



National Toxicology Program

Toxicity Report Series

Number 55

**NTP Technical Report
on the Toxicity Studies of**

***trans*-1,2-Dichloroethylene**

(CAS No. 156-60-5)

**Administered in Microcapsules in Feed
to F344/N Rats and B6C3F₁ Mice**

April 2002

U.S. Department of Health and Human Services

Public Health Service

National Institutes of Health

FOREWORD

The National Toxicology Program (NTP) is made up of four charter agencies of the U.S. Department of Health and Human Services (DHHS): the National Cancer Institute (NCI), National Institutes of Health; the National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health; the National Center for Toxicological Research (NCTR), Food and Drug Administration; and the National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention. In July 1981, the Carcinogenesis Bioassay Testing Program, NCI, was transferred to the NIEHS. The NTP coordinates the relevant programs, staff, and resources from these Public Health Service agencies relating to basic and applied research and to biological assay development and validation.

The NTP develops, evaluates, and disseminates scientific information about potentially toxic and hazardous chemicals. This knowledge is used for protecting the health of the American people and for the primary prevention of disease.

The studies described in this Toxicity Study Report were performed under the direction of the NIEHS and were conducted in compliance with NTP laboratory health and safety requirements and must meet or exceed all applicable federal, state, and local health and safety regulations. Animal care and use were in accordance with the Public Health Service Policy on Humane Care and Use of Animals.

These studies are designed and conducted to characterize and evaluate the toxicologic potential of selected chemicals in laboratory animals (usually two species, rats and mice). Chemicals selected for NTP toxicology studies are chosen primarily on the bases of human exposure, level of production, and chemical structure. The interpretive conclusions presented in this Toxicity Study Report are based only on the results of these NTP studies. Extrapolation of these results to other species and quantitative risk analyses for humans require wider analyses beyond the purview of these studies. Selection *per se* is not an indicator of a chemical's toxic potential.

Details about ongoing and completed NTP studies are available at the NTP's World Wide Web site: <http://ntp-server.niehs.nih.gov>. Abstracts of all NTP Toxicity Study Reports and full versions of the most recent reports and other publications are available from the NIEHS' Environmental Health Information Service (EHIS) <http://ehis.niehs.nih.gov> (800-315-3010 or 919-541-3841). In addition, printed copies of these reports are available from EHIS as supplies last.

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**U.S. Department of Health and Human Services
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National Institutes of Health**

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PEER REVIEW

The draft report on the toxicity studies of *trans*-1,2-dichloroethylene was evaluated by the reviewers listed below. These reviewers serve as independent scientists, not as representatives of any institution, company, or governmental agency. In this capacity, reviewers determine if the design and conditions of these NTP studies are appropriate and ensure that the Toxicity Study Report presents the experimental results and conclusions fully and clearly.

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SUMMARY

Background: 1,2-Dichloroethylene is used as a solvent for waxes and resins, in the extraction of rubber, as a refrigerant, and in the manufacture of artificial pearls. More than 1 million pounds are used annually in the United States. The chemical exists in two isomeric states, *cis* and *trans*; the *trans* isomer is used more widely in industry, and thus we tested that form.

Methods: Because 1,2-dichloroethylene is both volatile and insoluble in water, we prepared starch microcapsules containing the chemical and mixed them into the feed of rats and mice to test the toxicity of the chemical. For every dose group, 5% of the feed mixture consisted of starch microcapsules; the doses of *trans*-1,2-dichloroethylene ranged from 1,470 to 23,500 ppm. The highest doses were approximately 3,200 mg/kg body weight for rats and approximately 8,000 mg/kg for mice.

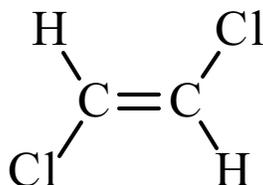
Results: Male rats and male and female mice receiving the highest concentrations of *trans*-1,2-dichloroethylene weighed less than the control animals. Liver weights of exposed female rats were greater than those of the control animals, and kidney weights of exposed rats were decreased. However, no lesions associated with the chemical were observed in the exposed rats or mice. *trans*-1,2-Dichloroethylene was not mutagenic in any of the genetic toxicity tests performed.

Conclusion: Very little toxicity was associated with ingestion of microencapsulated *trans*-1,2-dichloroethylene by rats or mice. The animals could have tolerated even higher doses than those used in this study with no adverse effects.

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ABSTRACT



trans-1,2-DICHLOROETHYLENE

CAS Number: 156-60-5

Chemical Formula: C₂H₂Cl₂ Molecular Weight: 96.95

Synonyms: *trans*-Acetylene dichloride; (E)-1,2-dichloroethene; (E)-(9Cl)-1,2-dichloroethene; *trans*-1,2-dichloroethene; (E)-1,2-dichloroethylene; *trans*-dichloroethylene

1,2-Dichloroethylene exists in two isomeric states: *trans*-1,2-dichloroethylene and *cis*-1,2-dichloroethylene. The *trans* isomer is used more widely in industry than the *cis* isomer. *trans*-1,2-Dichloroethylene is used as a solvent for waxes, resins, and acetylcellulose. It is also used in the extraction of rubber, as a refrigerant, and in the manufacture of pharmaceuticals and artificial pearls. F344/N rats and B6C3F₁ mice were administered *trans*-1,2-dichloroethylene in microcapsules in feed for 14 weeks. Animals were evaluated for clinical pathology, reproductive system effects, and histopathology. Genetic toxicity studies were conducted *in vitro* in *Salmonella typhimurium* and Chinese hamster ovary (CHO) cells, and *in vivo* in mouse bone marrow cells and peripheral blood erythrocytes.

In the 14-week feed studies, groups of 10 male and 10 female rats and mice were fed diets containing microcapsules with a chemical load of 45% *trans*-1,2-dichloroethylene. Dietary concentrations of 3,125, 6,250, 12,500, 25,000, and 50,000 ppm microencapsulated *trans*-1,2-dichloroethylene resulted in average daily doses of 190, 380, 770, 1,540, and 3,210 mg/kg for male rats; 190, 395, 780, 1,580, and 3,245 mg/kg for female rats; 480, 920, 1,900, 3,850, and 8,065 mg/kg for male mice; and 450, 915, 1,830, 3,760, and 7,925 mg/kg for female mice. Additional groups of 10 male and 10 female rats and mice served as untreated and vehicle controls. There were no exposure-related deaths of rats or mice. Mean body weights of male rats and male and female mice in the 50,000 ppm groups were

significantly less than those of the vehicle controls. The mean body weight gains of female mice in the 12,500 and 25,000 ppm groups were also significantly less than that of the vehicle controls.

On day 21 and at week 14, there were mild decreases in hematocrit values, hemoglobin concentrations, and erythrocyte counts in groups of male and female rats in the 25,000 and 50,000 ppm groups. At week 14, these effects were seen in male rats exposed to 6,250 and 12,500 ppm. There were no exposure-related alterations in clinical chemistry parameters in rats or mice.

The liver weights of female rats exposed to 6,250 ppm or greater were significantly greater than those of the vehicle controls. The absolute kidney weights of male rats exposed to 25,000 or 50,000 ppm were significantly decreased. No gross or microscopic lesions were observed in rats or mice that could be attributed to *trans*-1,2-dichloroethylene exposure.

Neither *cis*-, *trans*-, nor *cis,trans*-1,2-dichloroethylene was mutagenic in *S. typhimurium* strain TA97 (*cis* isomer only), TA98, TA100, TA1535, or TA1537, with or without S9 metabolic activation enzymes. In CHO cells *in vitro*, *cis*-1,2-dichloroethylene induced sister chromatid exchanges (SCEs) in the absence of S9; with S9, the single trial that was performed yielded equivocal results. The *cis,trans* isomer induced significant increases in SCEs in cultured CHO cells with and without S9. In contrast to these positive results, *trans*-1,2-dichloroethylene gave negative results in the SCE test, with and without S9. Neither *cis*-, *trans*-, nor *cis,trans*-1,2-dichloroethylene induced chromosomal aberrations (Abs) in cultured CHO cells, with or without S9. *In vivo*, no induction of SCEs or Abs was noted in bone marrow cells of male mice administered *cis*- or *trans*-1,2-dichloroethylene by intraperitoneal injection once, with sampling performed 23 hours (for SCE analyses) or 17 hours (for Abs analyses) after injection. In addition, negative results were obtained in a peripheral blood micronucleus test in male and female mice administered *trans*-1,2-dichloroethylene in microcapsules in feed for 14 weeks.

Very little toxicity was associated with ingestion of microencapsulated *trans*-1,2-dichloroethylene. Histopathology and clinical chemistry data, combined with body and organ weight data, revealed that the maximum tolerated dose was not reached in these studies.