Routledge
Taylor & Francis Group

Archives of Environmental Health: An International Journal

ISSN: 0003-9896 (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/vzeh20

Toxicology and Hazard Assessment of 1,3-Dichloropropene (Telone® II)

William N. Albrecht Ph.D., M.S.P.H.

To cite this article: William N. Albrecht Ph.D., M.S.P.H. (1987) Toxicology and Hazard Assessment of 1,3-Dichloropropene (Telone® II), Archives of Environmental Health: An International Journal, 42:5, 292-296, DOI: 10.1080/00039896.1987.9935823

To link to this article: https://doi.org/10.1080/00039896.1987.9935823

Toxicology and Hazard Assessment of 1,3-Dichloropropene (Telone® II)

WILLIAM N. ALBRECHT, Ph.D., M.S.P.H.
Hazard Evaluation of Technical Assistance Branch
National Institute for Occupational Safety and Health
Cincinnati, Ohio

ABSTRACT. Potential adverse health effects from occupational exposure to 1.3-dichloropropene (DCP) are reviewed and hazards assessed. Further toxicologic evaluations should be conducted using only high-purity material that is free from possibly confounding impurities and stabilizers. Safety considerations when handling the material are included.

PROBLEMS associated with the use and manufacture of the subsoil fumigants 1.2-dibromo-3-chloropropane (DBCP) and 1.2-dibromoethane (EDB) have elevated 1.3-dichloropropene (DCP) as the primary constituent of Telone® II (Dow Chemical, U.S.A.), to the status of "broad-spectrum fumigant of choice" for many agricultural applications. Increased usage portends a concomitant increase in the frequency of human exposure. To ascertain the overall potential risk to agricultural workers who contact DCP, a literature review and hazard assessment was done to identify potential adverse health effects which may result from these exposures. Additionally, the exposures of a group of workers involved in large-scale use of the fumigant were determined.

In addition to Telone, DCP is contained in D-D® (Shell Chemical Company), a mixture of 1.3-dichloropropene and 1.2:dichloropropane, and Vorlex® Soil Fumigants (Schering AG). In some studies it is unclear whether the material evaluated is a pure preparation of 1.3-dichloropropene or the technical preparation, i.e., Telone II. The material studied is identified as specifically as possible, since questions concerning toxic effects may result from impurities in the technical mixture.

Chemical characteristics and environmental fate

Work completed in the early 1940s showed fumigant potential for a series of halogenated propanes and propenes. Further study indicated they could control a variety of nematodes.[1]

Telone®II (Dow Chemical Company) is a mixture of (Z) or *cis*- and (E) or *trans*-isomers of the fumigant 1.3-dichloropropene. It is a white to amber-colored liquid with a sweet odor. When originally registered with the U.S. Environmental Protection Agency as a pesticide in 1975, commercial formulations contained 92% DCP, 3-5% 1.2-dichloropropane, with 1% epichlorohydrin added as a stabilizer. Preparations of higher purity are now in use. Telone II, as currenty marketed, is approximately 98% DCP and does not contain epichlorohydrin, but instead uses epoxidized soybean oil to stabilize the preparation. Traces of 1.2-dichloropropane are also contained in the product.[2] Telone II has a vapor pressure of 21 mm Hg at 20°C and a boiling point of 104°C and 112°C for the *cis* and *trans* isomer, respectively. It is soluble to 1000 ppm in water at 20°C[3] and in several organic solvents including acetone and toluene.

Both *cis*- and *trans*-isomers are hydrolyzed in wet soil to their corresponding 3-chloroallyl alcohol.[4-5] The 3-chloroacrylic acid of each isomer appears to be an end-product of the hydrolytic degradation.[5] One estimate of the total retention of *cis*-dichloropropene after injection at a depth of 30.5 cm (18") in warm, moist, sandy soil is 90-95%.[6] Half-lives of both isomers at 20°C were estimated to be between 3 and 25 days.[7] Limited amounts of fumigant may be introduced into the ambient atmosphere by diffusion upwards through the soil profile.[8]

Toxicity considerations

Acute and chronic toxicity. Dow researchers[9] evaluated the acute and chronic toxicity of DCP. An oral LD_{50} for male rats of 713 mg/kg and 410 mg/kg for female rats was determined. Upon gross necropsy, it was observed that the livers and kidneys of the animals were affected. After application to the shaved back of rabbits, dermal irritation was observed, with redness, edema, and eventual necrosis. Skin absorption was noted in rabbits, and doses of 0.125 and 0.25 g/kg caused death. The dermal LD_{50} was calculated to be 504 mg/kg. Rabbits that had DCP instilled into the eye evidenced severe conjunctival irritation and slight-to-moderate corneal injury which resolved after 8 days.[10]

Rats acutely exposed to a vapor concentration of 2,700 ppm developed mucous membrane irritation of the eyes and nose as well as severe lung, liver, and kidney damage. A 2-hr exposure at 1,000 ppm was lethal to rats. Liver and kidney damage were seen in rats and guinea pigs exposed to DCP vapor at 11 or 50 ppm for 7 hr/day, 5 days/wk (d/wk), for 1 month. Chronic exposure at 1 ppm for 7 hr/day, 5 day/wk, for 6 months showed no gross adverse effects on rats, guinea pigs, rabbits, or dogs. At 3 ppm histological examination revealed a cloudy swelling of the renal epithelium in male rats, but this was reversible upon cessation of exposure. A hematologic profile consisting of hematocrit, WBC count, hemoglobin, and differential count remained normal over the course of all dosages.

One ppm was administered via inhalation to rats without effect. The authors concluded this represented a "no observable" adverse effect level, and recommended 1 ppm as an acceptable threshold limit value for occupational exposure. Accordingly, this study became the basis for the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Value or TLV®.

A more recent study[11] subjected male and female rats and mice to vapors of D-D® mixture. After exposing groups of animals to concentrations of 0, 5, 15, or 50 ppm, for 6 hr/day, 5 days/wk for 6 or 12 wk, the exposure-related effects observed were an increase in the mean liver/body weight ratio in male rats and the mean kidney/body weight ratio of female rats at the 50 ppm level. Slight to moderate diffuse hepatic enlargement was seen in 12/21 (57%) of male mice at 50 ppm after 12 wk exposure.

A Soviet study[12] determined the effects of DCP on the exocrine function of the pancreas of rats. The dosage regimen for the study included an oral administration of 0.1, 0.5, or 2.5 mg/kg for 6 months. Enzymes indicative of pancreatic integrity which were measured included: trypsin, which was increased throughout the study; blood lipase, which was increased; and amylase, levels of which were reduced. No conclusions were offered as to the relevancy of the data.

Another Russian experiment[13] examined liver function in experimental animals (not specified) after giving daily oral doses of 2.2 mg/kg or 55 mg/kg for 30 days. At the conclusion of the experiment, hepatic excretory function was altered as evidenced by prolonged pigment circulation in the blood, thymol test turbidity (increased plasma protein content), increased cholesterol level (lipid metabolism), and an increase in the enzyme diphosphate aldolase (carbohydrate metabolism).

Metabolism. Radiolabeled *cis*- and *trans*-isomers of DCP were administered to rats to determine the rate of elimination of parent compound and all metabolites.[14] The excretion of radioactivity as a percent of the total administered dose was measured in the urine, feces, and expired air of Carworth Farm "E" strain rats at 24-hr intervals for 4 days. On the fourth day post dose, they were killed and the total residual radioactivity in the carcass was measured. Excretion of radiolabel was very rapid, with 80-90% eliminated within 24 hr. Urinary excretion accounted for 80% of the *cis*-DCP and 56% of the *trans*-DCP recovered. Most (92%) was present as the mercapturic acid conjugate. Approximately 2% of each isomer was found in the feces after 24 hr. After 96 hours, 4% of the *cis*- and 24% of the *trans*-isomer had been exhaled as radiolabeled carbon dioxide ($^{14}CO_2$). Residual ^{14}C accounted for about 2% of each isomer.

Approximately 50% of the administered dose of *trans*-DCP was eliminated within 24 hr, indicating an elimination constant of 0.03/hr. Excretion patterns differed among the structural isomers of DCP. Four percent of the *cis*-isomer was exhaled as $^{14}CO_2$, the preponderance being voided in the urine. Rats exhaled 24% of the *trans*-isomer as $^{14}CO_2$ with less being excreted in the urine. In summary, both isomers were eliminated rapidly from the rat, with only small amounts of residual material remaining after 4 days.

The mercapturic acid metabolite is formed via a glutathione-dependent conjugation reaction. When *cis*-DCP was incubated with glutathione and rat liver cytosol (containing glutathione S-alkyl transferase), a very rapid loss of *cis*-DCP was observed. The product of this reaction was S-[*cis*-3-chloroprop-2-enyl] glutathione.[15]

Osterloh, et al.[16] devised an assay for *cis*-DCP-*N*-acetyl cysteine in the urine of exposed workers.[16] Using gas chromatography-mass spectroscopy, it was confirmed that vapor phase exposure resulted in this conjugate being eliminated in the urine. Metabolite levels correlated well with exposure level and duration of exposure. This methodology may be useful in assessing the efficacy of control measures since it can definitively demonstrate exposure to DCP.

It is unclear if the small percentage of 1,2-dichloropropane in Telone II presents a potential human toxicity hazard. If this compound is *vic*-bisdechlorinated in a manner similar to some polychlorinated ethane subs-

trates examined by Town and Leibman,[17] the opportunity exists for formation of reactive epoxide metabolites. These metabolites could potentially alkylate nuclear material and result in a mutagenic hazard. DiPaolo and Doniger[18] examined the transforming ability of six epoxides of structurally related chloroalkenes including *cis*-1- and *trans*-1-chloropropene epoxide and *cis*-1,3- and *trans*-1,3-di-chloropropene epoxide. All induced neoplastic transformations in embryonic Syrian hamster cells. If these epoxides are metabolic intermediates of their parent chloropropenes, the authors concluded that they are probably proximate carcinogens.

Mutagenicity. Briefly, *Salmonella typhimurium* test strain TA1535 is used to detect mutagens causing base-pair substitutions (missense), and TA100 is test strain TA1535 with a resistance factor to ampicillin incorporated into it. Strain TA1538 is used to identify compounds which cause frameshift mutations, and strain TA98 contains the resistance factor. TA1535 and TA1538 are not able to carry out enzyme excision repair. Strains TA100 and TA98 are more effective in detecting classes of carcinogens that were not identified in the original Ames protocol, and are also more sensitive to a number of carcinogens which were only weakly mutagenic in previous testing.[18]

DeLorenzo et al.[20] determined that DCP was mutagenic to TA1535 and TA100, but not to TA1538 or TA98. Mutagenicity was observed with or without the addition of S-9 liver microsomal fraction. Some mutagens require "metabolic activation" before they are able to act on nuclear material.

In another study, Neudecker, Stefani, and Henschler[21] found the *trans*- and *cis*-isomers of DCP showed positive mutagenicity with test strains TA1535, TA1537, and TA1538. The (E) isomer was one-half as reactive as the (Z) isomer. At all concentrations tested, survival rates of bacteria exposed to *cis*-DCP were lower than those exposed to *trans*-DCP. There was a marked reduction in the rate of back-mutations after the addition of microsomes, and the cytotoxicity of both isomers was drastically reduced. Both isomers reacted strongly with 4-nitrobenzopyridine, suggesting a direct alkylating mechanism. These data indicate that DCP is a potential carcinogen and a potent mutagen under the experimental conditions used. Some of the results obtained by Neudecker et al.[19] are contrary to those of DeLorenzo et al.[18]

Stolzenberg and Hine[22] tested short-chain, 2- and 3-carbon halogenated hydrocarbons for mutagenicity using strain TA100 both with and without metabolic activation (S-9 fraction). The addition of S-9 caused a decrease in the mutagenic activity of most compounds containing a double bond. Furthermore, it was concluded that the position of the double bond in the molecule exerts an influence on the mutagenic activity. This would most likely be to due to the electron-donating properties of halogens which would enhance the reactivity of already nucleophilic double-bonded carbons.

Tomkins, Kwok, and Douglas[23] used Chinese hamster ovary cells to determine that DCP (purity unspecified) induced significant increases in sister chromatid exchange. This was found to occur with and without metabolic activation.

The work of Talcott and King[24] is of considerable importance and interest with regard to the mutagenicity and potential carcinogenicity of DCP. Because of the large variations observed in the mutagenicity of DCP to test strain TA100, they reexamined four commercially available preparations of DCP, all ultrapurified using silicic acid chromatography. They found that none of the DCP preparations retained mutagenic activity after purification, whereas all were mutagenic when the original preparation was reconstituted from its chromatographic fractions. Polar impurities of the preparations were too complex to be totally characterized, but two of them were tentatively identified as epichlorophydrin and 1,3-dichloro-2-propanol.

Watson et al.,[25] confirmed that impurities from commerical DCP (removed by silicic acid chromatography) were responsible for mutagenicity seen in TA100. These impurities, identified as *cis*- and *trans*-2-chloro-3-(chloromethyl) oxiranes, were the result of autoxidation of the compound. DCP tested after purification had no direct mutagenic activity. *cis*-DCP was converted to a bacterial mutagen in the presence of S-9, but it was shown that low concentrations of glutathione in standard bacterial mutagenicity assays were responsible for the inability of glutathione S-alkyl transferase-catalyzed detoxification to prevent the synthesis of mutagenic species. When the concentration of glutathione was adjusted to physiologic levels, mutagenic activity of *cis*-DCP was virtually eliminated. These results support the view that bacterial mutation assays should be a qualitative indicator of mammalian genotoxicity.

Teratogenicity and reproductive effects. No data were retrieved relative to teratogenic sequelae or of other adverse reproductive outcomes associated with maternal exposures to DCP.

Carcinogenicity. The *cis*-isomer of DCP was studied with other halogenated hydrocarbons by multiple bioassay. The compound was evaluated against male ICR/Ha Swiss mice according to three exposure protocols: (1) an initiation-promotion screen using phorbol myristate acetate as a promotor substance, (2) repeated skin applications on shaved skin, and (3) subcutaneous injection. In the initiator-promotor screen, there was no significant difference from the control group, as was the case with the dermal application test. Six out of 30 mice developed fibrosarcomas at the site of administration after subcutaneous injection as opposed to 0/100 control mice. This incidence was statistically significant. Related compounds also showed activity. A significant number of stomach tumors was induced by 1-chloropropene and 2-chloropropenal 1-chloropropene oxide (*cis*- and *trans*-) was inactive.[26]

Gavage studies recently reported by the National Toxicology Program (NTP)[27] using a commercial formulation of Telone II with 1% epichlorohydrin added as stabilizer found, according to NTP criteria, clear evidence of carcinogenicity in male F344/N rats, as indicated by increased incidence of squamous cell papillomas and carcinomas of the forestomach. There was also clear evidence of carcinogenicity in female $B6C3F_1$ mice, as demonstrated by an increased incidence of transitional cell carcinomas of the urinary bladder. Additionally, it

found tha Telone II caused an increase in the incidences of alveolar/bronchiolar adenomas of the lung and of squamous cell papillomas or carcinomas of the forestomach in female mice.

For female F344/N rats, there was some evidence of carcinogenicity when an increase in the incidence of squamous cell papillomas of the forestomach was observed. Because of poor survival in the control group of male $B6C3F_1$ mice, it was concluded that the study was inadequate to confirm or deny evidence of carcinogenicity. There were Telone II-related non-neoplastic lesions found in the forestomach of male and female rats and in the urinary bladder of male and female mice.

While still subject to revision, a draft report of the NTP gavage study of 1,2-dichloropropane[28] did not show any evidence of carcinogenicity for male F344/N rats, while in female rats there was equivocal evidence of carcinogenicity as indicated by a marginal increase in the incidence of adenocarcinomas of the mammary gland in the 250 mg/kg dose group. These malignancies were considered "borderline," and occurred concurrent with decreased survival and reduced weight gain. Some evidence of carcinogenicity was shown for male and female $B6C3F_1$ mice as indicated by an increased incidence of hepatocellular adenomas.

Studies nearing completion at Dow Chemical Co. using high purity Telone II have preliminary results which indicate that the product is not carcinogenic by inhalation (the most likely route of exposure in occupational situations) at doses of 5, 20, or 60 ppm after 1-yr of 2-yr exposure to rats and mice. Preliminary gross histopathology is negative.[2] Elimination of epichlorohydrin from the technical preparation may obviate further testing.

Van Duuren[29] prognosticated that DCP or its metabolites may be carcinogenic based upon its structural similarities to known carcinogens such as vinyl chloride.

Human health effects. Seven of 10 volunteers detected the odor of 1 ppm of DCP, although some reported a fatiguing of olfactory sensitivity after several minutes exposure.[8] During 1976 and 1977, 26 cases of occupationally-related injuries and illnesses resulting from exposures to DCP were reported in California, according to Maddy et al.[30] Six were systemic injuries, 11 were eye injuries, 7 were dermal, and 2 involved both the eyes and the skin. Most were reported to be due to spills, faulty equipment, or worker carelessness, according to the author.

Substantial vapor concentrations caused by an overturned tank truck transporting Telone II caused headache, dizziness, mucous membrane irritation, gasping, coughing, respiratory distress, nausea, and vomiting among 80 persons reported to be in the vicinity of the spill.[31] Eleven of 41 people tested had a slightly elevated SGOT, SPGT, or both. Eight of those 11 were retested within 48-72 hr and 5 still had slightly elevated SGOT. Twenty-eight people were interviewed 1-2 wk later. Heavy exposure was significantly correlated with persistent symptoms.

Three incidents of occupational exposure to DCP were reported by Markovitz and Crosby.[32] In one instance, nine firefighters experienced headache, nausea, and difficulty breathing after attending to a spill due to a tank truck accident. Seven yr after the incident, two of the firefighters died of non-Hodgkin's lymphoma. Similarly, a farmer who fumigated with DCP, and was exposed due to leaky equipment, died of complications resulting from myelomonocytic leukemia.

Forty-four male employees engaged in the production of DCP were the subject of a study to assess their fertility status. It was estimated that their time-weighted average exposures to DCP over the previous 5 yr was less than 1 ppm. In all groups studied, no association could be established between their fertility status and exposure to either allyl chloride, epichlorohydrin, or DCP.[33]

DCP is a skin irritant and is capable of causing blisters or burns on unprotected skin after brief exposures. A case of contact dermatitis has been reported in the literature.[34]

Hazard summary

The evaluations of inhalation toxicity of DCP by Torkelson and Oyen[8] and Parker, Coate, and Voelker[10] do not indicate an extreme potential for acute adverse health effects. High concentrations likely to cause injury following an acute exposure would have a strong and objectionable odor, thus serving as a warning that the area should be avoided. Nevertheless, it is advised that approved organic vapor respiratory protection be employed whenever performing operations which vent to the atmosphere, bulk-transfer, or when entering any confined space which may contain DCP. Cartridge-type respirators will not serve in oxygen-deficient atmospheres or as protection in atmospheres above 1,000 ppm DCP.

Similarly, any cleanup of large-volume spills should include the wearing of respiratory protection and impervious suits and gloves. Absorption through intact skin is likely, and clothing should be removed at once in the event of a dousing. Skin should be washed for 15 min with soap and water. Contaminated clothing should be considered a fire hazard until cleaned or completely dry. Heavy thickness (3 + mil) polyethylene, rubber, and neoprene are recommended materials for protective clothing. While not requiring personal respiratory or skin protection, low level, chronic exposure by inhalation during manufacturing or field applications are of potential consequence. These situations should rely on monitoring of ambient levels to assess the potential for health hazards.[35]

Contact with the eyes must be prevented when handling the bulk liquid. If eye splash occurs, the worker should have the affected eyes irrigated immediately and for the ensuing 15 min. He should then be escorted to an emergency room for treatment.

Teratogenic or other data relative to adverse reproductive outcome among females apparently do not exist. No decrease in fertility was seen in a small cohort of male employees exposed to less than 1 ppm for 5 yr. Mutagenic hazards are not well-defined and perhaps require retesting. However, DCP has been determined to possess mutagenic activity in some screens. Carcinogenic activity by dermal exposure was negative. Gavage studies using technical-grade DCP/Telone II have demonstrated evidence of carcinogenicity in two species of animals. It

remains unclear whether or not pure DCP has carcinogenic potential. High purity formulations which do not contain epichlorohydrin should be evaluated. Telone II is now being evaluated for oncogenic potential by inhalation route of exposure.

* * * * * * * * * *

The author wishes to acknowledge the expert consideration provided by Sandra Susten, Ph.D., DSDTT, NIOSH, Cincinnati, Ohio.

Submitted for publication December 31, 1986; revised; accepted for publication May 11, 1987.

Requests for reprints should be sent to: William N. Albrecht, Ph.D., Hazard Evaluation and Technical Assistance Branch, U.S. Department of Health and Human Services, Centers for Disease Control, NIOSH, Robert A. Taft Laboratories R-10, 4676 Columbia Parkway, Cincinnati, OH 45226.

* * * * * * * * * *

References

1. Carter, W. 1943. A promising new soil amendment and disinfectant. *Science* 97: 383.
2. O'Melia, F. 1986. Personal communication. Midland, MI: Dow Chemical USA.
3. Martin, H. and Worthington, C.R., Eds. 1974. *Pesticide Manual,* 4th ed. London: British Crop Protection Council.
4. Castro, C.E. and Belser, N.O. 1966. Hydrolysis of *cis-* and *trans-*1,3-dichloropropene in wet soil. *J Agric Food Chem* 14: 69-70.
5. Roberts, T.R. and Stoydin, G. 1976. The degradation of (*Z*)-and (*E*)-1,3-dichloropropenes and 1,2-dichloropropane in soil. *Pestic Sci* 7: 325-35.
6. Thomson, I.J. and McKenry, M.V. 1973. Movement and fate (of 1,3-dichloropropene and 1,2-dibromoethane) as affected by various conditions in several soils. Part I. *Hallgardia* 42: 393-420.
7. van Dijk, H. 1980. Dissipation rates in soil of 1,2-dichloropropane and 1,3- and 2.3-dichloropropenes. *Pestic Sci* 11: 625-32.
8. Albrecht, W.N. and Chenchin, K. 1985. Dissipation of 1,2-dibromo-3-chloropropane (DBCP), *cis*-1,3-dichloropropene (1.3-DCP), and dichloropropenes from soil to atmosphere. *Bull Environ Contam Toxicol* 34: 824-31.
9. Torkelson, T.R. and Oyen, F. 1977. The toxicity of 1,3-dichloropropene as determined by repeated exposure of laboratory animals. *Am Ind Hyg Assoc J* 38: 217-23.
10. Torkelson, T.R. and Rowe, V.K. 1981. Halogenated aliphatic hydrocarbons. In *Patty's Industrial Hygiene and Toxicology,* G.D. Clayton and F.E. Clayton, Eds., 3rd ed. 2B: 3573-77. John Wiley and Sons, New York.
11. Parker, C.M.; Coate, W.B.; and Voelker, R.W. 1982. Subchronic inhalation toxicity of 1,3-dichloropropene/1,2-dichloropropane (D-D®) in mice and rats. *J Toxicol Environ Health* 9: 899-910.
12. Strusevich, E.A. and Ekshtat, B.Y. 1974. The effect of certain chlorinated hydrocarbons on the exocrine function of the pancreas. *Gig Sanit* 1: 94-96.
13. Kurysheva, N.G. and Ekshtat, B.Y. 1975. Effect of 1,3-dichloropropylene and 1,2-dichloropropane on the functional state of liver in animal experiments. *Uch Zap Mosk Nauchno-Issled Inst Gig* 22: 89-93.
14. Hutson, D.H.; Moss, J.; and Pickering, B. 1971. Excretion and retention of components of the soil fumigant D-D® and their metabolites in the rat. *Food Cosmet Toxicol* 9: 677-80.
15. Climie, I.; Hutson, D.H.; Morrison, B.; and Stoydin, G. 1979. Glutathione conjugation in the detoxication of (Z)-1,3-dichloropropene (a component of the nematocide D-D) in the rat. *Xenobiotica* 9: 149-56.
16. Osterloh, J.D.; Cohen, B.S.; Popendorf, W.; and Pond, S.M. 1984. Urinary excretion of the *N*-acetyl cysteine conjugate of *cis*-1,3-dichloropropene by exposed individuals. *Arch Environ Health* 39: 271-75.
17. Town, C. and Leibman, K.C. 1984. The *in vitro* dechlorination of some polychlorinated ethanes. *Drug Metab Dispos* 12: 4-8.
18. DiPaola, J.A. and Doniger, J. 1982. Neoplastic transformation of Syrian hamster cells by putative epoxide metabolites of commercially utilized chloroalkenes. *J Natl Cancer Inst* 69: 531-34.
19. Kilbey, B.J., Ed. 1984. *Handbook of Mutagenicity Test Procedures,* 2nd ed. Amsterdam: Elsevier Science Publishing Company.
20. DeLorenzo, F.; Degl'Innocenti, S.; Ruocco, A.; Silengo, L.; and Cortese, R. 1977. Mutagenicity of pesticides containing 1,3-dichloropropene. *Cancer Res* 37: 1915-17.
21. Neudecker, T.; Stefani, A.; and Henschler, D. 1977. *In vitro* mutagenicity of the soil nematocide, 1,3-dichloropropene. *Experientia* 33: 1084-85.
22. Stolzenberg, S.J. and Hine, C.H. 1980. Mutagenicity of 2- and 3-carbon halogenated compounds in the Salmonella/mammalian-microsome test. *Environ Mutagen* 2: 59-66.
23. Tomkins, D.; Kwok, E.; and Douglas, G. 1980. Testing of pesticides for induction of sister chromatid exchange in Chinese hamster ovary cells. *Can J Genet Cytol* 22: 681.
24. Talcott, R.E. and King, J. 1984. Mutagenic impurities in 1,3-dichloropropene preparations. *J Natl Cancer Inst* 72: 1113-16.
25. Watson, W.P.; Brooks, T.M.; Huckle, K.R.; Hutson, D.H.; Lang, K.L.; Smith, R.J.; and Wright, A.S. 1987. Microbial mutagenicity studies with (z)-1,3-dichloropropene. *Chem Biol Interact* 61: 17-30.
26. Van Duuren, B.L.; Goldschmidt, B.M.; Loewengart, G.; Smith, A.C.; Melchionne, S.; Seidman, I.; and Roth, D. 1979. Carcinogenicity of halogenated olefinic and aliphatic hydorcarbons in mice. *J Natl Cancer Inst* 63: 1433-39.
27. National Toxicology Program. 1985. Technical report series No. 269. Toxicology and carcinogenesis studies of Telone®II (technical-grade 1,3-dichloropropene [CAS No. 542-75-6] containing 1% epichlorohydrin as a stabilizer) in F344/N rats and B6C3F$_1$ mice (gavage studies). U.S. Dept Health and Human Services.
28. National Toxicology Program. 1986. Draft technical report no. 263-Carcinogenesis studies of 1,2-dichloropropane in F344/N rats and B6C3F$_1$ mice. U.S. Dept. Health and Human Services.
29. Van Duuren, B.L. 1977. Chemical structure, reactivity, and carcinogenicity of halohydrocarbons. *Environ Health Perspect* 21: 17-23.
30. Maddy, K.T. and Edmiston, S 1978. *Occupational Illnesses and Injuries Due to Pesticides Containing 1,3-Dichloropropene as Reported by Physicians in California in 1976 and 1977.* [Report prepared by California Department of Food and Agriculture, Division of Pest Management, Environmental Protection and Worker Safety, Sacramento, California, ACF 59-479].
31. Flessl, P.; Goldsmith, J.; Kahn, E.; Wesolowski, J.; Maddy, K.; and Peoples, S. 1978. Acute and possible long-term effects of 1,3-dichloropropene-California. *Morbid Mortal Weekly Report* 27: 50,55.
32. Markovitz, A. and Crosby, W.H. 1984. A soil fumigant, 1,3-dichloropropene, as a possible cause of hematologic malignancies. *Arch Intern Med* 144: 1409-11.
33. Venable, J.R.; McClimans, C.D.; Flake, R.E.; and Dimick, D.B. 1980. A fertility study of employees engaged in the manufacture of glycerine. *J Occup Med* 22: 87-91.
34. Nater, J.P. and Gooskens, V.H.J. 1976. Occupational dermatosis due to a soil fumigant. *Contact Derm* 2: 4-6.
35. Anonymous. 1985. Telone® Products Safety Guide. Midland, MI: Dow Chemical U.S.A.