SUMMARY OF FINDINGS

The cancer potency of 1,2-dichloropropane was estimated from dose-response data for benign and malignant liver tumors among male mice exposed orally to 1,2-dichloropropane by gavage (NTP, 1986). The cancer potency estimate corresponds to the upper 95 percent confidence bound on the linear term of the multistage model fit to cancer dose-response data in animals. The potency derivation takes into account body size differences between humans and experimental animals. The Proposition 65 “no significant risk level” (NSRL) is defined in regulation as the daily intake level posing a $10^{-5}$ lifetime risk of cancer. The cancer potency estimate and the corresponding NSRL are given in Table 1.

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Cancer Potency (mg/kg-day)$^{-1}$</th>
<th>NSRL (µg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,2-Dichloropropane</td>
<td>0.072</td>
<td>9.7</td>
</tr>
</tbody>
</table>

INTRODUCTION

This report describes the derivation of a cancer potency estimate and NSRL for 1,2-dichloropropane (CAS No. 78-87-5; molecular weight 112.99, synonyms: propylene dichloride, dichloro-1,2-propane). “1,2-Dichloropropane” was listed on January 1, 1990, as a chemical known to the State to cause cancer under Proposition 65 (California Health and Safety Code 25249.5 et seq.). 1,2-Dichloropropane has been used as an insecticide for stored grain and as a soil fumigant. Most pesticidal uses of 1,2-dichloropropane have been discontinued in the U.S. In 2002 less than 400 pounds of 1,2-dichloropropane, applied as a mixture with 1,3-dichloropropene, was used in California as a pesticide (CDPR, 2003). Currently, 1,2-dichloropropane is used primarily as a chemical intermediate in the production of carbon tetrachloride and perchloroethylene, and as an industrial solvent (OEHHA, 1999). A more detailed discussion of the uses, production, and environmental occurrence of 1,2-dichloropropane is given in OEHHA (1999).
This document discusses the studies used for cancer dose-response assessment, and summarizes the derivation of the cancer potency estimate and NSRL.

**STUDIES SUITABLE FOR DOSE-RESPONSE ASSESSMENT**

The basis for the development of a dose response relationship for 1,2-dichloropropane based on the carcinogenicity endpoint is discussed at greater length in OEHHA (1999). Literature searches did not identify critical information released since the publication of that document that would impact on the derivation of the dose response relationship.

No epidemiological studies that have directly examined the carcinogenicity of 1,2-dichloropropane were identified in the scientific literature.

The most suitable carcinogenicity data for the assessment of cancer risk to humans from exposure to 1,2-dichloropropane come from the studies conducted by the National Toxicology Program (NTP, 1986) showing significant increases in liver tumors in male and female mice. A description of the study design and results from these studies, provided below, has been largely taken from OEHHA (1999).

1,2-Dichloropropane was administered to male and female B6C3F1 mice (50/sex/group) in corn oil by gavage five days/week for 103 weeks at doses of 0, 125 or 250 mg/kg (0, 89.3 and 178.6 mg/kg-day, respectively). Liver tumors were increased among both male and female treated mice. Since male mice were more sensitive to the hepatocarcinogenic effects of 1,2-dichloropropane than female mice, only the tumor incidence data for males are presented here, in Table 2. A significant dose-related trend was observed for liver adenomas in both sexes (p<0.05, Life Table Test), with the overall incidence statistically significant in high-dose males (p<0.05, Fisher Exact Test). There was an increase in the frequency of liver carcinomas in both sexes, but the incidences were not statistically significant. The overall incidences of combined liver tumors in high-dose males, and in low- and high-dose females, were significantly higher than those in controls. NTP concluded that there was some evidence of carcinogenicity for male and female B6C3F1 mice exposed to 1,2-dichloropropane.

<table>
<thead>
<tr>
<th>Dose (mg/kg)</th>
<th>Adenoma</th>
<th>Carcinoma</th>
<th>Adenoma or Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>7/50</td>
<td>11/50</td>
<td>18/50</td>
</tr>
<tr>
<td>125</td>
<td>10/47</td>
<td>17/47</td>
<td>26/47</td>
</tr>
<tr>
<td>250</td>
<td>17/50*</td>
<td>16/50</td>
<td>33/50*</td>
</tr>
</tbody>
</table>

1Tumor incidence based on the effective number of animals (i.e., the number of animals with the tumor / number of animals alive at week 54, the week the first liver tumor was identified in male mice.

* statistically significant increase in tumor incidence (p ≤ 0.05, Fisher exact test).

**APPROACH TO DOSE-RESPONSE ANALYSIS**

OEHHA is unaware of data on mechanism of action for this compound that would compel an analysis differing from the default approach. As noted in OEHHA (1999), 1,2-dichloropropane has shown positive mutagenic and clastogenic activity in short-term tests.
DOSE RESPONSE ASSESSMENT

Since male mice were the more sensitive species to the carcinogenic effect of 1,2-dichloropropane, the tumors that developed in these animals were used as the basis for the potency estimate. Using the incidence data for combined tumors of the liver (Table 2) and the lifetime average dose estimates of 0, 89.3, and 178.6 mg/kg-day, an animal cancer potency $^{1}$ ($q_{\text{animal}}$) of $5.7 \times 10^{-3}$ (mg/kg-day)$^{-1}$ was calculated by applying the linear multistage model to cancer dose response data (OEHHA, 1999). From this value, a human cancer potency is obtained, assuming the interspecies conversion set out in Proposition 65 regulations (Title 22, California Code of Regulations, section 12703). Following these regulations, a dose in units of milligram per unit surface area is assumed to produce the same degree of cancer effect in different species in the absence of information indicating otherwise. Under this assumption, scaling to the estimated human potency ($q_{\text{human}}$) can be achieved by multiplying the animal potency ($q_{\text{animal}}$) by the ratio of human to animal body weights ($b_{wh}/b_{wa}$) raised to the one-third power when animal potency is expressed in units (mg/kg-day)$^{-1}$:

$$q_{\text{human}} = q_{\text{animal}} \cdot (b_{wh} / b_{wa})^{1/3}$$

An average body weight for male mice of 0.035 kg and a default body weight of 70 kg for humans are assumed (OEHHA, 1999). The resulting scaling factor is 12.6, and a human cancer potency of 0.072 (mg/kg-day)$^{-1}$ is calculated. This number differs from that calculated in OEHHA (1999) (0.036 (mg/kg-day)$^{-1}$), under the Public Health Goals for Drinking Water program. Under that program, the interspecies conversion factor is given by the ratio of animal to human body weights raised to the one-fourth power. The regulations governing the calculation of NSRLs provide for deviations when there are more scientifically valid principles and assumptions. The different approaches to interspecies scaling given here are a matter of differing procedures between the two programs.

NO SIGNIFICANT RISK LEVEL

The NSRL for Proposition 65 is the intake associated with a lifetime cancer risk of $10^{-5}$.

$$\text{NSRL} = \frac{10^{-5} \times 70 \text{ kg}}{q_{\text{human}}}$$

The cancer potency estimate of 0.072 (mg/kg-day)$^{-1}$, based on benign and malignant liver tumors in male mice, was used to calculate an NSRL of 9.7 µg/day.

$^{1}$ The animal cancer potency is the upper 95% confidence bound on the linear term ($q_{1}$) of the multistage polynomial (probability of cancer = $1 - \exp[-(q_{0} + q_{1}d + q_{2}d^{2} + \cdots + q_{d}d^{d})]$, with constraint $q_{i} \geq 0$ for all $i$, and $d$ representing the dose).
REFERENCES


National Toxicology Program (NTP, 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). National Toxicology Program Technical Report Series No. 263. NIH Publication No. 86-2519.