (VC) contains a GC–>AT mutation at the Ki-ras codon 13. This mutation, however, has not been found in 5 ASL or 2 hepatocellular carcinomas (HCC) induced in rats by VC. These 2 HCC did contain a mutation at codon 61 of the Ha-ras gene. In order to extend this study and further explore the mechanisms of tumour induction, an addl 6 ASL and 6 HCC induced in rats by VC were analysed for ras gene point mutations, as well as 10 rat and 10 murine ASL induced by vinyl fluoride (VF), 5 ASL, 6 Kupffer cell sarcomas, 4 HCC and 2 cholangiocellular carcinomas induced by Thorotrast in rats. Tumour DNA was analysed by PCR-SSCP and direct sequencing. None of the rodent ASL contained a mutation at codon 13 of the Ki-ras gene showing that the ras gene mutational pattern is species-specific. The CAA–>CTA mutation, previously found at codon 61 of the Ha-ras gene in rat HCC, was observed in 5 further VC-induced HCC but was not detected in the Thorotrast-induced HCC, suggesting carcinogen-specificity. This mutation was also absent in VC-induced ASL, which supports the cell-specificity of the ras mutational pattern in chemically induced tumours. No predominant mutation was detected in VF- and Thorotrast-induced tumours. Thus, a given mutation in a tumour may be carcinogen-specific but also depend on the species and the cell type.

Vinyl chloride is a known human and animal carcinogen that induces angiosarcomas of the liver. The authors review here studies on the formation and repair of DNA adducts associated with vinyl chloride and vinyl fluoride in exposed and control rodents and unexposed humans. These vinyl halides induce etheno (epsilon) adducts that are identical to those formed after lipid peroxidation. Of these adducts, N2,3-ethenoguanine (epsilon G) is present in greatest amounts in tissues of exposed animals. After exposure to vinyl chloride for four weeks, epsilon G levels attain steady-state concns, such that the amount of newly formed adducts equals the number of adducts that are lost each day. We report the first dosimetry of epsilon G in rats exposed to 0, 10, 100 or
1100 ppm vinyl chloride for 5 days or 4 wk. The number of adducts increased in a supralinear manner. Exposure to 10 ppm vinyl chloride for 5 days caused a 2- to 3-fold incr in epsilon G over that of the controls, while 4 wk exposure resulted in a 5-fold incr. This was confirmed with [13C2]vinyl chloride & by measuring exogenous & endogenous adducts in the same animals. Exposure to 100 ppm vinyl chloride for 4 wk caused a 25-fold incr in epsilon G levels over that found in control rats, while exposure to 1100 ppm resulted in a 42-fold incr. The amount of endogenous epsilon G was similar in liver DNA from rats & humans. A comparable response to exposure was seen in rats & mice exposed to 0, 25, 250 or 2500 ppm vinyl fluoride for 12 months. There was a very high correlation between epsilon G levels in rat & mouse liver at 12 months & the incidence of haemangiosarcoma at 2 yr. /The authors/ were able to demonstrate that the target cell population for angiosarcoma, the nonparenchymal cells, contained more epsilon G than hepatocytes, even though nonparenchymal cells are exposed by diffusion of vinyl halide metabolites formed in hepatocytes. The expression of N-methylpurine-DNA glycosylase mRNA was induced in rat liver after exposure to either 25 or 2500 ppm vinyl fluoride. When this induction was investigated in hepatocytes & nonparenchymal cells, it was found that the latter had only 20% of the N-methylpurine-DNA glycosylase mRNA of hepatocytes, & that only the hepatocytes had induction of this expression after exposure to vinyl fluoride. Thus, the target cells for vinyl halide carcinogenesis have much lower expression of this DNA repair enzyme, which has been associated with etheno adduct repair. [Swenberg JA et al; IARC Sci Publ 150: 29-43 (1999)]**PEER REVIEWED**

Dose-response relationships of genotoxic agents differ greatly depending on the agent & the endpoint being evaluated. Simple conclusions that genotoxic effects are linear cannot be applied universally. The shape of the molecular dose of DNA adducts varies from linear, to supralinear, to sublinear depending on metabolic activation & detoxication, & repair of individual types of DNA adducts. For mutagenesis and other genotoxicity endpoints, the dose-response reflects the molecular dose of each type of DNA adduct, cell proliferation, as well as endogenous factors that lead to mutagenesis such as the formation & repair of endogenous DNA adducts. These same factors are important when interpreting the shape of dose-response data for carcinogenesis of genotoxic agents, however, tumor background variability adds additional complexity. Endogenously formed DNA adducts may be identical to those formed by chemicals, as in the case of vinyl chloride & ethylene oxide, or they may be those associated with oxidative stress. Data presented in this paper demonstrate that the exogenous number of adducts induced by 5 days of exposure to 10 ppm vinyl chloride is only 2.2-fold > that present as a steady-state amount in unexposed control rats. Similar data are shown for ethylene oxide. Extremely sensitive methods have been developed for measuring the molecular dose of genotoxins. These methods can detect DNA adducts as low as 1 per 10(9) to 10(10). However, in view of the high number of endogenous DNA adducts that are present in all cells, it is unlikely that causal relationships can be attributed to very low numbers of such DNA adducts. Effects of both exogenous & endogenous DNA adducts need to be factored into the interpretation of chemical exposures. [SWENBERG JA et al; MUTATION RESEARCH 464 (1): 77-86 (2000)]**PEER REVIEWED**

Etheno adducts in DNA bases are formed from exogenous agents such as vinyl chloride & urethane, but also via endogenous lipid peroxidation products like trans-4-hydroxy-2-nonenal. An immunohistochemical method was
developed to localize the promutagenic 1,N(6)-ethenodeoxyadenosine DNA adduct in liver of rats exposed to vinyl chloride or an iron overload with or without carbon tetrachloride. Six monoclonal antibodies, previously produced through collaborative efforts, were screened for their optimal adduct recognition & low background formation. The antibody generated by clone EM-A-4 was found to be most suitable. Semi-quantitative image analysis of relative pixel intensity showed approximately 1.5 times higher adduct levels (P < 0.05) in the livers of rats treated with vinyl chloride or an iron overload when compared with untreated controls. Significantly elevated adduct levels persisted in vinyl chloride-treated rat liver 14 days after cessation of exposure, suggesting that this adduct is not rapidly eliminated from rat liver DNA. Using the new immunohistochemical method it is possible to visualize this promutagenic etheno-DNA adduct that may play a role in oxidative stress & lipid peroxidation-induced DNA damage in carcinogenesis. [Yang Y et al; Carcinogenesis 21 (4): 777-781 (2000)]**PEER REVIEWED**

TSCA TEST SUBMISSIONS:
The ability of vinyl chloride (VC) to induce morphological transformation in the BALB/3T3 mouse cell line (Cell Transformation Assay) was evaluated. Based on preliminary toxicity determinations (exposure time=1 day), VC was tested as a gas in an exposure chamber which contained VC in the medium at concentrations of 0, 4, 20, 100 and 250 µg/ml in the medium (corresponding to a measured concentration in the chamber of 0, 4.1 and 9.0, 69, 506 and 1024 ppm, respectively) with cell survival ranging from 92% to 47% for treated cells. VC clearly exhibited a statistically significant increase in transformation activity when compared with controls.[Arthur D. Little, Inc.; Cell Transformation Assays of 11 Chlorinated Hydrocarbon Analogs. (1983), EPA Document No. 40-8324457, Fiche No. OTS0509392 ]**QC REVIEWED**

The effects of vinyl chloride were examined in the mouse hepatocyte primary culture/DNA repair assay. Based on preliminary toxicity tests, vinylchloride was tested at concentrations of 5, 10 and 15% and was found to be cytotoxic at the 15% concentration. Vinyl chloride was genotoxic at all concentrations tested.[Naylor Dana Institute; DNA Repair Tests of 11 Chlorinated Hydrocarbon Analogs. (1983), EPA Document No. 40-8324292, Fiche No. OTS0509403 ]**QC REVIEWED**

The effects of vinyl chloride were examined in the rat hepatocyte primary culture/DNA repair assay. Based on preliminary toxicity tests, vinyl chloride was tested at concentrations of 5, 10 and 15% as a gas in a desiccator exposure chamber. The highest concentration was too toxic to be evaluated in the assay. The lower two concentrations were nontoxic but did cause a significant increase in the unscheduled DNA synthesis over untreated controls.[Naylor Dana Institute; DNA Repair Tests of 11 Chlorinated Hydrocarbon Analogs. (1983), EPA Document No. 40-8324292, Fiche No. OTS0509403 ]**QC REVIEWED**

Chronic toxicity and oncogenicity were evaluated in groups of male and female Wistar rats (100/sex/group, except highest dose level, 50/sex/group) ingesting vinyl chloride (VC) in the diet at 0, 0.014, 0.13 and 1.3 mg VC/kg body weight/day, which was available for 4 hrs/day over the lifespan of the animals. There was a significant increase in the incidence of liver nodules suspected of being tumors in both sexes, especially in females, at the highest dose level. An increased incidence of foci of cellular alteration, neoplastic nodules, hepatocellular carcinomas, liver-cell polymorphism and cysts were observed at the highest
dose level. Two females and 1 male developed a hepatic angiosarcoma, while none were observed in the other groups. Females exhibited a significant increase of basophilic foci of cellular alterations in the low and mid-dose levels, and the number of females in the mid-dose group bearing foci of cellular alteration was significantly increased. There were no significant differences between treated groups and controls in the following: body weight, hematology, or glutathione levels of the liver.\textsuperscript{[Civo Institute TNO; Lifespan Oral Carcinogenicity Study of Vinyl Chloride in Rats. (1983), EPA Document No. FYI-AX-1084-0353, Fiche No. 0353]}

**QC REVIEWED**

**METABOLISM/PHARMACOKINETICS:**

**METABOLISM/METABOLITES:**


**PEER REVIEWED**

N-ACETYL-S-(2-CHLOROETHYL)CYSTEINE OR N-ACETYL-S-(2-HYDROXYETHYL)CYSTEINE MAY BE ISOLATED FROM RAT BODY FLUIDS DEPENDING ON METHOD OF PROTECTIVE ESTERIFICATION USED. \textsuperscript{[GREEN T, HATHWAY DE; CHEM-BIOL INTERACT 17 (2): 137 (1977)]}

**PEER REVIEWED**

Rats /were subjected/ to an airborne concn of (14)C-vinyl chloride ranging from 200-1,200 ppm in a closed system, ... the rate of decr of vinyl chloride levels in the chamber atmosphere /was measured/. ... Saturation of the vinyl chloride-metabolizing enzymes of the rat /was/ achieved at 250 ppm. \textsuperscript{[Bolt HM et al; Arch Toxicol 7: 179-88 (1977) as cited in USEPA, Office of Drinking Water; Criteria Document (Draft): Vinyl Chloride p.IV-7 (1983)]}

**PEER REVIEWED**

... DATA ... INDICATE DOSE-DEPENDENT FATE OF VINYL CHLORIDE AFTER INHALATION OR ORAL ADMIN IN RATS. PRIMARY MECHANISM OF DETOXIFICATION OF VINYL CHLORIDE OR ITS REACTIVE METABOLITES INVOLVES CONJUGATION WITH HEPATIC GLUTATHIONE. GLUTATHIONE CONJUGATES ... SUBJECT TO HYDROLYSIS YIELDING CYSTEINE CONJUGATES ... \textsuperscript{[National Research Council. Drinking Water & Health Volume 1. Washington, DC: National Academy Press, 1977.783]}

**PEER REVIEWED**

The principal center of the metabolic process is the liver, where the monomer undergoes a number of oxidative processes, being catalyzed partly by alcohol dehydrogenase, and partly by a catalase. \textsuperscript{[International Labour Office. Encyclopaedia of Occupational Health and Safety. 4th edition, Volumes 1-4 1998. Geneva, Switzerland: International Labour Office, 1998.104.244]}

**PEER REVIEWED**

Data suggest that the alcohol dehydrogenase pathway is the major route of metabolism below 50 ppm, while the microsomal oxidase pathway is the major route at higher concentrations. \textsuperscript{[Hefner RE et al; Ann NY Acad Sci 246: 135-48 (1975)]}

**PEER REVIEWED**

A STRONG CORRELATION WAS FOUND BETWEEN VINYL CHLORIDE (VC) CONCN AT WORKING PLACES AND THE INCR EXCRETION OF THIODIGLYCOLIC ACID OF 18 EXPOSED
WORKERS. THE VALUE OBTAINED WERE IN THE RANGE OF 0.14-7.00 PPM. THE EXCRETION OF THIODIGYLCOLIC ACID, MEASURED BY GC-MS ANALYSIS, AMOUNTED TO 0.3-4.0 MG/L. [MUELLER G ET AL; INT ARCH OCCUP ENVIRON HEALTH 41 (3): 199 (1978)]**PEER REVIEWED**

The first step in biotransformation of ... vinyl chloride ... has been proposed to involve microsomal oxidation leading to epoxide formation across the double bond. ... /It has been/ suggested that the resulting oxiranes are highly reactive and therefore can covalently bind to nucleic acids with the eventual end result of mutations and cancer. [Klaassen, C.D., M.O. Amdur, Doull J. (eds.). Casarett and Doull's Toxicology. The Basic Science of Poisons. 5th ed. New York, NY: McGraw-Hill, 1995.750]**PEER REVIEWED**

The metab & pharmacokinetics of vinyl chloride (VC) have been extensively studied in rodents & humans, but the max velocity (Vmax) & Michaelis constant (K(m)) for the activation of VC by microsomal monooxygenases in vitro have not yet been determined. ... The epoxidation of VC by rat liver microsomes (adult Sprague-Dawley) at concns from 1 ppm to 10(6) ppm in the gas phase was measured. In the assay, the reactive VC metabolites chloroethylene oxide & 2-chloroacetaldehyde were trapped with excess cAMP, yielding, 1,N6-etheno-cAMP (epsilon cAMP) ... . ... Activation of VC by rat liver microsomes followed Michaelis-Menten kinetics with K(m) = 7.42 +/- 0.37 (+/- SD) microM & Vmax = 4674 +/- 46 pmol.mg protein-1.min-1. Inhibitor studies & immunoinhibition assays showed that VC was activated by cytochrome P450 (CYP) 2E1 down to 1 ppm in the air phase. [el Ghissassi F et al; Biochem Pharmacol 55 (9): 1445-1452 (1998)]**PEER REVIEWED**

ABSORPTION, DISTRIBUTION & EXCRETION:

Male Sprague-Dawley rats were given single oral doses (gavage) of (14)C vinyl chloride at 0.05, 1.0 or 100 mg/kg, ... routes and rates of elimination of (14)C activity were followed for 72 hr. ... Of the samples examined (liver, skin, plasma, muscle, lung, fat, and carcass), liver retained the greatest percentage of admin radioactivity at all doses. [Watanabe PG et al; Toxicol Appl Pharmacol 36: 339-52 (1976) as cited in USEPA; Office of Drinking Water; Criteria Document (Draft): Vinyl Chloride p.IX-3 (1983)]**PEER REVIEWED**

Experiments with volunteers showed that 42% of an inhaled dose of vinyl chloride ... was retained in the lung. This value was independent of the concn of vinyl chloride in the air. Elim of vinyl chloride through the lung was negligible since its concn in expired air decreased immediately after cessation of exposure. [Krajewski J et al; Br J Ind Med 37 (4): 373-4 (1980)]**PEER REVIEWED**

ORAL DOSES OF 0.05-1.0 MG/KG IN RATS ... PULMONARY EXCRETION WAS
MONOPHASIC @ THESE DOSES, & URINARY METABOLITES ... /WERE 
N-ACETYL-S-(2-HYDROXYETHYL)CYSTEINE & THIODIGLYCOLIC ACID/. AT ... 100 
MG/KG, PULMONARY EXCRETION ... BIPHASIC & A GREATER PERCENTAGE ... 
EXPIRED AS VINYL CHLORIDE--67%, COMPARED WITH 1 OR 2% @ LOWER DOSE. 

The metabolic elimination of vinyl chloride in Rhesus monkeys /following 
inhalation exposure/ is a dose-dependent, saturable process. ... Below 
200-300 ppm elimination is first-order. [Buchter A et al; Tox Lett 6: 33-6 
(1980) as cited in USEPA, Office of Drinking Water; Criteria Document 
(Draft): Vinyl Chloride p.IV-8 (1983)]**PEER REVIEWED**

It is easily absorbed by the human organism through the respiratory system 
from where it passes into the blood circuit and from there to the various 
organs and tissues. It is also absorbed through the digestive system as a 
contaminant of food and beverages, and through the skin. [International 
Labour Office. Encyclopaedia of Occupational Health and Safety. 4th 
Office, 1998.104.244]**PEER REVIEWED**

Gastrointestinal absorption of vinyl chloride in rats occurs rapidly 
following ingestion of aqueous or vegetable oil treatment solutions. ... 
Quantitatively, absorption of 98.7% from the gut occurred at an oral dose 
of 450 mg/kg. (Withey JR; J Toxicol Environ Health 1 (3): 381-94 
(1976)]**PEER REVIEWED**

Animal and human studies have shown that vinyl chloride is readily and 
rapidly absorbed. The primary route of exposure to vinyl chloride is 
inhalation. However, the net uptake after exposure by inhalation is only 
30-40% of inspired vinyl chloride. This is due to the fact that vinyl 
chloride is taken up rapidly until it reaches a blood concentration in 
equilibrium with that based upon inspired concentration and the 
blood-to-air partition coefficient. Uptake then decreases to an amount 
sufficient to replace that metabolized. [WHO; Environmental Health 
Criteria 215: Vinyl Chloride p. 110 (1999)]**PEER REVIEWED**

While uptake by the oral route is near 100% any vinyl chloride not 
metabolized during first pass through the liver will be expired. Thus, the 
net dose may be less than the uptake, especially at high doses resulting 
in saturation of metabolizing enzymes. [WHO; Environmental Health Criteria 
215: Vinyl Chloride p. 110 (1999)]**PEER REVIEWED**

BILOGICAL HALF-LIFE:
THE PATTERN OF PULMONARY ELIMINATION OF 10 AND 1000 PPM VINYL CHLORIDE WAS 
DESCRIBED BY APPARENTLY SIMILAR FIRST-ORDER KINETICS, WITH HALF-LIVES OF 
20.4 AND 22.4 MINUTES RESPECTIVELY. THE HALF LIVES FOR THE INITIAL PHASE 
OF EXCRETION OF (14)C RADIOACTIVITY IN URINE WERE 4.6 AND 4.1 HOURS, 
RESPECTIVELY. [IARC. Monographs on the Evaluation of the Carcinogenic Risk 
Agency for Research on Cancer, 1972-PRESENT. (Multivolume work).V19 392 
(1979)]**PEER REVIEWED**

MECHANISM OF ACTION:
PRECARCINOGEN VINYL CHLORIDE CONVERTED TO ALKYLATING INTERMEDIATE 
RESPONSIBLE FOR INTRODUCTION OF 2-OXYETHYL GROUP ONTO NUCLEOPHILIC SITES 
IN DNA & PROTEINS OF MICE. [GOTHE ET AL; BIOCHEM BIOPHYS RES COMMUN 76
After metabolic activation to CEO by CYP2E1, vinyl chloride exerts various genotoxic effects (including gene mutations and chromosomal aberrations) in different organisms, including bacteria, yeasts, mammalian cells in culture, Drosophila, rodents and humans. Among the mutagenic events induced by vinyl chloride, base-pair substitutions appear, so far, to be the most frequent. Vinyl chloride in the presence of an activation system has a transforming activity on mammalian (rodent) cells in culture. [WHO; Environmental Health Criteria 215: Vinyl Chloride p. 187 (1999)]

The first step in biotransformation of ... vinyl chloride ... has been proposed to involve microsomal oxidation leading to epoxide formation across the double bond. ... /It has been/ suggested that the resulting oxiranes are highly reactive and therefore can covalently bind to nucleic acids with the eventual end result of mutations and cancer. [Klaassen, C.D., M.O. Amdur, Doull J. (eds.). Casarett and Doull's Toxicology. The Basic Science of Poisons. 5th ed. New York, NY: McGraw-Hill, 1995.750]

INTERACTIONS:

**SPRAGUE-DAWLEY MALE RATS RECEIVED EITHER 5% ETHANOL IN DRINKING WATER OR DRINKING WATER ONLY FOR 4 WK PRIOR TO BEGINNING INHALATION OF 600 PPM VINYL CHLORIDE FOR 4 HR/DAY ON 5 DAYS/WK FOR 12 MO. AFTER 60 WEEKS FROM THE FIRST VINYL CHLORIDE EXPOSURE, LIVER TUMORS WERE FOUND IN 75% OF THE VINYL CHLORIDE-ETHANOL RATS AND IN 38% OF THE VINYL CHLORIDE-ONLY GROUP.**


The metabolism of vinyl chloride /was inhibited/ by administering a single dose of 320 mg/kg pyrazole one hr prior to inhalation of /vinyl chloride/ gas. [Hefner RE Jr et al; Ann NY Acad Sci 246: 135-48 (1975) as cited in USEPA; Ambient Water Quality Criteria Doc: Vinyl Chloride p.C-21 (1980) EPA 440/5-80-078]

Vinyl chloride and ethylene are acutely hepatotoxic in rats pretreated with polychlorinated biphenyl. ... Trichloropropane oxide significantly incr vinyl chloride toxicity in fasted but not in fed rats. Diethylmaleate significantly lowered hepatic glutathione during exposure, but did not increase hepatotoxicity of either vinyl chloride or ethylene. ... In polychlorinated biphenyl-treated rats, hepatic glutathione and hepatic epoxide hydroxylase influence the acute hepatotoxicity of vinyl chloride. [Conolly RB, Jaeger RJ; Toxicol Appl Pharmacol 50 (3): 523-32 (1979)]

/Combining/ 1 mg/cu m vinyl chloride with 1 mg phenol/cu m antagonized the effects on the nervous system of rats in a 7 mo continuous inhalation study. The mixture did not affect the learning ability which was impaired by 1 mg/cu m of either /cmpd/ separately. Vinyl chloride alone ...
extended the blood clotting time. [Chyba A; Rocz Panstw Zakl Hig 32 (4): 357-61 (1981)]**PEER REVIEWED**

Inorganic arsenic (As), 1,2-dichloroethane (DCE), vinyl chloride (VC) & trichloroethylene (TCE) are frequently identified as groundwater contaminants near hazardous waste disposal sites. While the carcinogenicity of each of these chemicals has been extensively studied individually, little information exists regarding their carcinogenic potential in combination. Therefore, we investigated the carcinogenic promoting potential of chemical mixtures containing arsenic, DCE, VC and TCE following multiple initiator administration in a multiple organ carcinogenicity bioassay ... . Our results reveal a dose-responsive antagonistic effect of this four-chemical mixture on the development of preneoplastic hepatic lesions (altered hepatocellular foci and glutathione S- transferase pi positive foci) as well as bronchioalveolar hyperplasia and adenoma formation. [POTT WA et al; Cancer Letters 133 (2): 185-190 (1998)]**PEER REVIEWED**

PHARMACOLOGY:

INTERACTIONS:


The metabolism of vinyl chloride /was inhibited/ by administering a single dose of 320 mg/kg pyrazole one hr prior to inhalation of /vinyl chloride/ gas. [Hefner RE Jr et al; Ann NY Acad Sci 246: 135-48 (1975) as cited in USEPA; Ambient Water Quality Criteria Doc: Vinyl Chloride p.C-21 (1980) EPA 440/5-80-078]**PEER REVIEWED**

Vinyl chloride and ethylene are acutely hepatotoxic in rats pretreated with polychlorinated biphenyl. ... Trichloropropane oxide significantly incr vinyl chloride toxicity in fasted but not in fed rats. Diethylmaleate significantly lowered hepatic glutathione during exposure, but did not increase hepatotoxicity of either vinyl chloride or ethylene. ... In polychlorinated biphenyl-treated rats, hepatic glutathione and hepatic epoxide hydroxylase influence the acute hepatotoxicity of vinyl chloride. [Conolly RB, Jaeger RJ; Toxicol Appl Pharmacol 50 (3): 523-32 (1979)]**PEER REVIEWED**

/Combining/ 1 mg/cu m vinyl chloride with 1 mg phenol/cu m antagonized the effects on the nervous system of rats in a 7 mo continuous inhalation study. The mixture did not affect the learning ability which was impaired
Inorganic arsenic (As), 1,2-dichloroethane (DCE), vinyl chloride (VC) & trichloroethylene (TCE) are frequently identified as groundwater contaminants near hazardous waste disposal sites. While the carcinogenicity of each of these chemicals has been extensively studied individually, little information exists regarding their carcinogenic potential in combination. Therefore, we investigated the carcinogenic promoting potential of chemical mixtures containing arsenic, DCE, VC and TCE following multiple initiator administration in a multiple organ carcinogenicity bioassay ... . Our results reveal a dose-responsive antagonistic effect of this four-chemical mixture on the development of preneoplastic hepatic lesions (altered hepatocellular foci and glutathione S- transferase pi positive foci) as well as bronchoalveolar hyperplasia and adenoma formation. [POTT WA et al; Cancer Letters 133 (2): 185-190 (1998)]**PEER REVIEWED**

ENVIRONMENTAL FATE & EXPOSURE:

ENVIRONMENTAL FATE/EXPOSURE SUMMARY:

Vinyl chloride's production and use in the manufacture of polyvinyl chloride (PVC) and other chlorinated compounds may result in its release to the environment through various waste streams. Vinyl chloride is also an anaerobic biodegradation product of higher chlorinated compounds such as tetrachloroethylene and trichloroethylene. If released to air, a vapor pressure of 2,980 mm Hg at 25 deg C indicates vinyl chloride will exist solely as a gas in the ambient atmosphere. Gas-phase vinyl chloride will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 55 hours. Direct photolysis is not expected to be an important environmental fate process since this compound only absorbs light weakly in the environmental UV spectrum. If released to soil, vinyl chloride is expected to have high mobility based upon an estimated Koc value of 57. Volatilization from moist soil surfaces is expected to be an important fate process based upon a Henry's Law constant of 0.0278 atm-cu m/mole. Vinyl chloride may volatilize from dry soil surfaces based upon its vapor pressure. The volatilization half-life of vinyl chloride was estimated as 0.2 days when incorporated in a soil at a depth of 1 cm and 0.5 days at a depth of 10 cm. Biodegradation is expected to occur slowly in the environment under both aerobic and anaerobic conditions. Vinyl chloride was approximately 50% and 100% degraded in 4 and 11 weeks, respectively, in the presence of sand by methanogenic microorganisms under anaerobic conditions in laboratory scale experiments. In the absence of sand 20% and 55% degradation occurred in 4 and 11 weeks, respectively. If released into water, vinyl chloride is not expected to adsorb to suspended solids and sediment in water based upon the estimated Koc. The biodegradation half-life of vinyl chloride in aerobic and anaerobic waters was reported as 28 and 110 days, respectively. Volatilization from water surfaces is expected to be an important fate process based upon this compound's Henry's Law constant. Estimated volatilization half-lives for a model river and model lake are 1 hour and 3 days, respectively. A measured BCF value of less than 10 in fish suggest bioconcentration in aquatic organisms is low. Hydrolysis is not expected to be an important
environmental fate process based on a hydrolysis half-life of 9.91 years at pH 7 and 25 deg C. Vinyl chloride may undergo indirect photolysis in natural waters when photosensitizers such as humic material are available. This process is only expected to be important in sunlit surface waters containing humic material. Occupational exposure to vinyl chloride may occur through inhalation and dermal contact with this compound at workplaces where vinyl chloride is produced or used. The general population may be exposed to vinyl chloride via inhalation of ambient air, ingestion of food and drinking water. (SRC) **PEER REVIEWED**

PROBABLE ROUTES OF HUMAN EXPOSURE:

Inhalation is the major route of exposure for nearby residents and workers(1). Exposure is also possible by ingestion of contaminated foods, drinking water and absorption through skin from cosmetics(1). [(1) USEPA; Ambient Water Quality Criteria for Vinyl Chloride. p.C-2 USEPA-440/5-80-078 (1980)]**PEER REVIEWED**

NIOSH (NOES Survey 1981-1983) has statistically estimated that 21,018 workers (8,840 of these are female) are potentially exposed to vinyl chloride in the US(1). Occupational exposure to vinyl chloride may occur through inhalation and dermal contact with this compound at workplaces where vinyl chloride is produced or used(SRC). The mean TWA concentrations of vinyl chloride in various jobs of polyvinyl chloride factories were given as follows: tank supplier, 659.67 mg/cu m; PVC reliever, 153.07 mg/cu m; tank cleaner, 95.57 mg/cu m; vinyl chloride unloader, 12.56 mg/cu m; safety and health specialist, 12.04 mg/cu m; foreman, 9.04 mg/cu m; stripper operator, 4.51 mg/cu m; vinyl chloride recovery operator, 4.38 mg/cu m; control room operator, 4.01 mg/cu m; field supervisor, 3.42 mg/cu m; office personnel, 3.34 mg/cu m; maintenance, 2.69 mg/cu m; dryer, 1.84 mg/cu m; bagger and trucker, 0.93 mg/cu m; gatekeeper, 0.93 mg/cu m(2). The general population may be exposed to vinyl chloride via inhalation of ambient air, ingestion of food and drinking water(SRC). [(1) NIOSH; National Occupational Exposure Survey (NOES) (1983) (2) Du CL et al; Bull Environ Contam Toxicol 56: 534-42 (1996)]**PEER REVIEWED**

BODY BURDEN:
A STRONG CORRELATION WAS FOUND BETWEEN VINYL CHLORIDE (VC) CONCN AT WORKING PLACES AND THE INCR EXCRETION OF THIODIGLYCOLIC ACID OF 18 EXPOSED WORKERS. THE VALUES OBTAINED WERE IN THE RANGE OF 0.14-7.00 PPM. THE EXCRETION OF THIODIGLYCOLIC ACID, MEASURED BY GAS CHROMATOGRAPHY-MASS SPECTROMETRY ANALYSIS, AMOUNTED TO 0.3-4.0 MG/L. [MUELLER G ET AL; INT ARCH OCCUP ENVIRON HEALTH 41 (3): 199 (1978)]**PEER REVIEWED**

NATURAL POLLUTION SOURCES:
Vinyl chloride monomer is not known to occur in nature(1). [(1) IARC; Monograph Some Monomers, Plastics and Synthetic Elastomers, and Acrolein 19: 377-83 (1979)]**PEER REVIEWED**

ARTIFICIAL POLLUTION SOURCES:
Small quantities of chloroethene can be exposed to food by migration of chloroethene monomer present in polyvinyl chloride food wrappings and containers. [Gilbert SG et al; J Food Process Preserv 4 (1-2): 27-49]
Water pollution by tetrachloroethylene leaching from vinyl liners in asbestos-cement water pipelines for water distribution. [Yuskus LR; J Am Water Works Assoc 76 (2): 76-81 (1984)]**PEER REVIEWED**


ENVIRONMENTAL FATE:
AQUATIC FATE: The rate of bulk exchange of gaseous vinyl chloride between atmosphere and water is about twice that of oxygen. As a result, the loss of vinyl chloride by volatilization from water is probably the most significant process in its distribution. There is little information pertaining specifically to the rate of adsorption onto particulate matter. In a study on the behavior of vinyl chloride in water, no significant difference in the rate of loss from distilled water, river water, or effluent from a vinyl chloride plant stirred at the same rate was found, thus indicating negligible adsorption onto particulate matter. Aquatic sediments could exhibit long-term storage of low levels if extreme environmental conditions, such as continual high levels of vinyl chloride input were present in water. [Callahan, M.A., M.W. Slimak, N.W. Gabel, et al. Water-Related Environmental Fate of 129 Priority Pollutants. Volume II. EPA-440/4-79-029b. Washington, D.C.: U.S. Environmental Protection Agency, December 1979.49-6]**PEER REVIEWED**

AQUATIC FATE: In environments such as municipal water chlorination facilities, high concentrations of chloride would exist. Under certain conditions, vinyl chloride may be converted to more highly chlorinated compounds based on the reactivity of carbon-carbon double bonds with chlorine and hypo-halous acid. Dissolved vinyl chloride in water will readily escape into the gas phase, but chemical reactions can occur with water impurities which may inhibit its release. Many salts have the ability to form complexes with vinyl chloride and can increase its solubility. Therefore, the amounts of vinyl chloride in water could be influenced significantly by the presence of salts. [Callahan, M.A., M.W. Slimak, N.W. Gabel, et al. Water-Related Environmental Fate of 129 Priority Pollutants. Volume II. EPA-440/4-79-029b. Washington, D.C.: U.S. Environmental Protection Agency, December 1979.49-7]**PEER REVIEWED**

TERRESTRIAL FATE: Based on a classification scheme, an estimated Koc value of 57, calculated from a water solubility of 2,700 mg/l and a regression derived equation indicates that vinyl chloride is expected to have high mobility in soil. Volatilization of vinyl chloride from moist soil surfaces is expected to be an important fate process given a Henry's Law constant of 0.0278 atm-cu m/mole. Vinyl chloride may volatilize from dry soil surfaces based on a vapor pressure of 2,780 mm Hg at 25 deg C. The volatilization half-life of vinyl chloride was estimated as 0.2 days when incorporated in a soil at a depth of 1 cm and


**ATMOSPHERIC FATE:** According to a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere (1), vinyl chloride, which has a vapor pressure of 2,980 mm Hg at 25 deg C (2), is expected to exist solely as a gas in the ambient atmosphere. Gas-phase vinyl chloride is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals (SRC); the half-life for this reaction in air is estimated to be 55 hours (SRC), calculated from its rate constant of 6.96X10-12 cu cm/molecule-sec at 25 deg C (3). Vinyl chloride is not expected to undergo considerable direct photolysis since this compound does not absorb light appreciably in the environmental UV spectrum (SRC). [(1) Bidleman TF; Environ Sci Technol 22: 361-367 (1988) (2) Daubert TE, Danner RP; Physical and Thermodynamic Properties of Pure Chemicals Data Compilation Washington, DC: Taylor and Francis (1989) (3) Atkinson R; J. Phys Chem Ref Data Monograph 1 (1989) (4) Crutzen PJ et al; J Geophys Res 83: 345-63 (1978) (5) Dilling WL et al; Environ Sci Technol 9: 833-88]
ENVIRONMENTAL BIODEGRADATION:

Limited existing data indicate that vinyl chloride is resistant to biodegradation in aerobic systems (1,2). Vinyl chloride was approximately 50% and 100% degraded in 4 and 11 weeks, respectively, in the presence of sand by methanogenic microorganisms under anaerobic conditions in laboratory scale experiments (3). In the absence of sand 20% and 55% degradation occurred in 4 and 11 weeks, respectively (3). [(1) Helfgott TB et al.; An Index of Refractory Organics, p. 21 USEPA-600/2-77-174 (1977) (2) Callahan MA et al.; Water-related Environmental Fate of 129 Priority Pollutants Vol 2, p. 49-1 to 49-10 USEPA-440/4-79-029b (1979) (3) Brauch HJ et al; Vom Wasser 68: 23-32 (1987)]

Studies have shown that anaerobic bacteria can reduce tetrachloroethylene and trichloroethylene to vinyl chloride via reductive dechlorination (1,2). The resultant vinyl chloride is further reduced to ethene, but the dechlorination of vinyl chloride to ethene is very slow and as a result an accumulation of vinyl chloride is noticed (1). The biodegradation half-life of vinyl chloride in aerobic and anaerobic waters was reported as 28 and 110 days, respectively (3). The first-order anaerobic biodegradation rate constant of vinyl chloride was reported to range from 0.0062-0.00096 day⁻¹(4). These rate constants correspond to half-lives in the range of 112 to 722 days (SRC). [(1) Hunkeler D et al; Environ Sci Technol 33: 2733-38 (1999) (2) Yager RM et al; Environ Sci Technol 31: 3138-47 (1997) (3) Capel PD, Larson SJ; Chemosphere 30: 1097-1106 (1995) (4) Rathbun RE; US Geol Surv Prof Pap 1589: 1-151 (1998)]

ENVIRONMENTAL ABIOTIC DEGRADATION:

... Reacts at an extremely rapid rate with hydroxyl radicals, exhibiting a half-life on the order of a few hours with the subsequent formation of hydrogen chloride or formyl chloride as possible products. Formyl chloride, if formed, is reported to decompose thermally at ambient temperatures with a half-life of about 20 minutes, yielding carbon monoxide and hydrogen chloride. [Callahan, M.A., M.W. Slimak, N.W. Gabel, et al. Water-Related Environmental Fate of 129 Priority Pollutants. Volume II. EPA-440/4-79-029b. Washington, D.C.: U.S. Environmental Protection Agency, December 1979.49-1]

Vinyl chloride, in the vapor phase, does not absorb light of wavelengths greater than 220 nm, and in water it does not absorb above 218 nm. As a result, direct photolysis ... would be expected, at best, to be a very slow process due to lack of overlap between vinyl chloride absorption and sunlight radiation spectra. ... It is, however, possible that light-induced transformations of vinyl chloride could occur through indirect photolysis. Photolysis experiments were conducted ... in natural water and in distilled water containing photosensitizers that absorb light of wavelengths greater than 300 nm. It was found that vinyl chloride in soln decomposed rapidly when irradiated with ultraviolet light in the presence of acetone, a high energy triplet sensitizer, or hydrogen peroxide, a free radical source. [Callahan, M.A., M.W. Slimak, N.W. Gabel, et al. Water-Related Environmental Fate of 129 Priority Pollutants. Volume II. EPA-440/4-79-029b. Washington, D.C.: U.S. Environmental Protection Agency, December 1979.49-2]

Atmospheric photodissociation ... appears to be much less important than photochemical oxidation. Rapid photochemical oxidation is reported to
remove the compound from the troposphere with a half-life of a few hours. As a result, neither the chlorine in vinyl chloride nor vinyl chloride itself is likely to diffuse to the stratosphere. Experiments ... indicate ... that if reactive radicals are present in natural waters at significant concn, they may degrade vinyl chloride. Experimental results show that vinyl chloride will not be significantly degraded by molecular oxygen at temperatures and oxygen concn present in natural waters. [Callahan, M.A., M.W. Slimak, N.W. Gabel, et al. Water-Related Environmental Fate of 129 Priority Pollutants. Volume II. EPA-440/4-79-029b. Washington, D.C.: U.S. Environmental Protection Agency, December 1979.49-3]**PEER REVIEWED**

Hydrolysis over a pH range of 4.3 to 9.4 does not appear to be an important pathway for loss of vinyl chloride from water. The hydrolytic half-life ... has been estimated to be less than 10 years at 25 deg C. Since the volatilization rate ... is much more rapid than the predicted rate of hydrolysis, hydrolysis should not be a significant aquatic fate. [Callahan, M.A., M.W. Slimak, N.W. Gabel, et al. Water-Related Environmental Fate of 129 Priority Pollutants. Volume II. EPA-440/4-79-029b. Washington, D.C.: U.S. Environmental Protection Agency, December 1979.49-4]**PEER REVIEWED**

The rate constant for the gas-phase reaction of vinyl chloride with photochemically-produced hydroxyl radicals is 6.96X10^{-12} \text{ cu cm/molecule-sec at 25 deg C}. This corresponds to an atmospheric half-life of about 55 hours at an atmospheric concentration of 5X10^{+5} hydroxyl radicals per cu cm(1). Vinyl chloride may also be degraded in the atmosphere by reaction with ozone, but the rate of this reaction is too slow to be environmentally important(2). Vinyl chloride is not expected to undergo considerable direct photolysis since this compound does not absorb light appreciably in the environmental UV spectrum(SRC). Vinyl chloride may undergo indirect photolysis in natural waters when photosensitizers such as humic material are available(4). Hydrolysis is not expected to be an important environmental fate process based on hydrolysis half-lives of 9.91 years (pH = 7, 25 deg C) and 10.7 years (pH = 7, 10 deg C)(4). [(1) Atkinson R; J Phys Chem Ref Data Monograph 1 (1989) (2) Atkinson R, Carter WPL; Chem Rev 84: 437-70 (1984) (3) Mill T; Chemosphere 38: 1379-90 (1999) (4) Rathbun RE; US Geol Surv Prof Pap 1589: 1-151 (1998)]**PEER REVIEWED**

ENVIRONMENTAL BIOCONCENTRATION:

The BCF value of vinyl chloride in golden ide fish was reported as less than 10(1). The BCF value of vinyl chloride in green algae was reported as 40(2). According to a classification scheme(3), the BCF data suggest that bioconcentration in aquatic organisms is low(SRC). [(1) Freitag D et al; Chemosphere 14: 1589-1616 (1985) (2) Rathbun RE; US Geol Surv Prof Pap 1589: 1-151 (1998) (3) Franke C et al; Chemosphere 29: 1501-14 (1994)]**PEER REVIEWED**

SOIL ADSORPTION/MOBILITY:

VOLATILIZATION FROM WATER/SOIL: The Henry's Law constant for vinyl chloride is 0.0278 atm-cu m/mole (1). This Henry's Law constant indicates that vinyl chloride expected to volatilize rapidly from water surfaces (2). Based on this Henry's Law constant, the volatilization half-life from a model river (1 m deep, flowing 1 m/sec, wind velocity of 3 m/sec) (2) is estimated as 1 hour (SRC). The volatilization half-life from a model lake (1 m deep, flowing 0.05 m/sec, wind velocity of 0.5 m/sec) (2) is estimated as 3 days (SRC). Vinyl chloride's Henry's Law constant (1) indicates that volatilization from moist soil surfaces may occur (SRC). Vinyl chloride is expected to volatilize from dry soil surfaces based on a vapor pressure of 2,980 mm Hg at 25 deg C (3). The volatilization half-life of vinyl chloride was estimated as 0.2 days when incorporated into a soil surface 1 cm in depth and 0.5 days when incorporated at a depth of 10 cm (4). [(1) Gossett JM; Environ Sci Technol 21: 202-206 (1987) (2) Lyman WJ et al; Handbook of Chemical Property Estimation Methods. Washington, DC: Amer Chem Soc pp. 15-1 to 15-29 (1990) (3) Daubert TE, Danner RP; Physical and Thermodynamic Properties of Pure Chemicals Data Compilation Washington, DC: Taylor and Francis (1989) (4) Jury WA et al; J Environ Qual 13: 573-79 (1984)] **PEER REVIEWED**

ENVIRONMENTAL WATER CONCENTRATIONS: DRINKING WATER: In the National Organic Monitoring Survey (1976-77) 2 samples out of 113 contained detectable levels (> 0.1 ppb) and these averaged 0.14 ppb (1). 31 of 133 US cities using finished surface water contained vinyl chloride at concns of 0.1 to 9.8 ppb (2). A contaminated drinking water well located in New York contained 50 ppb vinyl chloride (3). Drinking water from PVC pipes contained 1.4 ppb vinyl chloride in a recent installation, while a 9 yr old system had 0.03 to 0.06 ppb (4). The concentration of vinyl chloride in various brands of bottled water was 0.6 ppb or less (5). A national screening program for US water supplies showed that 7 of 142 samples contained vinyl chloride at a max concn of 76 ppb (6). [(1) Drury JS, Hammons AS; Investigations of Selected Environmental Pollutants 1,2-dichloroethane. p. 63 USEPA-560/2-78-006 (1979) (2) Coniglio WA et al; The Occurrence of Volatile Organics in Drinking Water. USEPA Exposure Assessment Project (1980) (3) Burmaster DE; Environ 24: 6-13, 33-6 (1982) (4) USEPA; Ambient Water Quality Criteria for Vinyl Chloride. USEPA-440/5-80-078 (1980) (5) Fayad NM et al; J Environ Sci Health A32: 1065-83 (1997) (6) Cotruvo JA et al; p. 511-30 in Organic Carcinogens in Drinking Water (1986)] **PEER REVIEWED**

GROUNDWATER: Vinyl chloride was detected in 2 of 13 US cities groundwater supplies at concns of 2.2 to 9.4 ppb (1,2). Vinyl chloride was detected in 7% of all wells tested in a 9 state US survey at a max concn of 380 ppb (3). Vinyl chloride was identified, not quantified in 4 of 1,060 wells in New Jersey (4). After train derailment in Manitoba on Mar 10, 1980, in


EFFLUENT CONCENTRATIONS: Vinyl chloride was detected in gas samples from municipal landfill sites in Canada at concns of 3,508 and 7,470 ppb (1). Vinyl chloride was detected in landfill gas in Ontario, Canada at concns of 0.0023-0.0412 ug/cu m (2). The estimated amount of vinyl chloride emitted from 2 wastewater treatment plants in Los Angeles, CA were 14 kg/year and 3 kg/year (3). The only industry with appreciable waste water effluents of vinyl chloride is the organic chemicals mfg/plastic industry where mean levels are 750 ppb (4). Waste water from 12 polyvinyl chloride (PVC) plants in 7 US areas ranged from 0.05 to 20 ppm with typical levels being 2 to 3 ppm (5). Vinyl chloride was detected in landfill leachate at concns of 8-3,000 g/l and landfill gas at 0-83.2 mg/cu m (6). [(1) Brosseau J, Heitz M; Atmos Environ 28: 285-93 (1994) (2) Chandler DS et al; J Air Waste Manage Assoc 87th annual Meet (1994) (3) Mayer GJ et al; Wat Environ Res 66: 140-44 (1994) (4) USEPA; Treatability Manual. p.12.12-1 to 12.12-4 USEPA-600/2-82-001a (1981) (5) USEPA; Ambient Water Quality Criteria for Vinyl Chloride. USEPA-440/5-80-078 (1980) (6) Roy WR; pp. 411-6 in Contam Groundwaters. Adriano DC et al, eds., Northwood, UK: Sci Rev (1994)]**PEER REVIEWED**
SEDIMENT/SOIL CONCENTRATIONS:

SEDIMENT: After March 10, 1980 train derailment in Canada in which large quantities of vinyl chloride were spilled in the snow, soil samples reached levels as high as 500 ppm between one and two meters below the soil surface. ([1] Charlton J et al; pp. 245-67 in Hazard Assessment of Chemicals Vol 2. Saxena J ed (1983)] PEER REVIEWED


ATMOSPHERIC CONCENTRATIONS:


SOURCE DOMINATED: Ambient air near 2 vinyl chloride (VC) plants in Long Beach, CA contained 0.1-3.4 ppm [1]. Vinyl chloride was detected in new auto interiors at concns of 0.4 to 1.2 ppm [1]. After Mar 10, 1980 train derailment in Canada in which quantities of VC were spilled during a blizzard, levels in excess of 200 ppm were found at ground levels near some freight cars but levels outside of the spill area were < 0.02 ppm the detection limit [2]. Vinyl chloride was detected in ambient air near a waste site at 2-7.3 ppb [3]. Vinyl chloride was detected in eight highly industrialized areas in the US at concns of 0-0.513 ppb [4]. Vinyl chloride was detected in Houston, TX near vinyl chloride manufacturing plants at concns of 3.1-1,250 ppb [5, 6]. ([1] IARC; Monograph, Some Monomers, Plastics and Synthetic Elastomers, and Arolein 19: 380-3 (1979) (2) Charlton J et al; pp. 245-67 in Hazard Assessment of Chemicals Vol 2. Saxena J, ed (1983) (3) Stephens RD et al; pp. 265-87 in Pollutants in a Multimedia Environment. Cohen Y, ed. NY, NY: Plenum Press (1986) (4) Pellizzari ED; Quantification of Chlorinated Hydrocarbons in Previously Collected Air Samples USEPA-450/3-78-112 (1978) (5) McMurray JR, Tarr J; IES 24 Ann Mtg Fort Worth, TX 18-20 Apr 78 p 149-53 (1978) (6) Fishbein L; Sci Total Environ 11: 111-61 (1979)] PEER REVIEWED

INDOOR AIR: Vinyl chloride was detected in the air of homes from a neighborhood surrounding a landfill at concns of 4 ppb (avg) and 7 ppb (max concn) [1]. ([1] Stephens RD et al; pp. 265-87 in Pollutants in a Multimedia Environment. Cohen Y, ed. NY, NY: Plenum Press (1986)] PEER REVIEWED

FOOD SURVEY VALUES:

Vinyl chloride was detected at 20 mg/kg in alcoholic beverages which were packaged in products containing vinyl chloride [1, 2]. Vinyl chloride was detected in edible oils at concns of 0.05 to 2 ppm avg and in butter and margarine at unspecified concns [2]. ([1] IARC; Monograph Some Anti-Thyroid
OTHER ENVIRONMENTAL CONCENTRATIONS:
Vinyl chloride monomer has been found in polyvinyl chloride resins but these levels can be reduced by new processing techniques in food grade resins(1). For example, PVC delivered to a fabricator contained 250 ppm vinyl chloride monomer which was reduced to 0.5-20 ppm after fabrication(1). Residual vinyl chloride monomer found in food packing material ranged from 0.043-71 ppb for film and up to 7.9 ppm for plastic bottles(1). It has been found in domestic and foreign cigarettes and little cigars in concentrations of 5.6-27 mg/cigarette(1). [(1) IARC; Monograph Some Monomers, Plastics and Synthetic Elastomers, and Acrolein 19: 381-3 (1979)]**PEER REVIEWED**

ENVIRONMENTAL STANDARDS & REGULATIONS:

ACCEPTABLE DAILY INTAKES:
The ten day health advisory for vinyl chloride for a 10 kg child that consumes one liter of water/day is 2.6 mg/day or 0.26 mg/kg/day. [USEPA/ODW; Vinyl Chloride Health Advisory (Draft) p.7 (1985)]**PEER REVIEWED**

CERCLA REPORTABLE QUANTITIES:
Persons in charge of vessels or facilities are required to notify the National Response Center (NRC) immediately, when there is a release of this designated hazardous substance, in an amount equal to or greater than its reportable quantity of 1 lb or 0.454 kg. The toll free number of the NRC is (800) 424-8802; In the Washington D.C. metropolitan area (202) 426-2675. The rule for determining when notification is required is stated in 40 CFR 302.4 (section IV. D.3.b). [40 CFR 302.4 (7/1/2000)]**PEER REVIEWED**

RCRA REQUIREMENTS:
D043; A solid waste containing vinyl chloride may or may not become characterized as a hazardous waste when subjected to the Toxicity Characteristic Leaching Procedure listed in 40 CFR 261.24, and if so characterized, must be managed as a hazardous waste. [40 CFR 261.24 (7/1/2000)]**PEER REVIEWED**

U043; As stipulated in 40 CFR 261.33, when vinyl chloride, as a commercial chemical product or manufacturing chemical intermediate or an off-specification commercial chemical product or a manufacturing chemical intermediate, becomes a waste, it must be managed according to Federal and/or State hazardous waste regulations. Also defined as a hazardous waste is any residue, contaminated soil, water, or other debris resulting from the cleanup of a spill, into water or on dry land, of this waste. Generators of small quantities of this waste may qualify for partial exclusion from hazardous waste regulations (40 CFR 261.5). [40 CFR 261.33 (7/1/2000)]**PEER REVIEWED**

ATMOSPHERIC STANDARDS:
Emission standards for ... vinyl chloride ... and compliance to the following topic areas are considered: (1) Relief valve discharge; (2)
Fugitive emission sources; (3) Leakage from pump, compressor, and agitator seals; (4) Leaks from relief valves; (5) Manual venting of gases; (6) Opening of equipment; (7) Samples; (8) Leak detection and elimination; and (9) In process wastewater. [40 CFR 61.65 (7/1/90)]**PEER REVIEWED**

Vinyl chloride formation and purification: The concn of vinyl chloride in each exhaust gas stream from any equipment used in vinyl chloride formation and/or purification is not to exceed 10 ppm (average for 3 hr period), except as provided in 40 CFR 61.65(a). [40 CFR 61.63 (7/1/90)]**PEER REVIEWED**

This action promulgates standards of performance for equipment leaks of Volatile Organic Compounds (VOC) in the Synthetic Organic Chemical Manufacturing Industry (SOCMI). The intended effect of these standards is to require all newly constructed, modified, and reconstructed SOCMI process units to use the best demonstrated system of continuous emission reduction for equipment leaks of VOC, considering costs, non air quality health and environmental impact and energy requirements. Vinyl chloride is produced, as an intermediate or a final product, by process units covered under this subpart. [40 CFR 60.489 (7/1/2000)]**PEER REVIEWED**

Vinyl chloride has been designated as a hazardous air pollutant under section 112 of the Clean Air Act. [40 CFR 61.01 (7/1/2000)]**PEER REVIEWED**

Listed as a hazardous air pollutant (HAP) generally known or suspected to cause serious health problems. The Clean Air Act, as amended in 1990, directs EPA to set standards requiring major sources to sharply reduce routine emissions of toxic pollutants. EPA is required to establish and phase in specific performance based standards for all air emission sources that emit one or more of the listed pollutants. Vinyl chloride is included on this list. [Clean Air Act as amended in 1990, Sect. 112 (b) (1) Public Law 101-549 Nov. 15, 1990]**PEER REVIEWED**

CLEAN WATER ACT REQUIREMENTS:
Toxic pollutant designated pursuant to section 307(a)(1) of the Federal Water Pollution Control Act and is subject to effluent limitations.[40 CFR 401.15 (7/1/2000)]**QC REVIEWED**

FEDERAL DRINKING WATER STANDARDS:

STATE DRINKING WATER STANDARDS:
(CA) CALIFORNIA 0.5 ug/l[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)]**QC REVIEWED**

(FL) FLORIDA 1 ug/l[USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)]**QC REVIEWED**

STATE DRINKING WATER GUIDELINES:

(AZ) ARIZONA 0.015 ug/l [USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)]**QC REVIEWED**

(CT) CONNECTICUT 2 ug/l [USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)]**QC REVIEWED**

(ME) MAINE 0.15 ug/l [USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)]**QC REVIEWED**

(MN) MINNESOTA 0.2 ug/l [USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93)]**QC REVIEWED**

FDA REQUIREMENTS:

Vinyl chloride is an indirect food additive for use only as a component of adhesives. [21 CFR 175.105 (4/1/2000)]**PEER REVIEWED**

CHEMICAL/PHYSICAL PROPERTIES:

MOLECULAR FORMULA:


MOLECULAR WEIGHT:


COLOR/FORM:


ODOR:


BOILING POINT:

MELTING POINT:

CORROSIVITY:
VINYL CHLORIDE IS NOT CORROSIVE WHEN DRY BUT IN PRESENCE OF MOISTURE IT CORRODES IRON AND STEEL. [Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968.82]**PEER REVIEWED**

CRITICAL TEMPERATURE & PRESSURE:
424.61 deg K; 151.5 deg C; 304.6 deg F/5755 kPa; 57.55 bar; 834.7 psia; 56.8 atm [Braker W, Mossman Al; Matheson Gas Data Book 6th ED p.695 (1980)]**PEER REVIEWED**

DENSITY/SPECIFIC GRAVITY:

HEAT OF VAPORIZATION:
20.9 kJ/mole at -13.4 deg C [Environment Canada; Tech Info for Problem Spills: Vinyl Chloride (Draft) p.4 (1981)]**PEER REVIEWED**

SOLUBILITIES:


In water, 8.8X10+3 mg/l @ 25 deg C [Delassus PT, Schmidt DD; J Chem Eng Data 26: 274-6 (1981)]**PEER REVIEWED**

SPECTRAL PROPERTIES:


SURFACE TENSION:
23.1 dyn/cm at -20 deg C [Braker W, Mossman A; Matheson Gas Data Book 6th ED p.695 (1980)]**PEER REVIEWED**

VAPOR DENSITY:

VAPOR PRESSURE:

VISCOSITY:
Viscosity, gas at 101.325 kPa at 20 deg C is 0.01072 cP; viscosity, liquid at -20 deg C is 0.280 cP [Braker W, Mossman A; Matheson Gas Data Book 6th ED p.695 (1980)]**PEER REVIEWED**

OTHER CHEMICAL/PHYSICAL PROPERTIES:

Henry's Law constant= 0.0278 atm-cu m/mole @ 25 deg C [Gossett JM; Environ Sci Technol 21: 202-6 (1987)]**PEER REVIEWED**

Hydroxyl radical rate constant = 6.96X10-12 cu cm/molecule-sec @ 25 deg C [Atkinson R; J Phys Chem Ref Data. Monograph No. 1 (1989)]**PEER REVIEWED**

CHEMICAL SAFETY & HANDLING:

DOT EMERGENCY GUIDELINES:
Fire or explosion: EXTREMELY FLAMMABLE. Will be easily ignited by heat, sparks or flames. Will form explosive mixtures with air. Silane will ignite spontaneously in air. Those substances designated with a "P" may polymerize explosively when heated or involved in a fire. Vapors from liquefied gas are initially heavier than air and spread along ground. Vapors may travel to source of ignition and flash back. Containers may explode when heated. Ruptured cylinders may rocket. /Vinyl chloride; vinyl chloride, inhibited; or vinyl chloride, stabilized/ [U.S. Department of Transportation. 2000 Emergency Response Guidebook. RSPA P 5800.8 Edition. Washington, D.C: U.S. Government Printing Office, 2000,p. G-116]**QC REVIEWED**

Health: Vapors may cause dizziness or asphyxiation without warning. Some may be toxic if inhaled at high concentrations. Contact with gas or liquefied gas may cause burns, severe injury and/or frostbite. Fire may produce irritating and/or toxic gases. /Vinyl chloride; vinyl chloride, inhibited; or vinyl chloride, stabilized/ [U.S. Department of Transportation. 2000 Emergency Response Guidebook. RSPA P 5800.8 Edition.**


Evacuation: ... Fire: If tank, rail car or tank truck is involved in a fire, ISOLATE for 1600 meters (1 mile) in all directions; also, consider initial evacuation for 1600 meters (1 mile) in all directions. /Vinyl chloride; vinyl chloride, inhibited; or vinyl chloride, stabilized/ [U.S. Department of Transportation. 2000 Emergency Response Guidebook. RSNA P 5800.8 Edition. Washington, D.C: U.S. Government Printing Office, 2000,p. G-116]**QC REVIEWED**

Fire: DO NOT EXTINGUISH A LEAKING GAS FIRE UNLESS LEAK CAN BE STOPPED. Small fires: Dry chemical or CO2. Large Fires: Water spray, fog or regular foam. Move containers from fire area if you can do it without risk. Fire involving tanks: Fight fire from maximum distance or use unmanned hose holders or monitor nozzles. Cool containers with flooding quantities of water until well after fire is out. Do not direct water at source of leak or safety devices; icing may occur. Withdraw immediately in case of rising sound from venting safety devices or discoloration of tank. ALWAYS stay away from tanks engulfed in fire. For massive fire, use unmanned hose holders or monitor nozzles, if this is impossible withdraw from area and let fire burn. /Vinyl chloride; vinyl chloride, inhibited; or vinyl chloride, stabilized/ [U.S. Department of Transportation. 2000 Emergency Response Guidebook. RSNA P 5800.8 Edition. Washington, D.C: U.S. Government Printing Office, 2000,p. G-116]**QC REVIEWED**

Spill or leak: ELIMINATE all ignition sources (no smoking, flares, sparks or flames in immediate area). All equipment used when handling the product must be grounded. Stop leak if you can do it without risk. Do not touch or walk through spilled material. Do not direct water at spill or source of leak. Use water spray to reduce vapors or divert vapor cloud drift. Avoid allowing water runoff to contact spilled material. If possible, turn leaking containers so that gas escapes rather than liquid. Prevent entry into waterways, sewers, basements or confined areas. Isolate area until gas has dispersed. /Vinyl chloride; vinyl chloride, inhibited; or vinyl chloride, stabilized/ [U.S. Department of Transportation. 2000 Emergency Response Guidebook. RSNA P 5800.8 Edition. Washington, D.C: U.S. Government Printing Office, 2000,p. G-116]**QC REVIEWED**

First aid: Move victim to fresh air. Call 911 or emergency medical
service. Apply artificial respiration if victim is not breathing. Administer oxygen if breathing is difficult. Remove and isolate contaminated clothing and shoes. In case of contact with liquefied gas, thaw frosted parts with lukewarm water. Keep victim warm and quiet. Ensure that medical personnel are aware of the material(s) involved, and take precautions to protect themselves. /Vinyl chloride; vinyl chloride, inhibited; or vinyl chloride, stabilized/ [U.S. Department of Transportation. 2000 Emergency Response Guidebook. RSPA P 5800.8 Edition. Washington, D.C: U.S. Government Printing Office, 2000,p. G-116]**QC REVIEWED**

ODOR THRESHOLD:
Although vinyl chloride has an odor at high concn, it is of no value in preventing excessive exposure. The actual vapor concn that can be detected has never been adequately determined and varies from one individual to another, from impurities in the sample and probably from duration of exposure. [Clayton, G.D., F.E. Clayton (eds.) Patty's Industrial Hygiene and Toxicology. Volumes 2A, 2B, 2C, 2D, 2E, 2F: Toxicology. 4th ed. New York, NY: John Wiley &amp; Sons Inc., 1993-1994.4176]**PEER REVIEWED**

SKIN, EYE AND RESPIRATORY IRRITATIONS:
... Primary irritant for skin ... . [Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968.82]**PEER REVIEWED**

FIRE POTENTIAL:

... /FORMS/ FLAMMABLE MIXT WITH AIR ABOVE -78 DEG C. [Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press Inc., 1968.81]**PEER REVIEWED**


NFPA HAZARD CLASSIFICATION:
Health: 2. 2= Materials that, on intense or continued (but not chronic) exposure, could cause temporary incapacitation or possible residual injury, including those requiring the use of respiratory protective equipment that has an independent air supply. These materials are hazardous to health, but areas may be entered freely if personnel are provided with full-face mask self-contained breathing apparatus that provides complete eye protection. [Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997. 325-92]**PEER REVIEWED**

Flammability: 4. 4= This degree includes flammable gases, pyrophoric liquids, and Class IA flammable liquids. The preferred method of fire attack is to stop the flow of material or to protect exposures while allowing the fire to burn itself out. [Fire Protection Guide to Hazardous Materials. 12 ed. Quincy, MA: National Fire Protection Association, 1997. 325-92]**PEER REVIEWED**
Reactivity: 2. 2= This degree includes materials that are normally unstable and readily undergo violent chemical change, but are not capable of detonation. This includes materials that can undergo chemical change with rapid release of energy at normal temperatures and pressures and materials that can undergo violent chemical changes at elevated temperatures and pressures. This also includes materials that may react violently with water or that may form potentially explosive mixtures with water. In advanced or massive fires involving these materials, fire fighting should be done from a safe distance or from a protected location.


FLAMMABLE LIMITS:

FLASH POINT:

AUTOIGNITION TEMPERATURE:

FIRE FIGHTING PROCEDURES:
If material on fire or involved in fire: Do not extinguish fire unless flow can be stopped. Use water in flooding quantities as fog. Cool all affected containers with flooding quantities of water. Apply water from as far a distance as possible. [Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994.1109]**PEER REVIEWED**


TOXIC COMBUSTION PRODUCTS:

FIREFIGHTING HAZARDS:

EXPLOSIVE LIMITS & POTENTIAL:

HAZARDOUS REACTIVITIES & INCOMPATIBILITIES:
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. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990244]**PEER REVIEWED**

HAZARDOUS DECOMPOSITION:
WHEN HEATED TO DECOMP, IT EMITS HIGHLY TOXIC FUMES OF /HYDROGEN CHLORIDE/.

HAZARDOUS POLYMERIZATION:
Polymerization occurs if heated in sunlight or presence of air; reaction is exothermic. [Environment Canada; Tech Info for Problem Spills: Vinyl Chloride (Draft) p.1 (1983)]**PEER REVIEWED**


Prolonged exposure of cylinders or tank cars to heat or fire may cause the material to polymerize with possible container rupture. [Association of American Railroads. Emergency Handling of Hazardous Materials in Surface Transportation. Washington, DC: Association of American Railroads, Bureau of Explosives, 1994.1109]**PEER REVIEWED**

... Tends to self-polymerize explosively if peroxidation occurs, and several industrial explosions have been recorded. [Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990.244]**PEER REVIEWED**


PRIOR HISTORY OF ACCIDENTS:
After a train derailment in Canada on Mar 10, 1980, in a blizzard in which 2 of 12 boxcars were found to be leaking and large quantities of vinyl chloride were spilled in the snow, a max of 10 ppm was found in groundwater at the center of the spill site. Levels dropped below the detection limit of 0.02 ppm 10 weeks after the spill. [Charlton J et al; p.245-67 in Hazard Assessment of Chemicals Vol 2; Saxena J ed (1983)]**PEER REVIEWED**

Travelling from Belgium to the BUNA works in Schkopau, ten of eighteen tank wagons filled with vinyl chloride (VC) derailed on the Magdeburg-Halle railway line just outside Schonebeck station. One wagon exploded & 4 others went up in flames. Buildings & trees in gardens located in the immediate vicinity of the track caught fire & burned. 4 owners of garden plots suffered burns. A total of 28 people received inpatient treatment in a nearby hospital, another 268 people were treated as outpatients. The typical symptoms of fume poisoning such as headache, nausea, irritations of respiratory tract & eyes were the primarily diagnosed problems. The vegetation was damaged by flue gases & developing HCl causing fire & caustic burns. Fire brigades & special task forces succeeded to control the looming danger of health & environmental hazards by cooling the burning wagons & pumping the liquid gases from the tank wagons. Vinyl chloride which was released over several days was measured in residential areas to be 0.06-8 ml/m³
air. Vinyl chloride is a gas which is heavier than air. When exposed to light it will be degraded within a few days. A technical guide concn of 3 ml/m3 air has been adopted for its cancerogenic potential. Dioxin values measured in soils & plants were in the natural range of 20 ng I-TE/kg DS. These values increased to 8300 ng at the very seat of the fire only. With the water used for fire fighting vinyl chloride penetrated into the groundwater revealing values of up to 73 mg/litre. A total of 292 urine samples taken from patients & members of the rescue forces, residents & a control group were tested for their contents of the VC metabolite thiodiacetic acid. However, this number does not allow to draw any conclusions with regard to a potential incr in the risk of cancer. With 0.27, 0.43 and 0.37 mg/litre of urine, the mean values are in the normal range for unexposed people. Only 3 cases showing values of up to 3.1 mg/litre indicated that a real exposure had taken place. The environmental & health authorities have evaluated the results of the measurements at site. [Thriene B et al; Gesundheitswesen 62 (1): 34-38 (2000)]**PEER REVIEWED**

**IMMEDIATELY DANGEROUS TO LIFE OR HEALTH:**

**PROTECTIVE EQUIPMENT & CLOTHING:**

Respiratory protection is as follows for the following concentrations of vinyl chloride: Not over 10 ppm: Combination type C supplied-air respirator, demand type, with half facepiece, and auxiliary self-contained breathing air supply, or type C supplied air respirator, demand type, with half facepiece, or any chemical cartridge respirator with an organic vapor cartridge which provides a service life of at least 1 hr for concentrations up to 10 ppm; Not over 25 ppm: A powered air purifying respirator with hood, helmet, full or half facepiece, and a canister which provides a service life of at least 4 hours for concentrations of vinyl chloride up to 25 ppm, or gas mask, front- or back-mounted canister which provides a service life of at least 4 hours for concentrations of vinyl chloride up to 25 ppm; Not over 100 ppm: Combination type C supplied air respirator, demand type, with full facepiece, and auxiliary self-contained air supply, or open circuit self-contained breathing apparatus with full facepiece in demand mode, or type C supplied air respirator, demand type, with full facepiece; Not over 1000 ppm: Combination type supplied air respirator, continuous flow type with full or half facepiece, and auxiliary self-contained air supply; Not over 3600 ppm: Combination type C supplied air respirator, pressure demand type, with full or half facepiece, and auxiliary self-contained air supply; Unknown, or above 3600 ppm: Open circuit, self-contained breathing apparatus, pressure demand type with a full facepiece. [Mackison, F. W., R. S. Stricoff, and L. J. Partridge, Jr. (eds.). NIOSH/OSHA - Occupational Health Guidelines for Chemical Hazards. DHHS(NIOSH) Publication No. 81-123 (3 VOLS). Washington, DC: U.S. Government Printing Office, Jan. 1981.5]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": ... Dispensers of liq detergent /should be
available. ... Safety pipettes should be used for all pipetting. ... In animal laboratory, personnel should ... wear protective suits (preferably disposable, one-piece & close-fitting at ankles & wrists), gloves, hair covering & overshoes. ... In chemical laboratory, gloves & gown should always be worn ... however, gloves should not be assumed to provide full protection. Carefully fitted masks or respirators may be necessary when working with particulates or gases, & disposable plastic aprons might provide addnl protection. ... Gowns ... should be/ of distinctive color, this is a reminder that they are not to be worn outside the laboratory. /Chemical Carcinogens/ [Montesano, R., H. Bartsch, E. Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A. B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979.8]**PEER REVIEWED**

Wear appropriate personal protective clothing to prevent the skin from becoming frozen from contact with the liquid or from contact with vessels containing the liquid. [NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997.331]**PEER REVIEWED**

Wear appropriate eye protection to prevent eye contact with the liquid that could result in burns or tissue damage from frostbite. [NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997.331]**PEER REVIEWED**

Quick drench facilities and/or eyewash fountains should be provided within the immediate work area for emergency use where there is any possibility of exposure to liquids that are extremely cold or rapidly evaporating. [NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997.331]**PEER REVIEWED**

Recommendations for respirator selection. Condition: At concentrations above the NIOSH REL, or where there is no REL, at any detectable concentration. Respirator Class(es): Any self-contained breathing apparatus that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode. Any supplied-air respirator that has a full facepiece and is operated in a pressure-demand or other positive-pressure mode in combination with an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive-pressure mode. [NIOSH. NIOSH Pocket Guide to Chemical Hazards. DHHS (NIOSH) Publication No. 97-140. Washington, D.C. U.S. Government Printing Office, 1997.331]**PEER REVIEWED**


PREVENTIVE MEASURES:
Nobody may keep tobacco or food either in his work clothes or at his workplace. Meals should be eaten in appropriate canteens, which should be ventilated separately and isolated from the work premises. The work clothing should be specially designed for this use and left at the end of the shift. [International Labour Office. Encyclopedia of Occupational Health and Safety. Vols. I & II. Geneva, Switzerland: International Labour Office, 1983.2258]**PEER REVIEWED**


PRECAUTIONS FOR "CARCINOGENS": Smoking, drinking, eating, storage of food or of food & beverage containers or utensils, & the application of cosmetics should be prohibited in any laboratory. All personnel should remove gloves, if worn, after completion of procedures in which carcinogens have been used. They should ... wash ... hands, preferably using dispensers of liq detergent, & rinse ... thoroughly. Consideration should be given to appropriate methods for cleaning the skin, depending on nature of the contaminant. No standard procedure can be recommended, but the use of organic solvents should be avoided. Safety pipettes should be used for all pipetting. [Chemical Carcinogens/ [Montesano, R., H. Bartsch, E. Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A. B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979.8]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": In animal laboratory, personnel should remove their outdoor clothes & wear protective suits (preferably disposable, one-piece & close-fitting at ankles & wrists), gloves, hair covering & overshoes. ... clothing should be changed daily but ... discarded immediately if obvious contamination occurs ... /also, workers should shower immediately. In chemical laboratory, gloves & gowns should always be worn ... however, gloves should not be assumed to provide full protection. Carefully fitted masks or respirators may be necessary when working with particulates or gases, & disposable plastic aprons might provide addnl protection. If gowns are of distinctive color, this is a reminder that they should not be worn outside of lab. [Chemical Carcinogens/ [Montesano, R., H. Bartsch, E. Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A. B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979.8]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": ... Operations connected with synth & purification ... should be carried out under well-ventilated hood.
Analytical procedures ... should be carried out with care & vapors evolved during ... procedures should be removed. ... Expert advice should be obtained before existing fume cupboards are used ... & when new fume cupboards are installed. It is desirable that there be means for decreasing the rate of air extraction, so that carcinogenic powders can be handled without ... powder being blown around the hood. Glove boxes should be kept under negative air pressure. Air changes should be adequate, so that concn of vapors of volatile carcinogens will not occur. /Chemical Carcinogens/ [Montesano, R., H. Bartsch, E. Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A. B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979.8]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Vertical laminar-flow biological safety cabinets may be used for containment of in vitro procedures ... provided that the exhaust air flow is sufficient to provide an inward air flow at the face opening of the cabinet, & contaminated air plenums that are under positive pressure are leak-tight. Horizontal laminar-flow hoods or safety cabinets, where filtered air is blown across the working area towards the operator, should never be used ... Each cabinet or fume cupboard to be used ... should be tested before work is begun (eg, with fume bomb) & label fixed to it, giving date of test & avg air-flow measured. This test should be repeated periodically & after any structural changes. /Chemical Carcinogens/ [Montesano, R., H. Bartsch, E. Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A. B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979.9]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Principles that apply to chem or biochem lab also apply to microbiological & cell-culture labs ... Special consideration should be given to route of admin. ... Safest method of administering volatile carcinogen is by injection of a soln. Admin by topical application, gavage, or intratracheal instillation should be performed under hood. If chem will be exhaled, animals should be kept under hood during this period. Inhalation exposure requires special equipment. ... unless specifically required, routes of admin other than in the diet should be used. Mixing of carcinogen in diet should be carried out in sealed mixers under fume hood, from which the exhaust is fitted with an efficient particulate filter. Techniques for cleaning mixer & hood should be devised before extn begun. When mixing diets, special protective clothing & possibly, respirators may be required. /Chemical Carcinogens/ [Montesano, R., H. Bartsch, E. Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A. B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979.9]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": When ... admin in diet or applied to skin, animals should be kept in cages with solid bottoms & sides & fitted with a filter top. When volatile carcinogens are given, filter tops should not be used. Cages which have been used to house animals that received carcinogens should be decontaminated. Cage-cleaning facilities should be installed in area in which carcinogens are being used, to avoid moving of ... contaminated /cages/. It is difficult to ensure that cages
are decontaminated, monitoring methods are necessary. Situations may exist in which the use of disposable cages should be recommended, depending on type and amount of carcinogen and efficiency with which it can be removed. /Chemical Carcinogens/ [Montesano, R., H. Bartsch, E. Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A. B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979.10]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": To eliminate risk that contamination in lab could build up during conduct of expt, periodic checks should be carried out on lab atmospheres, surfaces, such as walls, floors and benches, and interior of fume hoods and air ducts. As well as regular monitoring, check must be carried out after cleaning-up of spillage. Sensitive methods are required when testing lab atmospheres for chemicals such as nitrosamines. Methods should where possible, be simple and sensitive. /Chemical Carcinogens/ [Montesano, R., H. Bartsch, E. Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A. B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979.10]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Rooms in which obvious contamination has occurred, such as spillage, should be decontaminated by lab personnel engaged in expt. Design of expt should avoid contamination of permanent equipment. Procedures should ensure that maintenance workers are not exposed to carcinogens. Particular care should be taken to avoid contamination of drains or ventilation ducts. In cleaning labs, procedures should be used which do not produce aerosols or dispersal of dust, for example, wet mop or vacuum cleaner equipped with high efficiency particulate filter on exhaust, which are available commercially, should be used. Sweeping, brushing and use of dry dusters or mops should be prohibited. Grossly contaminated cleaning materials should not be re-used. If gowns or towels are contaminated, they should not be sent to laundry, but decontaminated or burnt, to avoid any hazard to laundry personnel. /Chemical Carcinogens/ [Montesano, R., H. Bartsch, E. Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A. B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979.10]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Doors leading into areas where carcinogens are used should be marked distinctively with appropriate labels. Access limited to persons involved in expt. A prominently displayed notice should give the name of the Scientific Investigator or other person who can advise in an emergency and who can inform others (such as firemen) on the handling of carcinogenic substances. /Chemical Carcinogens/ [Montesano, R., H. Bartsch, E. Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A. B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979.11]**PEER REVIEWED**

Personnel protection: Avoid breathing vapors. Keep up wind. Do not handle broken packages unless wearing appropriate personal protective

SRP: Contaminated protective clothing should be segregated in such a manner so that there is no direct personal contact by personnel who handle, dispose, or clean the clothing. Quality assurance to ascertain the completeness of the cleaning procedures should be implemented before the decontaminated protective clothing is returned for reuse by the workers. **PEER REVIEWED**


STABILITY/SHELF LIFE:

SHIPMENT METHODS AND REGULATIONS:
No person may /transport,/ offer or accept a hazardous material for transportation in commerce unless that person is registered in conformance ... and the hazardous material is properly classed, described, packaged, marked, labeled, and in condition for shipment as required or authorized by ... /the hazardous materials regulations (49 CFR 171-177)./ [49 CFR 171.2 (7/1/2000)]**PEER REVIEWED**

The International Air Transport Association (IATA) Dangerous Goods Regulations are published by the IATA Dangerous Goods Board pursuant to IATA Resolutions 618 and 619 and constitute a manual of industry carrier regulations to be followed by all IATA Member airlines when transporting hazardous materials. [IATA. Dangerous Goods Regulations. 41st Ed.Montreal, Canada and Geneva, Switzerland: International Air Transport Association, Dangerous Goods Regulations, 2000. 234]**PEER REVIEWED**

The International Maritime Dangerous Goods Code lays down basic principles for transporting hazardous chemicals. Detailed recommendations for individual substances and a number of recommendations for good practice are included in the classes dealing with such substances. A general index of technical names has also been compiled. This index should always be consulted when attempting to locate the appropriate procedures to be used when shipping any substance or article. [IMDG; International Maritime Dangerous Goods Code; International Maritime Organization p.2186 (1998)]**PEER REVIEWED**

STORAGE CONDITIONS:

Containers of vinyl chloride shall be legibly labeled either: VINYL CHLORIDE: EXTREMELY FLAMMABLE GAS UNDER PRESSURE: CANCER SUSPECT AGENT or ... with the additional legend CANCER-SUSPECT AGENT applied near the label or placard. [29 CFR 1910.1017 (7/1/90)]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Storage site should be as close as practicable to lab in which carcinogens are to be used, so that only small quantities required for ... ext need to be carried. Carcinogens should be kept in only one section of cupboard, an explosion-proof refrigerator or freezer (depending on chemicophysical properties ...) that bears appropriate label. An inventory ... should be kept, showing quantity of carcinogen & date it was acquired ... Facilities for dispensing ... should be contiguous to storage area. /Chemical Carcinogens/ [Montesano, R., H. Bartsch, E.Boylan, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979.13][**PEER REVIEWED**

Suitable precautions ... including the use of 20-30% aqueous sodium hydroxide soin to destroy the peroxide. [Bretherick, L. Handbook of Reactive Chemical Hazards. 4th ed. Boston, MA: Butterworth-Heinemann Ltd., 1990][**PEER REVIEWED**

CLEANUP METHODS:
Land Spill: Construct barriers to contain spill. Absorb small amounts of spill with natural or synthetic sorbents, shovel into containers with covers. [Environment Canada; Tech Info for Problem Spills: Vinyl Chloride (Draft) p.2 (1980)][**PEER REVIEWED**

Water Spill: Contain contaminated water with dams or natural barriers. [Environment Canada; Tech Info for Problem Spills: Vinyl Chloride (Draft) p.2 (1980)][**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": A high-efficiency particulate arrestor (HEPA) or charcoal filters can be used to minimize amt of carcinogen in exhausted air ventilated safety cabinets, lab hoods, glove boxes or animal rooms ... Filter housing that is designed so that used filters can be transferred into plastic bag without contaminating maintenance staff is avail commercially. Filters should be placed in plastic bags immediately after removal ... The plastic bag should be sealed immediately ... The sealed bag should be labelled properly ... Waste liquids ... should be placed or collected in proper containers for disposal. The lid should be secured & the bottles properly labelled. Once filled, bottles should be placed in plastic bag, so that outer surface ... is not contaminated ... The plastic bag should also be sealed & labelled. ... Broken glassware ... should be decontaminated by solvent extraction, by chemical destruction, or in specially designed incinerators. /Chemical Carcinogens/ [Montesano, R., H. Bartsch, E.Boylan, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979.15][**PEER REVIEWED**

Eliminate all ignition sources. Stop or control the leak, if this can be

**DISPOSAL METHODS:**

Generators of waste (equal to or greater than 100 kg/mo) containing this contaminant, EPA hazardous waste numbers U043; D043 must conform with USEPA regulations in storage, transportation, treatment and disposal of waste. [40 CFR 240-280, 300-306, 702-799 (7/1/2000)]**PEER REVIEWED**

**PRECAUTIONS FOR "CARCINOGENS":** There is no universal method of disposal that has been proved satisfactory for all carcinogenic compounds & specific methods of chem destruction ... published have not been tested on all kinds of carcinogen-containing waste. ... summary of avail methods & recommendations ... /given/ must be treated as guide only. /Chemical Carcinogens/ [Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979.14]**PEER REVIEWED**

**PRECAUTIONS FOR "CARCINOGENS":** Total destruction ... by incineration may be only feasible method for disposal of contaminated laboratory waste from biological ext. However, not all incinerators are suitable for this purpose. The most efficient type ... is probably the gas-fired type, in which a first-stage combustion with a less than stoichiometric air:fuel ratio is followed by a second stage with excess air. Some ... are designed to accept ... aqueous & organic-solvent solutions, otherwise it is necessary to absorb soln onto suitable combustible material, such as sawdust. Alternatively, chem destruction may be used, esp when small quantities ... are to be destroyed in laboratory. /Chemical Carcinogens/ [Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979.15]**PEER REVIEWED**

**PRECAUTIONS FOR "CARCINOGENS":** HEPA (high-efficiency particulate arrestor) filters ... can be disposed of by incineration. For spent charcoal filters, the adsorbed material can be stripped off at high temp & carcinogenic wastes generated by this treatment conducted to & burned in an incinerator. ... LIQUID WASTE: ... Disposal should be carried out by incineration at temp that ... ensure complete combustion. SOLID WASTE: Carcasses of lab animals, cage litter & misc solid wastes ... should be disposed of by incineration at temp high enough to ensure destruction of chem carcinogens or their metabolites. /Chemical Carcinogens/ [Montesano, R., H. Bartsch, E.Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979.15]**PEER REVIEWED**

**PRECAUTIONS FOR "CARCINOGENS":** Small quantities of ... some carcinogens can be destroyed using chem reactions ... but no general rules can be given. ... As a general technique ... treatment with sodium dichromate in strong sulfuric acid can be used. The time necessary for
destruction ... is seldom known ... but 1-2 days is generally considered sufficient when freshly prep'd reagent is used. ... Carcinogens that are easily oxidizable can be destroyed with milder oxidative agents, such as sat soln of potassium permanganate in acetone, which appears to be a suitable agent for destruction of hydrazines or of compounds containing isolated carbon-carbon double bonds. Concns or 50% aqueous sodium hypochlorite can also be used as an oxidizing agent. /Chemical Carcinogens/ [Montesano, R., H. Bartsch, E. Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979.16]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": Carcinogens that are alkylating, arylating or acylating agents per se can be destroyed by reaction with appropriate nucleophiles, such as water, hydroxyl ions, ammonia, thiols & thiosulfate. The reactivity of various alkylating agents varies greatly ... & is also influenced by sol of agent in the reaction medium. To facilitate the complete reaction, it is suggested that the agents be dissolved in ethanol or similar solvents. ... No method should be applied ... until it has been thoroughly tested for its effectiveness & safety on material to be inactivated. For example, in case of destruction of alkylating agents, it is possible to detect residual compounds by reaction with 4(4-nitrobenzyl)-pyridine. /Chemical Carcinogens/ [Montesano, R., H. Bartsch, E. Boyland, G. Della Porta, L. Fishbein, R. A. Griesemer, A.B. Swan, L. Tomatis, and W. Davis (eds.). Handling Chemical Carcinogens in the Laboratory: Problems of Safety. IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer, 1979.17]**PEER REVIEWED**

A potential candidate for fluidized bed incineration at a temperature range of 450 to 980 deg C and residence times of seconds for liquids and gases, and longer for solids. A potential candidate for rotary kiln incineration at a temperature range of 820 to 1,600 deg C and residence times of seconds for liquids and gases, and hours for solids. [USEPA; Engineering Handbook for Hazardous Waste Incineration p.3-11 (1981) EPA 68-03-3025]**PEER REVIEWED**

Vinyl chloride is a waste chemical stream constituent which may be subjected to ultimate disposal by controlled incineration; preferably after mixing another combustible fuel. Care must be taken to assure complete combustion to prevent the formation of phosgene. An acid scrubber is necessary to remove the halo acids produced. [USEPA; Engineering Handbook for Hazardous Waste Incineration p.2-10 (1981) EPA 68-03-3025]**PEER REVIEWED**

The following wastewater treatment technologies have been investigated for vinyl chloride: Biological treatment. [USEPA; Management of Hazardous Waste Leachate, EPA Contract No. 68-03-2766 p.E-51 (1982)]**PEER REVIEWED**

PRECAUTIONS FOR "CARCINOGENS": There is no universal method of disposal that has been proved satisfactory for all carcinogenic compounds & specific methods of chem destruction ... published have not been tested on all kinds of carcinogen-containing waste. ... summary of avail methods & recommendations ... /given/ must be treated as guide only. /Chemical Carcinogens/ [Montesano, R., H. Bartsch, E. Boyland, G. Della Porta, L.
OCCUPATIONAL EXPOSURE STANDARDS:

OSHA STANDARDS:
No employee may be exposed to vinyl chloride at concentrations greater than 1 ppm averaged over any 8 hr period and no employee may be exposed to vinyl chloride at concentrations greater than 5 ppm averaged over any period not exceeding 15 min. No employee may be exposed to vinyl chloride by direct contact with liquid vinyl chloride. [29 CFR 1910.1017(c) (7/1/2000)]**PEER REVIEWED**

THRESHOLD LIMIT VALUES:
8 hr Time Weighted Avg (TWA) 1 ppm [American Conference of Governmental Industrial Hygienists. TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH. 2000.71]**PEER REVIEWED**

A1: Confirmed human carcinogen. [American Conference of Governmental Industrial Hygienists. TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH. 2000.71]**PEER REVIEWED**

Excursion Limit Recommendation: Excursions in worker exposure levels may exceed three times the TLV-TWA for no more than a total of 30 min during a work day, and under no circumstances should they exceed five times the TLV-TWA, provided that the TLV-TWA is not exceeded. [American Conference of Governmental Industrial Hygienists. TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH. 2000.6]**PEER REVIEWED**

NIOSH RECOMMENDATIONS:


IMMEDIATELY DANGEROUS TO LIFE OR HEALTH:

OTHER OCCUPATIONAL PERMISSIBLE LEVELS:
Australia (1973): 25 ppm; Finland (1975), Holland (1973), Poland (1976), Switzerland (1976), and USSR (1977): 10 ppm; Italy (1975): 5 ppm; Japan
(1975) and Sweden (1978): 1 ppm. [American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati, OH: American Conference of Governmental Industrial Hygienists, 1986.616]**PEER REVIEWED**

MANUFACTURING/USE INFORMATION:

MAJOR USES:


COMONOMER-EG, WITH VINYL ACETATE OR VINYLIDENE CHLORIDE. [SRI]**PEER REVIEWED**

CHEM INTERMED FOR METHYL CHLOROFORM & 1,1,1-TRICHLOROETHANE. [SRI]**PEER REVIEWED**

CHEM INTERMED FOR OTHER ORG CHEMS-EG, CHLOROACETALDEHYDE. [SRI]**PEER REVIEWED**

MONOMER & COMONOMER FOR FIBERS-EG, VINYON & SARAN FIBERS. [SRI]**PEER REVIEWED**

OXIDN INHIBITOR IN ETHYLENE OXIDE PRODN. [SRI]**PEER REVIEWED**

REFRIGERANT & EXTRACTION SOLVENT (FORMER USE). [SRI]**PEER REVIEWED**

Vinyl chloride ... is used in the manufacture of numerous products in building and construction, automotive industry, electrical wire insulation and cables, piping, industrial and household equipment, medical supplies, and is depended upon heavily by the rubber, paper, and glass industries. [USEPA; Ambient Water Quality Criteria Doc: Vinyl Chloride p.A-1 (1980) EPA 440/5-80-078]**PEER REVIEWED**


Vinyl chloride ... was formerly a component of aerosol propellants. Vinyl chloride and vinyl acetate copolymers are used extensively to produce vinyl asbestos floor tiles. [DHHS/NTP; Fourth Annual Report On Carcinogens p.200 (1985) NTP 85-002]**PEER REVIEWED**

Limited quantities of chloroethene were used in the United States as an aerosol propellant ... and as an ingredient of drug and cosmetic products. (Former use) [USEPA; Health and Enviromental Effects Profile for Chloroethene; p.4 (1985) ECAO-CIN-P155]**PEER REVIEWED**

MANUFACTURERS:
Borden Chemicals and Plastics, Hq, Hwy 73, Geismar, LA 70734, (224)
METHODS OF MANUFACTURING:
CRACKING OF ETHYLENE DICHLORIDE OBTAINED VIA OXYCHLORINATION OR DIRECT
CHLORINATION OF ETHYLENE; VAPOR-PHASE REACTION OF ACETYLENE & HYDROGEN
CHLORIDE IN THE PRESENCE OF MERCURIC CHLORIDE. [SRI]**PEER REVIEWED**

From ethylene dichloride and alcoholic potassium ... by halogenation of
ethylene ... [Budavari, S. (ed.). The Merck Index - An Encyclopedia of
Chemicals, Drugs, and Biologicals. Whitehouse Station, NJ: Merck and Co.,
Inc., 1996.1705]**PEER REVIEWED**

GENERAL MANUFACTURING INFORMATION:

... SOMETIMES STABILIZED BY ADDING HYDROQUINONE, BUTYL CATECHOL, OR PHENOL. [Lefaux, R. Practical Toxicology of Plastics. Cleveland: CRC Press
Inc., 1968.83]**PEER REVIEWED**


Dichloroethane used for pyrolysis to vinyl chloride must be of purity greater than 99.5 wt % because cracking process is exceedingly susceptible to inhibitors. It must also be dry to prevent corrosion. [Kirk-Othmer Condensed Encyc Chem Tech 1985 p.1230]**PEER REVIEWED**

**FORMULATIONS/PREPARATIONS:**


**IMPURITIES:**


Specifications for a typical commercial product call for maxima in mg/kg by weight of the following impurities: unsaturated hydrocarbons - 10; acetaldehyde - 2; dichloro compounds - 16; water - 15; hydrogen chloride - 2; nonvolatiles - 200; iron - 0.4. Phenol at levels of 25-50 mg/kg by weight is used as a stabilizer to prevent polymerization. [IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work).V7 292 (1972)]**PEER REVIEWED**

The impurities of vinyl chloride are as follows:/ acetic aldehyde 5 ppm, butane 8 ppm, 1,3-butadiene 10 ppm, chlorophene 10 ppm, diacetylene 4 ppm, vinyl acetylene 10 ppm, propine 3 ppm, methylchloride 100 ppm. [Hiatt HH et al; Origins of Human Cancer Book A: Incidence of Cancer in Humans Vol #4 p.120 (1977)]**PEER REVIEWED**

**CONSUMPTION PATTERNS:**

MONOMER FOR POLY(VINYL CHLORIDE) RESINS, 85%; EXPORTS, 13.5%; MISCELLANEOUS (MOSTLY COPOLYMER USE), 1.5% (1982) [SRI]**PEER REVIEWED**

95% FOR POLYVINYL CHLORIDE HOMOPOLYMER AND COPOLYMER RESIN; 4% FOR SYNTHESIS OF METHYL CHLOROFORM; 1% FOR MISC APPLICATIONS (1972) [SRI]**PEER REVIEWED**

CHEMICAL PROFILE: Vinyl Chloride. Polyvinyl chloride, 91%; exports, 7%; other, including chlorinated solvents, 2%. [Kavaler AR; Chemical Marketing Reporter 235 (22): 46 (1989)]**PEER REVIEWED**


U. S. PRODUCTION:
(1977) 2.72X10+12 G [SRI]**PEER REVIEWED**
(1982) 2.22X10+12 G [SRI]**PEER REVIEWED**
(1985) 4.30X10+12 G [USITC. SYN ORG CHEM-U.S. PROD/SALES 1985 p.268]**PEER REVIEWED**
(1986) 8.41X10+9 lb [USITC. SYN ORG CHEM-U.S. PROD. PRELIMINARY FEB 1988 (SERIES C/P-87-5)]**PEER REVIEWED**
(1995) 6,316,000 tons; (1996) 6,487,000 tons [Kirk-Othmer Encyclopedia of

U. S. IMPORTS:
(1977) 6.05X10+5 G [SRI]**PEER REVIEWED**
(1982) 2.30X10+10 G [SRI]**PEER REVIEWED**


U. S. EXPORTS:
(1978) 4.08X10+11 G [SRI]**PEER REVIEWED**
(1983) 3.11X10+11 G [SRI]**PEER REVIEWED**

LABORATORY METHODS:

CLINICAL LABORATORY METHODS:

ANALYTIC LABORATORY METHODS:
NIOSH Method 1007. Analyte: Vinyl chloride. Matrix: Air. Procedure: Gas chromatography, flame ionization detector. For vinyl chloride this method has an estimated detection limit of 0.00004 mg/sample. The precision/RSD is not determined and the recovery is not determined. Applicability: The working range is 0.4 to 40 mg/cu m (0.16 to 16 ppm) for a 5 liter air sample. Interferences: Other than the possibility of loss of sample upon storage of two weeks or more at room temperature, none have been noted. [U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health. NIOSH Manual of Analytical Methods. 4th ed. Methods A-Z & Supplement. Washington, DC: U.S. Government Printing Office, Aug 1994.]*PEER REVIEWED**

EPA Method 8010. Direct Injection or Purge and Trap GC with
halogen-specific detector for the analysis of halogenated volatile organics including vinyl chloride in solid waste. Under the prescribed conditions for vinyl chloride, the method has a detection limit of 0.18 ug/l. Precision and method accuracy were found to be directly related to the concentration of the parameter and essentially independent of the sample matrix. [USEPA; Test Methods for Evaluating Solid Waste SW-846 (1986)]**PEER REVIEWED**

EPA Method 8240. GC/MS for the determination of volatile organics. This method can be used to quantify most volatile organic compounds including vinyl chloride that have boiling points below 200 deg C and are insoluble or slightly soluble in water. The detection limit is not given. Precision and method accuracy were found to be directly related to the concentration of the analyte and essentially independent of the sample matrix. [USEPA; Test Methods for Evaluating Solid Waste SW-846 (1986)]**PEER REVIEWED**

EPA Method 601. Purge and Trap GC with electrolytic conductivity detection for the analysis of purgeable halocarbons including vinyl chloride in municipal and industrial discharges. Under the prescribed conditions, the method detection limit for vinyl chloride is 0.18 ug/l. The method is recommended for use in the concentration range from the method detection limit to 1000 times that limit. Precision and method accuracy were found to be directly related to the concentration of the parameter and essentially independent of the sample matrix. [40 CFR 136, App. A (7/1/90)]**PEER REVIEWED**

EPA Method 624. Purge and Trap GC/MS for the analysis of purgeable organics including vinyl chloride in the municipal and industrial discharges. Under the prescribed conditions for vinyl chloride, the method detection limit is not given. Precision and method accuracy were found to be directly related to the concentration of the parameter and essentially independent of the sample matrix. [40 CFR 136, App. A (7/1/90)]**PEER REVIEWED**

EPA Method 1624. Isotope Dilution Purge and Trap GC/MS. This method is applicable for the determination of volatile organic compounds in municipal and industrial discharges. By adding a known amount of an isotopically labeled compound to every sample prior to purging, a correction of recovery of the pollutant can be made. If isotopically labeled compounds are not available, an internal standard method is used. Under the prescribed conditions for both the isotopically labeled and unlabeled vinyl chloride the method has a minimum detection level of 50 and 10 ug/l with no interferences present. [40 CFR 136, App. A (7/1/90)]**PEER REVIEWED**

EPA Method 524.2. Purge and Trap GC/MS for the determination of volatile aromatic compounds in finished drinking water, raw source water, or drinking water in any treatment stage. For vinyl chloride the method has a detection limit of 0.17 ug/l and a relative standard deviation of 6.7% with a wide bore capillary column, and a method detection limit of 0.04 ug/l and a relative standard deviation of 0.2% with a narrow bore capillary column. [USEPA; Methods for the Determination of Organic Compounds in Finished Drinking Water and Raw Source Water (1986)]**PEER REVIEWED**

EPA Method 524.1. Purge and Trap GC/MS. The method is applicable for the determination of volatile organic compounds in water, finished drinking
water, raw source water, or drinking water in any treatment stage. For vinyl chloride the method has a detection limit of 0.31 ug/l and a standard deviation of 10.8%. [USEPA; Methods for the Determination of Organic Compounds in Finished Drinking Water and Raw Source Water (1986)] **PEER REVIEWED**

EPA Method 502.2: Purge and Trap Capillary Column GC with Photoionization and Electrolytic Conductivity Detectors in Series. The method is applicable for the determination of volatile organic compounds in finished drinking water, raw source water, or drinking water in any treatment stage. For vinyl chloride the method has a detection limit of 0.02 ug/l, a percent recovery of 109%, and a standard deviation of 5.4 using the photoionization detector; and a method detection limit of 0.04 ug/l, a percent recovery of 95%, and a standard deviation of recovery of 5.6 using the electrolytic conductivity detector. [USEPA; Methods for the Determination of Organic Compounds in Finished Drinking Water and Raw Source Water (1986)] **PEER REVIEWED**

EPA Method 502.1. Purge and Trap GC with a halogen-specific detector for the determination of halogenated volatile compounds including vinyl chloride in finished drinking water, raw source water, or drinking water in any treatment stage. Under the prescribed conditions for vinyl chloride, the method detection limit is 0.006 ug/l. [USEPA; Methods for the Determination of Organic Compounds in Finished Drinking Water and Raw Source Water (1986)] **PEER REVIEWED**

EPA Method 8260. GC/MS for the determination of volatile organic compounds. This method can be used to quantitate most volatile organic compounds including vinyl chloride that have boiling points below 200 deg C and are insoluble or slightly soluble in water. Under the prescribed conditions for vinyl chloride the method has a detection limit of 0.17 ug/l, a percent recovery of 98%, and a percent relative standard deviation of 6.7% using a wide bore capillary column; and a detection limit of 0.04 ug/l, a percent recovery of 104% and a percent relative standard deviation of 0.2% using a narrow bore capillary column. [USEPA; Test Methods for Evaluating Solid Waste SW-846 (1986)] **PEER REVIEWED**

EPA Method 5030. Purge and Trap extraction procedure for the analysis of volatile organics. Such cmpds include low-molecular-weight halogenated hydrocarbons, aromatics, ketones, nitriles, acetates, acrylates, ethers and sulfides. An inert gas is bubbled through the solution at ambient temperature, and the volatile components are efficiently transferred from the aqueous phase to the vapor phase. After purging is complete, the sorbent column is heated and backflushed with inert gas to desorb the components onto a GC column. Water samples can be analyzed directly, while preparation is necessary for water-miscible liquids, solids, wastes and soil/sediments. [USEPA; Test Methods for Evaluating Solid Waste SW-846 (1986)] **PEER REVIEWED**

EPA Method 5040. Protocol for Analysis of Sorbent Cartridges from Volatile Organic Sampling Train. This method covers the determination of volatile principal organic hazardous constituents collected on Tenax and Tenax/charcoal sorbent cartridges using a volatile organic sampling train, from wet stack gas effluents from hazardous waste incinerators. The contents of the sorbent cartridges are thermally desorbed, bubbled, and trapped on an analytical adsorbent trap. The desired target detection limit of the analytical method is 0.1 ng/l. Interferences include
phthalate esters, detectable levels of volatile principal hazardous constituents in blanks, and soap residue on the glassware. [USEPA; Test Methods for Evaluating Solid Waste SW-846 (1986)]**PEER REVIEWED**


SAMPLING PROCEDURES:


EPA Method 8010. For the analysis of solid waste, a representative sample (solid or liquid) is collected in a standard 40 ml glass screw-cap VOA vial equipped with a Teflon-faced silicone septum. Sample agitation, as well as contamination of the sample with air, must be avoided. Two vials are filled per sample location, then placed in separate plastic bags for shipment and storage. [USEPA; Test Methods for Evaluating Solid Waste SW-846 (1986)]**PEER REVIEWED**

SPECIAL REFERENCES:
SPECIAL REPORTS:


A REVIEW CONTAINING OVER 100 REFERENCES OF SAMPLING AND ANALYTICAL METHODS FOR VINYL CHLORIDE IN WORKPLACE ATMOSPHERE, AMBIENT AIR, WATER, FOOD, CIGARETTE SMOKE, AND POLYVINYL CHLORIDE. EGAN H ET AL, EDS, ENVIRONMENTAL CARCINOGENS SELECTED METHODS OF ANALYSIS VOL 2, VINYL CHLORIDE (IARC SCIENTIFIC PUBLICATIONS NUMBER 22) LYON (1979).


DHHS/ATSDR; Toxicological Profile for Vinyl Chloride (Update) TP-92/20 (1993)

SYNONYMS AND IDENTIFIERS:

SYNONYMS:
CHLORETHENE **PEER REVIEWED**
CHLORETHYLENE **PEER REVIEWED**
CHLOROETHENE **PEER REVIEWED**
CHLOROETHYLENE **PEER REVIEWED**
CHLORURE DE VINYLE (FRENCH) **PEER REVIEWED**
CLORURO DI VINILE (ITALIAN) **PEER REVIEWED**
Ethen, chloro- **PEER REVIEWED**
ETHYLENE, CHLORO- **PEER REVIEWED**
ETHYLENE MONOCHLORIDE **PEER REVIEWED**
MONOCHLOROETHENE **PEER REVIEWED**
MONOCHLOROETHYLENE **PEER REVIEWED**
Monovinyl chloride (MVC) **PEER REVIEWED**
Trovidur **PEER REVIEWED**
VC **PEER REVIEWED**
VCM **PEER REVIEWED**
VINILE (CLORURO DI) (ITALIAN) **PEER REVIEWED**
VINYL CHLORIDE MONOMER **PEER REVIEWED**
VINYLCHLORID (GERMAN) **PEER REVIEWED**
VINYLE (CHLORURE DE) (FRENCH) **PEER REVIEWED**
VINYL C MONOMER **PEER REVIEWED**
WINYLU CHLOREK (POLISH) **PEER REVIEWED**

ASSOCIATED CHEMICALS: Chloroethylene oxide; 7763-77-1

FORMULATIONS/PREPARATIONS:


SHIPPING NAME/ NUMBER DOT/UN/NA/IMO:
UN 1086; Vinyl chloride, inhibited or stabilized
IMO 2.0; Vinyl chloride, inhibited or stabilized

STANDARD TRANSPORTATION NUMBER:
49 057 92; Vinyl chloride

EPA HAZARDOUS WASTE NUMBER:
U043; A toxic waste when a discarded commercial chemical product or manufacturing chemical intermediate or an off-specification commercial product or manufacturing chemical intermediate.

D043; A waste containing vinyl chloride may or may not be characterized as a hazardous waste following testing by the Toxicity Characteristic Leaching Procedure as prescribed by the Resource Conservation and Recovery Act (RCRA) regulations.
ADMINISTRATIVE INFORMATION:

HAZARDOUS SUBSTANCES DATABANK NUMBER: 169

LAST REVISION DATE: 20030829

LAST REVIEW DATE: Reviewed by SRP on 1/20/2001

UPDATE HISTORY:
  Complete Update on 2003-08-29, 1 fields added/edited/deleted
  Complete Update on 02/14/2003, 1 field added/edited/deleted.
  Complete Update on 11/08/2002, 1 field added/edited/deleted.
  Complete Update on 10/16/2002, 1 field added/edited/deleted.
  Complete Update on 05/31/2002, 1 field added/edited/deleted.
  Complete Update on 05/13/2002, 1 field added/edited/deleted.
  Complete Update on 02/13/2002, 1 field added/edited/deleted.
  Complete Update on 01/18/2002, 2 fields added/edited/deleted.
  Complete Update on 08/09/2001, 1 field added/edited/deleted.
  Complete Update on 05/23/2001, 85 fields added/edited/deleted.
  Field Update on 10/18/2000, 1 field added/edited/deleted.
  Complete Update on 02/11/2000, 1 field added/edited/deleted.
  Complete Update on 08/26/1999, 1 field added/edited/deleted.
  Complete Update on 07/20/1999, 8 fields added/edited/deleted.
  Complete Update on 03/29/1999, 2 fields added/edited/deleted.
  Field Update on 03/19/1999, 1 field added/edited/deleted.
  Complete Update on 02/24/1999, 1 field added/edited/deleted.
  Complete Update on 02/11/1999, 2 fields added/edited/deleted.
  Complete Update on 11/16/1998, 1 field added/edited/deleted.
  Complete Update on 11/12/1998, 1 field added/edited/deleted.
  Complete Update on 02/25/1998, 1 field added/edited/deleted.
  Complete Update on 10/17/1997, 1 field added/edited/deleted.
  Complete Update on 09/08/1997, 1 field added/edited/deleted.
  Complete Update on 08/13/1997, 1 field added/edited/deleted.
Complete Update on 07/09/1997, 1 field added/edited/deleted.
Complete Update on 03/27/1997, 2 fields added/edited/deleted.
Complete Update on 10/12/1996, 1 field added/edited/deleted.
Complete Update on 04/26/1996, 1 field added/edited/deleted.
Complete Update on 04/16/1996, 7 fields added/edited/deleted.
Complete Update on 01/18/1996, 1 field added/edited/deleted.
Complete Update on 11/10/1995, 1 field added/edited/deleted.
Complete Update on 02/13/1995, 1 field added/edited/deleted.
Complete Update on 01/24/1995, 1 field added/edited/deleted.
Complete Update on 12/19/1994, 1 field added/edited/deleted.
Complete Update on 09/23/1994, 1 field added/edited/deleted.
Complete Update on 08/04/1994, 1 field added/edited/deleted.
Complete Update on 06/08/1994, 1 field added/edited/deleted.
Complete Update on 05/05/1994, 1 field added/edited/deleted.
Complete Update on 03/25/1994, 1 field added/edited/deleted.
Complete Update on 01/12/1994, 69 fields added/edited/deleted.
Field Update on 11/05/1993, 1 field added/edited/deleted.
Field Update on 08/03/1993, 1 field added/edited/deleted.
Field Update on 04/30/1993, 1 field added/edited/deleted.
Field Update on 12/11/1992, 1 field added/edited/deleted.
Complete Update on 08/17/1992, 66 fields added/edited/deleted.
Field Update on 05/29/1992, 1 field added/edited/deleted.
Field Update on 04/16/1992, 1 field added/edited/deleted.
Field Update on 04/01/1992, 1 field added/edited/deleted.
Complete Update on 01/23/1992, 1 field added/edited/deleted.
Complete Update on 08/23/1990, 1 field added/edited/deleted.
Complete Update on 05/23/1990, 50 fields added/edited/deleted.
Field Update on 05/04/1990, 1 field added/edited/deleted.
Field Update on 01/15/1990, 1 field added/edited/deleted.
Complete Update on 01/11/1990, 43 fields added/edited/deleted.
Field Update on 10/03/1989, 1 field added/edited/deleted.
Field Update on 05/05/1989, 1 field added/edited/deleted.
Complete Update on 04/20/1989, 34 fields added/edited/deleted.
Complete Update on 04/03/1989, 91 fields added/edited/deleted.
Complete Update on 06/01/1987
Created 19830301 by DS