1,2-Dichloropropane; CASRN 78-87-5

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 1,2-Dichloropropane

File First On-Line 12/01/1991

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

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — 1,2-Dichloropropane
CASRN — 78-87-5

Not available at this time.

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

Substance Name — 1,2-Dichloropropane
CASRN — 78-87-5
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
Hyperplasia of the nasal mucosa **Rat 13-week Inhalation Study** **Nitschke et al., 1988**	NOAEL: None LOAEL: 69.3 mg/cu.m (15 ppm) LOAEL(ADJ): 12.4 mg/cu.m LOAEL(HEC): 1.3 mg/cu.m	300	1	4E-3 mg/cu.m

*Conversion Factors: MW = 112.99. Assuming 25C and 760 mmHg, LOAEL(mg/cu.m) = LOAEL(ppm) x MW/24.45 = 69.3 mg/cu.m. LOAEL(ADJ) = LOAEL(mg/cu.m) x 6 hours/day/24 hours/day x 5 days/7 days = 12.4 mg/cu.m. The LOAEL(HEC) was calculated for a gas:respiratory effect in the ExtraThoracic region. MVa = 0.14 cu.m/day, MVh = 20 cu.m/day, Sa(ET) = 11.6 sq. cm., Sh(ET) = 177 sq. cm. RGDR(ET) = (MVa/Sa) / (MVh/Sh) = 0.107. LOAEL(HEC) = LOAEL(ADJ) x RGDR = 1.3 mg/cu.m.

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

Nitschke K.D., K.A. Johnson, D.L. Wackerle, J.E. Phillips and D.A. Dittenber. 1988. Propylene dichloride: A 13-week inhalation toxicity study with rats, mice, and rabbits. Dow Chemical Company, Mammalian and Environmental Toxicology Research Laboratory, Midland, MI. OTS Doc. #86-870001397

Male and female F344 and B6C3F1 mice (10/group) were exposed to 0, 15, 50, or 150 ppm dichloropropane (0, 69.3, 231, or 693 mg/cu.m) for 6 hours/day, 5 days/week for 13 weeks (duration-adjusted concentrations = 0, 12.4, 41.3, and 124 mg/cu.m). New Zealand rabbits (7/sex/group) were exposed to 0, 150, 500, or 1000 ppm dichloropropane (0, 693, 2310, or 4621 mg/cu.m) according to the same regimen (duration-adjusted concentrations = 0, 124, 413, and 825 mg/cu.m). The animals were observed daily after exposure for overt signs of toxicity as well as changes in behavior pattern and nervous system activity. Body weights were measured weekly. Hematology, clinical chemistry, and urinalysis were done prior to exposure and 2 weeks before study termination. Histopathology was conducted on 52 tissues in the control and high-concentration groups for all three species. The nasal tissues, larynx, trachea, and lungs were evaluated in all concentration groups for all three species. Histopathological examinations were also made on the liver and kidney in mice and on the liver, bone marrow, and spleen in rabbits at all exposure concentrations. The number of sections of the nasal cavity was not stated; it was assumed that four sections were taken as was done in the preliminary 2-week study in the same lab (Nitschke and Johnson, 1983). No treatment-related deaths were observed in any species. Body weights were statistically significantly reduced in the male rats (90% of control) and female rats (92-94% of control) exposed to 150 ppm, and slightly reduced at 50 ppm dichloropropane. No significant treatment-related effects on any hematological, clinical chemistry, or urinalysis parameters studied were noted in the rats or mice. Histopathological effects were seen in the upper respiratory tract of the rats that were concentration-related in incidence and severity. Very slight to slight hyperplasia of the respiratory epithelium of the nasal cavity was observed (0/10, 2/9, 5/10 and 9/10 in males and 0/10, 3/10, 7/10 and 9/10 in females at 0, 15, 50, and 150 ppm, respectively). This hyperplasia occurred primarily in the anterior regions of the nasal cavity. Very slight to slight degeneration of the olfactory mucosa in the rostral portion of the nasal cavity was noted for all male and female rats exposed to 50 or 150 ppm dichloropropane, but not in the control and 15-ppm groups. Statistical analysis of these results was not reported. Slight inflammation of the larynx was also noted in several male rats exposed to 150 ppm dichloropropane; no other treatment related effects were observed in the respiratory tract of rats. No effects were observed in the liver, spleen, or bone marrow in rats exposed to 150 ppm.

No treatment-related pathological effects were observed in the mice. Anemia was seen in the rabbits exposed to dichloropropane in a concentration related manner. Red blood cell counts

(RBC), hemoglobin concentration, and percent packed cell volume were statistically significantly decreased in the animals exposed to 150 ppm (red blood cell count only), 500, or 1000 ppm dichloropropane. Animals in the 500- and 1000-ppm groups exhibited evidence of a regenerative response (bone marrow hyperplasia and hemosiderin-laden macrophages). Minimal degeneration of the olfactory epithelium was also observed in the nasal cavity of some rabbits from all exposure groups and the controls, but the incidence and severity were higher in the 1000 ppm male animals. This study demonstrates that respiratory effects are apparently the most sensitive endpoint of dichloropropane-induced toxicity, and that species vary considerably with regard to their susceptibility to these effects. A LOAEL of 15 ppm [LOAEL(HEC) = 1.3 mg/cu.m] can be estimated for this study, based on nasal epithelial hyperplasia in female rats. This LOAEL should be considered minimal because of the low incidence and severity of the lesion seen at this concentration. Despite the minimal nature of the effects, they are considered to be adverse because of the increase in incidence and severity with increasing exposure concentration. This relationship is additionally supported by the short-term data (described later). Based on the exposure concentrations used in this study, rats are more than 10 times more sensitive than mice and 100 times more sensitive than rabbits to the nasal effects.

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

UF — The uncertainty factor of 300 reflects a factor of 10 to protect sensitive individuals. A factor of 3 is used for extrapolation from a subchronic study, since study of the critical effect shows little progression with exposure time. A factor of 3 is used for the use of a minimal LOAEL due to the minimal nature of the effect. A factor of 3 is used for interspecies extrapolation due to the use of dosimetric adjustments. The factors of 3 represent operational application of a geometric half of the standard factor of 10, rounded to a single significant figure. As a result, multiplication of 3 factors of 3 results in a composite factor of 30.

MF — None

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

Nitschke and Johnson (1983) exposed groups of 5 male and female F344 rats and male rabbits to 0, 100, 300, or 1000 ppm (0, 462, 1386, or 4621 mg/cu.m) 6 hours/day for 2 weeks (9 exposures) in a preliminary study to the critical study. Male and female B6C3F1 mice were exposed to 0, 30, 100, or 300 ppm (0, 139, 462, or 1386 mg/cu.m) with the same protocol. Hematology, serum chemistry, and urine chemistry measurements were made either prior to or after the ninth exposure. Histopathological examination of the respiratory tract (nasal turbinates - four sections, larynx, trachea, lungs), adrenals, liver, kidney, testes, bone marrow, and thymus was performed. Body weights of male and female rats were significantly reduced compared with controls in all groups. No exposure-related changes in hematology, serum chemistry, or urinalysis were found

in rats. Slight to moderate degeneration of the nasal olfactory epithelium was observed in all 5 male and 5 female rats exposed to 100 or 300 ppm. Severe degeneration was observed in 4/5 males and 5/5 females at 1000 ppm. In the critical study, degeneration of the olfactory epithelium was described as slight to very slight in all male and female rats exposed to 50 or 150 ppm, indicating a very limited progression of this lesion between 2 and 13 weeks. In contrast, the hyperplasia of the respiratory epithelium noted in the 13-week study was not reported in the 2-week study. This suggests that some progression of the lesion occurs since an area of the nasal epithelium was affected at 13 weeks, but not at 2 weeks. The severity of the lesion at 13 weeks was characterized as slight to very slight. Slightly reduced cellularity of the bone marrow was also reported in males exposed to 1000 ppm and females exposed to 300 or 1000 ppm.

In mice, body weight was not affected by exposure (Nitschke and Johnson, 1983). Mild liver lesions were observed in male and female mice exposed to 300 ppm and absolute and relative liver weight increases were found in females. Mice exposed to 300 ppm also had decreased RBC, decreased hemoglobin concentration, and decreased packed cell volume, but these were within the range of historical controls. Slight degeneration of the nasal olfactory epithelium was observed in 4/5 males exposed to 300 ppm and in females exposed to 100 ppm (2/5) or 300 ppm (4/5). Moderate degeneration was observed in 1 male and 1 female exposed to 300 ppm. No nasal lesions were observed in the critical study in mice exposed to 50 or 150 ppm, suggesting that these lesions may resolve with time and do not progress substantially. The only clearly exposure-related lesion in rabbits was slight degeneration of the nasal olfactory epithelium in 2/5 males exposed to 1000 ppm. This result is similar to the critical study in which minimal degeneration was seen in a few rabbits exposed to 1000 ppm and no effect was observed in the nasal epithelium at 500 ppm. These results agree with those of Nitschke et al. (1988) in showing that the nasal epithelium is the most sensitive target tissue in rats, mice, and rabbits. The rat appears to be somewhat more sensitive than the mouse and considerably more sensitive than the rabbit. In addition, comparison of the results at 2 weeks and 13 weeks for three species shows little or no increase in incidence or severity of this lesion, suggesting that the lesion does not progress substantially between 2 weeks and 13 weeks of exposure. Although not directly addressing the issue of progression during a lifetime exposure, these data reduce the concern about progression and the uncertainty in extrapolation to chronic exposure.

In a study conducted by Heppel et al. (1946), dogs, rats, mice, rabbits, and guinea pigs were exposed to 1000-2200 ppm dichloropropane 7 hours/day, "nearly always" 5 days/week. Deaths were observed in rats, rabbits, and guinea pigs after less than 8 exposures to 2200 ppm dichloropropane. Most animals could survive 35 exposures to 1500 ppm dichloropropane. Deaths were observed in dogs, guinea pigs, and rats exposed to 1000 ppm dichloropropane. Mice died after only a few hours of exposure to 1000 ppm dichloropropane. Food intake and body weight were adversely affected at all exposure levels. Hematological evaluation failed to reveal any treatment-related effects. Although clinical tests of liver function failed to reveal any adverse

effects, histopathological evaluation of the animals that died after only 2-11 exposures to 1000-2200 ppm dichloropropane revealed a friable fatty liver with fatty degeneration characterized by fat accumulation in the centrilobular hepatocytes and coagulation necrosis in guinea pigs. Pulmonary congestion was seen in similarly exposed rats. Hepatic lesions were also noted in rabbits, dogs, and mice exposed to dichloropropane at varying concentrations. Fatty degeneration was also observed in the kidneys of most test species, while lipoid depletion or extensive necrosis was seen in the adrenal cortices of rats and guinea pigs, respectively. Histopathological effects in the respiratory tract were not discussed. It appears that if animals survived the first several exposures, they became resistant to most of these toxic effects because marked splenic hemosiderosis in rats and subcortical fibrosis of the adrenal in guinea pigs were the only notable treatment-related lesions seen in animals that survived 35 exposures.

In a subsequent experiment, Highman and Heppel (1946) compared the pathological findings occurring in guinea pigs and rats after 1-5 7-hour exposures to 2200 ppm dichloropropane with those found in the same species exposed once for 7 hours to 2200 ppm dichloropropane and sacrificed at various intervals up to 21 days after exposure. Treatment-related lesions noted in guinea pigs following either exposure regimen included fatty degeneration of the liver and the kidneys and degeneration and necrosis of both the cortex and the medulla of the adrenal glands. Rats also exhibited hepatic lesions and depletion of lipoid material of the adrenal cortex. The effects were most severe 24-48 hours after the first exposure, and appeared to resolve with time regardless of whether exposure was continued. For example, in rats after one exposure, slight diffuse fatty degeneration was observed in the liver that progressed, after an additional exposure, to marked diffuse fatty degeneration and extensive, often confluent centrilobular coagulation and focal hemorrhagic necrosis. The hepatic lesions appeared to diminish at this point until only minimal fatty changes were observed after five exposures to dichloropropane.

Because of the high mortality observed in most species at concentrations greater than or equal to 1000 ppm dichloropropane, Heppel et al. (1948) investigated the effects of exposure to 400 ppm dichloropropane in rats, mice, guinea pigs, and dogs. The animals received 7-hour exposures, 5 days/week for 25-30 weeks. The rats were killed at various intervals during the exposure period and several were observed for 6-8 months after they had received 140 exposures. High mortality was observed in the mice during the first 12 exposures. The majority of the mice (5/8) that were killed within 48 hours of the first exposure exhibited slight fatty degeneration of the liver, and slight fatty degeneration of the kidney was observed in 1/2 mice killed after the second exposure. In a group of 80 C3H mice given up to a total of 37 4- to 8-hour exposures to 400 ppm dichloropropane, only 3 survived the entire treatment and observation period. Those mice that died during the exposure period were found to have moderate to marked congestion and fatty degeneration of the liver, extensive centrilobular coagulation necrosis of the liver, and slight to moderate fatty degeneration of the kidney. Multiple hepatomas were found in the three mice that survived the full 37 exposures. The most prominent treatment-related effect observed in the other

species was decreased body weight gain in rats. The only other exposure-related effect in rats was slight hemosiderin deposition in the liver. Most of the control and exposed guinea pigs exhibited minimal fatty changes in the heart, liver, or kidney and slight to moderate hemosiderosis of the spleen and adrenal gland, but the severity of these changes was slightly greater in the exposed animals. No treatment-related effects were observed in the dogs. Histology of the lungs was performed and no respiratory tract effects were reported.

Drew et al. (1978) exposed rats to 1000 ppm dichloropropane for 4 hours and then measured several serum enzyme indicators of hepatic function immediately after exposure and at 24 and 48 hours after exposure. They found that SGOT, SGPT, and ornithine carbamyl transferase activities were significantly elevated by at least 1-day post exposure, but that glucose-6-phosphatase activity was unaffected. Although no histopathology was conducted in this study, these results, together with the earlier studies that demonstrated liver histopathology after one exposure to comparable concentrations of dichloropropane, indicate that serum enzymes may serve as a reliable early biomarker of dichloropropane-induced liver toxicity. The respiratory tract was not examined in this study.

Oral subchronic and chronic studies have demonstrated toxic effects in the liver, spleen, testes, and blood. Bruckner et al. (1989) exposed male Sprague-Dawley rats to 0, 100, 250, 500, or 750 mg/kg/day in corn oil gavage on 5 days/week for 13 weeks. Increased mortality occurred in the 500- and 750-mg/kg/day groups. Body weight reduction was significant in all groups. Manifestations of hemolytic anemia included decreased hematocrit, decreased hemoglobin concentration, increased serum bilirubin, and hemosiderosis and hyperplasia of the erythropoietic elements of the spleen. Some of these effects were evident in the 100-mg/kg/day group. Relative spleen weight was increased in the 250- and 500-mg/kg/day groups. Testicular degeneration was observed in 500- and 750-mg/kg/day animals and not in the lower dose groups. Liver toxicity was indicated by increased serum OCT levels, histopathological changes, and increased liver weight in the 250- and 500-mg/kg/day groups.

The NTP (1986) exposed female rats and male and female mice to 0, 125, and 250 mg/kg/day, and male rats to 0, 62, and 125 mg/kg/day in corn oil by gavage 5 days/week for 103 weeks. Decreased body weight was observed in the high- dose males (86% of control) and females (76% of control). Liver histopathological effects showed focal clear cell changes in females (3/50, 5/50, and 11/50 in 0-, 125-, and 250-mg/kg/day groups) and necrosis in the high-dose group only. No liver effects were seen in males at either dose. Increased hemosiderosis was also observed in the high-dose female rats. In mice, liver lesions were observed in dosed males but not in females. Hepatocytomegaly occurred in 3/50, 5/49, and 15/50 and necrosis was seen in 2/50, 5/49, and 10/50 in 0-, 125-, and 250-mg/kg/day dose groups, respectively.

In the NTP 13-week study, rats were dosed by gavage with 0, 60, 125, 250, 500, or 1000 mg/kg/day on 5 days/week. High-dose rats showed liver histopathology including congestion in 5/10 males and 2/10 females and necrosis and fatty change in 2/10 females. Mice were dosed with 0, 30, 60, 125, 250, and 500 mg/kg/day and no treatment-related histological effects were observed. Taken together the oral studies indicate that the LOAEL for liver effects in mice and rats is at 250 mg/kg/day for chronic exposures. The subchronic LOAEL in rats was 1000 mg/kg/day and in mice the NOAEL was 500 mg/kg/day. Body weight reduction occurred at 125 mg/kg/day in male rats in the chronic study and at 250 mg/kg/day in the females. Blood effects in rats show a clear LOAEL at 250 mg/kg/day with mild effects at 100 mg/kg/day.

Kirk et al. (1989) conducted an oral teratology study with dichloropropane in Sprague-Dawley rats. Groups of 30 bred females were administered 0, 10, 30, or 125 mg dichloropropane/kg/day in corn oil by gavage on gestation days 6-15. Based on the findings of the study, dichloropropane is fetotoxic in Sprague-Dawley rats at the maternally toxic dose of 125 mg/kg/day. Maternal toxicity was evidenced in the high-dose group by the clinical findings including significantly decreased body weight gain during days 8-16, decreased movement, decreased muscle tone, decreased extensor thrust reflex, increased salivation, decreased food consumption (25%) during gestation days 6-9, and increased water consumption (25%) during days 9-15. These effects were not seen in controls and in the 10- and 30-mg/kg/day dose groups. Although no teratogenic effects were seen, a statistically significant increase in the incidence of delayed ossification of skull bones was evident among fetuses in the 125-mg/kg/day dose group. Thus, dichloropropane is fetotoxic in rats at a maternally toxic dose; the NOAEL and LOAEL for this study were 30 and 125 mg/kg/day, respectively.

In an oral teratology study with dichloropropane in New Zealand White rabbits (Hanley et al., 1989), groups of 18 inseminated females were administered 0, 15, 50, or 150 mg dichloropropane/kg/day in corn oil by gavage on gestation days 7-19. The results of the study indicate that oral administration of dichloropropane at 150 mg/kg/day caused anemia, anorexia, and a statistical decrease in the body weight gain of the maternal animal. There was a significant decrease in RBC count, hemoglobin concentration, and hematocrit, and significant elevation in the WBC, platelet, and reticulocyte counts. Maternal toxicity was not observed in the 15- and 50-mg/kg/day groups. A statistically significant increase in the incidence of delayed ossification of skull bones among fetuses in the 150 mg/kg/day group was noted. An increased incidence of delayed skeletal ossification (not statistically significant) was observed at 50 mg/kg/day. No such effects were seen in the 15-mg/kg/day dose group and in controls. Under the conditions of the study, dichloropropane is fetotoxic to rabbits at the highest dose and also causes deleterious effects on the maternal physiology; the NOAEL and LOAEL for developmental and maternal effects were 50 and 150 mg/kg/day, respectively.

In a 2-generation reproduction study in Sprague-Dawley rats (Kirk et al., 1990), groups of 30 rats/sex/dose were provided access to drinking water that contained 0, 0.024, 0.10, or 0.24% (w/v) dichloropropane over 2 generations. Premating exposure of male and female F0 generation rats to 0.24% dichloropropane caused a statistically significant decrease in body weight gain. There was also a significant decrease in water consumption (50% less than controls) and a decrease in body weight gain during gestation and lactation in F0 generation females and a statistically significant decrease in neonatal body weight and survival. RBC counts, hemoglobin concentration, and hematocrit were significantly decreased in F0 females. Although some of these effects were seen at 0.10 and 0.024%, they were not significant. Treatment- related histopathological changes in the liver were seen at all exposure levels but were more remarkable in the 0.24% group. No treatment-related changes in the reproductive organs or in other reproductive indices, including fertility, mating index, conception index, viable litters, gestation length, litter size, live pups, and sex ratio, were noted.

In F1 generation animals, water consumption and weight gain decreased significantly during gestation and lactation, but no statistically significant decrease in survival was noted among F2 neonates. There were no treatment- related histologic changes in the reproductive organs of parental rats. Some sporadic hematological and histopathological changes in the liver and kidney were seen in parental F1 animals but these findings were not biologically meaningful, except mild liver lesions at 0.24%. Under the conditions of the study, dichloropropane did not affect fertility but decreased neonatal body weight and survival at the 0.24% concentration and produced deleterious effects on the maternal animal. The NOAEL and LOAEL for reproductive toxicity were 0.10 and 0.24%, respectively. Based on measured drinking water intake, the doses were calculated for males and females for prebreeding, post-breeding in males, and pregestation and gestation in females. The NOAEL and LOAEL levels correspond to approximate doses of 100 and 200 mg/kg/day, respectively.

The oral studies indicate that fetotoxicity, minor developmental effects, and a NOAEL for reproductive effects are found at doses approximating those found to adversely affect blood and body weight, and approaching doses found to affect the liver in chronic and subchronic studies. Because of the lack of inhalation, developmental, and reproductive studies, these oral studies were used to infer that developmental and reproductive effects are not significantly more sensitive than liver and blood effects. This supports the use of the respiratory effect as the critical effect, since respiratory effects are considerably more sensitive than liver and blood effects in rats in inhalation studies.

Pharmacokinetic studies conducted by Timchalk et al. (1989) indicate that dichloropropane appears to be rapidly absorbed, metabolized, and excreted after oral gavage or inhalation exposure. No meaningful sex-related differences were found in these studies. The majority of the radioactivity was excreted within 24 hours. The principle routes of elimination following oral or

inhalation exposure were via the urine (37-52%) and expired air (37- 40%). The major urinary metabolites after oral or inhalation exposure were identified as three mercapturates, the N-acetylcysteine conjugates of dichloropropane. The majority (61-80%) of the expired volatile material was the parent dichloropropane after oral exposure. After inhalation exposure, recovery of label was 56-65% in the urine and 16-23% in the expired air (primarily CO2). The peak blood dichloropropane concentrations in the inhalation study showed a dose-dependent nonlinearity in the blood clearance of dichloropropane; however, upon termination of exposure, dichloropropane was rapidly eliminated (T1/2 = 24-30 minutes). Elimination route and metabolites were studied after 6-hour inhalation exposure to 5, 50, or 1000 ppm dichloropropane. With increasing concentration, a greater proportion of the recovered dose was eliminated as expired organics (1.7, 2.1-3.4, and 6.3- 6.7%), although relative urinary excretion and relative elimination as expired CO2 were not affected in a concentration related way. These results suggest saturation of oxidative metabolism at the highest concentrations. Repeated exposure resulted in a slight shift in the urinary metabolite profile and reduced urinary excretion. However, repeated dose studies were only performed at the 1-mg/kg/day oral dose level, and changes in metabolism with repeated higher doses or inhalation exposures were not studied.

Overall, this study appears to be well conducted with a few deficiencies noted during the evaluation of data. These are that the position of radiolabel in relation to chemical structure was not stated and the rates of absorption and excretion were not determined. Although the study author stated that the test solution was stable even after 8 days (94.4% of the initial concentration), no supporting data were provided. Comparison of the area under the curve and peak plasma C-14 concentrations indicated no clear pattern of dose-dependent C-14 elimination after oral or inhalation exposure.

Dichloropropane is used extensively in Italy as a commercial solvent and in the commercial stain remover formulation Trielina, which contains 60-100% dichloropropane. Pozzi et al. (1985) reported two cases of dichloropropane intoxication following inhalation exposure to Trielina. In the first case, a 20-year-old woman was admitted to the hospital with oliguria, epistaxis, hematuria, uterine bleeding, and periorbital and conjunctival hemorrhages. Two days before admission she had abdominal pain, vomiting, fever, facial edema, and erythema. She admitted to sniffing Trielina every night. Clinical tests confirmed severe renal failure, acute liver damage, hemolytic anemia, and disseminated intravascular coagulation. Following transfusions with fresh blood and four hemodialfiltration sessions, the patient was discharged with complete recovery of her renal and liver function and normal coagulation tests. In the second case, a 55-year-old woman was admitted to the hospital with severe liver failure, hemolytic anemia, and slight disseminated intravascular coagulation 3 days after she had spent 6 hours cleaning her flat using 2 liters of solvent containing dichloropropane. She had been suffering from membranoproliferative glomerulonephritis and was on home hemodialysis when exposure to dichloropropane occurred. Hemodialysis treatments continued in the hospital, and within a week

the hemolytic anemia and intravascular coagulation disappeared, and her liver disease improved considerably. These two cases demonstrate that acute as well as repeated high-level inhalation exposure to dichloropropane (level not specified in either case) are associated with adverse effects on the liver, kidney, and hematopoietic systems in humans, and that these effects can be reversed following cessation of exposure. No respiratory symptoms were reported.

The health effects in humans (truck drivers, highway patrol officers, fire fighters, and hospital employees) that were exposed to dichloropropane following the accidental spill of 2000 gallons from a truck were described by Rubin (1988). The exposed individuals complained of chest discomfort, dyspnea, and cough, and some had persistent chest pain or discomfort and fatigue. These symptoms indicate that dichloropropane is a respiratory irritant. The level of exposure to dichloropropane was not quantified.

I.B.5. Confidence in the Inhalation RfC

Study — High
Database — Medium
RfC — Medium

The Nitschke et al. (1988) study used an adequate number of animals, exposure concentrations, and controls, examined three species, focused on known target organs, and the incidence and severity of the nasal lesions were exposure-related. The database is given a medium confidence rating because there are no chronic inhalation studies. A medium confidence rating for 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, 1987a,b

Agency Work Group Review — 07/17/1991

Verification Date — 07/17/1991

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 1,2-Dichloropropane conducted in September 2002 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 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 (internet address).

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — 1,2-Dichloropropane
CASRN — 78-87-5

This substance/agent has not undergone a complete evaluation and determination under US EPA's IRIS program for evidence of human carcinogenic potential.

III. [reserved]
IV. [reserved]
V. [reserved]

VI. Bibliography

Substance Name — 1,2-Dichloropropane
CASRN — 78-87-5

VI.A. Oral RfD References

None

VI.B. Inhalation RfC References

Bruckner, J.V., W.F. MacKenzie, R. Ramanathan, S. Muralidhara, H.J. Kim and C.E. Dallas. 1989. Oral toxicity of 1,2-dichloropropane: Acute, short-term, and long-term studies in rats. Fund. Appl. Toxicol. 12: 713-730.

Drew, R.T., J.M. Patel and F-N. Lin. 1978. Changes in serum enzymes in rats after inhalation of organic solvents singly and in combination. Toxicol. Appl. Pharmacol. 45: 809-819.

Hanley, T.R., N.M. Berdasco, J.E. Battjes and K.A. Johnson. 1989. Propylene dichloride: Oral teratology study in New Zealand White Rabbits. Mammalian and Environmental Toxicology Research Laboratory, Health and Environmental Sciences, The Dow Chemical Company, Midland, MI.

Heppel, L.A., P.A. Neal, B. Highman and V.T. Porterfield. 1946. Toxicology of 1,2-dichloropropane (propylene dichloride). I. Studies on effects of daily inhalations. J. Ind. Hyg. Toxicol. 28(1): 1-8.

Heppel, L.A., B. Highman and E.G. Peake. 1948. Toxicology of 1,2- dichloropropane (propylene dichloride). IV. Effect of repeated exposures to a low concentration of the vapor. J. Ind. Hyg. Toxicol. 30: 189-191.

Highman, B. and L.A. Heppel. 1946. Toxicology of 1,2-dichloropropane (propylene dichloride). III. Pathologic changes produced by a short series of daily exposures. Arch. Pathol. 42: 525-534.

Kirk, H.D., T.R. Hanley, K.A. Johnson and F.K. Dietz. 1989. Propylene dichloride: Oral teratology study in Sprague-Dawley rats. Mammalian and Environmental Toxicology Research Laboratory, Health and Environmental Sciences, The Dow Chemical Company, Midland, MI.

Kirk, H.D., T.R. Hanley, Jr., D.M. Bond, et al. 1990. Propylene dichloride: Two-generation reproduction study in Sprague-Dawley rats. Mammalian and Environmental Toxicology Research Laboratory, Health and Environmental Sciences, The Dow Chemical Company, Midland, MI.

Nitschke, K.D. and K.A. Johnson. 1983. Propylene dichloride: One day and two week inhalation toxicity study in rats, mice, and rabbits. Mammalian and Environmental Toxicology Research Laboratory, Health and Environmental Sciences, Dow Chemical Company, Midland, MI.

Nitschke, K.D., K.A. Johnson, D.L. Wackerle, J.E. Phillips and D.A. Dittenber. 1988. Propylene dichloride: A 13-week inhalation toxicity study with rats, mice, and rabbits. Dow Chemical Company, Mammalian and Environmental Toxicology Research Laboratory, Midland, MI. OTS Doc. #86-870001397

NTP (National Toxicology Program). 1986. Toxicology and Carcinogenesis studies of 1,2-dichloropropane (Propylene dichloride) (CAS No. 78-87-5) in F344/N rats and B6C3F1 mice (gavage studies). TR-263, NIH Publication No. 86-2519. National Toxicology Program, Research Triangle Park, NC.

Pozzi, C., P. Marai, R. Ponti, et al. 1985. Toxicity in man due to stain removers containing 1,2-dichloropropane. Br. J. Ind. Med. 42(11): 770-772.

Rubin, D.F. 1988. Occupational health implications of a toxic spill of propylene dichloride. Western J. Med. 148(1): 78-79.

Timchalk, C., M.J. Bartels, M.D. Dryzga and F.A. Smith. 1989. Propylene dichloride: Pharmacokinetics and metabolism in Fischer 344 rats following oral and inhalation exposure. Mammalian and Environmental Toxicology Research Laboratory, Health and Environmental Sciences, The Dow Chemical Company, Midland, MI.

U.S. EPA. 1987a. Drinking Water Criteria Document for 1,2-Dichloropropane. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Drinking Water, Washington, DC. EPA/600/x-84/162-2.

U.S. EPA. 1987b. Health Effects Assessment for 1,2-Dichloropropane. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Emergency and Remedial Response, Washington, DC. EPA/600/8-88/029.

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — 1,2-Dichloropropane
CASRN — 78-87-5

Date	Section	Description
12/01/1991	I.B.	Inhalation RfC on-line
12/03/2002	I.B.6.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — 1,2-Dichloropropane
CASRN — 78-87-5
Last Revised — 12/01/1991

- 78-87-5
- Propane, 1,2-dichloro-
- Propylene dichloride
- 1,2-DICHLOROPROPANE
- AI3-15406
- alpha,beta-DICHLOROPROPANE
- alpha,beta-PROPYLENE DICHLORIDE
- BICHLORURE DE PROPYLENE [French]
- Caswell No. 324
- CCRIS 951
- Dichloro-1,2 propane [French]
- Dichlorure de propylene [French]
- Dicloruro de propileno [Spanish]
- Dwuchloropropan [Polish]
- ENT 15,406
- EPA Pesticide Chemical Code 029002
- HSDB 1102
- NCI-C55141
- Propylene chloride