

## Allyl chloride; CASRN 107-05-1

Human health assessment information on a chemical substance is included in the IRIS database only after a comprehensive review of toxicity data, as outlined in the [IRIS assessment development process](#). Sections I (Health Hazard Assessments for Noncarcinogenic Effects) and II (Carcinogenicity Assessment for Lifetime Exposure) present the conclusions that were reached during the assessment development process. Supporting information and explanations of the methods used to derive the values given in IRIS are provided in the [guidance documents located on the IRIS website](#).

### STATUS OF DATA FOR Allyl chloride

**File First On-Line 09/01/1990**

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	not evaluated	
Inhalation RfC (I.B.)	yes	12/01/1991
Carcinogenicity Assessment (II.)	yes	09/01/1990

## I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

### I.A. Reference Dose for Chronic Oral Exposure (RfD)

Substance Name — Allyl chloride  
CASRN — 107-05-1

Not available at this time.

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### I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)

Substance Name — Allyl chloride  
CASRN — 107-05-1  
Last Revised — 12/01/1991

The inhalation Reference Concentration (RfC) is analogous to the oral RfD and is likewise based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. The inhalation RfC considers toxic effects for both the respiratory system (portal-of-entry) and for effects peripheral to the respiratory system (extrarespiratory effects). It is expressed in units of mg/cu.m. In general, the RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily inhalation exposure of the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Inhalation RfCs were derived according to the Interim Methods for Development of Inhalation Reference Doses (EPA/600/8-88/066F August 1989) and subsequently, according to Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry (EPA/600/8-90/066F October 1994). RfCs can also be derived for the noncarcinogenic health effects of substances that are carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

**I.B.1. Inhalation RfC Summary**

Critical Effect	Exposures*	UF	MF	RfC
<b>Functional and histological peripheral neurotoxicity</b>	NOAEL: 17 mg/cu.m NOAEL(ADJ): 3.6 mg/cu.m NOAEL(HEC): 3.6 mg/cu.m	3000	1	1E-3 mg/cu.m
<b>Rabbit Subchronic Inhalation Study</b>	LOAEL: 206 mg/cu.m LOAEL(ADJ): 44 mg/cu.m LOAEL(HEC): 44 mg/cu.m			
<b>Lu et al., 1982</b>				

\*Conversion Factors:  $MW = 73.53$ .  $NOAEL(ADJ) = NOAEL(mg/cu.m) \times 6 \text{ hours/day} \times 6 \text{ days/7 days} = 3.6 \text{ mg/cu.m}$ . The NOAEL(HEC) was calculated for a gas:extrarespiratory effect assuming periodicity was attained. Since the b:a lambda values are unknown for the experimental animal species (a) and humans (h), a default value of 1 is used for this ratio.  $NOAEL(HEC) = NOAEL(ADJ) \times (b:a \text{ lambda}(a)/\text{lambda}(h)) = 3.6 \text{ mg/cu.m}$ .

### **I.B.2. Principal and Supporting Studies (Inhalation RfC)**

Lu, B, D. Shuwei, Y. Airu, X. YinLin, G. Taibao and C. Tao. 1982. Studies on the toxicity of allyl chloride. *Ecotoxicol. Environ. Saf.* 6: 19-27.

The neurological effects of allyl chloride were studied in rabbits, cats, and rats (Lu et al., 1982; data also reported in He et al., 1985). A group of six male rabbits and 1 female cat were exposed to 206 mg/cu.m allyl chloride 6 hours/day, 6 days/week for 3 months (duration-adjusted concentration, 44 mg/cu.m) and an equal number of animals served as controls. Clinical observations, body weight, hematology, urinalysis (protein, blood, cells), liver function (SGPT), serum chemistry (total nonprotein sulfhydryls, creatinine), electromyography (EMG, rabbits only), organ weights, and histopathological examination including brain, spinal cord, heart, trachea, lung, liver, kidney, spleen, adrenals, and peripheral nerves, were conducted. Four rabbits were examined at the end of the exposure and two were used to study recovery. EMG changes indicative of peripheral nerve damage were noted in the rabbits at the end of the first month of exposure. Changes noted by month 2 in all of the exposed rabbits included muscle weakness of the extremities, lurching motion, and unsteady gait. This developed into paralysis in three of the exposed rabbits. Relative lung and liver weights were significantly increased in rabbits compared with controls. Histopathological examination of the rabbits revealed degeneration of peripheral nerve fibers consistent with the abnormal clinical and EMG findings. Other changes observed in the rabbits included dilation of sinusoids and vacuolar degeneration in the liver, congestion or cloudy swelling and fatty degeneration of the epithelium of the renal convoluted tubules, and thickening of the alveolar septa in the lungs. The exposed cat exhibited only muscle weakness and unsteady gait toward the end of the exposure period. No other treatment-related effects were observed in the parameters measured.

Rabbits (n=6, 5 male and 1 female) and 10 male rats were exposed to 17 mg/cu.m allyl chloride 6 hours/day, 6 days/week for 5 months (duration-adjusted concentration is 3.6 mg/cu.m) (Lu et al., 1982; data also reported in He et al., 1985). An equal number served as controls. The exposure protocol and analyses performed at the end of exposure were essentially identical to the exposure to 206 mg/cu.m. No data are presented regarding the results of this experiment but it is stated that no evidence of adverse treatment-related effects was found after exposure to 17 mg/cu.m. This study identifies a NOAEL for neurological effects of 17 mg/cu.m [NOAEL(HEC) = 3.6 mg/cu.m for extrarespiratory effects assuming periodicity is attained and using the default value of 1 for  $b:a \lambda(a)/\lambda(h)$ ].

### **I.B.3. Uncertainty and Modifying Factors (Inhalation RfC)**

UF — Two uncertainty factors of 10 each are used for protection of sensitive human subpopulations and for extrapolation from a subchronic study. An additional factor of 10 is

applied due to database deficiencies including lack of adequate developmental and reproductive toxicity data. A factor of 3 is applied for uncertainty in the extrapolation from laboratory animal to humans.

MF — None

#### **I.B.4. Additional Studies/Comments (Inhalation RfC)**

Chronic toxic polyneuropathy in humans associated with allyl chloride exposure was first reported in 17 Chinese women employed in the manufacture of sodium allyl sulfonate who were also exposed to sodium sulfite (He et al., 1980). The exposure levels were not specified and the women were exposed for durations that ranged from 7 months to 5 years. Physical and neurological examinations, electromyography (EMG), nerve conduction measurements, and rheography of the extremities were conducted. Laboratory determinations conducted on some or all of the subjects included routine blood and urine tests, liver function tests (SGPT, thymol turbidity, and thymol flocculation), blood glucose, electrolytes, nonprotein nitrogen, erythrocyte sedimentation rate, PSP (phenosulfonothalein clearance) test, EKG, EEG, and BMR (basal metabolic rate). Clinical signs of polyneuropathy were observed in 17 cases, including impairment of pain and touch sensation, decreased vibration sensation, slightly decreased posture sensation, weakened muscle strength, loss of ankle reflex, decreased skin temperature, hyperhidrosis of the hands and feet, and tenderness of the calf. Electromyographs indicated the presence of neuropathy in 8 of 13 cases. Nerve conduction velocity in the tibial and peroneal nerves was slowed in seven cases, and in five of these cases, motor nerve distal latencies were also prolonged in both nerves. Rheographic abnormalities were also observed in 14 of 15 patients. Liver function and other laboratory findings were normal.

After the discovery of polyneuropathy associated with allyl chloride exposure, He et al. (1985) conducted an epidemiological study of sodium allyl sulfonate workers in two different factories (data also reported in He and Zhang, 1985). Twenty-six workers in factory A were exposed to 2.6-6650 mg/cu.m allyl chloride for 2.5 months to 6 years. The exposure is reported as 138 mg/cu.m with a standard deviation of 12 based on 68 area samples (He, 1991). No information is available regarding location, duration, or timing of samples. Workers (n=27) in factory B were exposed to 0.2-25.13 mg/cu.m allyl chloride for 1 to 4.5 years based on only 10 area samples (He, 1991; no mean concentration or other sampling details provided). The reference group consisted of 50 healthy adults with an age range similar to that of the exposed groups (He, 1991). No other information is available for comparison of the exposed and control groups. Physical and neurological examinations, visual acuity, visual field detection, rheography of the extremities, electrocardiography, electromyography (EMG), and nerve conduction measurements were conducted. Laboratory determinations conducted on some or all of the subjects included routine blood and urine tests, liver function tests (SGPT, thymol turbidity, and thymol

flocculation), blood glucose, electrolytes, nonprotein nitrogen, erythrocyte sedimentation rate, PSP test, EEG, and BMR. All factory A workers experienced lacrimation and sneezing when first exposed. Most of the workers in factory A reported neurological signs that included muscle weakness, paresthesia, numbness and cramping pain of the extremities, sensory impairment in the glove-stocking distribution, and reduced ankle reflexes. EMG revealed abnormalities in 53% of the workers studied in factory A. Significant decreases in motor nerve conduction velocity and increased motor distal latency were observed in workers from factory A and B compared to a reference group. Results are reported for five to nine factory A workers and all factory B workers. The same neurological signs were present in the factory B workers, but to a lesser degree. Cramping was reported much less in these workers. However, evidence of mild neuropathy was revealed by EMG in 13 of 27 factory B workers. Although He et al. (1985) identify the peripheral nervous system as a sensitive target in humans, inadequate exposure characterization precludes the use of this study as the basis for derivation of the RfC. Because of the small number of samples and the use of area samples without further characterization of proximity of workers and sampling locations, the available data are not considered to be adequate to quantitatively characterize the exposure of these subjects.

The effects of occupational exposure to allyl chloride were studied in 45 male and 15 female workers in an allyl chloride manufacturing plant who were exposed to concentrations of allyl chloride ranging from 1-113 ppm for 16 months (Hausler and Lenich, 1968 as reported in NIOSH, 1976). No information was given regarding the sampling and analytical method or the number and location of samples. Medical examinations were conducted on the workers, including urinalyses and liver function tests (thymol, cadmium, and serum bilirubin tests, in addition to LDH, SGOT, SGPT, sorbose dehydrogenase, and glutamic acid dehydrogenase determinations). Clinical examinations revealed only the presence of a garlic-like odor of the body and exhaled breath in 20 of the workers. Urinalyses revealed traces of protein, a few erythrocytes, epithelial cells, and leukocytes in the urine of two workers, and urobilinogen levels were slightly elevated in five workers. Liver function tests showed 5 subjects with SGOT above 45 U and 25 with SGPT above 17 U. Actual values were not provided for this or other measurements. The plant was subsequently redesigned and exposure to allyl chloride was generally 1 ppm or less, with the exception of the pumphouse, where the concentration was 15-36 ppm. After 6 months of exposure to these lower levels, the workers reported to have abnormal liver findings had normal liver and urine tests, but the data are not presented to support this conclusion. Although the authors claim that the liver function tests indicate the presence of early liver damage due to allyl chloride, the absence of pre-exposure control values, inadequate exposure characterization, and poor reporting of results preclude consideration of this study as the basis for derivation of the RfC.

Quast et al. (1982a) exposed Fisher 344 rats and B6C3F1 mice (n=10/sex/concentration) to 0, 1, 3, 10, and 20 ppm allyl chloride (0, 3, 9, 30, and 60 mg/cu.m, respectively) 6 hours/day, 5

days/week for up to 3 months (duration-adjusted concentrations are 0, 0.54, 1.6, 5.4, and 11 mg/cu.m, respectively) with an interim sacrifice at 1 month. Clinical observations were conducted, and body weights, hematology, urinalysis, clinical chemistry, organ weights, gross pathology, and histopathological evaluations of several organs (including the lungs and two sections of the nasal turbinates) were done. No treatment-related changes in any of the parameters evaluated were noted in either species. Elevated SGPT and SGOT values in the 20-ppm male mice sacrificed at 1 month were accompanied by microscopic changes in the liver described as multifocal acute coagulation necrosis accompanied by glycogen depletion. The lesions were not observed in the male mice after 3 months of exposure, and they were not observed in the female mice or rats of either sex.

In a follow-up study, Quast et al. (1982b) exposed 25 male and female Fisher 344 rats and 25 male and female B6C3F1 mice to 0, 50, 100, or 250 ppm allyl chloride (0, 150, 301, and 752 mg/cu.m) 6 hours/day, 5 days/week for 90 days (duration-adjusted concentrations are 0, 27, 54, and 134 mg/cu.m, respectively) with an interim sacrifice at 30 days. Clinical observations were conducted, and body weights, hematology (10 animals/group), urinalysis (10 animals/group), clinical chemistry, organ weights, gross pathology, and histopathological evaluations of several organs (including the lungs) were performed. No treatment-related effects on mortality, clinical observations, body weight, urinalysis, hematology, clinical chemistry, or organ weights were noted in either species. The absolute and relative liver weights were increased in the male rats exposed to 100 and 250 ppm allyl chloride and in all exposed female rats. There were no accompanying changes in serum liver enzyme activity or microscopic appearance of the liver, so the biological significance of the liver weight change is not clear. The livers of the male and female mice exposed to 250 ppm allyl chloride showed increased glycogen in the periportal hepatocytes with variable staining of the centrilobular hepatocytes without degeneration or necrosis. The toxicological significance of this effect is not clear. These results do not corroborate the finding of liver effects in the interim sacrifice at 20 ppm in Quast et al. (1982a). No exposure-related changes in the lungs were noted in rats or mice. The only microscopic effect considered to be related to allyl chloride exposure was observed in the kidneys of both male and female rats exposed to 100 and 250 ppm allyl chloride. The animals exposed to 100 ppm exhibited a slight increase in the cytoplasmic granularity and eosinophilic staining of the cortical epithelial cells when compared with the control rats. These changes were also observed in the 250-ppm animals as well as an increase in the number of tubules showing focal collapse and atrophy. This study identifies a NOAEL at 50 ppm for kidney effects [NOAEL(HEC) = 27 mg/cu.m].

Torkelson et al. (1959) exposed 5 rats/sex, 4 male guinea pigs, and 1 female rabbit to 8 ppm (24 mg/cu.m) allyl chloride 7 hours/day, 5 days/week for 35 days, with equal numbers of animals as controls. No clinical signs of toxicity were evident in these animals, nor did they exhibit any reductions in weight gain compared with the control animals. Histopathological examination of

the liver in all three species revealed dilation of the sinusoids, cloudy swelling, and focal necrosis. The kidneys of all three species were found to have changes in the glomeruli, necrosis of the epithelium of the convoluted tubules, and proliferation of the interstitial tissues. These changes were reported to have occurred in all animals, but results in controls were not described. These findings contradict the reports of Quast et al. (1982a,b) who found kidney effects and questionable liver effects only at much higher concentrations. There is no obvious explanation for the difference between the two studies. In a second experiment, Torkelson et al. (1959) exposed 24 rats, 3 rabbits, 9 guinea pigs, and 1 dog of each sex to 3 ppm allyl chloride (9 mg/cu.m) 7 hours/day, 5 days/week for 6 months (duration-adjusted value is 1.88 mg/cu.m). Untreated controls were included for each species. The animals were split into two groups: one group was killed immediately after the last exposure, and the other group was held for an additional 2 months to observe recovery from any adverse effects that may have occurred. No changes related to treatment were observed in any of the animals exposed to 3 ppm allyl chloride with regard to mortality, behavior, gross appearance, final body weight, or clinical or hematological parameters. The only histopathological change observed was slight central lobular degeneration in the livers of the female rats. The effect was not observed in the control groups, any other species, or in the female rats allowed to recover for 2 months. The small number of animals, poor reporting of results, and contradiction of these findings by better designed studies rule out the use of this study as the basis for the RfC.

Effects in the respiratory tract have been reported in animals exposed to high concentrations of allyl chloride. Lu et al. (1982) found marked congestion, hemorrhage, and edema on post-mortem examination after 2-hour exposures in a study designed to identify the LC50. Individual exposure levels are not reported, but the 2-hour LC50 values for mouse, rat and guinea pig are 11,500, 11,800, and 6000 mg/cu.m, respectively. Nielson and Bakbo (1985) studied sensory irritation in mice exposed to 1100-3770 ppm allyl chloride for 10-30 minutes. The RD50 (concentration causing a 50% decrease in respiratory rate) was identified as 2330 pm (7000 mg/cu.m) in mice. No decrease in respiratory rate was observed when mice were exposed to 3770 ppm via a tracheal cannula, indicating that the effect occurs by upper respiratory tract irritation and not irritation in the thoracic region. Lack of effects in the respiratory system at much lower concentrations in the Quast et al. (1982a,b) studies indicate the lower sensitivity of the respiratory tract effects compared with neurotoxic and renal effects.

Renal toxicity and neurotoxicity have also been observed in animals exposed to allyl chloride by oral and subcutaneous administration. He et al. (1981) administered allyl chloride in arachis oil by gavage to mice at doses of 300 or 500 mg/kg 3 times a week for 2-17 weeks. Clinical signs of neurotoxicity observed in animals treated with 500 mg/kg within the first month included hind limb weakness, hunching of the back, and a sprawling gait, but no paralysis. Mice dosed with 300 mg/kg allyl chloride developed some hind limb weakness by the third month of treatment. Light and electron microscopy revealed that animals exhibiting clinical signs of neurotoxicity

also had definite peripheral nerve fiber degeneration. Nerve damage was also found in animals that were asymptomatic. Degeneration of the axons was seen in many peripheral nerves and roots, and tended to be more severe in the distal portions and in motor rather than sensory nerves. Degenerated fibers were also found in the dorsal, ventral, and lateral columns of the spinal cord. The kidneys were examined by light microscopy in 10 exposed and 4 control animals, and large foci of inflammatory cells including lymphocytes and plasma cells were seen in 7 of these animals. The liver appeared unaffected in the treated animals. He et al. (1980) treated 6 rabbits with 50 mg/kg allyl chloride subcutaneously 3 times in 1 week followed by 100 mg/kg, 3 times/week for 38-80 days. A peripheral neuropathy with EMG abnormalities developed in all treated animals at 5-6 weeks of treatment. Hunched posture in rats treated by gavage with 55 or 75 mg/kg/day and incoordination in male mice surviving to 48 weeks of gavage treatment with 200 mg/kg/day were reported in the NCI (1978) study. Detailed examination of the peripheral nerves was not performed.

John et al. (1983) exposed pregnant Sprague-Dawley rats to 0, 30, or 300 ppm (0, 90, or 270 mg/cu.m) 7 hours/day on days 6-15 of gestation and New Zealand rabbits to the same concentrations on days 6-18 of gestation. Maternal body weight and food and water consumption were recorded until the uterine contents were removed and examined on gestational day 21 (rats) or 29 (rabbits). Maternal liver weights, and the number and position of live, dead or resorbed fetuses were recorded. After being weighed and measured, fetuses were examined for external malformations, cleft palate, soft tissue and cranial alterations (1/3 were examined), and skeletal malformations. Maternal toxicity was evident in both species at the high dose based on reduced weight gain on the first few days of exposure, increases in liver weight (both species) and increased kidney weight (rats only). The data showing the extent of these effects was not presented. There was no evidence of a significant treatment-related effect on corpora lutea, implantation, live fetuses/litter, or incidence of resorptions in either species. A slight delay in skeletal development was seen in the rat fetuses from the 300-ppm group, but no other developmental effects were seen in either species.

Hardin et al. (1987) reported a screening developmental study in which pregnant CD-1 mice were dosed by gavage with 500 mg/kg/day on days 6-13 of gestation. Parameters evaluated as a screen for developmental toxicity were litter size, birth weight, and neonatal survival to postnatal day 3. Under this protocol, no effects on developing fetuses were observed. This study is compromised by the occurrence of 50% maternal mortality, and the evaluation of a small number of litters. A developmental study in which rats were dosed intraperitoneally with 80 mg/kg on days 1-15 of gestation showed an increase in fetal resorptions, craniofacial defects, and edema (Hardin et al., 1981).

### **I.B.5. Confidence in the Inhalation RfC**

Study — Low  
Database — Low  
RfC — Low

The confidence in the principal study is low because it used a small number of animals and reported detailed results for only the higher concentration with poor reporting of results for the NOAEL exposure. The confidence in the database is low because there is conflicting information on possible liver effects and no data on reproductive toxicity and because chronic animal studies are lacking. Low confidence in the RfC follows.

### **I.B.6. EPA Documentation and Review of the Inhalation RfC**

Source Document — This assessment is not presented in any existing U.S. EPA document.

Other EPA Documentation — U.S. EPA, 1986

Agency Work Group Review — 12/19/1990

Verification Date — 12/19/1990

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the RfC for allyl chloride conducted in August 2003 identified one or more significant new studies. IRIS users may request the references for those studies from the IRIS Hotline at [hotline.iris@epa.gov](mailto:hotline.iris@epa.gov) or 202-566-1676.

### **I.B.7. EPA Contacts (Inhalation RfC)**

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or [hotline.iris@epa.gov](mailto:hotline.iris@epa.gov) (internet address).

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## **II. Carcinogenicity Assessment for Lifetime Exposure**

Substance Name — Allyl chloride  
CASRN — 107-05-1  
Last Revised — 09/01/1990

Section II provides information on three aspects of the carcinogenic assessment for the substance in question; the weight-of-evidence judgment of the likelihood that the substance is a human carcinogen, and quantitative estimates of risk from oral exposure and from inhalation exposure. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10,000, 1 in 100,000 or 1 in 1,000,000. The rationale and methods used to develop the carcinogenicity information in IRIS are described in The Risk Assessment Guidelines of 1986 (EPA/600/8-87/045) and in the IRIS Background Document. IRIS summaries developed since the publication of EPA's more recent Proposed Guidelines for Carcinogen Risk Assessment also utilize those Guidelines where indicated (Federal Register 61(79):17960-18011, April 23, 1996). Users are referred to Section I of this IRIS file for information on long-term toxic effects other than carcinogenicity.

## **II.A. Evidence for Human Carcinogenicity**

### **II.A.1. Weight-of-Evidence Characterization**

Classification — C; possible human carcinogen

Basis — Classification is based on a low (but biologically important) incidence of forestomach tumors in female mice and positive results in a variety of genetic toxicity tests. Allyl chloride is an alkylating agent and structurally related to probable human carcinogens.

### **II.A.2. Human Carcinogenicity Data**

None.

### **II.A.3. Animal Carcinogenicity Data**

Limited. The results from a chronic gavage study, a short-term lung adenoma bioassay, and a skin painting study are suggestive of carcinogenicity, but interpretation is limited by inadequacies in the data.

Groups of Osborne-Mendel rats and B6C3F1 mice (50 animals/sex/dose) were administered technical grade allyl chloride in corn oil by gavage, 5 times/week for 78 weeks (NCI, 1978). Twenty animals/sex/group served as vehicle controls and untreated controls for each species. As the material was highly toxic, the initial doses were adjusted downward. Final TWAs for the low- and high-dose groups over the 78-week dosing period were as follows: 57 and 77

mg/kg/day for male rats; 55 and 73 mg/kg/day for female rats; 172 and 199 mg/kg/day for male mice; and 129 and 258 mg/kg/day for female mice. Rats were observed for an additional 30-33 weeks and mice for an additional 14 weeks after the dosing period. Mortality in the high-dose groups of rats (both sexes) and male mice was very high; fifty percent mortality in these groups was reached in 14-38 weeks. Adequate numbers of animals survived in all low-dose groups and in the high-dose female mice to evaluate the risk from late-developing tumors. In rats, no statistically significant increases in tumor incidence at any sites were observed.

In mice of both sexes, proliferative nonneoplastic lesions of the stomach were observed. In female mice, squamous cell papillomas and carcinomas of the forestomach were observed in 0/39 control (19 vehicle and 20 untreated), 3/47 low-dose (2 carcinomas), and 3/45 high-dose animals (all papillomas). Sufficient numbers of high-dose females survived to evaluate risk from late developing tumors. In male mice, squamous cell carcinomas of the forestomach occurred in 0/29 (17 vehicle and 12 untreated) control, 2/36 low-dose, and 0/10 high-dose animals (only 10 high-dose males survived past 52 weeks). The incidence of these tumors was not significantly greater than that in the concurrent controls at either dose level for either sex. The combined incidence in females, however, was significantly increased at both doses relative to historical vehicle controls (1/180 female mice with squamous cell papilloma or carcinoma of the forestomach). The incidence of carcinomas in the low-dose males was also significantly elevated compared with historical controls (1/180). The time period during which the historical control data were collected was not specified. Because the stomach tumors were considered to be a rare tumor type, and because the proliferative lesions could represent an early stage in the neoplastic process, the findings were interpreted by the authors to be strongly suggestive of carcinogenicity in mice. The Data Evaluation/Risk Assessment Subgroup of the Clearinghouse on Environmental Carcinogens reviewed the NCI bioassay. The reviewers considered this study inadequate for drawing any conclusion about the carcinogenicity of allyl chloride because of the poor survival in the high dose groups.

Male and female Strain A/St mice (10/sex/group) were given intraperitoneal injections of allyl chloride (unknown purity) in tricapylin 3 times/week for 8 weeks, for total doses of 1.2, 2.9, and 5.9 g/kg (Theiss et al., 1979). After 24 weeks from beginning of the exposure, the mice were sacrificed and their lungs examined for gross lesions (adenomas). The average numbers of adenomas per mouse (20 animals/group, both sexes combined) were 0.19, 0.60, 0.50, and 0.60 in the vehicle control, low-, medium- and high-dose groups, respectively. The average in the high-dose group was reported as significantly increased relative to the vehicle controls by either the Student's t test or the chi-square test, but not both. While the results may indicate carcinogenic activity, the statistical analyses were not well reported, and there was no indication of a dose-related increase in tumor multiplicity.

Van Duuren et al. (1979) tested allyl chloride (of unknown purity) in skin painting experiments with female Ha:ICR Swiss mice (30 mice/dose, housed 6 mice/cage). Allyl chloride in acetone, administered 3 times/week (31 or 94 mg/mouse) for 63-85 weeks did not induce skin tumors. Lung and stomach papillomas were observed in both dose groups: 14 lung and 3 stomach papillomas in the low-dose group and 12 lung and 3 stomach papillomas in the high-dose group. One adenocarcinoma of the glandular stomach was reported in the high-dose group. The authors indicated that these incidences were not significantly elevated compared with vehicle or nontreated controls (control incidence not reported). A single application of allyl chloride to Ha:ICR Swiss mice (94 mg/mouse) followed by repeated applications of phorbol myristate acetate resulted in an accelerated onset and a statistically significant increase in skin tumor incidence (10 total papillomas/7 tumor-bearing animals, control incidence not reported).

#### **II.A.4. Supporting Data for Carcinogenicity**

Allyl chloride is an alkylating agent. Mutagenicity assays of allyl chloride in *Salmonella typhimurium* have been generally positive with or without metabolic activation (for example, Bignami et al., 1980), but have greatly decreased activity in the presence of an exogenous activating system (Eder et al., 1980). It produced gene conversion in *Saccharomyces cerevisiae* but no mutations in *Aspergillus nidulans* or chromosome aberrations in rat liver cells (Bignami et al., 1980). Allyl chloride at a concentration of 1 mM induced unscheduled DNA synthesis in HeLa cells (Schiffman et al., 1983). Allyl chloride epoxide is epichlorohydrin, a nasal carcinogen for rats by inhalation and a probable human carcinogen, although the likelihood of formation of this metabolite is unknown. Allyl chloride is structurally similar to dibromochloropropane, a probable human carcinogen.

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#### **II.B. Quantitative Estimate of Carcinogenic Risk from Oral Exposure**

Not available.

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#### **II.C. Quantitative Estimate of Carcinogenic Risk from Inhalation Exposure**

Not available.

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#### **II.D. EPA Documentation, Review, and Contacts (Carcinogenicity Assessment)**

### **II.D.1. EPA Documentation**

Source Document — U.S. EPA, 1986, 1979

The 1986 Health and Environmental Effects Profile received OHEA review. The Preliminary Risk Assessment is an internal EPA document.

### **II.D.2. EPA Review (Carcinogenicity Assessment)**

Agency Work Group Review — 11/12/1986, 02/24/1988, 04/05/1989

Verification Date — 04/05/1989

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the cancer assessment for allyl chloride conducted in August 2003 did not identify any critical new studies. IRIS users who know of important new studies may provide that information to the IRIS Hotline at [hotline.iris@epa.gov](mailto:hotline.iris@epa.gov) or 202-566-1676.

### **II.D.3. EPA Contacts (Carcinogenicity Assessment)**

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or [hotline.iris@epa.gov](mailto:hotline.iris@epa.gov) (internet address).

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**III. [reserved]**

**IV. [reserved]**

**V. [reserved]**

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## **VI. Bibliography**

Substance Name — Allyl chloride

CASRN — 107-05-1

## VI.A. Oral RfD References

None

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## VI.B. Inhalation RfC References

Hardin, B.D., G.P. Bond, M.R. Sikov, F.D. Andrew, R.P. Beliles and R.W. Niemeier. 1981. Testing of selected workplace chemicals for teratogenic potential. *Scand. J. Work Environ. Health.* 7: 66-75.

Hardin, B.D., R.L. Shuler, J.R. Burg, et al. 1987. Evaluation of 60 chemicals in a preliminary developmental toxicity test. *Teratogen. Carcinogen. Mutagen.* 7: 29-48.

Hausler, M. and R. Lenich. 1968. Effect of chronic occupational allyl chloride exposure. *Arch. Toxicol. (Berl.)* 23: 209-214.

He, F. and S.L. Zhang. 1985. Effects of allyl chloride on occupationally exposed subjects. *Scand. J. Work Environ. Health.* 11(Suppl 4): 43-45.

He, F., D. Shen, Y. Guo and B. Lu. 1980. Toxic polyneuropathy due to chronic allyl chloride intoxication: A clinical and experimental study. *Chin. Med. J.* 93(3): 177-182. (Eng. ed.)

He, F., J.M. Jacobs and F. Scaravilli. 1981. The pathology of allyl chloride neurotoxicity in mice. *Acta Neuropathol.* 55(2): 125-133.

He, F., B. Lu, S. Zhang, S. Dong, A. Yu and B. Wang. 1985. Chronic allyl chloride poisoning. An epidemiology, clinical, toxicological and neuropathological study. *G. Ital. Med. Lav.* 7(1): 5-15.

He, F. 1991. Institute Occupational Medicine, Chinese Academy of Preventative Medicine/WHO Collaborating Centre Occupational Health, Beijing, China. Letter to Daniel Guth, U.S. EPA, Research Triangle Park, NC. September 16.

John, J.A., T.S. Gushow, J.A. Ayres, T.R. Hanley Jr., J.F. Quast and K.S. Rao. 1983. Teratologic evaluation of inhaled epichlorohydrin and allyl chloride in rats and rabbits. *Fund. Appl. Toxicol.* 3: 437-42.

Lu, B., D. Shuwei, Y. Airu, X. YinLin, G. Taibao and C. Tao. 1982. Studies on the toxicity of allyl chloride. *Ecotoxicol. Environ. Saf.* 6: 19-27.

NCI (National Cancer Institute). 1978. Bioassay of allyl chloride for possible carcinogenicity. CAS No. 107-05-1. NCI-CG-TR-73. DHEW Publ. No. (NIH) 78-1323.

Nielson, G.D. and J.C. Bakbo. 1985. Sensory irritating effects of allyl halides and a role for hydrogen bonding as a likely feature at the receptor site. *Acta Pharmacol. Toxicol.* 57: 106-16.

NIOSH (National Institute for Occupational Safety and Health). 1976. Criteria for a recommended standard...Occupational exposure to allyl chloride. U.S. DHEW, PHS, CDC, Rockville, MD. HEW Publ. No. (NIOSH) 76-204.

Quast, J.F., J.W. Henck, D.J. Schuetz and M.J. McKenna. 1982a. Allyl chloride - Subchronic Studies. IA - 90-day inhalation study in laboratory rodents (CDF-Fisher 344 rats and B6C3F1 mice). OTS Document #FYI-AX-0782- 0199.

Quast, J.F., J.W. Henck, D.J. Schuetz, D.A. Dittenber and M.J. McKenna. 1982b. Allyl chloride - Subchronic studies. IB - Results of an inhalation 4-day probe and 90-day subchronic study in laboratory rodents. OTS Document #FYI- AX-0782-0199.

Torkelson, T.R., M.A. Wolf, F. Oyen and V.K. Rowe. 1959. Vapor toxicity of allyl chloride as determined on laboratory animals. *Am. Ind. Hyg. Assoc. J.* 20: 217-223.

U.S. EPA. 1986. Health and Environmental Effects Profile for Allyl Chloride. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response, Washington, DC. EPA/600/X-86/198.

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### **VI.C. Carcinogenicity Assessment References**

Bignami, M., G. Conti, L. Conti, R. Crebelli, F. Misuraca, A.M. Puglia, R. Randazzo, G. Sciandrello and A. Carere. 1980. Mutagenicity of halogenated aliphatic hydrocarbons in salmonella typhimurium, *Streptomyces coelicolor* and *Aspergillus nidulans*. *Chem.-Biol. Interaction.* 30(1): 9-23.

Eder, E., T. Neudecker, D. Lutz and D. Henschler. 1980. Mutagenic potential of allyl and allylic compounds: Structure-activity relationship as determined by alkylating and direct in vitro mutagenic properties. *Biochem. Pharmacol.* 29(3): 993-998.

NCI (National Cancer Institute). 1978. Bioassay of Allyl Chloride for Possible Carcinogenicity. Carcinogenesis Technical Report Series. NCI-CG-TR-73. PB-287516.

Schiffmann, D., E. Eder, T. Neudecker and D. Henschler. 1983. Induction of unscheduled DNA synthesis in HeLa cells by allylic compounds. *Cancer Letters*. 20(3) 263-269.

Theiss, J.C., M.B. Shimkin and L.A. Poirer. 1979. Induction of pulmonary adenomas in strain A mice by substituted organohalides. *Cancer Res.* 39: 391-395.

U.S. EPA. 1979. The Carcinogen Assessment Group's Preliminary Risk Assessment on Allyl Chloride. Type 1-Air Program.

U.S. EPA. 1986. Health and Environmental Effects Profile for Allyl Chloride. Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH. ECAO-Cin-P186.

Van Duuren, B.L., B.M Goldschmidt, G. Loewengart, A.C. Smith, S. Melchionne, I. Seldman and D. Roth. 1979. Carcinogenicity of halogenated olefinic and aliphatic hydrocarbons in mice. *J. Natl. Cancer Inst.* 63(6): 1433-1439.

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## VII. Revision History

Substance Name — Allyl chloride  
CASRN — 107-05-1

Date	Section	Description
09/01/1990	II.	Carcinogen assessment on-line
12/01/1991	I.B.	Inhalation RfC on-line
10/28/2003	I.B.6., II.D.2.	Screening-Level Literature Review Findings message has been added.

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## VIII. Synonyms

Substance Name — Allyl chloride

CASRN — 107-05-1

Last Revised — 09/01/1990

- 107-05-1
- ALLILE (CLORURO DI) [ITALIAN]
- ALLYLCHLORID [GERMAN]
- ALLYL CHLORIDE
- ALLYLE (CHLORURE D') [FRENCH]
- P-AMINOPROPIOFENON [CZECH]
- CHLORALLYLENE
- 3-CHLOROPRENE
- 1-CHLORO-2-PROPENE
- 3-CHLOROPROPENE-1
- 1-CHLORO PROPENE-2
- 3-CHLOROPROPENE
- 3-CHLORO-1-PROPENE
- 3-CHLOROPROPYLENE
- ALPHA-CHLOROPROPYLENE
- 3-CHLORPROPEN [GERMAN]
- CHLORURE D'ALLYLE [FRENCH]
- CLORURO DE ALILO [SPANISH]
- HSDB 178
- NCI-C04615
- NSC 20939
- 1-PROPENE, 3-CHLORO-
- PROPENE, 3-CHLORO-
- 2-PROPENYL CHLORIDE
- UN 1100