2. RELEVANCE TO PUBLIC HEALTH

2.1 BACKGROUND AND ENVIRONMENTAL EXPOSURES TO 1,1-DICHLOROETHANE IN THE UNITED STATES

The production and use of 1,1-dichloroethane as a solvent, cleaning agent, and degreaser, and in the manufacture of 1,1,1-trichloroethane, vinyl chloride, and high vacuum rubber may result in its release to the environment. Volatilization is expected to be high based on its vapor pressure and Henry’s Law constant. Atmospheric photooxidation occurs slowly in the environment, as does biodegradation and hydrolysis. 1,1-Dichloroethane has high mobility in soil and has the potential to leach from surface soils into groundwater. The bioaccumulation potential of 1,1-dichloroethane is low.

Monitoring data indicate that the general population may be exposed to 1,1-dichloroethane via inhalation for people living near source areas, ingestion of contaminated drinking water, and use of consumer products such as paint removers, which may contain this compound. Ingestion of food sources contaminated with 1,1-dichloroethane is not an important exposure pathway.

A National Health and Nutrition Survey of the U.S. population in 2003–2004 screened for 1,1-dichloroethane in blood from 1,367 participants (670 males and 679 females) in the age range of 20–59 years old. The portion of the data below the limit of detection (LOD) was too high to provide valid results.

2.2 SUMMARY OF HEALTH EFFECTS

Relatively little information is available on the health effects of 1,1-dichloroethane in humans or animals. Chlorinated aliphatics as a class are known to cause central nervous system depression and respiratory tract and dermal irritation when humans are exposed by inhalation to sufficiently high levels. In the past, 1,1-dichloroethane was used as an anesthetic; however, this use was discontinued due to the risk of cardiac arrhythmia induction in humans at anesthetic doses (approximately 26,000 ppm). A small number of animal studies have examined the toxicity and carcinogenicity of 1,1-dichloroethane; these studies have failed to conclusively identify the critical targets of toxicity. Nonneoplastic effects are limited to renal toxicity in cats, maternal and fetal toxicity in rats, and alterations in body weight gain. Crystal precipitations and obstruction in the renal tubule lumina and increases in serum urea and creatinine were observed in cats exposed to 500 ppm for 13 weeks followed by a 13-week exposure to 1,000 ppm for 13 weeks. However, these effects were not observed in rats, guinea pigs, or rabbits similarly exposed to 1,1-dichloroethane, and renal effects have not been observed following gavage administration of 764 or
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950 mg/kg/day in rats or 2,885 or 3,331 mg/kg/day in mice 5 days/week for 78 weeks or in mice exposed
to 465 mg/kg/day 1,1-dichloroethane in drinking water for 52 weeks. Kidney effects have also been
observed in mice administered a lethal intraperitoneal injection of 1,1-dichloroethane; the effects included
increased glucose and protein in the urine and tubular swelling. The toxicological significance of the
nephrotoxicity observed in cats and the mice with regard to human health is not known given the small
number of animals tested (cats), the lack of a nephrotoxic effect in other species and in other studies
where 1,1-dichloroethane was administered orally.

The liver is the only other organ that has been examined in multiple studies; no hepatic effects have been
reported following intermediate-duration inhalation exposure of rats, guinea pigs, rabbits, or cats,
intermediate-duration oral exposure of mice, or chronic-duration exposure of rats and mice. The potential
reproductive toxicity, immunotoxicity, and neurotoxicity of 1,1-dichloroethane have not been examined
following inhalation, oral, or dermal exposure. A single developmental toxicity study reported retarded
fetal development (delayed ossification of vertebrae) in rats at 6,000 ppm (7 hours/day on gestation
days 6–15); an 11% decrease in maternal body weight gain and a decrease in maternal food consumption
were also reported at this concentration. There is inconclusive evidence that 1,1-dichloroethane may be
carcinogenic in rodents. A significant positive dose-related trend was observed for the incidence of
hemangiosarcomas and mammary adenocarcinomas in female rats, hepatocellular carcinomas in male
mice, and endometrial stromal polyps in female mice. However, only the incidence of endometrial
stromal polyps in female mice was significantly increased over the corresponding control animals.
Limitations in this study, particularly the poor survival in treated and control animals, preclude the
consideration of these results as conclusive evidence of carcinogenicity. A 52-week drinking water study,
testing much lower doses, did not find increases in the incidence of lung, liver, or kidney tumors in mice.
Based on the available carcinogenicity data for 1,1-dichloroethane and supporting data on 1,2-dichloro-
ethane, the EPA has classified 1,1-dichloroethane as a possible human carcinogen (group C). Neither the
Department of Health and Human Services nor the International Agency for Research on Cancer have
classified the carcinogenic potential of 1,1-dichloroethane.

An overview of these data is presented in Figures 2-1 and 2-2.
Figure 2-1. Health Effects for Following Inhalation Exposure to 1,1-Dichloroethane

**Dose (ppm)** | **Effects in Animals**
--- | ---
6,000 | Maternal and developmental effects in rats^a^
750 (TWA) | Renal effects in cats^b^; no liver or kidney effects in rats, guinea pigs, or rabbits

^a 11% decrease in maternal body weight gain and increased incidence of fetuses with delayed ossification
^b Increased serum urea and creatinine levels, crystal precipitations and obstruction in tubule lumina and dilatation of proximal section of renal tubules

TWA = time-weighted average
Figure 2-2. Health Effects for Following Oral Exposure to 1,1-Dichloroethane

Dose (mg/kg/day)$^a$

<table>
<thead>
<tr>
<th>Dose</th>
<th>Effects in Animals</th>
</tr>
</thead>
<tbody>
<tr>
<td>2,061 (males); 2,379 (females)</td>
<td>Highest no-effect level in mice following chronic exposure</td>
</tr>
<tr>
<td>546 (males); 679 (females)</td>
<td>Highest no-effect level in rats following chronic exposure</td>
</tr>
<tr>
<td>401 (males)</td>
<td>Decreases in body weight gain in rats following 5 week exposure$^a$</td>
</tr>
</tbody>
</table>

$^a$Doses adjusted for intermittent exposure (5 days/week)
2.3 MINIMAL RISK LEVELS (MRLs)

Inhalation MRLs

There are limited data to derive inhalation MRLs for 1,1-dichloroethane; the database consists of two inhalation studies. Hofmann et al. (1971) examined the potential for 1,1-dichloroethane to induce liver and/or kidney effects in rats, guinea pigs, rabbits, and cats exposed to 500 ppm 6 hours/day, 5 days/week for 13 weeks followed by a second 13-week exposure period to 1,000 ppm. No adverse effects were observed in the rats, guinea pigs, or rabbits. In three of four cats, increases in serum urea and creatinine levels and renal tubular effects (crystalline precipitates, obstruction of lumina, and dilatation) were observed at the end of the 26-week period. Tubular degeneration and periglomerular fibrosis were also noted; however, it is not known if this was observed in all affected cats. In a developmental toxicity study (Schwetz et al. 1974), decreases in maternal body weight gain and decreases in maternal food consumption were observed in rats exposed to 3,800 or 6,000 ppm 1,1-dichloroethane on gestation days 6–15 (7 hours/day); the magnitude of the decrease in weight gain was 8 and 11%, respectively. Increases in the incidence of fetuses with delayed ossification of sternebrae were also observed at 6,000 ppm. No other developmental effects, including alterations in fetal resorptions, fetal growth, or incidences of gross or soft tissue anomalies, were observed.

These studies examined a limited number of end points and there is a great deal of uncertainty regarding the primary targets of toxicity following inhalation exposure. The lowest adverse effect level that has been identified is 750 ppm (time-weighted average) for renal effects in cats following a 26-week exposure (Hofmann et al. 1971). However, this effect has not been corroborated in other species following inhalation (Hofmann et al. 1971) or oral (Klaunig et al. 1986; NCI 1977) exposure. Additionally, it is not known if cats are a good model for 1,1-dichloroethane-induced crystal formation and tubular damage and there is uncertainty regarding the threshold concentration for these renal effects due to the exposure protocol, which involved increasing the exposure concentration mid-way through the study. Both maternal and fetal growth retardation were observed at 6,000 ppm in an acute-duration study; however, it is not known if systemic or neurological effects would occur at lower concentrations. 1,1-Dichloroethane has anesthetic properties at fairly high concentrations (approximately 26,000 ppm) (Miller et al. 1965), a concentration also associated with cardiac arrhythmias (Reid and Muinanga 2012). It is not known if exposure to lower concentrations would also result in central nervous system depressive effects or cardiotoxic effects because these end points have not been examined. Uncertainties associated with
identification of the most sensitive target and the associated concentration-response relationships, precludes deriving inhalation MRLs for 1,1-dichloroethane.

*Oral MRLs*

Two studies have examined the oral toxicity of 1,1-dichloroethane following intermediate- or chronic-duration exposure. No lung, liver, or kidney effects were observed in mice exposed to doses as high as 465 mg/kg/day 1,1-dichloroethane in drinking water for 52 weeks (Klaunig et al. 1986); no other potential targets were examined. Similarly, no nonneoplastic effects were noted in major tissues and organs of rats and mice administered 1,1-dichloroethane in corn oil 5 days/week for 78 weeks (NCI 1977). The highest doses tested were 764 and 950 mg/kg/day, respectively, in male and female rats and 2,885 and 3,331 mg/kg/day, respectively, in male and female mice. A 6-week study found decreases in body weight gain (>16%) in male rats administered 562 mg/kg/day and female rats administered 1,780 mg/kg/day 1,1-dichloroethane 5 days/week in corn oil (NCI 1977). No additional information was reported, and the cause of the decreased weight gain is not known. The chronic-duration rat study did not find significant alterations in body weight gain at higher concentrations in the male rats. Thus, the oral studies have not identified a target of toxicity, precluding the derivation of oral MRLs for 1,1-dichloroethane.