RISK ASSESSMENT

OF

1,3-DICHLOROPROPENE

DEPARTMENT OF PESTICIDE REGULATION
CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY

JANUARY 10, 1997

I. BACKGROUND

A Commercial reentry of Telone II soil fumigant into California has been proposed by DowElanco. Permits for its use in California were suspended by the California Department of Food and Agriculture in 1990 because of the high ambient air concentrations of 1,3-dichloropropene (1,3-D) detected in Merced county during a routine air monitoring. This monitoring was part of DPR implementation of Assembly Bill 1807 of 1983 (sometimes called the Toxic Air Contaminant Act of 1983). The primary toxicological concern was the potential for risk of cancer. 1,3-D is listed by U.S. EPA as a B2 carcinogen, a Probable Human Carcinogen (IRIS, 1994). It is also listed as a chemical known to the state of California to cause cancer under Proposition 65, the Safe Drinking Water and Toxic Enforcement Act of 1986.

Since the suspension in 1990, DowElanco has conducted various field trials of Telone II applications in which the airborne concentration of 1,3-D was monitored. Air dispersion models were used to simulate air concentrations associated with specific application scenarios. Estimates of risk for each separate application of Telone II permit conditions have been conducted by DPR to address the specific individual applications.

This risk assessment evaluates the potential risks of acute, subchronic/seasonal, and chronic exposures to 1,3-D associated with the proposed use of Telone II for 1994-95.

II. PROPOSED USE OF TELONE FOR 1994-95

The proposed application conditions were specific for the following counties: Fresno, Imperial, Kern, Kings, Madera, Merced, Monterey, Riverside, Santa Barbara, San Joaquin, San Luis Obispo, Stanislaus, and Tulare. The county that has the highest proposed acreage of use is Kern county with a maximum of 8,000 acres. Ninety percent of this Kern county acreage are for carrots (DowElanco, 1994). The proposed maximum acreage of application per day per section is 80 acres. The proposed maximum application rate is 12 gallons per acre. Applicators must have a valid certificate from DowElanco indicating completion of the Stewardship and Safety Training Program and Application Rig Specification Training.

III. RISK ASSESSMENT

The scope of this risk assessment is limited to addressing the proposed use of Telone II during 1994-95. This assessment may not be applicable to conditions beyond the extent of use specified in this permit condition.

III.A. Hazard Identification and Dose-Response Assessment

Under the Birth Defect Prevention Act of 1984 (SB 950), toxicological data from a battery of studies are required to be submitted to DPR in support of the registration of a pesticide in California. These studies are reviewed by DPR toxicologists for the determination of the acceptability to fill the data requirements and for the identification of adverse effects of the pesticide. A summary of the

submitted toxicological studies for 1,3-D is included in Appendix A. To date, data requirements for all types of toxicity studies are filled. Unless otherwise indicated, the studies submitted to DPR and described in this section are the ones that met the guidelines under Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). They were accepted for fulfilling the SB 950 data requirements.

The database in the open literature was searched up to June 1994. Pertinent information from the published literature was also included in this section.

Inhalation is the primary route of 1,3-D exposure both for occupational activities and for the general population from the use of Telone II. Dietary exposures are not of concern because no tolerances have been set for 1,3-D in foods. The following information focuses on data critical to addressing the potential inhalation exposure scenarios associated with the currently proposed use of Telone II.

III.A.1. Acute Inhalation Toxicity

Studies in rats

One acute inhalation toxicity study is on file at DPR. In this study by Streeter *et al* (1987), groups of 5 Fischer 344 rats per sex were exposed to 775, 855, or 1,035 ppm Telone II (97.5% cis/trans 1,3-D) for 4 hours. The rats were kept for a 2-week post-exposure observation period before terminal sacrifice. The estimated 4-hour LC_{50} was 855 to 1,035 ppm for male rats and 904 ppm for female rats. Throughout the experimental period, all rats at 775 ppm had some of the following signs of toxicity: salivation, lacrimation, lethargy, and urine and fecal stains. One of the 5 females at 855 ppm and all the rats at 1035 ppm died. Rats that died had hemorrhages in multiple lung lobes. A NOEL could not be established from this study. Based on the clinical signs, the 775 ppm was determined to be the LOEL. Using the default assumption that a NOEL could be 10-fold lower than the LOEL, the NOEL for 4 hours of exposure was estimated as 77.5 ppm. The potential dose of an inhalation exposure can be estimated by the equation:

$$Dose_{Potential} = ppm \times purity \times 4.53\ (mg/m^3)/ppm \times BR\ m^3/kg/day \times F_{day} \times F_{week} \qquad \text{Eq. 1}$$

where 4.53 (mg/m^3)/ppm is the conversion factor from concentration in ppm (by volume) to mg/m^3 (by weight); BR is the breathing rate; F_{day} is the fraction of a day that the exposure occurs (i.e., hours of exposure/24 hours); and F_{week} is the fraction of a week that the repeated exposures occurs (i.e., days/7 days).

Using Eq. 1, chemical purity of 97.5%, and the default breathing rate of 0.96 m^3/kg/day for rats, the calculated potential dose at the estimated 4-hour NOEL was 54.8 mg/day:

$$(77.5 \times 0.975 \times 4.53)\ mg/m^3 \times 0.96\ m^3/kg/day \times (4/24)\ day = 54.8\ mg/kg$$

The estimated NOEL of 54.8 mg/kg was used in characterizing the risk of acute inhalation exposures to 1,3-D.

Observations in humans

The immediate effects of acute exposures to 1,3-D in humans were noted in a publication by Markovitz and Crosby (1984). Observations were made of 9 firemen involved in a clean-up of a tank truck spill of 1,3-D in 1973. The initial signs of toxicity included headache, neck pain, nausea, and breathing difficulty. Information on acute toxicity in humans can also be found in the DPR illness report database. Between 1982 and 1990, prior to the suspension of Telone II use, there were 55 cases of accidental exposures related to 1,3-D. Most were from workers receiving splash or spray due to accident, and equipment failure or repair. The signs of toxicity included burning eyes and sinuses, skin irritation and rash, eye irritation and conjunctivitis, bitter taste in mouth, nausea, vomiting, stomach ache, headache, cough, chest pains, and loss of consciousness.

III.A.2. Subchronic Inhalation Toxicity

Two subchronic (90-day or 13-week) inhalation studies on Telone II in rats and mice (Coate, 1979; Stott *et al*., 1984) were submitted to DPR (see Appendix A). The strain of rats used in both studies was Fischer 344. While CD-1 mice were used by Coate (1979), B6C3F1 mice were used by Stott *et al* (1984). Groups of 10 animals per sex were exposed to 0, 10, 30, or 90 ppm Telone II (90.9% 1,3-D used in Stott *et al*., 1984), 6 hours/day and 5 days/week, for 13 weeks. An additional dose level of 150 ppm was also included in the study by Stott *et al* (1984). In both studies, no effects were observed at 10 ppm. Changes in the nasal epithelium were reported at the next higher exposure level of 30 ppm. The nasal epithelial effects noted by Coate (1979), in 9 of 10 female rats, included loss of cytoplasm, disorganization of the nuclei, and occasional necrotic cells. Hyperplasia of the respiratory epithelium was additionally observed in two of the 10 males in the study by Stott *et al* (1984). The severity of nasal effects and the number of endpoints increased at higher exposure levels. The effects in rats and mice at 90 and 150 ppm included olfactory epithelial degeneration and lesions, nasal turbinate epithelial metaplasia, and lower terminal body weight (by approximately 20% in rats and 11% in mice at 150 ppm). In addition, Stott *et al* (1984) reported hyperplasia of the urinary bladder transitional epithelium in female mice; 7 of 10 mice at 90 ppm and 6 of 10 mice at 150 ppm.

Based on the nasal effects reported in rats, a subchronic NOEL of 10 ppm (6 hours/day, 5 days/week) was established. Using Eq.1, the chemical purity of 90.9%, and the default breathing rate of 0.96 m^3/kg/day for rats, the calculated potential dose at the NOEL (6 hr/day, 5 days/week) was 7.1 mg/kg/day:

$$(10 \times 0.909 \times 4.53)\ mg/m^3 \times 0.96\ m^3/kg/day \times (6/24) \times (5/7) = 7.1\ mg/kg/day$$

The estimated NOEL of 7.1 mg/kg/day is used in this risk assessment to characterize the risk of subchronic/seasonal exposures to 1,3-D. A comparable NOEL based on different toxicity endpoints was also established in an inhalation study of D-D published by Parker *et al* (1982). D-D contained both 1,3-dichloropropene (54%) and 1,2-dichloropropane (29%). Groups of 28 animals per sex were exposed to 0, 15, or 50 ppm D-D, 6 hours/day and 5 days/week, for 12 weeks. Histopathological examination of the nasal tissue was not performed. No effects were observed at 15 ppm. At 50 ppm, increases in the relative weight (organ to body weight ratio) of liver (approximately 9% in male rats) and kidney (approximately 11% in female rats) and hepatocytic

enlargement (male mice) were reported. Using Eq. 1, the chemical purity of 54%, and the default breathing rates of 0.96 m^3/kg/day for rats and 1.8 m^3/kg/day for mice, the calculated potential dose at the NOEL of 15 ppm D-D (6 hours/day, 5 days/week) was 6.3 mg/kg/day for rats and 11.8 mg/kg/day for mice:

$$(15 \times 0.54 \times 4.53)\ mg/m^3 \times 0.96\ m^3/kg/day \times (6/24) \times (5/7) = 6.3\ mg/kg/day$$

$$(15 \times 0.54 \times 4.53)\ mg/m^3 \times 1.8\ m^3/kg/day \times (6/24) \times (5/7) = 11.8\ mg/kg/day$$

A brief discussion on the toxicity of epichlorohydrin (ECH) is helpful in understanding the toxicity of 1,3-D. The earlier Telone II formulation used in the toxicity studies contained a small amount of ECH (approximately 1%). ECH has been shown to be nasal irritant in rats and rabbits after inhalation exposures. The lowest exposure for these effects was 9 to 16 ppm after 20 days of exposure (NAS, 1980). However, these levels were much higher than the amount of ECH present in the 1,3-D toxicity studies using Telone II. For example, the Telone II used by Stott *et al* (1984) contained 1.2% ECH. The ECH concentration at the NOEL of 10 ppm Telone II would be 0.12 ppm. Therefore, unless potentiation by 1,3-D occurred, it is not likely that ECH would contribute significantly to the toxicity observed with Telone II.

III.A.3. Reproductive Toxicity

A two-generation inhalation study by Breslin *et al* (1987) was submitted for the evaluation of reproductive toxicity potential of 1,3-D. Groups of 30 Fischer 344 rats per sex were exposed to 0, 5, 20, or 60 ppm Telone II (92% cis/trans 1,3-D) for 7 days initially. The exposure levels were subsequently raised to 0, 10, 30, 90 ppm for a total of 10 to 12 weeks before mating. The rats were exposed for 6 hours/day and 5 days/week. Reproductive toxicity and effects on neonatal growth and survival were examined, and no effects were observed. Paternal toxicities were present only at the highest exposure level of 90 ppm. They included changes in the nasal epithelium (degeneration of the olfactory epithelium, hyperplasia of the respiratory epithelium) and lower body weight (3-7% in the males). The paternal NOEL of 30 ppm is higher than the NOEL determined from the subchronic studies.

III.A.4. Teratogenicity

One inhalation study in Fischer 344 rats (John *et al*., 1983a) and one in New Zealand rabbits (John *et al*., 1983b) were submitted for the evaluation of developmental toxicity of 1,3-D. Groups of 30 pregnant rats and rabbits were exposed to 0, 20, 60, or 120 ppm Telone II (90.1% cis/trans 1,3-D) for 6 hours per day. Rats were exposed from day 6 to 15 of gestation. Rabbits were exposed from day 6 to 18 of gestation. Developmental endpoints were examined, but no developmental effects were observed.

In rats, maternal toxicity was evident in lower food consumption and weight gain during the exposure period. The total maternal weight gain during the exposure period was lowered by 6, 13, and 25 grams at 20, 60, and 120 ppm, respectively. The 6 grams was approximately 3% of the rat body weight at 20 ppm. At the higher doses, the maternal weight gain returned to levels comparable to the controls as soon as the exposures ceased. Because the effect at the lowest level

of 20 ppm was marginal ($p < 0.05$, Dunnett's test) and the effects were transient, the relevance of this endpoint in addressing subchronic exposures was not clear. Maternal weight gain reduction was also observed in rabbits at 60 and 120 ppm, but the effects were not consistently observed throughout the study.

III.A.5. Genotoxicity

Many studies on gene mutation, chromosomal effects and other types of DNA damage were submitted for filling data requirements under SB 950. The results were summarized in Appendix A. In addition, several studies reported in the open literature were also reviewed for the purpose of risk assessment.

The overall database showed genotoxic potential of 1,3-D in multiple tests with multiple endpoints. Although impurities and the stabilizer ECH in 1,3-D formulations may have contributed to the positive results in some studies, in the absence of additional studies for clarification, it was concluded that 1,3-D is mutagenic in both prokaryotes and eukaryotes (Appendix A).

III.A.6. Chronic Inhalation Toxicity

Chronic toxicity and oncogenicity of 1,3-D have been studied through oral, inhalation, and dermal routes of exposures (Appendix A). In the inhalation studies with Fischer 344 rats by Lomax *et al* (1987) and with B6C3F1 mice by Stott *et al* (1987), groups of 70 animals per sex were exposed to 0, 5, 20, or 60 ppm Telone II (92.1% cis/trans 1,3-D), 6 hours/day and 5 days/week, for 2 years. Ten animals per group were sacrificed at 6 and 12 months of exposure. The Telone II formulation used in these studies contained epoxidized soybean oil, instead of ECH, as a stabilizer.

No clinical signs of toxicity or significant effect on survival were observed in rats or mice. Chronic effects in rats included changes in nasal epithelium (decreased thickness and erosion of the olfactory epithelium, submucosal fibrosis) and decreased body weight gain observed at the highest exposure level of 60 ppm.

Chronic effects observed in mice at the highest exposure level of 60 ppm included degeneration, hyperplasia and hypertrophy of the nasal epithelial cells, lower body weight (2-11%), cytological changes in kidney and liver cells (decreased vacuolization of the proximal tubular epithelium and hepatocytes), and hyperplasia of the urinary bladder mucosa. The increase in the incidence of hyperplasia and hypertrophy of the respiratory epithelium (28/50) and hyperplasia of urinary bladder mucosa (19/48) were also statistically significant ($p < 0.01$) at 20 ppm in female mice. Based on these effects in the nasal epithelium and urinary bladder, the NOEL was established at 5 ppm.

U.S. EPA established the Reference Concentration (RfC) of 0.02 mg/m^3 based on the NOEL of 5 ppm. The RfC is "the 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" (IRIS, 1994). It is established for the protection of non-oncogenic effects. U.S. EPA calculated the RfC by multiplying the NOEL with an inter-species dosimetric adjustment factor (Regional Gas Dose Ratio; RGDR) and dividing the adjusted NOEL by an overall uncertainty factor (UF) of 30 (10 for

inter-individual variation, 3 for interspecies variation):

$$RfC = (NOEL\ Dose_{potential} \times RGDR) / UF$$

$$RfC = (5 \times 0.92 \times 4.53)\ mg/m^3 \times (6/24) \times (5/7) \times 0.1831 \times 1/30 = 0.02\ mg/m^3$$

III.A.7. Oncogenicity

The oncogenicity of 1,3-D through inhalation exposures was investigated in the aforementioned two chronic inhalation studies. No evidence of oncogenicity was indicated in rats (Lomax *et al*., 1987). Conversely, evidence of oncogenicity was shown in mice (Stott *et al*., 1987). There was a positive trend of increase with dose ($p<0.01$; Cochran-Armitage trend test) in bronchioloalveolar adenomas in male mice. The incidences, based on the number of animal at risk, were 9/49 (18%), 6/50 (12%), 13/49 (27%), and 22/50 (44%) respectively at 0, 5, 20, and 60 ppm. The increase in tumor incidence was statistically significant ($p<0.01$; Fisher Exact test) at the high dose. The biological significance of benign lung adenomas in the absence of carcinomas may be debatable. However, according to the NTP guidelines for evaluation of rodent carcinogenesis studies (McConnell *et al*., 1986), it is appropriate to combine the incidence of lung adenoma and carcinoma for consideration because of the progressive nature of alveologenic lesions in mice. Moreover, not just adenomas but also malignant alveolar/bronchiolar carcinomas were observed in male mice exposed to Telone II by oral gavage (NTP, 1985).

III.A.7.a. Weight of Evidence for Oncogenicity in Humans

In a publication, Markovits and Crosby (1984) reported 2 of the 9 firemen who were involved in a clean-up of a tank truck spill of 1,3-D developed histiocytic lymphoma within 7 years after the acute exposure episode that required immediate medical attention. The authors also reported a case of leukemia in an applicator who had prolonged (30 days initially) and extensive (impregnated clothes from leaky hose) exposure to 1,3-D. The available oncogenicity data in humans are inadequate for a determination of the oncogenicity in humans.

Given the evidence of tumors in male mice from the inhalation exposure study, additional weight of evidence for the oncogenic potential of 1,3-D is noted by: (i) multiple tumors observed in oral and dermal exposure studies in rodents, (ii) positive genotoxic potential, and (iii) the structural similarity to known oncogens. Based on the same weight-of-evidence consideration, U.S.EPA classified 1,3-D as a B2 carcinogen, a probable human carcinogen (IRIS, 1994).

Oral and dermal oncogenicity studies

The following studies are scientifically valid and contained supporting data although they were not acceptable for filling the chronic/oncogenicity data requirements in rodents because of deviation from the FIFRA guidelines. The SB 950 data requirements were filled by the chronic inhalation studies.

In the oral study conducted by National Toxicology Program (NTP, 1985), male and female F344/N rats and B6C3F1 mice were administered Telone II by oral gavage (corn oil vehicle) 3 times a week for 104 weeks. The treatments resulted in statistically significant increase in multiple tumors, both at and away from the site of initial contact with Telone II (Table 1). Although the Telone II formulation contained ECH (1.0%), it is unlikely that ECH alone could account for the tumors observed in the rats unless 1,3-D remarkably potentiates the oncogenic effect of ECH. This is supported by the following comparison. The dose of ECH in the high dose group (50 mg/kg, 3 days/week) was 0.21 mg/kg/day (50 x 0.01 x 3/7). On the other hand, the ECH dose for eliciting similar level of tumor response in the forestomach was much higher. In an oncogenicity study of ECH by Konishi *et al* (1980), Wistar rats that received drinking water containing 750 ppm ECH for 81 weeks had 10% incidence of papilloma and 10% incidence of carcinoma of the forestomach. The potential ECH dose was estimated to be 64 mg/kg/day (16 mg/day). Thus, the ECH dose in the NTP study (1985) with Telone II was approximately 300-fold lower (0.21/64) than the ECH in the study by Konishi *et al* (1980). Therefore, the oncogenicity of 1,3-D as observed in the NTP study (1985) cannot be dismissed.

In the dermal study by Van Duuren *et al* (1979), female Ha:ICR Swiss mice were administered Telone II for 77 weeks either by topical application (3 times per week) or by subcutaneous injection (once a week). Topical treatments resulted in tumors not only at the site of initial contact (skin papilloma) but also at a site away from Telone II administration (lung papilloma). The increase in lung papilloma (30/100, 19/30, 17/30 at 0, 41, and 122 mg per mouse) was statistically significant ($p < 0.01$, Fisher Exact test) at both treatment groups. Subcutaneous injection also resulted in increased fibrosarcoma (0/30 and 6/30 at 0 and 3 mg per mouse) at the site of injection.

Genotoxic Potential

The overall weight of evidence indicated that 1,3-D is mutagenic in both prokaryotes and eukaryotes (see Section III.A.6. - Genotoxicity).

Structural similarity to known oncogens

1,3-D is structurally related to other short-chain halogenated hydrocarbons that are known oncogens such as vinyl chloride and ethylene dibromide.

III.A.7.b. Quantitative Estimate of Oncogenic Potency

The oncogenic potency was estimated using the default assumption that a threshold dose does not exist for an oncogenic effect. The dose-response relationship from the dose range used in the animal studies was extrapolated to the low dose range generally experienced by humans using a linearized multistage (LMS) mathematical model. The dose-response relationship is described by an exponential polynomial equation and the coefficients are estimated using the statistical technique of a maximum likelihood. The

Table 1. Tumor incidences[a] in F344/N rats and B6C3F1 mice exposed (3 times/week) to Telone II for 2 years through oral gavage dosing (NTP, 1985).

Tumor Site/Type	Species/Sex	Tumor incidence		
		0 mg/kg	25 mg/kg	50 mg/kg
Forestomach squamous cell papilloma/carcinoma	Rats; M	1/59 (2%)$^{++}$	1/58 (2%)	17/61 (28%)**
	Rats; F	0/58 (0%)$^{++}$	2/59 (3%)	8/62 (13%)**
Liver neoplastic nodule/carcinoma	Rats; M	1/59 (2%)$^{+}$	6/58 (10%)	9/61 (15%)**
Thyroid follicular cell adenoma/carcinoma	Rats; F	0/50 (0%)$^{+}$	2/49 (4%)	4/52 (8%)
Mammary fibroadenoma	Rats; F	14/50 (28%)$^{+}$	20/49 (41%)	24/52 (48%)*
		0 mg/kg	50 mg/kg	100 mg/kg
Forestomach squamous cell papilloma/carcinoma	Mice; M	0/37 (0%)	2/47 (4%)	3/50 (6%)
	Mice; F	0/50	(0%)$^{+}$ 1/50 (2%) 4/47 (9%)	
Urinary bladder transitional cell carcinoma	Mice; M	0/37 (0%)	0/47 (0%)	2/50 (4%)
	Mice; F	0/50 (0%)$^{++}$	8/50 (16%)**	21/47 (45%)**
Lung alveolar/bronchiolar adenoma/carcinoma	Mice; M	1/37 (3%)$^{++}$	13/47 (28%)**	12/50 (24%)**
	Mice; F	2/50 (4%)$^{+}$	4/50 (8%)	8/47 (17%)*

[a] The incidences are adjusted for number of animals at risk (excluding animals that died before week 52 or the time tumors were first detected). Only tumors with statistically significant increase in the treatment groups were presented.

Symbols for levels of statistical significance:
- Cochran-Armitage trend test (given at the control group): "+" for $p<0.05$; "++" for $p<0.01$.
- Fisher Exact test (given at each dose group): "*" for $p<0.05$; "**" for $p<0.01$.

model is constrained to linearity in the low-dose region. The "potency" is defined as the maximum likelihood estimate (MLE; Q_1) of the linear term in the model equation and/or its upper 95% confidence limit (UCL; Q_1^*). The potency estimated from animal data is extrapolated to humans. The current DPR default approach in interspecies dose scaling is to assume dose equivalence between animals and humans based on 3/4 power of the body weight (BWt). Therefore, potency in the unit of $(mg/kg/day)^{-1}$ derived from animal data is extrapolated to humans by a factor of $(BWt_{human}/BWt_{animal})^{1/4}$. The current default extrapolation factor from mice to humans is $(70\ kg/0.03\ kg)^{1/4}$, or 6.95. Risk is then calculated as the potency multiplied by the exposure or dose. It is an estimate of the excess cumulative probability of tumor occurrence in a lifetime (70 years for humans).

Tumor incidence data from broncheoloalveolar adenomas observed in male mice in the inhalation study by Stott *et al* (1987) were used for the extrapolation using the Global 86 program. The potential doses for the inhalation exposures of 5, 20, and 60 ppm (6 hr/day, 5 days/wk) were calculated using Eq. 1, the chemical purity of 92%, and the default breathing rate of 1.8 m^3/kg/day for mice. An example calculation for the dose at 5 ppm (6 hrs/day, 5 days/week) is:

$$(5 \times 0.92 \times 4.53)\ mg/m^3 \times (6/24) \times (5/7) \times 1.8\ m^3/kg/day = 6.7\ mg/kg/day$$

Based on the animal data, the Q_1 (MLE) and Q_1^* (UCL) of the mathematical equation were 0.0035 and 0.0079 $(mg/kg/day)^{-1}$, respectively. The MLE and UCL potency for humans, using the extrapolation factor of 6.95, were 0.025 and 0.055 $(mg/kg/day)^{-1}$, respectively. These potency values were slightly higher than the UCL potency of 0.045 $(mg/kg/day)^{-1}$ used in estimating the risk based on air monitoring data of Merced county in 1990 which resulted in the suspension of Telone II use. The difference was due to the adjustment of chemical purity of Telone II used for the inhalation study and the update of DPR's default values of body weight for humans (70 kg) and mice (0.03 kg). The use of current default body weights resulted in a change of the default potency extrapolation factor for mice-to-humans from 6.06 to 6.95.

The current potency value used by the U.S. EPA for calculating the oncogenic risk of inhalation exposures is 0.0966 $(mg/kg/day)^{-1}$ (Engler, 1994). This is the UCL of potency estimated from the LMS model and assumed the equivalence of dose between species based on 2/3 power, instead of 3/4 power, of body weight. For mice-to-humans extrapolation, the different interspecies dose scaling approaches would result in approximately 1.9-fold difference in potency values.

One of the concerns regarding the approach to oncogenicity risk estimation has been the use of annual or lifetime average exposure to estimate the risk of repeated episodically high exposures. For some chemicals, oncogenic risks at a given level of lifetime average exposure could be much greater when exposures occurred at higher levels for shorter durations. This was demonstrated in a study of 1,3-butadiene by the National Toxicology Program (NTP, 1993). However, current knowledge on the impact of short-term, high level of exposures on oncogenicity is not sufficient for a quantitative extrapolation of dose-respone relationship from a long-term continuous lifetime studies other than to assume that the oncogenic potential is proportional to the lifetime annual average exposures.

III.B. Exposure Assessment

The use of Telone II as a field fumigant will result in the presence of 1,3-D in the air. The exposures of two groups of populations were assessed. One group was the workers who, in addition to exposures to 1,3-D present in the ambient air, also received exposures in occupational settings. The other group was the general population who received exposures as a result of 1,3-D off-gassing from the fields. The exposures of the general population were characterized both by a township in Kern county that has the highest anticipated Telone II use and the locations near the application fields.

During the past 4 years, many air monitoring studies have been conducted by DowElanco and Cal/EPA (Air Resources Board and DPR). The monitoring data were useful not only for characterizing the flux pattern of 1,3-D from application fields under various use and weather conditions but also for validating air dispersion models that were used in estimating the air concentrations of 1,3-D.

III.B.1. Occupational Exposures

An exposure assessment for loaders and applicators has been conducted. Details of the assessment are provided in Appendix B. The exposures were estimated based on biomonitoring data from an interim report of a study conducted in Washington by DowElanco (Houtman, 1993). Urinary samples were collected for 3 days post exposure from groups of 5 workers performing loading or application. The exposure period was approximately 4 hours during which time 250 gallons of Telone II were loaded and applied at the rate of 25 gallon/acre. The Absorbed Daily Dosage (ADD) was estimated based on the recovery of urinary metabolite, N-acetyl-S-(3-chloroprop-2-enyl)cysteine (3C-NAC). The correlation between the 3C-NAC and the absorbed dose of 1,3-D was based on a recent pharmacokinetic study in which 6 humans were exposed to 1 ppm 1,3-D for 6 hours (Waechter et al., 1992). The biomonitoring data of Houtman (1993) were adjusted downward proportionally for the California application rates (12 gallon/acre) and the Personal Protection Equipment (PPE) specified in the California permit conditions. The respective protection factors for a half-face and a full-face respirator were assumed to be 90 and 95%.

The seasonal ADD (SADD), annual ADD (AADD), and lifetime ADD (LADD) were calculated based on the geometric mean ADD of the 5 workers. For a loader, the duration and frequency for occupational exposures were assumed to be approximately 24 minutes in an 8-hour day, 40 days per year and 270 days per career or lifetime. For an applicator, the duration and frequency of occupational exposures were assumed to be 6.8 hours per day, 36 days per year and 270 days per career or lifetime. These exposure parameters were based on a recent survey conducted by DowElanco in California in response to a Data Call-In (DCI) by the U.S. EPA (Houtman, 1992). It was believed that a worker would not be performing both loading and application of Telone II. The ADD, SADD, AADD, and LADD estimated in Appendix B are provided in Table 2.

Table 2. Occupational Exposures of 1,3-D[a].

Work Tasks	Absorbed Dose (ug/kg/day)				
	ADD[b]		SADD[c]	AADD[d]	LADD[e]
	high	mean			
Loaders	2.48	0.73	0.16	0.08	0.007
Applicators	21.2	1.13	0.23	0.11	0.012

[a] Data taken from Appendix B.
[b] The high value was estimated based on the highest biomonitoring data of 5 workers. The mean is the geometric mean of these 5 workers. The ADD for applicators was calculated assuming 6.8 hours of work per day.
[c] The SADD was calculated from the geometric mean ADD assuming 20 and 18 days of work per 90 days for the loaders and applicators, respectively.
[d] The AADD was calculated from the geometric mean ADD assuming 40 and 36 days of work for loader and applicators, respectively.
[e] The LADD was calculated from the geometric mean ADD assuming 270 days of work per 70 years lifetime.

III.B.2. Ambient Air Exposures for the general population

The estimation of potential acute, subchronic/seasonal, and chronic/lifetime exposures of the general population consisted of two steps: (1) the simulation of air concentrations and (2) the Monte Carlo simulation of the potential exposures.

III.B.2.a. Simulation of Air Concentrations - Area-wide

A distribution of annual average ambient air concentration was simulated using a modified ISCST model (Industrial Source Complex dispersion model - Short Term) and conducted for 9 townships in Kern county that are expected to have the highest density of Telone II use based on the historical data for the location of carrot fields. In addition, air concentration simulation was also performed for one township that has the highest anticipated use. The size for each field was set at 80 acres. In the simulation, no field was assumed to be treated more than once in a three year period. The DowElanco report by Calhoun *et al* (1994) has a detailed description of the simulation conditions and approach. The section-centered simulation from DowElanco was modified to yield a distribution for a finer grid (36 receptors per section). The detailed description regarding the derivation of the final distribution was provided in the report of Johnson (1994a). The area-wide distribution of air concentration at the highest use township was used in a Monte Carlo simulation for subchronic and

lifetime exposures of the general population living in townships and counties in which Telone II will be used according to the current proposal. The simulated distribution of air concentrations for use in the assessment of subchronic and lifetime exposures was the time-weighted average daily air concentration for the specific period of exposure (i.e., average over 62 days for a subchronic exposure and 3 years for an annual average exposure).

To characterize the risk of acute exposures, the off-site distribution simulated by Johnson (1994b) was used to find the highest air concentrations at 100 meters from fields. These were 0.54 mg/m^3 for a 4-hour period and 0.19 mg/m^3 for a 24-hour period (Barry, 1994). Conservative assumptions and methodology that resulted in high estimates of air concentration were used in this simulation. Some of these assumptions were: application to 11 fields in one township and the highest flux rates. The highest air concentration reflected the least favorable meteorological conditions over the 15-day simulation period. Therefore, these values could be considered as the highest bound of air concentrations that have very low likelihood of occurrence.

III.B.2.b. Simulation of Exposures

Acute Exposures

At a given concentration of a chemical in the air, children will generally receive higher exposures per unit body weight than adults because of the higher breathing rate per unit body weight. Therefore, the potential dose for the highest acute exposure was calculated for both a child and an adult. Using Eq. 1 and the default breathing rate of 0.46 $m^3/kg/day$ for a child and 0.26 $m^3/kg/day$ for an adult, the calculated potential dose at the highest 24-hour air concentration of 0.19 mg/m^3 at 100 meters from fields is 0.087 mg/kg/day for a child and 0.049 mg/kg/day for an adult:

$$0.19\ mg/m^3 \times 0.46\ m^3/kg/day = 0.087\ mg/kg/day$$

$$0.19\ mg/m^3 \times 0.26\ m^3/kg/day = 0.049\ mg/kg/day$$

Subchronic and Lifetime Exposures

Monte Carlo simulations of the average daily dose for subchronic and lifetime exposures were conducted using the simulated distributions of average air concentrations under the area-wide scenarios. The subchronic period was set at 62 days, representing one of the two 2-month windows of use in accordance with the current proposed use. The lifetime average daily dose was assumed to result from 30 or 70 years of exposure. The current default exposure duration to a pesticide in a lifetime is 70 years. The scenario of a 30 years of 1,3-D exposure was included for the purpose of comparison with the Monte Carlo analysis conducted by DowElanco (Calhoun *et al*., 1994) which assumed a distribution of residence time at one location between 30 and 70 years and equated this to the potential duration for 1,3-D exposures in a lifetime. It has not been demonstrated, however, that a change of residence would assure no further potential for exposure to 1,3-D.

Distributions of exposure parameters applied to the Monte Carlo analyses included daily geographic mobility and age-specific body weight and breathing rates at various activity levels. For the subchronic exposures, simulations were performed for male and female age groups including infants and children. For the lifetime exposures, the residence time factor that defined the expected years of exposure to 1,3-D were set at 30 and 70 years. A detailed description and the rationale for the choice of parameters are presented in Appendix B. The results are summarized in Table 3 for subchronic exposures and Table 4 for lifetime exposures. Simulations were performed for males and females separately. Because of the overall similarity of the results for the two genders, only the results of the males are presented in these tables.

III.B.3. Combined occupational and ambient air exposures for workers.

In the biomonitoring study by Houtman (1993) that formed the basis for the estimation of occupational exposures, no information was available regarding the ambient air exposure for workers outside of the occupational settings. The exposure of a worker who may live in an area with 1,3-D in the ambient air may be estimated.

The scenario for a high end of exposure range could be modeled by using an applicator living 100 meters from an application field. The total acute exposure would be the sum of the ADD for occupational exposure (21.2 ug/kg/day for 6.8 hours) and the ambient air exposure at 100 meter from the application fields (49 ug/kg/day; see section III.B.2.b) for the remainder of a day (17.2 hours). Because the exposure under the occupational setting is lower than the ambient air exposures, the total exposure would be expected to be lower than the ambient air exposure for 24 hours. This would also apply to subchronic/
seasonal and lifetime exposure scenarios. The estimated occupational LADD of 0.007-0.012 ug/kg/day is 2-3% of the estimated 95th percentile of the 70-year average exposure distribution for a lifetime. Therefore, the ambient air exposures can be used to address the risk of 1,3-D exposures in California.

Table 3. Monte Carlo simulation of the potential subchronic average daily exposures to 1,3-D in the ambient air[a].

Percentile of Exposure Distribution	Area-wide Exp[b] (ug/kg/day)	
	child[c]	adult[d]
5	0.470	0.188
10	0.558	0.228
25	0.770	0.314
50	1.207	0.459
75	2.052	0.676
90	3.126	0.930
95	3.750	1.103
99	4.711	1.468
Mean	1.551	0.5297
s.d.	1.042	0.2904

[a] Data taken from Appendix B. Exposures of males and females were similar. Data for males are presented.

[b] The simulation of exposures utilized the distribution of 62-day average air concentrations in a high-Telone-use township within a 9 townships area where Telone II is proposed to be applied to a total of 25, 80-acre fields per year.

[C] Children 1-2 years old which represented the highest exposure age group from infants to 12 years old.

[d] The 18-25 years old age group which represented the highest exposure age group from 18 to 70 years old.

Table 4. Monte Carlo simulation of the potential lifetime average daily exposures to 1,3-D in the ambient air[a].

Percentile of Exposure Distribution	Area-wide Exp[b] (ug/kg/day)	
	30 yrs	70 yrs
5	0.027	0.053
10	0.032	0.063
25	0.044	0.087
50	0.066	0.129
75	0.103	0.193
90	0.150	0.277
95	0.179	0.326
99	0.230	0.425
Mean	0.080	0.151
s.d.	0.048	0.087

[a] Data taken from Appendix B. Exposures of males and females were similar. Data for males were presented. Lifetime exposure periods of 30 and 70 years were assumed.

[b] The simulation of exposures utilized the distribution of 3-year average exposures in a high-Telone-use township within a 9 townships area where Telone II is proposed to be applied to a total of 25, 80-acre fields per year.

III.C. Risk Characterization

The risk of acute and subchronic/seasonal exposures were based on non-oncogenic adverse endpoints that were assumed to have a threshold level of exposure below which no deleterious effects are expected. The risk of a non-oncogenic effect was characterized by the margin-of-safety (MOS). The MOSs for 1,3-D exposures were calculated as the ratio of the NOEL to the ADD or SADD. Oncogenicity is the most sensitive endpoint for chronic/lifetime exposures and is assumed to have no biological threshold. The risk for lifetime exposures was calculated as the product of the LADD and the potency, using both the MLE and UCL of the potency estimates.

III.C.1. Acute MOS

The potential dose at the estimated acute NOEL was 54.8 mg/kg based on the clinical signs of toxicity observed at the dose 10-fold higher. This NOEL is used in the MOS calculation.

Occupational exposures for workers

The occupational ADDs for loaders and applicators were taken from data in Table 2. The MOSs are calculated using the high ADD of 2.48 ug/kg/day for a loader and 21.2 ug/kg/day for an applicator. These values were estimated from the highest urinary biomonitoring data of 5 workers loading or applying Telone II for 4 hours.
The MOSs are:

$$\text{Acute MOS}_{\text{loader}}: \ 54.8/(2.48 \times 10^{-3}) = 22{,}000$$

$$\text{Acute MOS}_{\text{applicator}}: \ 54.8/(21.2 \times 10^{-3}) = 2{,}600$$

Ambient Air Exposures for general population

The dose at the highest simulated 24-hour ambient air concentration of 0.19 mg/m^3 at 100 meters from fields was calculated as 0.087 mg/kg/day for a child (see Section III.B.2.b.). The MOS for the acute exposure at 100 meters from the fields is:

$$\text{Acute MOS}_{100\ \text{m}}: \ 54.8/0.087 = 630$$

III.C.2. Subchronic MOS

The potential dose at the subchronic NOEL was 7.1 mg/kg/day based on the effects on the nasal epithelium in rats at a dose that was 3-fold higher.

Occupational exposures for workers

The SADDs for loaders and applicators were taken from data in Table 2. The MOSs are calculated from the SADD of 0.16 ug/kg/day for a loader and 0.23 ug/kg/day for an applicator. The MOSs for a loader and an applicator are:

Subchronic MOS_{loader} : $7.1/(0.16 \times 10^{-3}) = 44{,}000$

Subchronic $MOS_{applicator}$: $7.1/(0.23 \times 10^{-3}) = 31{,}000$

Ambient Air Exposures for general population

Data in Table 3 showed that the high range of the average daily exposure was 4.711 ug/kg/day for a child (1-2 years old). This was the highest simulated potential exposure. The MOS is:

Subchronic MOS: $7.1/(4.711 \times 10^{-3}) = 1{,}500$

III.C.3. Lifetime oncogenic risk

The MLE and UCL potency values extrapolated from the dose-response relationship of lung tumors in male mice were 0.025 and 0.055 (mg/kg/day)-1, respectively.

Occupational exposures for workers

The LADDs for loaders and applicators were taken from data in Table 2. The potential oncogenic risk in a lifetime are calculated from the LADD of 0.007 ug/kg/day for a loader and 0.012 ug/kg/day for an applicator, using both MLE and UCL of potency values. The risks are:

MLE $Risk_{loader}$: $0.025\ (mg/kg/day)^{-1} \times (0.007 \times 10^{-3})\ (mg/kg/day) = 1.8 \times 10^{-7}$
UCL $Risk_{loader}$: $0.055\ (mg/kg/day)^{-1} \times (0.007 \times 10^{-3})\ (mg/kg/day) = 3.9 \times 10^{-7}$

MLE $Risk_{appl.}$: $0.025\ (mg/kg/day)^{-1} \times (0.012 \times 10^{-3})\ (mg/kg/day) = 3.0 \times 10^{-7}$
UCL $Risk_{appl.}$: $0.055\ (mg/kg/day)^{-1} \times (0.012 \times 10^{-3})\ (mg/kg/day) = 6.6 \times 10^{-7}$

Ambient air exposures for general population

The potential oncogenic risks at the 50th and 95th percentile of the simulated distribution of average daily exposure, for area-wide scenarios (Table 4), are presented in Table 5. Risks were calculated using both the MLE and UCL of potency estimates.

Table 5. The potential lifetime oncogenic risk from 30 and 70 years of exposures to 1,3-D in the ambient air[a].

Geographic locations	50th percentile		95th percentile	
	MLE	UCL	MLE	UCL
		30 years		
Area-wide[b]	1.7×10^{-6}	3.6×10^{-6}	4.5×10^{-6}	9.8×10^{-6}
		70 years		
Area-wide[b]	3.2×10^{-6}	7.1×10^{-6}	8.2×10^{-6}	1.8×10^{-5}

[a] Risk was calculated as the exposure multiplied by the potency. The exposures data were taken from Table 4. The MLE and UCL potency values extrapolated from the dose-response relationship of lung tumors in male mice were 0.025 and 0.055 (mg/kg/day)-1, respectively.

[b] The simulation of exposures utilized the distribution of 3-year average exposures in a high-Telone-use township within a 9 townships area where Telone II is proposed to be applied to a total of 25, 80-acre fields per year.

IV. CONCLUSION

The potential risk from the proposed use of Telone II in California for 1994-95 has been assessed. The occupational exposure appeared to be minimal compared to the potential ambient air exposures for the general public. The MOSs for the estimated high values of acute and subchronic/seasonal exposures for the general public were at least 630. The MOS exceeded the MOS of 100 which is generally considered as sufficient for protection against non-oncogenic effects when the NOEL used to calculate the MOS was established in laboratory animals.

The potential lifetime oncogenic risk was calculated based on the DPR potency values and the exposure distributions generated from Monte Carlo simulations. The calculated risk is approximately 2-fold lower using DPR potency when compared to the risk using U.S. EPA potency. The exposure used in risk calculation was the average exposure over a lifetime. Although the risk may be higher for the potential episodically high exposures, the current toxicity data are not sufficient for a quantitative assessment other than to assume that the risk is proportional to the lifetime annual average exposures. The simulations of exposures utilized distributions of annual average ambient air concentrations simulated from a modified ISCST dispersion model and with the assumption that a field is treated with Telone II once every three years. Air concentrations were simulated for characterizing the air concentrations of a township in Kern county that has the highest anticipated use of Telone II. Using the distributions of air concentrations, the subsequent Monte Carlo simulation of lifetime average exposures incorporated parameters of exposure such as daily geographic mobility and age-related breathing rates and body weights. The lifetime average exposures were simulated both for a 30- and a 70-year exposure. The current DPR default duration for a lifetime exposures to a pesticide is 70 years. The simulated lifetime exposures represent the exposures for areas with proposed Telone II use. The exposure for a 30-year duration was simulated for the purpose of comparison to the risk assessment submitted by DowElanco (Calhoun, 1994).

At the 95th percentile of the area-wide exposure scenario, the MLE and UCL of risk for a 30-year exposure were 4.5×10^{-6} and 9.8×10^{-6}. They were approximately 50-67% higher than the risks estimated by Calhoun *et al* (1994) using different input parameters for the Monte Carlo simulation.

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Appendix A

SUMMARY OF TOXICOLOGY DATA

TELONE II (1,3-dichloropropene)

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

TELONE II (1,3-dichloropropene)

Chemical Code # 000573, Tolerance # 50046
SB 950 # 137

August 18, 1986
Revised 4/16/87, 7/18/88, 5/23/89, 4/27/90, 6/1/90, 6/15/94, 8/10/94

I. DATA GAP STATUS

Combined (onco + chronic) rat: No data gap, possible adverse chronic effects

Chronic dog: No data gap, possible adverse effect.

Onco mouse: No data gap, possible adverse effects

Repro rat: No data gap, no adverse effects

Terato rat: No data gap, no adverse effects.

Terato rabbit: No data gap, no adverse effects.

Gene mutation: No data gap, possible adverse effect

Chromosome: No data gap, no adverse effect.

DNA damage: No data gap, possible adverse effect

Neurotox: Not required at this time.

Note, Toxicology one-liners are attached
All record numbers through 117410 in 061 were examined.
** indicates an acceptable study.
Bold face indicates a possible adverse effect.
Original Summary prepared by F. Martz, revised April 16, 1987, July 18, 1988, May 23, 1989, April 27, 1990, June 1, 1990, June 15, 1994 and August 10, 1994 by J. Gee
Filename: T940810
See also "Guidance for the Reregistration of Pesticide Products (Reregistration Standard) Containing 1,3-Dichloropropene (Telone II) as the Active Ingredient", US EPA, 9/18/86, CDFA Record # 050620. The position of EPA (1986) was that if significant residues were found, oral studies would be required in addition to the inhalation studies. Gee, 5/23/89.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

ONCOGENICITY/CARCINOGENICITY

COMBINED RAT

010 036552 "Toxicology and Carcinogenesis Studies of Telone II in F344/N Rats and B6C3F1 Mice." (NTP, Frederick Cancer Research Center, 5/85) Rats, F344 strain; Telone II (1,3-dichloropropene, 87.5% pure) with epichlorohydrin as stabilizer; 50, 25, or 0 mg/kg by oral gavage "3 times a week"; 52/sex/group with an additional 28/sex/group (3 as substitutes) in satellite groups with sacrifices at 9, 16, 21, 24 and 27 months of 5/sex/group. Study scientifically valid but UNACCEPTABLE and not upgradeable due to guideline deviations. ONCO effects with NO NOEL: forestomach cancer at 50 mg/kg, liver cancer in males at 25 and 50 mg/kg, trend for thyroid cancer in females, mammary cancer in females at 50 mg/kg with trend at 25 mg/kg, stomach epithelial hyperplasia at 25 and 50 mg/kg. (Reviewed 1/16/86 by Martz).

**** 031, 005 060677, 036218** "Telone II Soil Fumigant: 2-Year Inhalation 0hronic Toxicity-Oncogenicity Study in Rats." (Dow Chemical, Midland, MI, 7/13/87, M-003993-009R) 1,3-Dichloropropene, 92.1% (cis 49.5% and trans, 42.6%), 1,2-dichloropropane, 0.7%; 1,3-dichloropropane; 1.8%, 1-chlorohexane, 1.1% with remaining 4.3% a mixture of isomers of chlorohexane, chlorohexene and trichloropropene, stabilized with soybean oil; 70/sex/group exposed by inhalation 6 hours/day, 5 days/week for 2 years - whole body exposure - at 0, 5, 20 or 60 ppm nominal; 10/sex/group sacrificed at 6 and at 12 months (interim report, # 036218); NOEL = 20 ppm (decreased weight gain, changes in nasal tissues in males and females), no evidence of an oncogenic effect reported; ACCEPTABLE with a possible adverse chronic effect. (Gee, 7/11/88).

005 036218 Dow, 9/85 (1 year interim report - see above); F344 strain; exposure conditions identical to those of mouse study listed below (#36219). UNREMARKABLE at 1 year; nasal changes noted in mice not reproduced in rats; no effects except slight weight-gain inhibition in high dose group. (Martz, 1/13/86).

010 36551 "90-day Inhalation Toxicity Study in Rats and Mice; Telone II" (Hazleton Laboratories, 5/15/79, Project No. 174-127) Fischer 344 rats, 10/sex/dose, were exposed to 0, 10, 30 or 90 ppm nominal (actual - 0, 11.98, 32.14, and 93.02 ppm) 6 hours per day, 5 day/wk for 13 weeks; terminal body weights were significantly reduced (8-11%) in the high dose male and female rats; dose-related alterations of the nasal epithelium were observed in high dose of both sexes (10/10 and 10/10)and in mid-dose females (9/10) as reported in the Addendum to the Final Report, dated 7/9/79 giving a NOEL = 10 ppm in female rats and 30 ppm in males; UNACCEPTABLE (deficiencies include no hematology, no serum chemistry performed, not all required tissues were examined histologically in control and high dose groups); not upgradeable. Initially reviewed by Martz, 4/29/86; re-reviewed by C. Lewis, 7/6/89 and updated by J. Gee, 6/15/94. No worksheets.

038 071713 "Telone II Soil Fumigant: A 13-Week Inhalation Study in Rats and Mice." (Dow, 11/30/84) Telone II, 90.9%, lot WP-82-1111-56; given by inhalation 6 hr/day, 5 day/week, 10 Fischer 344 rats per sex, exposed

to 0, 10, 30, 90 or 150 ppm nominal; 13-week exposure; only findings were degeneration in the olfactory epithelium and hyperplasia of the respiratory epithelium in both sexes, especially at 90 and 150 ppm; body weight gains were significantly lower at 90 and 150 ppm; NOEL = 10 ppm based on hyperplasia in 2/10 males at 30 ppm. Supplementary data. (Gee, 5/22/89).

CHRONIC DOG

****50046-061 117410** Stott, W.T., Stebbins, K.E., Haut, K.T., Quast, J.F., and Shabrang, S.N.; "Telone*II soil fumigant: One-year dietary toxicity study in beagle dogs", The Dow Chemical Co., Midland, Study ID M-003993-024, 7/22/92. Dogs were fed diets containing microencapsulated Telone*II at 0, 0.5, 2.5, or 15 mg/kg/day for 1 year. NOEL = 2.5 mg/kg/day [hematology profile typical of hypochromic, microcytic anemia: related to increased hematopoiesis in bone marrow and extramedullary hematopoiesis in spleen in both sexes]. Clinical signs in 2 high dose males of pale skin/mucous membranes apparently reflected the anemia. Body weights were depressed and relative liver weights were increased in both sexes at 15 mg/kg/day. The relatively low NOEL for signs of anemia constitutes a "**possible adverse effect**". **Acceptable**; Aldous, 11/15/93.

046 075537 "Telone II: 13-Week Dietary Toxicity Study in Beagle Dogs." Quast, J. F., Dow Chemical Company, August 1, 1989. The 3-page letter was submitted as an adverse effects disclosure for microcytic hypochromic anemia in the 13-week study in beagle dogs. Doses were 0, 130, 380 or 1000 ppm with Telone II incorporated in a starch sucrose matrix and administered in the dog chow. The letter contains no data but states the anemia was dose-related. Some dogs were being maintained after dosing for further study. The final report has not yet been received by CDFA. (Gee, 4/27/90).

Document 50046-043 contains a protocol (dated 4/12/89) for a 13-week study with beagle dogs. Title: Telone II: 13-Week Dietary Toxicity Study in Beagle Dogs. Record # 073875. The purpose was to evaluate the affects of dietary exposure of non-rodents to doses of 0, 130, 380 or 1000 ppm in the diet prepared with 1,3-dichloropropene formulated by microencapsulation in a starch/sucrose matrix. The document summarized several studies on dosing of dogs by several routes. A cover letter, dated April 27, 1989, from the registrant still questioned the need for a chronic study. (Gee, 5/23/89).

025 050620 The EPA Registration Standard, dated September 18, 1986, indicates that the requirement for a chronic feeding study in nonrodent species, namely dog, is dependent on the outcome of residue tests. If residues are found in food/feed commodities, chronic feeding studies in rat and dog may be required. Residue data for crop field trials are due in March, 1989. Requirements for residues in food/feed, etc., are reserved. (Gee, 4/16/87). See 061 117410 for the full study (Gee, 6/15/94)

ONCOGENICITY, MOUSE

007 28361, 28362 and 28363 Parts of published report on three different exposure scenarios. See 010 036554 for complete copy of the publication in: J. National Cancer Institute 63 (6): 1433-1439 (1979)

010 036553, "Toxicology and Carcinogenesis Studies of Telone II in F344/N Rats and B6C3F1 Mice." (NTP, Frederick Cancer Research Center, 5/85) Mice, B6C3F1 strain; Telone II (87.5% 1,3-dichloropropene); 100, 50, or 0 mg/kg/day

by oral gavage "3 times a week"; 50/sex/group. UNACCEPTABLE and not upgradeable due to guideline deviations, but scientifically valid for female data. ONCO effects with NO NOEL; in females, cancer of urinary bladder at 100 and 50 mg/kg, forestomach and lung at 100 mg/kg; results in males inconclusive due to inadequate randomization and poor control group survival. (Martz, 1/17/86).

010 036554 "Carcinogenicity of Halogenated Olefinic and Aliphatic hydrocarbons in Mice." (Van Duuren, B. L. et al., NYU Med Ctr., JNCI 63: 1433-1439, 1979) Ha:ICR Swiss strain; cis-1,3-dichloropropene (Chemical Samples Co., Columbus, OH), 122 mg/mouse or 41 mg/mouse by dermal application 3/week for about 77 weeks; initially reviewed as having caused no local or distant tumors. UNACCEPTABLE and not upgradeable. Reviewed: 6/3/85 by A.Aspostolou, peer review 2/20 and 8/18/86 by Martz. Re-review as part of the risk assessment process noted that the incidence of lung tumors in both groups of treated mice was statistically significant by Fisher's Exact Test although not so noted in the publication table. The incidences were 30/100 for controls and 19/30 and 17/30 at low and high doses respectively. Remains UNACCEPTABLE but with a possible adverse effect. (Gee, 5/31/90).

010 036554 "Carcinogenicity of Halogenated Olefinic and Aliphatic Hydrocarbons in Mice." (NYU Med Ctr, JNCI 63: 1433-1439, 1979) Ha:ICR Swiss strain; cis-1,3-dichloropropene (Chemical Samples Co., Columbus, OH), 3 mg/mouse once weekly x 77 weeks by subcutaneous injection; examined injection site and liver only; fibrosarcoma at injection site, 6/30 vs 0/30 vehicle control, probably due to irritation by physical-chemical properties of AI. Otherwise, insufficient for assessment. UNACCEPTABLE and not upgradeable. (A.A., 6/3/85; Martz 2/20 and 8/18/86).

010 036554 "Carcinogenicity of Halogenated Olefinic and Aliphatic Hydrocarbons in Mice." (NYU Med Ctr., JNCI 63: 1433-1439, 1979) Ha:ICR Swiss strain; cis-1,3-dichloropropene (Chemical Samples Co., Columbus, OH), 122 mg/mouse by dermal application once followed by promotion with 5 mg phorbol myristate acetate dermally 3/week for about 77 weeks; no tumors. UNACCEPTABLE and not upgradeable. (Reviewed: 6/3/85 by A.A., peer review 2/20 and 8/18/86 by Martz).

**** 029, 006 060675, 036219** "Telone II Soil Fumigant: 2-Year Inhalation Chronic Toxicity-Oncogenicity Study in Mice." (Dow, 7/13/87, M-003993-009) 1,3-Dichloropropene, 92.1% (cis 49.5% and trans, 42.6%) plus 1,2-dichloropropane 0.7%, 1,3-dichloropropane 1.8%, 1-chlorohexane 1.1% and the remainder a mixture of isomers of chlorohexane, chlorohexene and trichloropropene, lot TB831213-4; given by inhalation at 0, 5, 20 or 60 ppm nominal uncorrected for 92% purity, 6 hours/day, 5 days/week for 2 years; 70/sex/group with intermediate sacrifices of 10/sex/group at 6 months and at 12 months (interim report # 036219 in 006); daily analytical data for 1,3-dichloropropene concentration. Hyperplasia of the urinary bladder mucosa was found in females at 20 and 60 ppm and in males at 60 ppm with a trend at 20 ppm. Increase in benign lung bronchioloalveolar adenomas in males at 60 ppm. Degeneration of the olfactory epithelium and hyperplasia of the respiratory epithelium, bilateral, at 60 ppm in both sexes. Decreased liver vacuolation in females at 60 ppm. NOEL = 5 ppm. ACCEPTABLE with possible adverse effects. (Gee, 7/12/88).

006 036219 Dow, 9/85 (1 year interim report; B6C3F$_1$ strain; Telone II (lot# TB831213-4); 60, 20, 5, or 0 ppm 6 hours/day x 5 days/week x 6 or 12 months. NO TUMORS; slight focal hyperplasia and hypertrophy of epithelium of nasal turbinates at 20 ppm in males and at 60 ppm and in both sexes; liver glycogen and kidney lipid decrease in males at 60 ppm (decreased organ weights and vacuolation); urinary bladder hyperplasia of transitional epithelium in females at 60 ppm; **possible adverse effects**; NOEL = 5 ppm. (Martz, 1/14/86).

SUBCHRONIC

10 036551 "90-Day Inhalation toxicity Study in Rats and Mice." (Hazleton, (VA), 5/79) CD-1 strain; Telone II, purity unspecified; 90, 30, 10, or 0 ppm 6 hours/day x 5 days/week x 13 weeks (65 exposures). Unacceptable and not upgradeable - was intended as range finder for future study. EFFECTS: In 90 ppm females - epithelium of dorsal nasal septum and turbinates - decreased cytoplasm and single cell necrosis; slight weight gain reduction @ 90 ppm; NOEL = 30 ppm. (Martz, 4/29/86). In addition, alterations in nasal epithelium were noted in high-dose female mice but not in male mice; NOEL = 30 ppm in females and 90 ppm in males. Revised by Gee, 6/15/94.

038 071713 "Telone II Soil Fumigant: A 13-Week Inhalation Study in Rats and Mice." (Dow, 11/30/84) Telone II, 90.9%, lot WP-82-1111-56; given by inhalation 6 hr/day, 5 day/week, 10 B6C3F1 mice per sex, exposed to 0, 10, 30, 90 or 150 ppm nominal; 13-week exposure; findings were degeneration in the olfactory epithelium and hyperplasia of the respiratory epithelium in both sexes, especially at 90 and 150 ppm; body weight gains were significantly lower at 90 and 150 ppm; females in 90 and 150 ppm showed effects in the epithelial cells of the urinary bladder; NOEL = 30 ppm. Supplementary data. (Gee, 5/22/89).

REPRODUCTION AND FERTILITY

010 036555 "D-D: A 10 Week Inhalation Study of Mating Behavior in Male and Female Rats." (Shell (UK), 4/80) Wistar strain; technical D-D ("epi-chlorohydrin free"), 53.7% 1,3-dichloropropene, remaining constituents mainly chlorinated isomers/analogs; 96, 32, 14, or 0 ppm for 6 hours/day x 5 days/week; treated males mated with naive females after 2, 4, 7, and 10 weeks exposure; treated females mated with naive males after 10 weeks exposure; hematology, serum chemistry, urinalysis, and histopathology on satellite animals; 30 males and 24 females per group with 20 and 15 respectively for reproduction performance and the remainder for hematology, etc. UNACCEPTABLE and not upgradeable: only 1 generation and inadequate group sizes. Otherwise, appears to be a well conducted and documented study with scientifically valid results. NO reproductive effects. Liver and kidney weight elevation at 96 ppm, reversible upon withdrawal, except female kidney values. (Martz, /20/86)

** 030 060676 "Telone II Soil Fumigant: Two-Generation Inhalation Reproduction Study in Fischer 344 Rats." (Dow Chemical, 7/13/87, M-003993-015) 1,3-Dichloropropene, 91.2%, lot #TB831213-4; exposures of 0, 5, 20 or 60 ppm for 7 days increased to 0, 10, 30 or 90 ppm on day 8, 6 hours/day, 5 days/week, two generations, two litters each; 30/sex/group;; maternal animals removed from chamber after gestation day 20 until day 4 postpartum when separated from pups for the 6 hours exposure; parental NOEL =

30 (decreased weight gain, nasal tissue changes at 90 ppm), reproduction NOEL ≥ 90 ppm (no adverse effect on reproduction parameters); ACCEPTABLE. (Gee, 7/13/88).

TERATOLOGY, RAT

** 010 036561 "Telone II: Inhalation Teratology Study in Fischer 344 Rats and New Zealand White Rabbits." (Dow, 10/83) F344 strain; Telone II (1,3-dichloropropene; 90.1% pure); 120, 60, 20, or 0 ppm via inhalation; 30/group. Study and report ACCEPTABLE. NO developmental effects (NOEL = 120 ppm for malformations/developmental effects); maternal NOEL < 20 ppm (reduced maternal weight gain at all 3 treatment levels.) (Martz, 2/21/86).

TERATOLOGY, RABBIT

** 010 036562 "Telone II: Inhalation Teratology Study in Fischer 344 Rats and New Zealand White Rabbits." (Dow, 10/83) New Zealand White; Telone II (1,3-dichloropropene; 90.1% pure); 120, 60, 20, or 0 ppm via inhalation; 17 - 24 pregnant rabbits per group. Study OK, but report incomplete: reviewed as upgradeable with submission of historical control data, 2/21/86. The historical control data are in #50619, Document 50046-025. The study has been rereviewed as ACCEPTABLE, 3/26/87. NO developmental effects (NOEL = 120 ppm for malformations); NOEL = 20 ppm for reduced maternal weight gain. (Martz, 2/21/86 and 3/26/87).

GENETIC TOXICOLOGY

GENE MUTATION

016, **004282** & 004293 "Mutagenicity of 1,3-Dichloropropene using Ames Testing." (Schering AG, summary report 9/82) Formulated mixtures containing 1,3-dichloropropene in addition to various other constituents, were tested for mutagenic activity in the Ames Salmonella Test. Results were conflicting and insufficient for independent assessment. UNACCEPTABLE but upgradeable upon submission of complete report(s). Summary contains statement that positive effects were seen with TA1535 and TA100 but no data. Report contains a statement that the methyl isothiocyanate in the sample tested caused cytotoxicity before the mutagenic effect was detectable. No data. (Reviewed: 6/3/85 BY A.A., peer review 8/18/86 by Martz and 7/18/88 by Gee).

010 036556 "Mutagenicity of 1,3-Dichloropropene in Bacteria Test System." (Nomura Sogo Res. Inst., 12/78) E. coli strain B/r, Wp 2, Try⁻; 49.8%-cis and 46.3%-trans 1,3-dichloropropene, 5000, 2500, 1000, 500, 250, 100, 25, or 0 µg/plate, ±S9. Unacceptable and not upgradeable due to design deficiencies. No mutagenic effects reported. (Gee, 2/24/86).

010 036558 "Mutagenicity of 1,3-Dichloropropene in Bacteria Test System." (Nomura Sogo Res. Inst., 12/78) Five Salmonella strains for plate assay; 49.8%-cis and 46.3%-trans 1,3-dichloropropene, 0-5000 µg/plate ± S9; G46 for host-mediated assay in ICR mice at 30 or 60 mg/kg x 3 times/3 hours. UNACCEPTABLE and not upgradeable: single plates. Significant **Positive response** in several strains indicative of base-pair substitution; negative in host-mediated assay. (Gee, 2/24/86).

** 019 042945 "The Evaluation of Telone II Soil Fumigant in the CHO Cell/HGPRT Forward Mutation Assay." (Dow, 2/27/86) CHO/HGPRT assay; Telone II (48.9% cis and 43.2% trans 1,3-dichloropropene); 250, 200, 150, 100, 50, or 0 mM without S9 (3 trials) and 200, 150, 125, 100, 50, or 0 µM with S9 (1 trial). Report complete and study ACCEPTABLE. NO evidence of mutagenicity. (Gee, 7/24/86).

No record number "Chemical Mutagenesis Testing in Drosophila. III. Results of 48 Coded Compounds Tested for the National Toxicology Program." (Valencia, R., et al., Environmental Mutagenesis 7: 325 - 348 (1985)) 1,3-Dichloropropene technical, 95.5% was tested with male Canton-S wild-type stock by feeding at 5,570 ppm for 72 hours from soaked filter paper. The males were mated to Basc females for 3, 2 and 2 days. No more than 40 females per parental male were mated from each brood. A total of 6584 tests were performed. The percent lethals were 0.12 for control broods and 0.30 for treated broods - **considered positive by the authors.** The translocation test was negative. No worksheet. [Review done in connection with the risk assessment.] (Gee, 5/31/90).

Summary: Although the test in mammalian cells was negative, there appear to be several studies with Salmonella giving positive results although none of those on file are acceptable. The positive effect reported in #036558 was quite significant. The possible adverse effect for gene mutation, therefore, stands at this time. One problem is the volatility of the test material and care must be taken to control samples for this property. From the text of the study with CHO, the flasks were tightly capped and loss of test material should not have been a factor. (Gee, 7/18/88).

CHROMOSOMES

** 010 036560 "Evaluation of Telone II Soil Fumigant in the Mouse Bone Marrow Micronucleus Test." (Dow, 5/85) Telone II (49.5%-cis and 42.6%-trans 1,3-dichloropropene), 380, 115, 38, or 0 mg/kg by oral gavage in CD-1 mice, 5/sex/group, 24 or 48 hour sac. Reviewed 2/25/86 as incomplete but upgradeable with justification of the use of only two sacrifice times. This has been submitted as Record #55630 in 50046-025, based on excretion of 93% within 48 hours. The study is now reviewed as ACCEPTABLE. NO increase in MN-PCE's reported. (Gee, 2/25/86 and 4/16/87).

Note: The reregistration standard of 1986 indicates that EPA is requiring additional testing for chromosomal effects, notably in vivo testing of bone marrow in rats.

DNA/OTHER

010 036557 "Mutagenicity Test on 1,3-Dichloropropene in Bacteria Test System." (Nomura Sogo Res. Inst., 12/78) Bacillus subtilis rec assay, strains H17 and M45; 49.8% cis- and 46.3% trans-1,3-dichloropropene, 1250, 500, 125, 50, or 0 µg/well without activation. UNACCEPTABLE and not upgradeable due to design deficiencies. **Slight growth differences at highest level.** Reviewed 2/24/86 by Gee.

** 010 036559 "Evaluation of Telone II in the Rat Hepatocyte Unscheduled DNA Synthesis Assay." (Dow, 4/85) UDS in rat hepatocytes; Telone II (49.5% cis and 42.6% trans-1,3-dichloropropene) $1x10^{-7}$ to $3x10^{-3}$ M concentration

(solubility limit), plus control. Report complete and study ACCEPTABLE. NO evidence of UDS even when cytotoxicity was noted. (Gee, 2/24/86).

Summary: These two tests measure different endpoints so no one conclusion can be reached and a possible adverse genotoxic effect is noted. Gee, 7/18/88.

Note: The reregistration standard of 1986 noted requirements for in vitro/in vivo primary hepatocyte UDS testing both in vitro and in vivo exposure - species not specified. Record # 036559 is not cited. (Gee, 5/23/89).

Note: In addition to the studies formally submitted by the registrant, publications in the open literature have been reviewed (no worksheets). The conclusion is that exposure to telone was genotoxic in multiple tests with multiple endpoints. The registrant has presented the position that the effects in early studies were due to mutagenic impurities and to the stabilizer. The stabilizer has been changed in recent products. In the absence of additional studies, however, which clearly demonstrate negative results, the overall weight-of-evidence indicates that telone is mutagenic in both prokaryotes and eukaryotes. (Gee, 8/10/94)

NEUROTOXICITY

Not required at this time.

GENERAL INFORMATION

007, 932850; Communication to EPA from Dow dated 2/9/82; contains risk assessment based on data from NTP rat and mouse studies (# 036552 & 53) as well as published dermal studies (# 036554), and refers to oncogenic effects noted in the former. (Martz, 8/18/86).

016, 932849, 932853, and 022757; Contain preliminary summary of NTP studies (# 036552 & 53), summary of mutagenicity studies showing positive effects (# 036556-58), and summary of the one generation reproduction study with technical D-D (# 36555), respectively. (Martz, 8/18/86).

APPENDIX B

EXPOSURE ASSESSMENT

Human Exposure Assessment for 1,3-dichloropropene

by

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HS 1634

May 26, 1989
Revised July 20, 1994

California Environmental Protection Agency
Department of Pesticide Regulation
Worker Health and Safety Branch
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ABSTRACT

The soil fumigant 1,3-dichloropropene (1,3-D) is used to control soil parasitic nematodes and other soil pests in annual crops and some perennials before planting. Metabolism and pharmacokinetic data on 1,3-D indicate facile conjugation as a mercapturate, and renal elimination after inhalation. The primary mode of exposure is inhalation, with dermal absorption of the vapor considered unimportant. Inadvertent exposure of humans during application equipment failure or repair has resulted in skin and/or eye irritation. Biological monitoring of workers demonstrated an estimated Absorbed Daily Dosage of 1.9 ug/kg/day (1.13 and 0.73 ug/kg/day for application and loading, respectively) when adjusted for respiratory protection worn during the entire fumigation cycle. These adjusted numbers are reflective of practices to be implemented in California should 1,3-D be reinstated, including spill control, dry disconnects and vapor recovery measures. Non-occupational inhalation exposure for residents of a Telone reinstatement area was estimated by stochastic simulation. Estimated 95th percentile Lifetime Average Daily Dosages ranged from 0.167 ug/kg/day for residents living 500 m from treated fields for 30 years, to 0.373 ug/kg/day for residents living 100 m from fields for 70 years. Estimated 95th percentile 62-day Average Daily Dosages ranged from 0.674 ug/kg/day for infants living 500 m from treated fields, to 6.272 ug/kg/day for young children living 100 m from fields. This report was prepared as Appendix B to the Department's risk assessment document for 1,3-D. The necessity for this risk document stemmed from the identification of adverse effects in acute and chronic studies as well as characterization of 1,3-D as an oncogen in rat chronic feeding and mouse inhalation studies.

APPENDIX B

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
WORKER HEALTH AND SAFETY BRANCH

HUMAN EXPOSURE ASSESSMENT

1,3-DICHLOROPROPENE

May 26,1989
Revised July 20, 1994

INTRODUCTION

The fumigant 1,3-dichloropropene (1,3-D) (CAS # 542-75-6, molecular formula $C_3H_4Cl_2$) is a liquid used as a soil treatment for the control of plant parasitic nematodes and other soil pests. The physical properties of 1,3-D are listed below:

Boiling point 108^{o}C (Composite of *cis/trans* isomers: higher BP 112.0^{o}C, lower BP 104.3^{o}C)
Vapor pressure 27.3 mm at 25^{o}C
Density 1.2 g/ml at 25^{o}C
Water solubility 2180 ppm (*cis-),* 2320 ppm (*trans-)*
Octanol/water partition coefficient 104
Cis-/*trans-* ratio 1:1

EPA STATUS

A Registration Standard was issued in September 1986 for 1,3-D which includes exposure and risk assessments for workers handling 1,3-D. These assessments assume that inhalation is the primary route of exposure, and that dermal exposure may only contribute during episodes of equipment repair or failure. Respirators, chemically resistant clothing and gloves are required during mixing and loading.

USAGE

1,3-D is manufactured by Dow Chemical Co. as a formulation containing 94% active ingredient (1:1 *cis-*:*trans-* isomer ratio) and 6% inert ingredients. Commercial 1,3-D is sold under the name Telone II™ and contains 9.5 lbs a.i. per gallon. 1,3-D is registered for use on more than 120 crops and ornamentals. It is used for preplant soil treatments for vegetable crops, field crops, deciduous fruit trees, nut trees and vines. It is recommended that soils where annual crops are grown be treated each year before planting. Over 15 million pounds were reported sold in California in 1987 (California Department of Food and Agriculture, 1988). Application rates of 1,3-D depend on crop and soil type, and range from 43 to 970 lbs a.i./acre. The soil surface is sealed by covering or rolling after application to increase efficacy by reduction of vapor loss. Application equipment injects 1,3-D to a depth of at least 12 inches below the sealed soil surface.

LABEL PRECAUTIONS

The label for Telone II contains the signal word "WARNING" and the following precautionary statements:

PRECAUTIONARY STATEMENTS

HAZARDOUS TO HUMANS AND DOMESTIC ANIMALS, HAZARDOUS LIQUID AND VAPOR

- o MAY CAUSE ALLERGIC SKIN REACTION
- o MAY BE FATAL IF INHALED, ABSORBED THROUGH SKIN, OR SWALLOWED
- o CAUSES SEVERE EYE DAMAGE
- o CAUSES BURNS OF SKIN
- o MAY CAUSE LUNG, LIVER AND KIDNEY DAMAGE AND RESPIRATORY SYSTEM UPON PROLONGED CONTACT
- o Do not breathe vapor
- o Do not get in eyes, on skin, on clothing
- o Do not take internally
- o Use only with adequate ventilation
- o Wear eye and skin protection necessary to prevent contact when handling TELONE II
- o Wash thoroughly with soap and water after handling and before eating or smoking
- o If protective gear, such as boots or gloves, becomes contaminated, immediately wash with soap and water. Never wear protective gear having the odor of 1,3-dichloropropene. Aerate and wash all protective gear thoroughly after each use until odor is gone.
- o Render unusable and dispose of contaminated leather goods, including shoes.
- o Do not apply this product in such a manner as to directly or through drift expose workers or other personnel. The area being treated must be vacated by unprotected persons.

California regulations and permit conditions: Additional requirements

California regulations require respiratory protection when inhalation exposure potential is high (e.g., during loading and equipment repair). Eye and skin protection (gloves and chemical resistant clothing) are required when handling Telone II.

The California permit conditions will require additional protective equipment. Loaders will be required to wear full-face respirators. Applicators must either wear a half-face respirator or be inside a charcoal-filtered cab during application. Workers re-entering a treated area during the first 7 days post application will be required to wear a one-half face respirator.

WORKER ILLNESS

Table 1 shows that from 1982-1990 there were 55 illnesses that were related to exposure to 1,3-D. In terms of type of illness, they were almost equally divided between systemic (16), eye (14) and skin (18). With respect to the causality most of the illnesses were classified as definite (33), followed by probable (9) and possible.

Table 1. 1,3-dichloropropene illnesses in California (1982-1990)

Year	Type				Causality		
	Systemic	Eye	Skin	Eye/Skin	Definite	Probable	Possible
1982	4	2	1	0	1	2	4
1983	2	3	1	0	5	1	0
1984	1	3	2	0	4	1	1
1985	0	2	3	0	4	1	0
1986	1	0	2	1	1	2	1
1987	1	0	0	0	1	0	0
1988	1	2	7	0	6	2	2
1989	1	2	1	2	5	0	1
1990	5	0	1	0	6	0	0

METABOLISM/PHARMACOKINETICS

ANIMAL STUDIES

Inhalation

Rats exposed nose-only to 30, 90, 300 or 900 ppm of 1,3-dichloropropene (*cis*- 49.3%, *trans*-42.8%) for three hours absorbed 14, 29, 85, and 171 mg/kg, respectively, or 82, 65, 66, 62 percent, respectively, of the exposure dose (Stott and Kastl, 1986). Decreases in percent absorbed as the exposure concentration increases are apparently related to the decreased ventilation frequency at higher exposure levels. Tissue distribution of inhaled vapors indicated the lungs contained approximately 50 percent of the total inhaled vapors and the nasal passages contained an additional 10-16 percent. Depuration of 1,3-D in the blood was biphasic with the initial half-life estimated to be 3-6 minutes and the terminal half-life 30-40 minutes. Levels of protein sulfhydryl amino acids were reduced, but no reduction in pulmonary sulfhydryl amino acids was observed. Similar results for rats were reported for tissue distribution and glutathione depletion after a one-hour exposure (Fisher and Kilgore, 1988a).

The characterization of the primary urinary metabolite from rats after inhalation was accomplished by Fisher and Kilgore (1988b) who found a mercapturate after a one hour exposure to 1,3-D at 40, 107, 284, 398, or 789 ppm. The excretion of the conjugate was nearly linear with respect to 1,3-D exposure up to 400 ppm. Above 400 ppm, the excretion of the mercapturate declined relative to this initial linearity. This may have been due to decreased ventilation frequency in rats exposed three hours to doses greater than 90 ppm as reported by Stott and Kastl (1986). Alternatively, it may have been due to depletion of conjugable glutathione.

Oral dosing

Several investigators have examined the metabolic fate of 1,3-D in animals after an oral dose. Hutson *et al*., (1971) reported that 81% of 10-mg doses of *cis*-1,3-D, and 57% of 10-mg doses of *trans*-1,3-D, were eliminated in the urine. Dietz *et al., (*1984 a,b) reported 50-80 percent renal elimination and 14-17 percent elimination as CO_2 in rats or mice treated with 1,3-D. No evidence of saturation of metabolic pathways was observed up to 50 mg/kg in these later studies. Urinary elimination of ^{14}C-equivalents was estimated to have a half-life of approximately 5.5 hours.

The primary metabolite in urine of rodents dosed orally with 1,3-D is *N*-acetyl-*S-(*3-chloroprop-2-enyl) cysteine (DCPMER) and its sulfoxide. This indicates that 1,3-D is metabolized and conjugated via a glutathione pathway in rodents. The formation of this metabolite is consistent with the loss of non-protein sulfhydryl levels in the liver and stomach after *per os* doses with 1,3-D (Dietz *et al*., 1984, Climie *et al*., 1979).

HUMANS

Inhalation

In workers exposed to 1,3-D during loading and application, Osterloh *et al.* (1984, 1989), Brouwer *et al.* (1991) and van Welie *et al.* (1991) observed DCPMER as a urinary metabolite. The common urinary metabolite in rodents and humans indicates that these species metabolize 1,3-D by similar metabolic pathways.

A PB/PK study was conducted by the registrant in which six humans were exposed to 1,3-D in an inhalation chamber at 1 ppm for 6 hours (Waechter *et al.,* 1992). Estimates of respiratory uptake, made from analysis of exhaled breath during the exposure, averaged 78% for the two isomers. Urine was collected during and after exposure (84 hrs post exposure). Excretion of the *cis*- and *trans*-mercapturates was complete 36 hours post exposure. The combined conversion of inhaled 1,3-D to the two mercapturates was found to be 24% (Stott, 1992).

DERMAL ABSORPTION

The high vapor pressure of 1,3-D (27.3 mm) reduces its dermal absorption potential. There is a single report in the literature concerning dermal absorption of 1,3-D and other low-boiling organic chemicals (Cohen and Poppendorf, 1989). The experimental details are not complete as the paper reported the values from a thesis by the first author. The values reported for dermal absorption of 1,3-D in rats *in vivo* were 0.62 and 1.5% for doses of 1.9 and 19 ug/cm^2, respectively. This range of absorption values was found for exposed skin that was not occluded.

WORKER EXPOSURE

Inhalation

Worker inhalation exposure assessed by breathing zone measurements during loading, application or equipment repair are summarized in Table 2.

Table 2. Breathing zone air concentrations of workers handling 1,3-dichloropropene during loading and application

ppm	Reference	Date
0.37[a/]	Davies and Fraser	1988
0.04-0.40	Tobol and Axe	1982[b/]
0.38[a/]	Maddy *et al*.	1980
0.71[a/]	Maddy *et al*.	1982
0.17[a/]	Fong and Maykoski	1985
<1.0[a/]	Albrecht	1987
<0.2[a/]	Cook	1982[b/]

[a/] Time-weighted average
[b/] Cited by Davies and Fraser (1988)

These studies suggest that workers are exposed to time-weighted average levels that are below the recommended 1 ppm Permissible Exposure Limit set by the Occupational Safety and Health Administration.

Since concentrations were measured in the workers' breathing zones while they performed a variety of tasks (some loaded and some applied, others loaded or applied and some unspecified), the reported inhalation exposure results from a composite of work tasks. The individual studies did not always report exposures by task, nor did they report any more than TWA values or monitoring results, making it difficult to obtain an absorbed dose for each work task.

Table 3. Potential inhalation exposure for 1,3-dichloropropene estimated from reported breathing zone concentrations, assuming a respiratory rate of 29 L/min

Study	mg/8-hr day
Poppendorf *et al.,*(1983)	142.3
Maddy *et al.*, (1980)	24.0
Maddy *et al*.(1982)	44.8
Fong and Maykoski(1985)	10.8
Davies and Fraser, (1988)	23.3
Cook,(1983)	12.6
Albrecht,1987)	63.1
Geometric Mean	31.5

The air monitoring results of several studies have been converted to potential inhalation exposures in mg/8-hr day, by assuming a respiration rate of 29 L/min (Table 3). The geometric mean of these data is reported because the data are log-normally distributed (Shapiro and Wilk, 1965). It is conventional to treat exposure data by this statistical method as it allows the use of all the environmental or exposure data that may be widely variant (Owen and DeRouen, 1980). If the mean for potential inhalation exposure from breathing zone measurements is mitigated by a respirator (90 reduction in exposure), corrected for respiratory uptake (78 %, Waechter *et al.,* 1992)) and a 70-kg person is assumed, then the ADD (Absorbed Daily Dosage) is 35.1 ug/kg/day.

Hand Exposure

The data available on potential hand exposure to 1,3-D are conflicting. Maddy *et al*., (1980, 1982) reported hand a contamination level of 16.4 ug/hr for workers wearing gloves. The other data on hand exposure (Table 4) were taken from the work of Davies and Fraser (1988), on an application of 1,3-D in Canada. The range of the data for the eight individuals' hand residues was 0.1-570 mg/hr with a geometric mean of 9.7 mg/hr.

Table 4. Hand exposure to 1,3-dichloropropene during loading[a/]

Worker	mg/hr
1	14
2	0.8
3	26.5
4	193
5	570
6	0.7
7	33.3
8	0.1
Geometric Mean	9.7

[a/] Davies and Fraser (1988)

This exposure value for the hand of 9.7 mg/hr is almost 600-fold greater than that reported by Maddy, (1982). The reasons for this large difference may be in the experimental design. In the Davies and Fraser (1988) study, the protocol was a cotton glove-polyethylene glove (1 mm)-cotton glove arrangement where the inner cotton gloves were analyzed for 1,3-D. The inner glove provides an absorptive sink whereas the outer glove compared to the smooth protective glove normally worn, provides a sponge for liquid 1,3-D for eventual penetration through the thin polyethylene glove. This type of thin glove (polyethylene) is not normally utilized in application of this material as it would not withstand the physical abuse of daily operations during loading the fumigant into the tanks. It is likely that in the studies of Maddy *et al*. (1982) where hand residues were monitored under normal work conditions, that thicker gloves were worn. Further, Maddy suggests that hand washes may not be an effective means for the removal of residues because some evaporation may have occurred as well as some dermal absorption. Even so, the analysis of hand washes in the work reported by Maddy *et al*., reported microgram amounts of 1,3-D rather than the milligram amounts in the work of

Davies and Fraser. While the Maddy data is very likely an underestimate of dermal exposure, the dermal estimates of Davies and Fraser are overestimates due to the experimental design. Since the hand exposure values are for 1.2 hrs/day (estimated daily loading time), the dermal component becomes a minor contributor of the overall human exposure which is primarily via inhalation.

Annual and Lifetime Exposure Days

Estimates of worker exposure time are provided by the US EPA Data Call-In for handlers of 1,3-D in crops grown in California that have been treated with 1,3-D (Houtman, 1992). This survey provided information on the number days per year for each crop that 1,3-D was handled for applicators and loaders in California (Table 5). The maximum number of days per career was estimated to be 270. The number of days per career ranged from a low of 24 for potatoes to a high of 270 for brassica. It is possible that the same individuals applying for brassica could be applying in vegetables, which could mean that an individual's exposure days per year or career could be as high as the total for all crops. However, it is likely to be much less because the calendar window for application to each crop prevents any one person from working all of them.

Table 5. Annual and lifetime handling days for loaders (L), applicators (A) and repairs (R)

	Tomato L,A,R	Potato L,A,R	Cotton L,A,R	Vegetables L,A,R	Brassica L,A,R	Beets L,A,R	Tree/Vine L,A,R
			Annual				
Custom	16,23,34	4,4,4	40,36,26	18,35,24	36,36,36	10,10,10	22,9,8
Grower	1,1,1,	1,1,1	2,2,13	3.5,3.5,3.5	0,0,0	1,1,1	4,4,4,
			Lifetime				
Custom	104,150,221	24,24,24	260,234,169	108,210,144	270,270,270	65,65,65	198,81,72
Grower	4.5,4,5,4.5	2.5,2.5,2.5	9,9,58.5	8.75,8.75,8.75	0,0,0	4.5,4.5,4.5	12,12,12

Biological Monitoring

Osterloh *et al*. (1984, 1989 a and b) reported human exposure studies with 22 workers loading and applying, in which they conducted urinary monitoring for *N*-acetyl-*S*-(3-chloroprop-2-enyl)cysteine (DCPMER). Respiratory protection (half-face) was worn only during loading and not during application. An average of 3.4 mg of DCPMER was excreted in the 24-hour period after exposure. Correction for the molecular weight difference between 1,3-D (111) and DCPMER (237) gives an ADD of 1.6 mg/person/day or 22.7 ug/kg/day. Using the data of Davies and Fraser (1988), it is possible to calculate the percentage of the exposure received during application and loading. In Davies and Fraser it was determined that 26.1 percent of the exposure occurred during application, 73.9% during loading. Osterloh *et al*. assumed 90% protection from the half-face respirator worn during loading, hence the inhaled dose was 0.1 times the exposure. During application, 1.0 (0% respiratory protection) indicates the absence of respirators. The absorbed dose for each activity may be found by the following equation.

$$\underline{\text{Loading}} \qquad \underline{\text{Application}}$$
$$(73.9\ \%)(X)(0.1) + (26.1\%)(X)(1.0) = 22.7\ \text{ug/kg/day} \qquad (1)$$

where X is exposure. Solving for X gives 67.8 ug/kg/day. Putting this value back into equation (1), and adding respiratory protection (half-face respirators) during application gives

$$\underline{\text{Loading}} \qquad \underline{\text{Application}}$$
$$(73.9\%)(67.8)(0.1) + (26.1\ \%)(67.8)(0.1) = 6.8\ \text{ug/kg/day}$$

The value of 6.8 ug/kg/day is the expected ADD if half-face respirators are worn during *both* loading and application.

Houtman (1993) monitored five individuals loading or applying 1,3-D in Washington state. The same individual did not do both tasks. These applicators and loaders carried out one application per day, at a rate of 25 gal/acre, lasting about four hours. One application was done without mitigation measures, while the others used various mitigation measures specified by the US EPA including dry disconnects (with and without vapor recovery), spill control at the end of the rows, and a cab with charcoal-filtered air. Houtman collected urinary monitoring data only for the application conducted without mitigation measures. To estimate the absorbed daily dose from these unmitigated conditions, respiratory protection factors of 0.9 and 0.95 for half-face and full-face respirators were used for applicators and loaders, respectively. The human chamber PB/PK exposure study data were used in the absorbed dose calculation. These respiratory protection requirements for loaders and applicators were part of the Permit Conditions in California for the flux studies and the Monterey Commercial Use Project. These same respiratory protection conditions will be required if 1,3-D is reinstated in California.

The exposure data, shown in Table 6 as geometric means, have been normalized to an 6.8-hour day, which is consistent with the data of Davies and Fraser (1988) and allows comparison with the data of Osterloh *et al.* where one person performed both loading and application.

Houtman (1993) found that utilizing spill control during application reduced the ambient air concentrations by 79%. The urinary metabolite data were adjusted by this factor. The absorbed dose was adjusted for the wearing of a one-half face respirator from the unmitigated application in Washington. The final adjustment of the data from Washington was the factoring of the reduced rate in California (12 gal/acre) as compared to the 25 gal/acre that were used in the studies in Washington. The loader exposure data were not adjusted for the reduced rate in California as the exposure occurs primarily during the connecting and disconnection of the hose from the nurse tank and is unrelated to the amount placed in the tank on the tractor.

With respect to the estimation of AADD and LADD, the range of values for loading and applying were obtained from the crop specific data compiled in Table 5.
There are several reasons for the reduced exposure of a combined (one person doing both tasks) load and apply (1.9 ug/kg/day) in the Washington study (Houtman, 1993) as compared to the earlier combined estimate of Osterloh *et al.* (6.8 ug/kg/day). Firstly, for the loader, the Washington study used dry disconnects and vapor recovery devices. For the applicator, spill control was used at the end of the rows. Each of these mitigation strategies reduces ambient air concentration which resulted in lower estimated exposure value of more than three-fold. It is further likely that the soil moisture content will be higher in California than occurred during the applications in Washington. This will further reduce emissions.

Table 6. ADD, AADD and LADD values for loading and application of 1,3- dichloropropene.

Study	Task	ADD[1/] (ug/kg/d)	Days/ Year	SADD[4/] (ug/kg/d)	AADD[5/] (ug/kg/d)	Days/ Career	LADD[6/] (ug/kg/d)
Osterloh *et al.*	Load/Apply	6.80					
Houtman	Load	0.73[3/]	4	0.016	0.008	24	6.9×10^{-4}
			40	0.16	0.08	270	7.7×10^{-3}
	Apply	1.13[3/]	4	0.025	0.012	24	1.1×10^{-3}
			36	0.23	0.11	270	1.2×10^{-2}
	Total[2/]	1.86					

1 Absorbed Daily Dosage, two load and application cycles/day; body weights of study volunteers used in calculations

2 One person doing both loading and applying-for comparison to studies of Osterloh *et al.*

3 Normalized to 6.8 hrs based on registrant study (Davies and Fraser, 1988), for one person doing both tasks to be compared with Osterloh *et al.,*

4 Split application for brassica, 90-day window (see Table 5)

5 Annual Average Daily Dosage (365 days/year)

6 Lifetime Average Daily Dosage 70 years life (25,550 days)

Exposure Appraisal

The exposure estimates based on the Houtman (1993) study, in which exposures were measured separately for loading and application, should be used for the assessment of risk. These estimates are based on biological monitoring that assessed both *cis*- and *trans*-mercapturate metabolites in the urine and utilized the pharmacokinetic information developed from exposure of humans under controlled conditions. Hand exposure information developed by previous investigators was not used as this route of exposure would be reflected in the total exposure measured by the biological monitoring.

None of the occupational exposure studies in which biological monitoring was conducted employed exactly the mitigation measures that would be required in California. These requirements are for full-face respiratory protection during loading and half-face protection during application.

NON-OCCUPATIONAL EXPOSURE

Inhalation exposure was estimated for residents of an area where Telone is used in carrot growing. Both lifetime and subchronic (seasonal) exposures were estimated for residents of the area in general, and for residents with homes at specified distances from Telone-treated fields (100, 200 and 500 meters). The estimated lifetime exposure distributions are given in Tables 7 through 10, seasonal exposures in Tables 11 through 14.

The exposure assessment relied on simulated air concentrations from a study provided by the registrant (Calhoun *et al.*, 1994), in which the ISCST simulation model (Wagner, 1987) was used to predict concentrations of 1,3-D in air for a scenario of limited reintroduction of Telone II™ soil fumigant in carrots. In the use scenario modeled, Telone is applied to 25 80-acre fields (2000 acres total) per year in a 9-township (324-square-mile) area in Kern County. Under this scenario, there is no other use of Telone. All applications are at the rate of 12 gallons per acre, and no field is treated more than once in three years. Calhoun *et al.* simulated three years of daily air concentrations for one point at the center of each section in the reintroduction area to produce an annual average daily concentration for each point. The locations of treated fields were assigned randomly in their model, so that concentrations at the section centers vary in part due to being different distances and directions from applications. The modeled concentrations thus represent long-term ambient concentrations for the reintroduction area. Calhoun *et al.* presented separately the concentrations for the township of highest Telone use within the 9-township area. These concentrations were used in the exposure assessment.

Probability distributions of exposure were estimated using stochastic simulation ("Monte Carlo") methods, implemented with the program @RISK (Palisades Corporation, 1992). The distribution of lifetime average daily dose (LADD), as ug of 1,3-D inhaled per kg of body weight per day (ug/kg/day), was estimated separately for persons living 1) the first 30 years of, and 2) all of a 70-year lifetime in the reintroduction area. Seasonal exposure was estimated for July-August, the period of greatest Telone use, by adjusting the long-term air concentrations for proportional use and mass loss during that 62-day period. Additional simulated air concentrations provided by the Environmental Monitoring Branch (Johnson, 1994a) were incorporated to estimate both lifetime and 62-day exposures to residents whose dwellings are close to treated fields. Exposure distributions were estimated separately for residents living 100, 200 and 500 meters from the edges of treated fields. Each estimated exposure distribution is based on a simulation with 10,000 trials.

LADD (ug/kg/day) was calculated by the following equation.

$$\mathrm{LADD} = \sum_{i=1}^{10} \mathrm{RT}_i \left[\left(\mathrm{Conc}_i \times \mathrm{BR}_i \right) / \mathrm{BW}_i \right] / 70$$

where the summation is over 10 age intervals,

RT_i = number of years in age interval *i* that the person resides in the Telone use area,

Conc_i = average of air concentrations (ug/m^3) in 5 locations weighted by the proportion of time spent in each location in interval *i*,

BR_i = average breathing rate (m^3/day) at each of 4 activity levels weighted by proportion of time spent at each level in interval *i*,

BW_i = body weight (kg) in interval *i*, and

70 years is the assumed lifetime.

Seasonal exposure (62-day average ug/kg/day) was calculated separately for each age interval, as

$$\text{Average daily dose} = \frac{\text{Conc x BR}}{\text{BW}}$$

where concentration, breathing rate and body weight are as defined above for LADD, but with air concentrations modified to approximate seasonal averages as explained in the next section.

Concentration, breathing rate and body weight were stochastic variables in the exposure simulation model. The statistical distributions used to simulate them are described in the sections on specific input variables following Tables 7-14.

Table 7. Lifetime average daily dose (ug/kg/day) of 1,3-D inhaled by residents of an area where Telone is applied to a total of 25 80-acre fields each year.

	Residence Time			
	Birth to age 30		Birth to age 70	
	Male	Female	Male	Female
Mean	0.0800	0.0783	0.1510	0.1436
Std Deviation	0.0480	0.0487	0.0867	0.0902
Percentile				
5	0.027	0.026	0.053	0.047
10	0.032	0.031	0.063	0.056
25	0.044	0.042	0.087	0.078
50	0.066	0.063	0.129	0.116
75	0.103	0.101	0.193	0.186
90	0.150	0.148	0.277	0.270
95	0.179	0.179	0.326	0.330
97.5	--[a]	--	--	--
99	0.230	0.236	0.425	0.444

a not calculated

Table 8. Lifetime average daily dose (ug/kg/day) of 1,3-D inhaled by residents living 100 m from treated fields in an area where Telone is applied to a total of 25 80-acre fields each year.

	Residence Time			
	Birth to age 30		Birth to age 70	
	Male	Female	Male	Female
Mean	0.1022	0.1001	0.1892	0.1829
Std Deviation	0.0514	0.0515	0.0926	0.0959
Percentile				
5	0.042	0.04	0.078	0.071
10	0.048	0.047	0.091	0.084
25	0.063	0.061	0.12	0.111
50	0.09	0.087	0.168	0.159
75	0.129	0.128	0.238	0.233
90	0.176	0.174	0.319	0.319
95	0.204	0.201	0.373	0.371
97.5	0.228	0.227	0.416	0.423
99	0.262	0.257	0.481	0.481

Table 9. Lifetime average daily dose (ug/kg/day) of 1,3-D inhaled by residents living 200 m from treated fields in an area where Telone is applied to a total of 25 80-acre fields each year.

	Residence Time			
	Birth to age 30		Birth to age 70	
	Male	Female	Male	Female
Mean	0.0996	0.0973	0.1846	0.178
Std Deviation	0.0501	0.0499	0.0901	0.0932
Percentile				
5	0.039	0.038	0.073	0.067
10	0.046	0.044	0.087	0.08
25	0.061	0.06	0.116	0.108
50	0.088	0.086	0.165	0.156
75	0.127	0.124	0.234	0.227
90	0.171	0.168	0.311	0.307
95	0.199	0.196	0.36	0.363
97.5	0.222	0.22	0.408	0.414
99	0.253	0.248	0.458	0.465

Table 10. Lifetime average daily dose (ug/kg/day) of 1,3-D inhaled by residents living 500 m from treated fields in an area where Telone is applied to a total of 25 80-acre fields each year.

	Residence Time			
	Birth to age 30		Birth to age 70	
	Male	Female	Male	Female
Mean	0.084	0.0818	0.1577	0.1498
Std Deviation	0.0423	0.0419	0.0772	0.0781
Percentile				
5	0.034	0.033	0.065	0.059
10	0.04	0.039	0.076	0.069
25	0.053	0.051	0.101	0.093
50	0.074	0.071	0.14	0.13
75	0.106	0.103	0.198	0.189
90	0.144	0.141	0.265	0.259
95	0.169	0.167	0.31	0.305
97.5	0.191	0.189	0.352	0.352
99	0.216	0.212	0.4	0.4

Table 11. Average daily dose (ug/kg/day) of 1,3-D inhaled by residents during the 62-day period of highest Telone use in an area where Telone is applied to a total of 25 80-acre fields each year.

	Age Group									
	< 1		1 < 2		2 < 3		3 < 6		6 < 9	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Mean	0.2499	0.2707	1.5513	1.6841	1.3685	1.4366	1.1103	1.1467	1.0548	1.0651
Std Deviation	0.2270	0.2431	1.0419	1.1219	0.9039	0.9243	0.7460	0.7561	0.6797	0.6863
Percentile										
5	0.045	0.050	0.470	0.520	0.422	0.464	0.333	0.361	0.330	0.326
10	0.058	0.065	0.558	0.616	0.501	0.549	0.399	0.426	0.397	0.395
25	0.098	0.108	0.770	0.841	0.691	0.750	0.553	0.589	0.558	0.560
50	0.173	0.192	1.207	1.308	1.070	1.134	0.869	0.904	0.849	0.863
75	0.321	0.343	2.052	2.244	1.815	1.897	1.466	1.507	1.367	1.396
90	0.539	0.590	3.126	3.385	2.738	2.804	2.242	2.249	2.050	2.038
95	0.714	0.789	3.750	4.047	3.260	3.375	2.659	2.731	2.464	2.474
97.5	0.903	0.966	4.233	4.530	3.667	3.821	3.010	3.137	2.783	2.880
99	1.125	1.183	4.711	5.124	4.108	4.260	3.468	3.522	3.230	3.296
	9 < 12		12 < 15		15 < 18		18< 25		25 < 70	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Mean	0.7953	0.7730	0.6536	0.5394	0.5300	0.4984	0.5297	0.4964	0.4809	0.4414
Std Deviation	0.5168	0.4897	0.4050	0.3320	0.3172	0.2980	0.2904	0.2913	0.2688	0.2840
Percentile										
5	0.239	0.237	0.208	0.172	0.176	0.164	0.188	0.164	0.167	0.132
10	0.291	0.292	0.254	0.209	0.214	0.196	0.228	0.200	0.201	0.164
25	0.417	0.412	0.360	0.295	0.298	0.278	0.314	0.284	0.281	0.236
50	0.645	0.635	0.545	0.453	0.447	0.419	0.459	0.422	0.416	0.362
75	1.029	1.007	0.835	0.694	0.676	0.645	0.676	0.637	0.618	0.567
90	1.529	1.455	1.209	0.998	0.977	0.917	0.930	0.904	0.848	0.830
95	1.870	1.767	1.457	1.207	1.171	1.103	1.103	1.085	1.018	1.022
97.5	2.118	2.080	1.713	1.413	1.338	1.279	1.267	1.252	1.166	1.190
99	2.496	2.341	2.020	1.645	1.568	1.450	1.468	1.433	1.342	1.382

Table 12. Average daily dose (ug/kg/day) of 1,3-D inhaled during the 62-day period of highest Telone use by residents living 100 m from fields in an area where Telone is applied to a total of 25 80-acre fields each year.

	Age Group									
	< 1		1 < 2		2 < 3		3 < 6		6 < 9	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Mean	0.4940	0.5352	3.0723	3.3330	2.6876	2.7770	2.1802	2.2126	1.9918	1.9861
Std Deviation	0.3548	0.3830	1.4181	1.5406	1.2335	1.2549	1.0277	1.0370	0.9528	0.9564
Percentile										
5	0.118	0.128	1.368	1.490	1.206	1.263	0.942	0.968	0.852	0.833
10	0.152	0.166	1.545	1.672	1.347	1.418	1.069	1.098	0.969	0.965
25	0.238	0.258	1.924	2.096	1.697	1.757	1.366	1.393	1.255	1.254
50	0.395	0.425	2.710	2.949	2.360	2.470	1.918	1.960	1.760	1.766
75	0.641	0.699	4.008	4.347	3.502	3.620	2.833	2.868	2.545	2.529
90	0.976	1.076	5.137	5.567	4.481	4.594	3.657	3.725	3.371	3.371
95	1.217	1.331	5.792	6.272	5.021	5.177	4.158	4.258	3.831	3.879
97.5	1.450	1.563	6.306	6.950	5.536	5.720	4.615	4.647	4.261	4.271
99	1.680	1.784	6.915	7.610	6.021	6.204	5.033	5.157	4.801	4.847
	9 < 12		12 < 15		15 < 18		18< 25		25 < 70	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Mean	1.4857	1.4065	1.1533	0.9575	0.9336	0.8872	0.8833	0.8610	0.8063	0.8020
Std Deviation	0.7344	0.6874	0.5796	0.4659	0.4444	0.4134	0.3970	0.4030	0.3694	0.4061
Percentile										
5	0.603	0.573	0.464	0.396	0.393	0.379	0.383	0.359	0.350	0.305
10	0.701	0.667	0.539	0.459	0.454	0.438	0.447	0.422	0.405	0.366
25	0.923	0.890	0.723	0.610	0.599	0.571	0.584	0.558	0.526	0.499
50	1.314	1.244	1.020	0.849	0.833	0.792	0.802	0.770	0.733	0.704
75	1.899	1.795	1.456	1.209	1.184	1.126	1.111	1.091	1.007	1.034
90	2.530	2.389	1.927	1.605	1.549	1.481	1.436	1.433	1.316	1.382
95	2.925	2.770	2.287	1.863	1.809	1.695	1.662	1.661	1.524	1.604
97.5	3.280	3.076	2.623	2.102	2.000	1.867	1.841	1.818	1.725	1.790
99	3.678	3.463	3.033	2.434	2.278	2.101	2.083	2.029	1.922	2.018

Table 13. Average daily dose (ug/kg/day) of 1,3-D inhaled during the 62-day period of highest Telone use by residents living 200 m from fields in an area where Telone is applied to a total of 25 80-acre fields each year.

	Age Group									
	< 1		1 < 2		2 < 3		3 < 6		6 < 9	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Mean	0.4605	0.5018	2.8772	3.1305	2.5168	2.6084	2.0439	2.0856	1.8713	1.8739
Std Deviation	0.3227	0.3596	1.3044	1.4290	1.1309	1.1633	0.9438	0.9779	0.8750	0.8917
Percentile										
5	0.112	0.117	1.229	1.308	1.089	1.124	0.851	0.854	0.758	0.745
10	0.139	0.155	1.382	1.492	1.222	1.278	0.978	0.986	0.895	0.871
25	0.219	0.243	1.778	1.935	1.568	1.633	1.265	1.293	1.169	1.170
50	0.374	0.401	2.647	2.865	2.324	2.404	1.865	1.887	1.700	1.694
75	0.607	0.664	3.775	4.152	3.289	3.433	2.687	2.734	2.426	2.428
90	0.906	0.998	4.704	5.195	4.114	4.278	3.387	3.499	3.103	3.164
95	1.112	1.238	5.266	5.730	4.585	4.726	3.771	3.915	3.536	3.593
97.5	1.300	1.441	5.770	6.269	5.016	5.128	4.206	4.249	3.908	3.920
99	1.534	1.688	6.289	6.837	5.542	5.607	4.605	4.696	4.281	4.346
	9 < 12		12 < 15		15 < 18		18< 25		25 < 70	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Mean	1.3973	1.3308	1.0879	0.9069	0.8808	0.8389	0.8368	0.8156	0.7646	0.7564
Std Deviation	0.6736	0.6511	0.5331	0.4368	0.4053	0.3864	0.3650	0.3789	0.3405	0.3774
Percentile										
5	0.539	0.511	0.423	0.356	0.362	0.348	0.358	0.328	0.322	0.284
10	0.648	0.604	0.501	0.423	0.424	0.405	0.419	0.390	0.376	0.336
25	0.872	0.824	0.679	0.567	0.570	0.530	0.554	0.523	0.503	0.462
50	1.254	1.199	0.982	0.819	0.799	0.766	0.779	0.745	0.706	0.675
75	1.816	1.723	1.388	1.170	1.128	1.081	1.064	1.044	0.961	0.984
90	2.351	2.273	1.816	1.521	1.439	1.382	1.328	1.350	1.231	1.286
95	2.687	2.563	2.107	1.726	1.643	1.579	1.522	1.527	1.409	1.483
97.5	2.965	2.847	2.365	1.940	1.850	1.741	1.692	1.704	1.581	1.659
99	3.358	3.142	2.680	2.170	2.043	1.922	1.877	1.904	1.767	1.851

Table 14. Average daily dose (ug/kg/day) of 1,3-D inhaled during the 62-day period of highest Telone use by residents living 500 m from fields in an area where Telone is applied to a total of 25 80-acre fields each year.

Age Group

	< 1		1 < 2		2 < 3		3 < 6		6 < 9	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Mean	0.2906	0.3157	1.8121	1.9672	1.5953	1.6652	1.2951	1.3295	1.2146	1.2220
Std Deviation	0.1948	0.2105	0.7170	0.7709	0.6263	0.6341	0.5264	0.5343	0.4984	0.5174
Percentile										
5	0.078	0.085	0.934	1.024	0.826	0.878	0.655	0.659	0.588	0.584
10	0.099	0.107	1.041	1.141	0.920	0.977	0.724	0.750	0.671	0.666
25	0.147	0.161	1.257	1.387	1.111	1.185	0.892	0.940	0.840	0.842
50	0.242	0.264	1.653	1.777	1.457	1.523	1.180	1.209	1.114	1.116
75	0.378	0.413	2.232	2.419	1.974	2.044	1.596	1.633	1.494	1.494
90	0.550	0.592	2.797	3.022	2.460	2.547	2.028	2.059	1.897	1.936
95	0.674	0.724	3.194	3.462	2.803	2.891	2.301	2.344	2.167	2.204
97.5	0.809	0.878	3.536	3.831	3.097	3.174	2.574	2.652	2.438	2.478
99	0.957	1.046	3.922	4.256	3.424	3.539	2.853	2.981	2.705	2.881

	9 < 12		12 < 15		15 < 18		18< 25		25 < 70	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Mean	0.9136	0.8829	0.7399	0.6103	0.5984	0.5640	0.5913	0.5588	0.5364	0.5024
Std Deviation	0.3929	0.3854	0.3262	0.2660	0.2473	0.2308	0.2375	0.2331	0.2169	0.2240
Percentile										
5	0.418	0.399	0.330	0.285	0.280	0.274	0.280	0.264	0.254	0.223
10	0.481	0.463	0.381	0.324	0.321	0.310	0.327	0.305	0.292	0.258
25	0.621	0.603	0.501	0.418	0.418	0.392	0.415	0.385	0.373	0.336
50	0.841	0.805	0.677	0.556	0.557	0.517	0.553	0.516	0.501	0.455
75	1.127	1.084	0.917	0.749	0.732	0.689	0.724	0.689	0.658	0.624
90	1.458	1.401	1.188	0.961	0.927	0.877	0.908	0.872	0.833	0.813
95	1.674	1.633	1.373	1.129	1.069	1.009	1.044	0.999	0.947	0.922
97.5	1.843	1.818	1.532	1.256	1.208	1.112	1.175	1.101	1.055	1.031
99	2.078	2.087	1.729	1.481	1.323	1.276	1.306	1.277	1.190	1.210

INPUT VARIABLES FOR EXPOSURE SIMULATION

Air concentrations

Table 15 gives the probability distributions of air concentrations (in ug/m^3) used as input in the exposure simulations. The first column gives percentiles of the distribution, interpolated from a four-parameter logistic curve fit to the original Calhoun *et al.* frequency distribution. The interpolated concentrations were adjusted by factors developed by the Environmental Monitoring Branch of DPR (Johnson, 1994b), shown in the second column. Environmental Monitoring did additional modeling with ISCST to develop an adjustment to approximate the effect of using a 36-point-per-section spatial grid to model air concentrations, instead of the relatively coarse 1-point-per-section grid used by Calhoun *et al.* The effect of the adjustment is to increase the variability of the air concentrations, while the mean level is unchanged. The adjusted concentrations appear in the third column. These adjusted values, reflecting annual average daily concentrations for points on a 36-point-per-section grid, were used for the estimation of lifetime average exposure.

Table 15. Air concentration (ug/m^3) probability distributions used in exposure simulation.

Percentile	Concentrations interpolated from 4-parameter logistic curve[a]	Adjustment factors to approximate 36-point grid[b]	Adjusted concentrations used to estimate lifetime exposure	Adjusted concentrations used to estimate 62-day exposure
0.0001	0.103842	0.69359	0.072024	0.278587
0.01	0.106063	0.84461	0.089582	0.346503
0.1	0.128835	0.93182	0.120051	0.464356
0.2	0.160687	0.96331	0.154791	0.598731
0.3	0.201575	0.98483	0.198517	0.767865
0.4	0.254546	1.00283	0.255267	0.987372
0.5	0.323879	1.01963	0.330237	1.277356
0.6	0.415684	1.03671	0.430944	1.666892
0.7	0.538854	1.05566	0.568846	2.200298
0.8	0.706593	1.07924	0.762583	2.949673
0.9	0.938983	1.11571	1.047632	4.052242
0.95	1.088601	1.15040	1.252327	4.844000
0.99	1.228987	1.23092	1.512784	5.851450
0.999	1.263482	1.35000	1.705701	6.597652
0.9999	1.266995	1.49000	1.887822	7.302097

a Curve fit to high-end air concentration frequency distribution in Calhoun *et al.* (1994)
b Johnson (1994b)

Seasonal exposure was estimated for July-August, the period of historically highest Telone use. To estimate average daily concentrations for this 62-day period, the adjusted annual concentrations were modified as follows. In the Calhoun *et al.* simulation, all positive air concentrations occurred in two 74-day periods (60 days of Telone use plus 14 additional days for the material to dissipate), one in spring and the other in summer. In their simulation, 70.7% of the total Telone was applied during the summer use period, with 40% mass loss to air. In the spring period, 29.3% of the Telone was applied with a mass loss rate of 25%. To approximate the average daily concentrations during the summer period, the fraction of the annual concentration contributed by the summer period was assumed to be (70.7 x 40) / [(70.7 x 40) + (29.3 x 25)] = 0.794. This fraction was condensed into 74 days by multiplying by 365/74. Since actual Telone applications will probably not be restricted to the four months assumed by Calhoun *et al.,* historical use patterns were consulted. Pesticide use reporting data showed that in 1988 and 1989, 58.5% and 49.9%, respectively, of 1,3-D applied to carrots in Kern County was applied during July and August. The simulation summer-period concentrations were further modified to represent concentrations for the 62 days of July-August by multiplying by (58.5 / 70.7) x (74/62). The net effect was to multiply the annual concentrations by 3.868. The concentrations thus modified, shown in the fourth column of Table 15, were used for the estimation of seasonal exposure.

For both lifetime and seasonal exposure assessments, the average air concentration experienced by each person was simulated by randomly selecting five values from the relevant air distribution. These values represented five locations where the individual spent his or her time. A weighted average of the five concentrations, weighted by the proportion of time spent at each location, was used as the air concentration experienced by the individual. The same five locations were used throughout a person's life, but the division of time between them changed as a function of age. The division of time between locations was a random variable in the simulation, and is discussed in the section on individual mobility.

To estimate exposure to persons living close to fields, additional modeling with ISCST was done by the Environmental Monitoring Branch to provide annual average daily air concentrations at 100-meter increments from edges of treated fields (Johnson, 1994a). The probability distributions of concentrations at 100, 200 and 500 meters, which were used in this exposure assessment, are given in Table 16. In calculating the average concentration experienced by a person, the first "location" selected, at which the greatest portion of time is spent, was considered the home location. The concentration for the home location was simulated by selecting one value from, e.g., the 100-meter distribution and one from the general distribution, then calculating a weighted average with the two values weighted one-third and two-thirds, respectively, to reflect the fact that a field is treated only once in three years. The two values were chosen to have a rank order correlation coefficient of 0.80, based on an observed correlation of 0.86 between ambient concentrations in the same township from year to year (personal communication, Bruce Johnson, Environmental Monitoring Branch, DPR, June 22, 1994). For seasonal exposures, the home concentration was simply a value from the relevant distance distribution. This home location concentration was then used as described in the preceding paragraph in the calculation of the average concentration over five locations.

Table 16. Annual average air concentrations (ug/m^3) at specified distances from treated fields[a].

Percentile	100 meters	200 meters	500 meters
0.00333	0.35393	0.30113	0.24996
0.01	0.37037	0.31439	0.26472
0.05	0.46011	0.40619	0.29312
0.1	0.50768	0.44753	0.31998
0.15	0.55763	0.48264	0.35456
0.2	0.58246	0.51404	0.36323
0.25	0.60290	0.55147	0.37940
0.3	0.64604	0.58207	0.38904
0.35	0.70250	0.62520	0.40306
0.4	0.77585	0.74610	0.41207
0.45	0.87638	0.85215	0.45127
0.5	0.90497	0.90723	0.49474
0.55	0.97657	0.96199	0.55052
0.6	1.05653	1.02253	0.57466
0.65	1.17366	1.17403	0.62218
0.7	1.31421	1.25398	0.67783
0.75	1.43991	1.34267	0.75510
0.8	1.54023	1.42689	0.79173
0.85	1.63177	1.51078	0.83575
0.9	1.75806	1.59046	0.87488
0.95	1.95317	1.78902	0.99410
0.99	2.20345	1.98031	1.27958
0.99667	2.26113	2.04338	1.35822

a Johnson (1994a)

Individual mobility within the Telone use area

Individuals were assumed to divide their total time between five randomly selected locations within the Telone high-use area. The average air concentration to which an individual is exposed was calculated, as described above, as the mean of the five location concentrations weighted by the proportion of time spent in each location. The mean division of time between locations was derived for each age interval from Table 4.5 in the Arab's *Survey of Children's Activity Patterns* (Wiley, 1991a) and Table 3.3 in *Activity Patterns of California Residents* (Wiley, 1991b). Wiley's "time at home" was used as the time spent in the first selected location, his "time in transit" was divided equally between two locations, and the remaining time in the day divided between two others. The division of time between these last two locations was 70/30% for infants, stepping down by age interval to a 50/50% division for adults. Individual time divisions were allowed to vary from the mean by randomly generating them from a multinomial distribution with *n* chosen to give fairly small variability in the youngest intervals and greater variability in the adolescent and adult intervals. The distributions for time division are shown in Table 17.

Table 17. Probability distributions of time spent in five locations

Age interval	Multinomial *n* parameter		Average minutes per day spent in location				
			1	2	3	4	5
0 to 1	100	Male	1157	27	27	160	69
		Female	1151	38	38	150	63
1 to 2	100	Male	1157	27	27	160	69
		Female	1151	38	38	150	63
2 to 3	90	Male	1134	31	31	170	74
		Female	1099	44	44	151	102
3 to 6	90	Male	1134	31	31	170	74
		Female	1099	44	44	151	102
6 to 9	80	Male	1044	59	30	170	137
		Female	1021	27	26	256	110
9 to 12	80	Male	1020	31	31	250	108
		Female	968	47	46	265	114
12 to 15	70	Male	893	61	60	256	170
		Female	917	49	49	255	170
15 to 18	70	Male	893	61	60	256	170
		Female	917	49	49	255	170
18 to 25	60	Male	782	75	74	255	254
		Female	862	60	60	229	229
25 to 70	60	Male	798	60	59	262	261
		Female	960	51	51	189	189

Breathing rates

An individual's average breathing rate in each age interval was calculated as a weighted average of his rates at each of four activity levels: resting, light, moderate and heavy. The rate at each level was weighted by the proportion of time the individual was assumed to spend at that level. Breathing rate at each activity level was a random variable. The proportion of time at each level was a constant fixed for each age interval.

For infants (0-1 year), a triangular distribution of breathing rates was derived from the mean and range reported in the *Exposure Factors Handbook*, Table 3A-2 (USEPA, 1990). The mode of the triangular distribution was set equal to the lower limit of the range in order to match the EPA mean. For the other age intervals, uniform distributions were derived from data in the ARB's *Measurement of Breathing Rate and Volume* (Adams, 1993). In each case, the range was chosen to include all the reported rates relevant to an activity level for a specific sex and age group. These ranges are given in Table 18. Data were unavailable for children aged 1-3, so the breathing rates for 3-6-year-olds were used. The breathing rates of an individual at different activity levels, within and across ages, were assumed to have the rank order correlations shown in Table 19. (The value of 0.8 on the diagonal represents the correlation between breathing rates of the same individual at the same activity level, at different ages.) It was not possible to incorporate correlations between body weight and breathing rates because the software used did not handle them correctly. Correlation coefficients of body surface area and breathing rate within age intervals and activity levels, reported in Adams (1993), ranged from 0.06 to 0.84, with a mean of 0.40. The correlation of body weight and breathing rate may be similar. The effect of omitting this correlation from the simulation was probably to increase the estimated exposures to an unknown degree, because if the greater exposures associated with high breathing rates tended to be paired with high body weights, the exposure would be mitigated somewhat.

The proportion of time assumed to be spent at each activity level is shown in Table 20.

Body weight

Body weight distributions were taken directly from Tables 5A-1 through 5A-4 in the *Exposure Factors Handbook* (USEPA, 1990). The histograms reported in these tables were used without smoothing. Upper and lower bounds were supplied to produce a mean weight equal to the mean given in the EPA tables. An individual's weights in different age intervals were assumed to have the rank order correlations shown in Table 21.

Residence time and lifetime

In estimating lifetime exposures, lifetime length was fixed at 70 years. Exposure was estimated separately for fixed times of residence in the Telone use area of 30 and 70 years. Since the exposure assessment is viewed as applying to any areas where Telone may be reintroduced in the proposed way, and not just to the specific township in Kern County for which Calhoun *et al.* modeled air concentrations, it was not reasonable to define a distribution of residence time in the area. Instead, the estimated exposures are those expected to result from living the first 30 or 70 years of a 70-year lifetime in any area with Telone use like that described here.

Table 18. Breathing rates (L/min) as ranges of uniform distributions.

Age interval	Activity level	Male	Female
0 to 1	All	Triangular (0.25, 0.25, 2.09)	
1 to 2	Resting	5-7	
	Light	7-11	
	Moderate	8-15	
	Heavy	14-22	
2 to 3	Resting	5-7	
	Light	7-11	
	Moderate	8-15	
	Heavy	14-22	
3 to 6	Resting	5-7	
	Light	7-11	
	Moderate	8-15	
	Heavy	14-22	
6 to 9	Resting	5-9	
	Light	10-17	
	Moderate	11-23	
	Heavy	20-45	
9 to 12	Resting	5-9	
	Light	10-17	
	Moderate	11-23	
	Heavy	20-45	
12 to 15	Resting	6-12	5-10
	Light	7-17	7-15
	Moderate	17-35	15-27
	Heavy	25-72	24-59
15 to 18	Resting	6-12	5-10
	Light	7-17	7-15
	Moderate	17-35	15-27
	Heavy	25-72	24-59
18 to 25	Resting	7-11	5-10
	Light	8-18	6-15
	Moderate	18-42	15-28
	Heavy	48-80	39-62
25 to 70	Resting	7-11	5-10
	Light	8-18	6-15
	Moderate	18-42	15-28
	Heavy	48-80	39-62

Table 19. Rank order correlation coefficients between individual's breathing rates at different activity levels, within and across age intervals.

	Resting	Light	Moderate	Heavy
Resting	0.8	0.5	0.5	0.4
Light		0.8	0.5	0.4
Moderate			0.8	0.5
Heavy				0.8

Table 20. Proportion of time at each activity level (constant in exposure simulation).

Age interval		Activity level			
		Resting	Light	Moderate	Heavy
0 to 1	Male	1	0	0	0
	Female	1	0	0	0
1 to 2	Male	0.8	0.15	0.04	0.01
	Female	0.8	0.15	0.04	0.01
2 to 3	Male	0.75	0.2	0.04	0.01
	Female	0.75	0.2	0.04	0.01
3 to 6	Male	0.7	0.2	0.08	0.02
	Female	0.7	0.2	0.08	0.02
6 to 9	Male	0.7	0.17	0.10	0.03
	Female	0.7	0.2	0.08	0.02
9 to 12	Male	0.6	0.32	0.05	0.03
	Female	0.6	0.33	0.05	0.02
12 to 15	Male	0.6	0.32	0.05	0.03
	Female	0.6	0.33	0.05	0.02
15 to 18	Male	0.5	0.4	0.06	0.04
	Female	0.5	0.42	0.05	0.03
18 to 25	Male	0.4	0.50	0.06	0.04
	Female	0.4	0.52	0.05	0.03
25 to 70	Male	0.35	0.57	0.05	0.03
	Female	0.35	0.60	0.04	0.01

Table 21. Rank order correlation coefficients between the weights of an individual at different ages.

	0 to 1	1 to 2	2 to 3	3 to 6	6 to 9	9 to 12	12 to 15	15 to 18	18 to 25	25 to 70
0 to 1	1.00	0.92	0.82	0.72	0.61	0.61	0.61	0.61	0.61	0.61
1 to 2		1.00	0.92	0.82	0.72	0.61	0.61	0.61	0.61	0.61
2 to 3			1.00	0.92	0.82	0.72	0.61	0.61	0.61	0.61
3 to 6				1.00	0.92	0.82	0.72	0.61	0.61	0.61
6 to 9					1.00	0.92	0.82	0.72	0.61	0.61
9 to 12						1.00	0.92	0.82	0.72	0.61
12 to 15							1.00	0.82	0.82	0.72
15 to 18								1.00	0.82	0.82
18 to 25									1.00	0.82
25 to 70										1.00

Exposure appraisal

The estimated exposure distributions may be regarded as providing a reasonable idea of the highest exposures that should be expected under the use scenario. The distributions should not be interpreted as reflecting the exposures of a population of individuals, but as a set of values that are likely to bracket the exposure of an individual in this situation.

It should be noted that the large differences between estimated seasonal exposures of children less than one, and children from one to three, are largely produced by the input breathing rate distributions. The breathing rate data for infants under one came from a different source than all the other breathing rate data. In addition, no data were available for children from one to three, so the rates for three- to six-year-old children were used. In combination with the small body size of these children, this may have overestimated their exposures.

An important limitation of this exposure assessment is that it used 1,3-D concentrations in outdoor air to estimate 24-hour/day exposure, even though most people spend the greatest part of the day indoors. Since the registrant provided no data on indoor concentrations, and since no appropriate surrogate data were available to estimate them, it was judged that there was no alternative.

It is important to remember that these estimates of non-occupational exposure apply only to the use scenario of Calhoun *et al.*, which specified Telone applications to only 2000 acres per year in an area which has 8500 acres of carrots alone. Any change in the use scenario would require a new exposure assessment.

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