NATIONAL TOXICOLOGY PROGRAM
Technical Report Series
No. 275

TOXICOLOGY AND CARCINOGENESIS STUDIES OF 2-CHLOROETHANOL (ETHYLENE CHLOROHYDRIN) (CAS NO. 107-07-3) IN F344/N RATS AND SWISS CD-1 MICE (DERMAL STUDIES)

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health

NATIONAL TOXICOLOGY PROGRAM

The National Toxicology Program (NTP), established in 1978, develops and evaluates scientific information about potentially toxic and hazardous chemicals. This knowledge can be used for protecting the health of the American people and for the primary prevention of disease. By bringing together the relevant programs, staff, and resources from the U.S. Public Health Service, DHHS, the National Toxicology Program has centralized and strengthened activities relating to toxicology research, testing and test development/validation efforts, and the dissemination of toxicological information to the public and scientific communities and to the research and regulatory agencies.

The NTP is made up of four charter DHHS agencies: 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. In July 1981, the Carcinogenesis Bioassay Testing Program, NCI, was transferred to the NIEHS.

NTP TECHNICAL REPORT

ON THE

TOXICOLOGY AND CARCINOGENESIS STUDIES OF 2-CHLOROETHANOL (ETHYLENE CHLOROHYDRIN)

(CAS NO. 107-07-3)

IN F344/N RATS AND SWISS CD-1 MICE

(DERMAL STUDIES)

NATIONAL TOXICOLOGY PROGRAM
P.O. Box 12233
Research Triangle Park, NC 27709

November 1985

NTP TR 275

NIH Publication No. 86-2531

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health

NOTE TO THE READER

These studies are designed and conducted to characterize and evaluate the toxicologic potential, including carcinogenic activity, of selected chemicals in laboratory animals (usually two species, rats and mice). Chemicals selected for testing in the NTP Carcinogenesis Program are chosen primarily on the bases of human exposure, level of production, and chemical structure. Selection per se is not an indicator of a chemical's carcinogenic potential. Negative results, in which the test animals do not have a greater incidence of cancer than control animals, do not necessarily mean that a test chemical is not a carcinogen, inasmuch as the experiments are conducted under a limited set of conditions. Positive results demonstrate that a test chemical is carcinogenic for animals under the conditions of the test and indicate that exposure to the chemical has the potential for hazard to humans. The determination of the risk to humans from chemicals found to be carcinogenic in animals requires a wider analysis which extends beyond the purview of this study.

Five categories of interpretative conclusions were adopted in June 1983 for use in the Technical Reports series to specifically emphasize consistency and the concept of actual evidence of carcinogenicity. For each definitive study result (male rats, female rats, male mice, female mice), one of the following quintet will be selected to describe the findings. These categories refer to the strength of the experimental evidence and not to either potency or mechanism.

- **Clear Evidence of Carcinogenicity** is demonstrated by studies that are interpreted as showing a chemically related increased incidence of malignant neoplasms, studies that exhibit a substantially increased incidence of benign neoplasms, or studies that exhibit an increased incidence of a combination of malignant and benign neoplasms where each increases with dose.
- **Some Evidence of Carcinogenicity** is demonstrated by studies that are interpreted as showing a chemically related increased incidence of benign neoplasms, studies that exhibit marginal increases in neoplasms of several organs/tissues, or studies that exhibit a slight increase in uncommon malignant or benign neoplasms.
- **Equivocal Evidence of Carcinogenicity** is demonstrated by studies that are interpreted as showing a chemically related marginal increase of neoplasms.
- **No Evidence of Carcinogenicity** is demonstrated by studies that are interpreted as showing no chemically related increases in malignant or benign neoplasms.
- **Inadequate Study of Carcinogenicity** demonstrates that because of major qualitative or quantitative limitations, the studies cannot be interpreted as valid for showing either the presence or absence of a carcinogenic effect.

Additionally, the following concepts (as patterned from the International Agency for Research on Cancer Monographs) have been adopted by the NTP to give further clarification of these issues:

> The term *chemical carcinogenesis* generally means the induction by chemicals of neoplasms not usually observed, the earlier induction by chemicals of neoplasms that are commonly observed, or the induction by chemicals of more neoplasms than are generally found. Different mechanisms may be involved in these situations. Etymologically, the term *carcinogenesis* means induction of cancer, that is, of malignant neoplasms; however, the commonly accepted meaning is the induction of various types of neoplasms or of a combination of malignant and benign neoplasms. In the Technical Reports, the words *tumor* and *neoplasm* are used interchangeably.

This study was initiated by the National Cancer Institute's Carcinogenesis Bioassay Program, now part of the National Institute of Environmental Health Sciences, National Toxicology Program. The studies described in this Technical Report have been conducted in compliance with NTP chemical health and safety requirements and must meet or exceed all applicable Federal, state, and local health and safety regulations. All NTP toxicology and carcinogenesis studies are subjected to a data audit before being presented for peer review.

Although every effort is made to prepare the Technical Reports as accurately as possible, mistakes may occur. Readers are requested to identify any mistakes so that corrective action may be taken. Further, anyone who is aware of related ongoing or published studies not mentioned in this report is encouraged to make this information known to the NTP. Comments and questions about the National Toxicology Program Technical Reports on Toxicology and Carcinogenesis Studies should be directed to Dr. J.E. Huff, National Toxicology Program, P.O. Box 12233, Research Triangle Park, NC 27709 (919-541-3780).

These NTP Technical Reports are available for sale from the National Technical Information Service, U.S. Department of Commerce, 5285 Port Royal Road, Springfield, VA 22161 (703-487-4650). Single copies of this Technical Report are available without charge (and while supplies last) from the NTP Public Information Office, National Toxicology Program, P.O. Box 12233, Research Triangle Park, NC 27709.

CONTENTS

CONTENTS (Continued)

TABLES

TABLES (Continued)

FIGURES

APPENDIXES

APPENDIXES (Continued)

APPENDIXES (Continued)

$Cl-CH_2-CH_2-OH$
2-CHLOROETHANOL

CAS NO. 107-07-3

Synonyms: Ethylene Chlorohydrin; Chloroethanol; Glycol Chlorohydrin; β-Chloroethanol

C_2H_5ClO Molecular Weight: 80.51

ABSTRACT

Toxicology and carcinogenesis studies of 2-chloroethanol (99% pure), an industrial chemical and an intermediate in the synthesis of ethylene oxide, were conducted by dermal application of 2-chloroethanol dissolved in 70% ethanol:30% water (v/v) solutions to groups of 50 F344/N rats of each sex at doses of 0, 50, or 100 mg/kg for 103 weeks or to groups of 50 Swiss CD-1 mice of each sex at doses of 0, 7.5, or 15 mg per animal for 104 weeks (0, 253, or 630 mg/kg at week 1; 0, 180, or 411 mg/kg at week 100). The control groups received skin applications of the vehicle; the mouse studies also included untreated control groups of 50 males and 50 females.

2-Chloroethanol solutions were applied to the clipped interscapular area of the animals once daily, 5 days per week for the test period. Rats received a volume of 0.18-0.22 ml of solution; mice received 0.10 ml of solution. In the 13-week studies, mortality was observed in male and female rats receiving 250 mg/kg per day and higher and in male and female mice receiving 20 mg per day and higher. In the 104-week studies, the survival and body weights of dosed rats were unaffected by 2-chloroethanol. The survival of high dose male mice was lower ($P < 0.05$) than that of the vehicle controls (vehicle control, 26/50; 7.5 mg, 16/50; 15 mg, 12/50). Body weights of dosed mice were unaffected by 2-chloroethanol. The survival and body weight gain data suggest that the male and female rats and female mice could have tolerated a higher dose of 2-chloroethanol. Male mice probably could not have tolerated a higher dose than was applied to the skin. Seven high dose male mice died within 3 days of the start of dosing; all of these had inflammation at the site of dermal application. Five also had ulceration at the site of dermal application, and five had lung congestion, inflammation, or hemorrhage.

Marginal increases were found in the incidence of lymphomas or leukemias (combined) as well as in the incidence of alveolar/bronchiolar adenomas or carcinomas (combined) in low dose male mice. Since there was no dose-related trend for these tumor incidences and because the increases were observed in only one sex, the increases were not considered to be related to the dermal application of 2-chloroethanol.

2-Chloroethanol was mutagenic in *Salmonella typhimurium* strains TA100 and TA1535 (but not TA1537 or TA98) in either the presence or the absence of Aroclor 1254-induced male Sprague-Dawley rat or Syrian hamster liver S9. 2-Chloroethanol did not induce sex-linked recessive lethal mutations in *Drosophila melanogaster*.

An audit of the experimental data was conducted for these 2-year studies. No data discrepancies were found that influenced the final interpretations.

Under the conditions of these 2-year dermal studies, there was *no evidence of carcinogenicity** of 2-chloroethanol for male and female F344/N rats given 50 or 100 mg/kg per day or for male and female Swiss CD-1 mice given 7.5 or 15 mg per animal per day.

*Categories of evidence of carcinogenicity are defined in the Note to the Reader on page 2.

CONTRIBUTORS

The NTP Technical Report on the Toxicology and Carcinogenesis Studies of 2-Chloroethanol is based on the 13-week studies in rats which began in January 1978 and ended in April 1978, the 13-week studies in mice which began in June 1977 and ended in September 1977, and the 2-year studies that began in January 1980 and ended in January 1982 at Litton Bionetics, Inc.

National Toxicology Program
(Evaluated Experiment, Interpreted Results, and Reported Findings)

Dexter S. Goldman, Ph.D.,* Chemical Manager

Gary A. Boorman, D.V.M., Ph.D.
Rajendra S. Chhabra, Ph.D.
David M. DeMarini, Ph.D.
Joseph K. Haseman, Ph.D.
James Huff, Ph.D.
C.W. Jameson, Ph.D.
E.E. McConnell, D.V.M.
G.N. Rao, D.V.M., Ph.D.
Bernard A. Schwetz, D.V.M., Ph.D.
Raymond W. Tennant, Ph.D.

NTP Pathology Working Group
(Evaluated Slides and Prepared Pathology Report on 10/26/82)

Scot L. Eustis, D.V.M., Ph.D. (Chair)
NTP
Gary A. Boorman, D.V.M., Ph.D.
NTP
Paul K. Hildebrandt, D.V.M.
Tracor Jitco, Inc.
Hendricus A. Solleveld, D.V.M., Ph.D.
NTP

Principal Contributors at Litton Bionetics, Inc.
(Conducted Studies and Evaluated Tissues)

Richard H. Cardy, D.V.M.
Pathologist (Rat Studies)
Jerry Fitzgerald, Ph.D.
Chemist
Carter D. Johnson, Ph.D.
Principal Investigator
Alan G. Manus, D.V.M.
Principal Investigator
James Moe, D.V.M., Ph.D.
Pathologist (Mouse Studies)

Principal Contributors at Experimental Pathology Laboratory
(Provided Pathology Quality Assurance)

Deborah A. Banas, D.V.M.

Principal Contributors at Carltech Associates, Inc.
(Contractor for Technical Report Preparation)

William D. Theriault, Ph.D.
Project Manager
Abigail C. Jacobs, Ph.D.
Senior Scientist
John Warner, M.S.
Chemist/Statistician

---

*Present address: Office of Compliance Monitoring (EN342), U.S. Environmental Protection Agency, Washington, DC 20460

PEER REVIEW PANEL

The members of the Peer Review Panel who evaluated the draft Technical Report on 2-chloroethanol on July 27, 1984, are listed below. Panel members serve as independent scientists, not as representatives of any institution, company, or governmental agency. In this capacity, Panel members have five major responsibilities: (a) to ascertain that all relevant literature data have been adequately cited and interpreted, (b) to determine if the design and conditions of the NTP studies were appropriate, (c) to ensure that the Technical Report presents the experimental results and conclusions fully and clearly, (d) to judge the significance of the experimental results by scientific criteria, and (e) to assess the evaluation of the evidence of carcinogenicity and other observed toxic responses.

National Toxicology Program Board of Scientific Counselors
Technical Reports Review Subcommittee

Jerry B. Hook, Ph.D. (Chair)*
Vice President, Preclinical Research and Development
Smith Kline & French Laboratories
Philadelphia, Pennsylvania

Curtis Harper, Ph.D. (Acting Chair)
Associate Professor of Pharmacology
School of Medicine
University of North Carolina
Chapel Hill, North Carolina

James Swenberg, D.V.M., Ph.D.*
Chief of Pathology
Chemical Industry Institute of Toxicology
Research Triangle Park, North Carolina

Ad Hoc Subcommittee Panel of Experts

Louis S. Beliczky, M.S., M.P.H. (Principal Reviewer)
Director, Department of Industrial Hygiene
United Rubber Workers International Union
Akron, Ohio

Devra L. Davis, Ph.D.
Board on Toxicology and Environmental Health Hazards
National Academy of Sciences
Washington, D.C.

Seymour L. Friess, Ph.D.
Arlington, Virginia

Thomas C. Jones, D.V.M.
Professor, Comparative Pathology
New England Regional Primate Research Center
Harvard Medical School
Southborough, Massachusetts

Richard J. Kociba, D.V. M., Ph.D.
(Principal Reviewer)
Dow Chemical USA
Midland, Michigan

David Kotelchuck, Ph.D. (Principal Reviewer)
Research Department
United Electrical, Radio and Machine Workers of America
New York, New York

Tom Slaga, Ph.D.*
Science Park, Research Division
University of Texas System Cancer Center
Smithville, Texas

Steven R. Tannenbaum, Ph.D.
Professor, Department of Nutrition and Food Science
Massachusetts Institute of Technology
Cambridge, Massachusetts

Bruce W. Turnbull, Ph.D.
Professor and Associate Director
College of Engineering
Cornell University
Ithaca, New York

John R. Van Ryzin, Ph.D.
Division of Biostatistics
School of Public Health
Columbia University
New York, New York

*Unable to attend meeting

SUMMARY OF PEER REVIEW COMMENTS ON THE TOXICOLOGY AND CARCINOGENESIS STUDIES OF 2-CHLOROETHANOL

On July 27, 1984, the draft Technical Report on the toxicology and carcinogenesis studies of 2-chloroethanol received peer review by the National Toxicology Program Board of Scientific Counselors' Technical Reports Review Subcommittee and associated Panel of Experts. The review meeting began at 9:00 a.m. in the Conference Center, Building 101, South Campus, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina.

Mr. Beliczky, a principal reviewer, agreed with the conclusions. He commented that for this chemical the inhalation or gavage route of exposure may have been more appropriate, since inhalation would be the primary expected route of exposure in the industrial setting. Dermal application would be more meaningful if the degree of absorption and metabolism could be be better characterized. Dr. D. Goldman, NTP, stated that workers are exposed dermally. Mr. Beliczky added that examining urine from workers exposed to 2-chloroethanol may have practical value.

As a second principal reviewer, Dr. Kociba agreed with the conclusions. He commented on the apparent dose-related incidence of acute inflammation and ulceration of the skin in male mice and said that this incidence may have a possible relationship in the high dose group to 2-chloroethanol application. He also asked that the data for pancreatic acinar cell atrophy in male rats be evaluated to determine whether any degenerative change in the pancreatic acini during the 2-year study was compound related. [See p. 59.]

As a third principal reviewer, Dr. Kotelchuck did not fully agree with the conclusion for female rats. He believed that there was equivocal evidence of carcinogenicity of 2-chloroethanol for adenomas of the pituitary gland in female rats for the following reasons: (1) the differences between high dose and vehicle control groups were significant by the life table and Fisher exact tests; (2) two of the three trend tests showed a statistically significant increase; (3) in an earlier study by Mason and coworkers, the incidence of adenomas of the pituitary gland in female F344 rats exposed to 2-chloroethanol was increased; and (4) it is biologically plausible for there to be a sex-influenced effect of this chemical on an endocrine gland (the incidence in male rats was not increased). Dr. Kotelchuck proposed modifying the conclusions to reflect the marginal increase in adenomas of the pituitary gland in female rats.

Dr. J. Haseman, NIEHS, noted that for adenomas of the pituitary gland the appropriateness of the life table test instead of the incidental tumor test, which was not statistically significant, depends on whether the eight tumors occurring in the high dose group before the end of the study were related to the cause of death. Dr. E. McConnell, NTP, said that tumors of the pituitary gland are not generally thought of as being lethal. Dr. Kociba commented that there is a continuum of lesions in the pituitary gland from hyperplasias through adenomas to carcinomas. Dr. G. Boorman, NTP, agreed and said that other factors used to downgrade the importance of the adenomas in this study were that no increases were seen for hyperplasias and there was a decrease in the incidences of carcinomas of the pituitary gland from vehicle control to dosed groups. Dr. J. Huff, NTP, added that the findings in the study by Mason and coworkers were of borderline significance and that the incidences from different dose groups had to be combined to show an increase.

Dr. Harper asked for a vote on the conclusion of equivocal evidence of carcinogenicity for describing the marginal increase of adenomas of the pituitary gland in female rats. There was one affirmative vote. Dr. Kociba moved that the Technical Report on the toxicology and carcinogenesis studies of 2-chloroethanol be accepted with the conclusions as written. Dr. Friess seconded the motion, and the Technical Report was approved unanimously by the Peer Review Panel.

I. INTRODUCTION

$Cl–CH_2–CH_2–OH$
2-CHLOROETHANOL

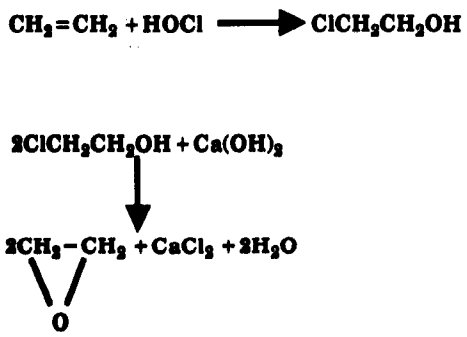
CAS NO. 107-07-3

Synonyms: Ethylene Chlorohydrin; Chloroethanol; Glycol Chlorohydrin; β-Chloroethanol

C_2H_5ClO Molecular Weight: 80.51

Use and Production

2-Chloroethanol is an intermediate in the synthesis of ethylene oxide and ethylene glycol and in the production of indigo, dichloroethyl formal (an intermediate for the production of polysulfide elastomers), and thiodiethylene glycol (used in textile printing); it is also an industrial solvent, a pre-emergent plant growth stimulator, an extractant in the dewaxing of mineral oil, and an antioxidant for textile printing dyes. The principal use of 2-chloroethanol was formerly in the production of ethylene oxide (Schultze, 1965). In this procedure, 2-chloroethanol is produced by reacting ethylene with hypochlorous acid; the 2-chloroethanol is dehydrochlorinated with slaked lime to form ethylene oxide:



2-Chloroethanol is an intermediate and is not isolated in this process. Before 1972, as much as 500 million pounds of ethylene oxide was prepared annually from 1,000 million pounds of 2-chloroethanol by this process (Blackford, 1976). Current production of ethylene oxide does not use this procedure. 2-Chloroethanol is no longer produced commercially in the United States (Riesser, 1979). 2-Chloroethanol is also prepared by reacting ethylene oxide with chloride ion or, commercially, with hydrochloric acid or magnesium chloride (Blackford, 1976).

Environmental Occurrence

The principal sources of 2-chloroethanol emissions are probably liquid wastes and still residues from manufacturing plants. 2-Chloroethanol poses no shipping hazards other than those caused by accidental spills or tank ruptures. The magnitude of vapor losses during transfer from transport to storage containers is unknown.

Toxicity

2-Chloroethanol is toxic when administered to laboratory animals at the concentrations and by the routes shown in Table 1. 2-Chloroethanol is highly irritating to mucous membranes but produces little if any reaction upon contact with rabbit skin. It is not a sensitizer in the guinea pig test. Toxic amounts can be absorbed through the skin without causing dermal irritation (Gleason et al., 1969). Toxic reactions in humans exposed to 2-chloroethanol dermally or by inhalation were first reported by Koelsch (1927). Human fatalities have resulted from ingestion, inhalation, or dermal contact with 2-chloroethanol (Goldblatt and Chiesman, 1944; Bush et al., 1949; Ballotta et al., 1953; Saitanov and Konanova, 1976). In all cases, neurotoxic symptoms were described. Death was attributed to cardiac and respiratory collapse.

Guess (1970), in a study of the response of rabbit tissues, showed that mucosal tissue was more sensitive to 2-chloroethanol than to ethanol; edema and erythema were produced by both. Of particular interest in this study were tissues that might come in contact with ethylene oxide-sterilized plastic devices used in medical or

TABLE 1. ACUTE TOXICITY OF 2-CHLOROETHANOL

Species	Strain	Route	LD_{50}/LC_{50}	Reference
Mouse		Inhalation	117 ppm	NIOSH (1975)
Mouse		Intraperitoneal	81 mg/kg	NIOSH (1975)
Mouse	Swiss	Intraperitoneal	98.3 mg/kg	Lawrence et al. (1971)
Mouse	Swiss	Oral	81 mg/kg	Lawrence et al. (1971)
Rat		Subcutaneous	84 mg/kg	NIOSH (1975)
Rat		Inhalation	32 ppm	Carpenter et al. (1949)
Rat	Sprague-Dawley	Intraperitoneal	64 mg/kg	Lawrence et al. (1971)
Guinea pig		Dermal	285 mg/kg	Wahlberg and Boman (1978)
Guinea pig	Huntley	Intraperitoneal	86 mg/kg	Lawrence et al. (1971)
Guinea pig		Inhalation	918 ppm	NIOSH (1977)
Rabbit	New Zealand	Intraperitoneal	85 mg/kg	Lawrence et al. (1971)
Rabbit	New Zealand	Dermal	68 mg/kg	Lawrence et al. (1971)

surgical procedures, devices that might contain residues of 2-chloroethanol. On intracutaneous administration, 2-chloroethanol was more toxic than ethanol; a 1:10 dilution caused hemorrhagic reactions within 15 minutes, and affected areas became necrotic within 24 hours. Histologic examination showed localized edema, cellular destruction, and infiltration by polymorphonuclear leukocytes and lymphocytes. Kronevi et al. (1979) studied the effects of several industrial solvents on the skin of guinea pigs. Exposure of guinea pig skin to 2-chloroethanol produced pyknosis of the basal cell nuclei; severity progressively increased and all epidermal layers were affected. Perinuclear edema was progressive, and cytoplasmic vacuolization occurred after 16 hours' exposure. The livers of animals administered 2-chloroethanol showed centrilobular hydropic changes characterized by large, clear spaces in the cytoplasm. Similar but less severe skin changes were induced by carbon tetrachloride, hexane, or toluene.

Chronic Toxicity and Carcinogenicity

Homburger (1968) studied the effects of 2-chloroethanol on the incidence of alveolar/bronchiolar adenomas in female CF_1 mice; a single intravenous dose of 1.2 mg 2-chloroethanol had no effect on the incidence of these tumors over a 12-month period. When the same dose was administered once per month for 7 months, the incidence of adenomas was increased in dosed animals (control, 2/18; dosed, 5/18).

Oral administration of 2-chloroethanol (0.01%-1.28% in the diet) to rats produced toxic effects at low doses (0.12%) and fatalities at higher doses (0.32% and higher) (Ambrose, 1950). 2-Chloroethanol was fatal to rats by inhalation (two 1-hour exposures at 4 ppm, exposures separated by a 2-hour interval), to rats by dermal application (0.12 ml per animal), to rabbits by dermal application (three applications of 0.5 ml per animal) (Ambrose, 1950; Strusevich and Ekshtat, 1973), and to FDRL rats by gavage (67.5 mg/kg per day for 21 days) (Oser et al., 1975).

Mason et al. (1971) found an increased incidence of pituitary gland adenomas in female F344 rats dosed with 2-chloroethanol. The dosed rats received subcutaneous injections of 2-chloroethanol (in saline) at levels of 0.3-10 mg/kg two times per week for 52 weeks followed by observation for an additional 26 weeks. The reported incidence of pituitary gland adenomas in the dosed female rats (all dose groups combined) was 7/100; the control rate was 1/50.

2-Chloroethanol and 2-bromoethanol were not found to be carcinogenic when administered by subcutaneous injection to female NMRI mice for approximately 70 weeks at doses of 0.3, 1.0, or 3.0 mg per week (Dunkelberg, 1983).

Genetic Toxicology

The genetic toxicity of 2-chloroethanol has been investigated in a wide variety of short-term

studies, and the results are summarized in Table 2. 2-Chloroethanol is a weak base-pair substitution mutagen in bacteria but is essentially negative in a variety of other systems, including fungi, Drosophila, mammalian cell cultures, and rodents. Of 17 studies in Salmonella, 14 show that 2-chloroethanol is a direct-acting base-pair substitution mutagen in *Salmonella typhimurium* strains TA1530, TA1535, and TA100 (Rosenkranz et al., 1974; Rosenkranz and Wlodkowski, 1974; Bartsch et al., 1975; Malaveille et al., 1975; McCann et al., 1975; Rannug et al., 1976; Lofroth, 1978; Nakamura et al., 1979; Rannug and Beije, 1979; Bignami et al., 1980a,b; Pfeiffer and Dunkelberg, 1980; Stolzenberg and Hine, 1980; NTP, Appendix F). Confirmatory results have been obtained in other bacteria, including *Klebsiella pneumoniae* (Voogd and van der Vet, 1969; Voogd et al., 1972; Voogd, 1973) and *Escherichia coli* (Norpoth et al., 1980); however, this chemical was negative in the bacterium *Streptomyces coelicolor* (Bignami et al., 1980a,b). The addition of rat liver S9 enhanced the mutagenicity of 2-chloroethanol in Salmonella, suggesting that 2-chloroethanol is metabolized to an additional mutagenic form.

2-Chloroethanol induced DNA damage in *E. coli* (Rosenkranz et al., 1974; Rosenkranz and Wlodkowski, 1974) but not in *Bacillus subtilis* (Elmore et al., 1976; Laumbach et al., 1977). 2-Chloroethanol was not mutagenic in yeast (Loprieno et al., 1977; Barale et al., 1979) and did not induce mitotic gene conversion in yeast (Loprieno et al., 1977); however, it was mutagenic in the fungus *Aspergillus nidulans* (Bignami et al., 1980a,b). 2-Chloroethanol did not induce sex-linked recessive-lethal mutations in Drosophila (Knaap et al., 1982; NTP, Appendix F), and it did not cause somatic crossing over in soybeans (Vig, 1975). However, it was reported to induce abnormal metaphase chromosomes in onion root tips (Barthelmess and Elkabarity, 1962).

In mammalian cells in vitro, 2-chloroethanol was not mutagenic (Huberman et al., 1975; Knaap et al., 1982) and did not inhibit DNA synthesis (Painter and Howard, 1982). However, it did induce DNA repair in human fibroblasts in vitro (Stich et al., 1976). Isakova et al. (1971) reported that 2-chloroethanol increased the frequency of chromosomal aberrations in rat bone marrow after the animals were exposed by inhalation; however, detailed data were not provided. Neither chromosomal aberrations nor micronuclei were found in mouse bone marrow cells after exposure to 2-chloroethanol by either the oral or intraperitoneal injection routes (Conan et al., 1979). In addition, 2-chloroethanol did not induce dominant-lethal mutations (Epstein et al., 1972) or heritable translocations in the mouse (Sheu et al., 1983).

Teratogenicity and Fetotoxicity

Malformations and high rates of embryo mortality occurred when chick embryos were administered 2-chloroethanol at doses of 50 or 100 mg/kg (egg weight) at 0 or 96 hours of incubation (Verrett, 1974). Fetotoxicity and maternal toxicity were produced when the compound was administered by gavage to pregnant Swiss CD-1 mice on days 4-12 of gestation (RTI, 1983a). No effect on the mother or offspring occurred when 2-chloroethanol was administered in drinking water to Swiss CD-1 mice on days 6-16 of gestation. No teratogenic effects were noted in New Zealand white rabbits administered 2-chloroethanol intravenously at doses (36 mg/kg per day) that produced significant levels of fetotoxicity or maternal toxicity (RTI, 1983b).

Environmental Fate of 2-Chloroethanol

Brominated 2- and 3-carbon compounds can be dehalogenated by a soil Flavobacterium (Castro and Bartnicki, 1968); 2-chloroethanol and 2-bromoethanol are probably dehalogenated to ethylene glycol by this system.

2-Chloroethanol is oxidized in an aqueous environment through 2-chloroacetaldehyde to 2-chloroacetic acid. 2-Chloroethanol is soluble in all proportions in water and can be expected to leach from soil and be transported by soil water. Neely et al. (1974) suggested that bioconcentration of water-soluble substances is unlikely.

TABLE 2. SUMMARY OF THE GENETIC TOXICOLOGY OF 2-CHLOROETHANOL

Test System	Endpoint	Result	References
Bacterial Systems			
Salmonella typhimurium	Gene mutation	+	Rosenkranz et al., 1974
		+	Rosenkranz and Wlodkowski, 1974
		+	Bartsch et al., 1975
		+	Malaveille et al., 1975
		+	McCann et al., 1975
		+	Rannug et al., 1976
		+	Lofroth, 1978
		+	Nakamura et al., 1979
		+	Rannug and Beije, 1979
		+	Bignami et al., 1980a,b
		+	Pfeiffer and Dunkelberg, 1980
		+	Stolzenberg and Hine, 1980
		+	NTP, Appendix F
		–	Elmore et al., 1976
		–	Laumbach et al., 1977
		–	Norpoth et al., 1980
Klebsiella pneumoniae	Gene mutation	+	Voogd and van der Vet, 1969
		+	Voogd et al., 1972
		+	Voogd, 1973
		+	Knapp et al., 1982
Streptomyces coelicolor	Gene mutation	–	Bignami et al., 1980a,b
Escherichia coli	Gene mutation	+	Norpoth et al., 1980
E. coli	DNA damage	+	Rosenkranz et al., 1974
		+	Rosenkranz and Wlodkowski, 1974
Bacillus subtilis	DNA damage	–	Elmore et al., 1976
		–	Laumbach et al., 1977
Nonmammalian Eukaryotes			
Schizosaccharomyces pombe	Gene mutation	–	Loprieno et al., 1977
		–	Barale et al., 1979
Aspergillus nidulans	Gene mutation	+	Bignami et al., 1980a,b
Drosophila melanogaster	Gene mutation	–	Knaap et al., 1982
		–	NTP, Appendix F
Saccharomyces cerevisiae	Chromosomal aberrations	–	Loprieno et al., 1977
Allium	Chromosomal aberrations	+	Barthelmess and Elkabarity, 1962
Glycine max	Chromosomal aberrations	–	Vig, 1975

TABLE 2. SUMMARY OF THE GENETIC TOXICOLOGY OF 2-CHLOROETHANOL (Continued)

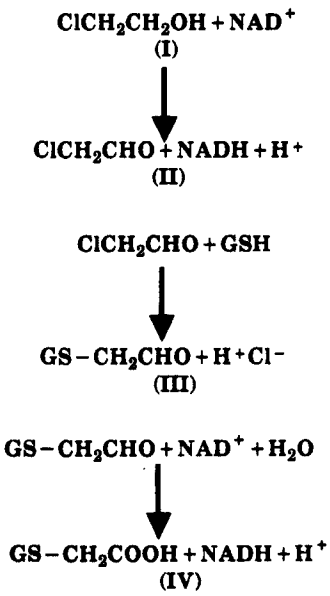
Test System	Endpoint	Result	References
Mammalian Cells (in vitro)			
Mouse lymphoma	Gene mutation	–	Knaap et al., 1982
Chinese hamster (V79)		–	Huberman et al., 1975
Human (HeLa)	DNA damage	–	Painter and Howard, 1982
Human fibroblasts		+	Stich et al., 1976
Mammals (in vivo)			
Rat (bone marow)	Chromosomal aberrations	+	Isakova et al., 1971
Mouse		–	Conan et al., 1979
	Micronucleus	–	Conan et al., 1979
	Heritable translocations	–	Sheu et al., 1983
	Dominant lethal	–	Epstein et al., 1972

Tissue Distribution and Metabolism

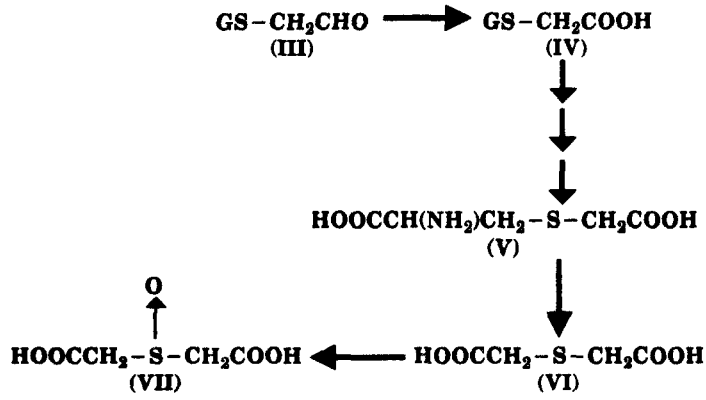
No reports were found on the kinetics of the dermal absorption of 2-chloroethanol or on the tissue distribution of 2-chloroethanol following dermal absorption. After a single oral dose of an aqueous solution of [1,2-^{14}C]-2-chloroethanol (5 or 50 mg/kg) was administered to adult male Wistar rats, 77%-80% of the administered radioactivity was recovered in the urine within 24 hours (Grunow and Altmann, 1982). In the same time period, another 3%-5% was recovered in the feces and expired air. No unchanged 2-chloroethanol was recovered in either feces or urine; expired ^{14}C was all in the form of $^{14}CO_2$. Peak levels of radioactivity were found in blood 1 hour after administration; these levels were reduced by 50% after approximately 4 hours. About 90% of the radioactivity in the urine was in the form of thiodiacetic acid and thionyldiacetic acid, the latter probably formed by the oxidation of the former metabolite.

Johnson (1965) suggested that the toxicity of 2-chloroethanol was due to the formation of chloroacetaldehyde by the test animal in amounts greater than could be detoxified by glutathione (GSH). 2-Chloroethanol is known to be a substrate for the purified cytoplasmic alcohol dehydrogenase of human liver (Blair and Vallee, 1966), rat liver, or yeast (Johnson, 1967). Johnson (1967) demonstrated the in vivo and in vitro formation of S-carboxymethyl-GSH in livers of rats dosed with 2-chloroethanol (I).

S-Carboxymethyl-GSH (IV) is presumably formed from GSH and chloroacetaldehyde (II), the dehydrogenation product of 2-chloroethanol (I); S-formylmethyl-GSH (III) is the presumed intermediate.



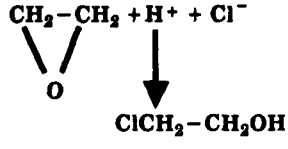
Grunow and Altmann (1982) reported finding thiodiacetic acid (VI) and thionyldiacetic acid (VII) in the urine of rats given an oral dose of 2-chloroethanol; both (VI) and (VII) are derivable from S-carboxymethylcysteine (V), the hydrolysis and deamination product of S-carboxymethyl-GSH (IV).



Thiodiacetic acid has been shown to be a metabolite of compounds that have the general property of being converted to chloroacetaldehyde; these compounds include vinyl chloride (Green and Hathway, 1975, 1977; Watanabe et al., 1976), 1,2-dichloroethanol (Yllner, 1971), and vinylidene chloride (Jones and Hathway, 1978).

Other Sources of 2-Chloroethanol

Ethylene oxide can react with chloride ions in aqueous systems to produce 2-chloroethanol:



The original report by Wesley et al. (1965) showing 2-chloroethanol residues (1-1,000 ppm) in foods sterilized by ethylene oxide was confirmed and extended by Ragelis et al. (1966, 1968). This work has been reviewed (Fishbein, 1969, 1976; Balazs, 1976; USEPA, 1978; FDA, 1978). Ethylene oxide and 2-chloroethanol residues (1-10 ppm) were found following ethylene oxide sterilization of pharmaceuticals (Adler, 1965; Holmgren and Diding, 1969) as well as in materials commonly used in surgical implants and medical procedures (Gunther, 1974a,b; Kozlenchkov and Medvedev, 1975; Brown, 1970; McGunnigle et al., 1975; O'Leary and Guess, 1968). Low-level exposure to 2-chloroethanol may be widespread because of the worldwide use of ethylene oxide as a sterilant. Current annual U.S. production of ethylene oxide is approximately 6.7 billion pounds (OSHA, 1982). Ethylene oxide is both toxic and carcinogenic (IARC, 1976, 1984; USEPA, 1978; OSHA, 1982; NIOSH, 1983; Generoso et al., 1981; Glaser, 1979). Ethylene oxide is currently under test by the NTP in 2-year inhalation studies at concentrations of 0, 50, or 100 ppm in mice.

Toxicology of Ethylene Oxide

The available studies of humans exposed occupationally to ethylene oxide were considered to be inadequate to evaluate the carcinogenic potential (IARC, 1976). No notable health problems were found in a group of current and former chemical plant employees exposed to ethylene oxide (Joyner, 1964); however, a 15-fold increase in the incidence of leukemia was observed in a group of 89 Swedish workers exposed to ethylene oxide at concentrations of 10-30 ppm for 4-10 years (expected number, 0.2; actual number, 3.0). Examination of workers exposed full time, part time, or not at all revealed significant increases in mortality in general and increases in death from stomach cancer or leukemia in workers with a history of exposure to ethylene oxide. Ethylene oxide exposure was estimated to range from 6 ppm in the 1970's to about 30 ppm in the 1950's and 1960's, and up to 700 ppm in the 1940's; however, these workers were also exposed to other chemicals (Hogstedt et al., 1979a,b). The Occupational Safety and Health Administration has proposed a reduction in the permissible exposure limit to ethylene oxide from 50 to 1 ppm averaged over an 8-hour workday (OSHA, 1983). The U.S. Environmental Protection Agency (USEPA,1984) recently published new labeling requirements for ethylene oxide containers to assure that workers using ethylene oxide would not be exposed

at concentrations greater than those proposed by OSHA.

Administration of ethylene oxide (75 or 150 mg/kg) to pregnant New Zealand rabbits at four different 2-day postfertilization periods (days 4-6, 6-8, 8-10, 10-12) of gestation produced no teratogenic effects, although maternal toxicity was dose related. A lowering of fetal body weight and average litter size and increases in maternal toxicity and structural malformations in pups occurred in a dose-related fashion when ethylene oxide (75 or 150 mg/kg) was administered to pregnant Swiss CD-1 mice at days 4-6, 6-8, 8-10, or 10-12 of gestation (Kimmel and LaBorde, 1979; LaBorde and Kimmel, 1980). Weanling F344 male and female rats were exposed to ethylene oxide (0, 10, 33, or 100 ppm) for 6 hours per day, 5 days per week for 12 weeks before being mated. The pregnant female rats in the 100-ppm dose group had longer gestation periods, reduced fertility index, and fewer pups per litter (Snellings et al., 1982).

Metabolism of vinyl chloride monomer may provide another source of exposure to 2-chloroethanol. Monochloroacetic acid was found in the urine of workers exposed to vinyl chloride monomer (Grigorescu and Toba, 1966). Chloroacetaldehyde, chloroethylene oxide, and 2-chloroethanol are likely intermediates in the metabolism of vinyl chloride (Green and Hathway, 1977; Watanabe et al., 1976). 2-Chloroethanol may be a metabolic intermediate common to both ethylene oxide and vinyl chloride monomer--two industrial chemicals produced worldwide in large amounts.

Regulatory Status of 2-Chloroethanol

The Food and Drug Administration (FDA, 1978) has proposed maximum residue limits and 30-day maximum exposure levels for ethylene oxide (30 µg/kg per day), 2-chloroethanol (15 µg/kg per day), and ethylene glycol (2.5 mg/kg per day). The U.S. Environmental Protection Agency (USEPA, 1978) proposed revoking all registrations and continuing registrations of pesticide products containing ethylene oxide.

Study Rationale

2-Chloroethanol was selected for testing because of its metabolic and chemical relationship to ethylene oxide and vinyl chloride monomer, its potential widespread exposure via ethylene oxide residues, and the lack of adequate carcinogenicity testing. Dermal application was selected because it is one of the two usual routes of exposure in humans, the other major route being inhalation. The F344/N rat and the Swiss mouse were chosen as the test animals.

II. MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION OF 2-CHLOROETHANOL
PREPARATION AND CHARACTERIZATION OF DOSE MIXTURES
DERMAL APPLICATION
SINGLE-ADMINISTRATION STUDIES
FOURTEEN-DAY STUDIES
THIRTEEN-WEEK STUDIES
TWO-YEAR STUDIES
- Study Design
- Source and Specifications of Test Animals
- Animal Maintenance
- Clinical Examinations and Pathology
- Statistical Methods

PROCUREMENT AND CHARACTERIZATION OF 2-CHLOROETHANOL

2-Chloroethanol was obtained in two batches. The first batch was obtained from Eastman Kodak Co. (lot no. A3X) and was identified as 2-chloroethanol by infrared, ultraviolet/visible, and nuclear magnetic resonance spectroscopy. All spectra were consistent with those expected for the structure of the chemical and with the available literature spectra (Appendix G). Cumulative data indicated that this batch of 2-chloroethanol was greater than 99% pure (Appendix G). This conclusion is based on elemental analyses in agreement with theoretical values, a value of 0.090% water as determined by Karl Fischer titration, and three gas chromatographic systems that indicated a single homogenous peak by one system and impurities totaling 0.20% and 0.39% by the other two systems.

The second batch of test chemical (lot no. C742) was obtained from Fischer Scientific Co. and was identified as 2-chloroethanol by spectroscopy, which produced results similiar to those for the first batch (Appendix G). This batch was estimated to be approximately 99% pure; the results of elemental analyses for carbon and hydrogen agreed with theoretical values, but values for chlorine were slightly higher than theoretical. A value of 0.082% water was obtained by Karl Fischer titration. The major impurity in this batch was identified as 2-(2-chloroethoxy)ethanol and quantitated at 0.9%.

2-Chloroethanol was stored in the dark at 5° C in its original container. Results of periodic reanalyses of the bulk chemical by infrared spectroscopy and gas chromatography indicated no notable degradation of the chemical throughout the study (Appendix G).

PREPARATION AND CHARACTERIZATION OF DOSE MIXTURES

2-Chloroethanol and 80% (single-administration, 14-day, and 13-week studies) or 70% (2-year studies) ethanol in water were mixed to yield the desired solution (Appendix H). Solutions of 2-chloroethanol (7.9% and 9.4% w/v) in 70% (v/v) ethanol/water were shown by the testing laboratory to be stable for 21 days when stored at room temperature. For these studies, formulated mixtures of 2-chloroethanol were stored at room temperature for no longer than 2 weeks.

Dose mixtures were analyzed at the testing laboratory every 8 weeks during the 2-year studies (Appendix I). In addition, referee samples were analyzed by the analytical laboratory approximately every 6 months as a quality assurance measure to check the mixing and analysis procedures at the testing laboratory (Appendix I). The concentrations of 3 of the 55 mixtures (5.5%) analyzed at the testing laboratory differed from the target concentration by more than 10% (Table 3; Appendix J, Table J1). Two of these three mixtures were not administered to the animals but were remixed and reanalyzed before dosing. The third, which was found to be 110.9% of the target concentration, was administered to the animals.

TABLE 3. CONCENTRATIONS OF 2-CHLOROETHANOL IN DOSE MIXTURES IN THE TWO-YEAR DERMAL STUDIES

	Percent of Target Concentration
Mean	101.0
Standard deviation	7.90
Coefficient of variation (percent)	7.82
Number of samples	55

DERMAL APPLICATION

For all animals, the interscapular skin was prepared by removing the hair with an electric clipper (No. 40 head). An area of about 3 × 3 cm was clipped on the mice and an area of about 6 × 6 cm on the rats. For all studies except the single-administration studies, the backs of the animals were clipped two times per week for the first 2 weeks of the studies and weekly thereafter.

SINGLE-ADMINISTRATION STUDIES

Male and female F344/N rats were obtained from Frederick Cancer Research Center, and male and female Swiss Webster mice were obtained from Charles River Breeding Laboratories. Rats were observed for 1 week and mice were observed for 3 weeks before the studies began. Rats were housed two per cage, and mice were housed five per cage. All animals received water and feed ad libitum during the observation period. Details of animal maintenance are given in Table 4.

Groups of two to eight male and two to nine female rats were given single dermal applications of 2-chloroethanol (7.5, 15, 20, 30, 40, 60, 80, 100, 119 [males only], 239, or 479 mg). Groups of five mice of each sex were given 10, 14.7, 21.5, 31.6, 46.4, or 68.1 mg. The 2-chloroethanol was applied either undiluted or in 80% ethanol/water depending on dose. There were no vehicle control animals. Animals were observed for 14 days for mortality. Body weights were recorded on the day of dosing and then on days 7 or 8 and 14. Necropsies were performed on all animals.

FOURTEEN-DAY STUDIES

Male and female F344/N rats and Swiss Webster mice were obtained from Charles River Breeding Laboratories and were held for 4 weeks before the studies began.

Groups of five males and five females of each species were given dermal applications of 2-chloroethanol in 80% ethanol in water for 14 consecutive days. Each day, rats received 0, 20, 30, 40, 60, or 80 mg per animal, and mice received 0, 2.5, 5, 10, 20, 30, 45, or 60 mg per animal. The 45-mg and 60-mg groups of mice were tested (without concurrent vehicle controls) after completion of the rest of the studies.

Animals were housed five per cage and received water and feed ad libitum. Details of animal maintenance are presented in Table 4. The rats and mice were observed twice per day and were weighed on days 0, 7, and 14 (rats) or days 1, 7, and 15 (mice). Necropsies were performed on all animals. Tissues examined are listed in Table 4.

THIRTEEN-WEEK STUDIES

Thirteen-week studies were conducted to evaluate the cumulative toxicity of 2-chloroethanol and to determine the doses to be used in the 2-year studies.

Four-week-old male and female F344/N rats were obtained from Harlan Industries, Indianapolis, Indiana, and 3-week-old male and female Swiss CD-1 mice were received from Charles River Breeding Laboratories, Portage, Michigan. Rats and mice were observed for 3 weeks before the studies began. Rats and mice were housed five per cage in polycarbonate cages. Diets consisting of Purina Lab Chow® and water (acidified with hydrochloric acid to pH 2.5 for bacterial control) were available ad libitum. Further experimental details are summarized in Table 4.

Groups of 10 rats of each sex were given dermal applications of 2-chloroethanol (0, 62, 125, 250, 500, or 1,000 mg/kg) in 80% ethanol in water, 5 days per week for 13 weeks. Groups of 10 mice of each sex received 0, 5, 10, 20, 30, or 45 mg per animal on the same schedule.

Rats were checked two times per day, and mice were checked once per day; moribund animals were killed. Clinical examinations were performed and animal weights recorded once per week.

At the end of the 13-week studies, survivors were killed. Necropsies were performed on all animals, except those excessively autolyzed or cannibalized. Tissues and groups examined are listed in Table 4.

TWO-YEAR STUDIES

Study Design

Groups of 50 rats of each sex were administered 0, 50, or 100 mg/kg 2-chloroethanol in 70% ethanol in water by dermal application, 5 days per week for 103 weeks. Groups of 50 mice of each sex were administered 0, 7.5, or 15 mg 2-chloroethanol in 70% ethanol in water by dermal application, 5 days per week for 104 weeks. Additional groups of 50 untreated mice of each sex were also included.

TABLE 4. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE DERMAL STUDIES OF 2-CHLOROETHANOL

Single-Administration Studies	Fourteen-Day Studies	Thirteen-Week Studies	Two-Year Studies
EXPERIMENTAL DESIGN			
Testing Laboratory			
Litton Bionetics, Inc.	Litton Bionetics, Inc.	Litton Bionetics, Inc.	Litton Bionetics, Inc.
Size of Test Groups			
Rats--2-8 males, 2-9 females; mice--5 of each sex	5 of each sex and species	10 of each sex and species	50 of each sex and species
Doses			
Rats--7.5, 15, 20, 30, 40, 60, 80, 100, 119 (males only), 239, or 479 mg; mice--10, 14.7, 21.5, 31.6, 46.4, or 68.1 mg 2-chloroethanol (undiluted or in 80% ethanol in water) by dermal application; dose vol: rats--0.05-0.4 ml; mice--0.1 ml	Rats--0, 20, 30, 40, 60, or 80 mg; mice--0, 2.5, 5, 10, 20, 30, 45, or 60 mg 2-chloroethanol in 80% ethanol in water by dermal application; dose vol: 0.1 ml	Rats--0, 62, 125, 250, 500, or 1,000 mg/kg; mice--0, 5, 10, 20, 30, or 45 mg 2-chloroethanol in 80% ethanol in water by dermal application; dose vol: rats--0.2 ml; mice--0.1 ml; interscapular dosing area was clipped weekly	Rats--0, 50, or 100 mg/kg; mice--0, 7.5, or 15 mg 2-chloroethanol in 70% ethanol in water by dermal application; dose vol: male rats--0.22 ml; female rats--0.18 ml; mice--0.10 ml; interscapular dosing area was clipped weekly
Date of First Dose			
Rats--7/21-7/29/77; mice--2/14-2/16/77	Rats--11/1/77; mice--3/23/77, 3/29/77 (60 mg), 4/5/77 (45 mg)	Rats--1/9/78; mice--6/21/77	Rats--2/8/80; mice--1/29/80
Date of Last Dose			
N/A	Rats--11/14/77; mice--4/5/77, 4/18/77 (45 mg)	Rats--4/7/78; mice--9/16/77	Rats--1/29/82; mice--1/25/82
Duration of Dosing			
Single dose	14 consecutive days	5d/wk for 13 wk	Rats--5 d/wk for 103 wk; mice--5 d/wk for 104 wk
Type and Frequency of Observation			
Rats--observed 1-2 h and 4 h after dosing on d 1 and 1 × d thereafter; weighed on d 1, 7, and 14; mice--weighed on d 1, 8, and 14	Observed 2 × d; rats--weighed on d 0, 7, 14; mice--weighed on d 1, 7, and 15	Rats--clinically examined 1 × wk; body weight measured 1 × wk; mice--observed 2 × d; body weight measured 1 × wk; observed 1-2 h and 4 h after dosing on d 1, and 1 × d thereafter	Observed 2 × d; clinical exam, palpation 1 × mo; weighed 1 × wk for 13 wk, then 1 × mo thereafter
Necropsy and Histologic Examination			
Necropsy performed on all animals	Necropsy performed on all animals; the following tissues were examined grossly; gross lesions; skin; mandibular lymph node; mammary gland; salivary gland; thigh muscle;	Necropsy performed on all animals; the following tissues were examined for vehicle control and 1,000 mg/kg group rats, and vehicle control, 20, 30, and 45 mg group mice,	Necropsy performed on all animals; histopath exam performed on the following tissues of all animals: gross lesions and tissue masses; blood smear; mandibular and

TABLE 4. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE DERMAL STUDIES OF 2-CHLOROETHANOL (Continued)

Single-Administration Studies	Fourteen-Day Studies	Thirteen-Week Studies	Two-Year Studies
Necropsy and Histologic Examination (Continued)			
	sciatic nerve; sternebrae, (including marrow); costochondral junction (rib); thymus; larynx; trachea; lungs and bronchi; tissue masses; adrenal glands; urinary bladder; regional lymph nodes; ileum; colon; cecum; rectum; mesenteric lymph node; liver; pancreas; spleen; kidneys; seminal vesicles/prostate/ testes or ovaries/uterus; no histopath exam	and all animals that died before the end of the study: gross lesions and tissue masses; mesenteric and cervical lymph nodes; salivary gland; sternebrae (including marrow); thyroid gland; parathyroids; small intestine; colon; liver; prostate/testes or ovaries/uterus; lungs and mainstem bronchi; mammary gland; heart; esophagus; stomach; brain; thymus; trachea; pancreas; spleen; kidneys; adrenal glands; skin; urinary bladder; pituitary gland; gallbladder (mice only); in addition, pancreas, lungs, and large intestine were examined histopathologically in all groups of dosed rats	mesenteric lymph nodes; salivary gland; sternebrae (including marrow); thyroid gland; parathyroids; colon; liver; urinary bladder; prostate/testes/seminal vesicles or ovaries/uterus; lungs and mainstem bronchi; skin (dosed and undosed sites); cecum; thigh muscle; brain; costochondral junction, rib; larynx; nasal cavity; heart; esophagus; stomach; thymus; trachea; pancreas; spleen; kidneys; adrenal glands; pituitary gland; mammary gland; duodenum; ileum; jejunum; sciatic nerve; rectum; gallbladder (mice); spinal cord (if neurologic signs were present); eyes (if grossly abnormal)
ANIMALS AND ANIMAL MAINTENANCE			
Species			
F344/N rats; Swiss Webster mice	Same as single-administration studies	F344/N rats; Swiss CD-1 mice	Same as 13-week studies
Animal Source			
Rats--Frederick Cancer Research Center (Frederick, MD); mice--Charles River Breeding Laboratories (Portage, MI)	Charles River Breeding Laboratories (Portage, MI)	Rats--Harlan Industries (Indianapolis, IN); mice--Charles River Breeding Laboratories (Portage, MI)	Charles River Breeding Laboratories (Portage, MI)
Time Held Before Start of Test			
Rats--1 wk; mice--3 wk	4 wk	Rats--20 d; mice--3 wk	Rats--2 wk; mice--3 wk
Age When Placed on Study			
Rats--6-9 wk; mice--6 wk	Rats--8 wk; mice--7 wk	Rats--7 wk; mice--6 wk	Rats--7 wk; mice--6 wk
Age When Killed			
Rats--8-11 wk; mice--8 wk	Rats--10 wk; mice--9 wk	Rats--20 wk; mice--20 wk	Rats--112 wk; mice--111 wk
Necropsy Dates			
Rats--8/4-8/12/77; mice--2/28/77	Rats--11/15/77; mice--4/6/77, 4/19/77	Rats--4/10-4/11/78; mice--9/19/77	Rats--2/8-2/11/82; mice--2/1-2/3/82

TABLE 4. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE DERMAL STUDIES OF 2-CHLOROETHANOL (Continued)

Single-Administration Studies	Fourteen-Day Studies	Thirteen-Week Studies	Two-Year Studies
ANIMALS AND ANIMAL MAINTENANCE (Continued)			
Method of Distribution			
So that average cage weights were approximately equal	Same as single-administration studies	Same as single-administration studies	Assigned to cages according to a table of random numbers; then cages assigned to groups according to another table of random numbers
Feed			
Purina Lab Chow® (Ralston Purina Co., St. Louis, MO); ad libitum	Same as single-administration studies	Same as single-administration studies	NIH 07 Open Formula Rat and Mouse Ration Pellets (Ziegler Bros., Gardners, PA); ad libitum
Bedding			
Ab-sorb-Dri® (Williams Feed and Bedding, Gaithersburg,) MD)	Same as single-administration studies	Same as single-administration studies	Ab-sorb-Dri® (Williams Feed and Bedding, Gaithersburg, MD) before 9/23/81; Sani-chips (P.J. Murphy Forest Products, Rochelle Pk, NJ) thereafter
Water			
Tap water acidified with hydrochloric acid to pH 2.5, provided ad libitum	Same as single-administration studies	Same as single-administration studies	Same as single-administration studies
Cages			
Polycarbonate (Lab Products, Inc., Garfield and Rochelle Pk, NJ, and Hazelton Systems, Aberdeen, MD)	Same as single-administration studies	Same as single-administration studies	Same as single-administration studies
Cage Filters			
Nonwoven polyester (Snow Filtration, Cincinnati, OH)	Same as single-administration studies	Same as single-administration studies	Same as single-administration studies
Animals per Cage			
Rats--2; mice--5	5	5	5
Cage Rotation			
None	None	None	None

TABLE 4. EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE DERMAL STUDIES OF 2-CHLOROETHANOL (Continued)

Single-Administration Studies	Fourteen-Day Studies	Thirteen-Week Studies	Two-Year Studies
ANIMALS AND ANIMAL MAINTENANCE (Continued)			
Animal Room Environment			
Rats--fluorescent light 12 h/d; temp--23° ± 2° C; hum--30%-70%; mice--fluorescent light 8 h/d; temp--22° ± 1° C; hum--30%-70%; 12-15 room air changes/h	Fluorescent light 12 h/d; temp: 23° ± 2° C; hum--30%-70%; room air changes not reported	Fluorescent light 12 h/d; hum--30%-70%; air changes not stated; temp--23° ± 2° C;	Fluorescent light 12 h/d; temp--23° ± 1° C; hum--30%-70% (Appendix M); 12-15 room air changes/h
Other Chemicals on Test in Same Room			
Rats--no record; mice--none	None	Rats--no record; mice--none	None
CHEMISTRY			
Lot Numbers Used			
A3X	A3X	A3X	A3X, C742
Date of Initial Use of Subsequent Lots			
N/A	N/A	N/A	December 1980
Supplier			
Eastman Kodak (Rochester, NY)	Same as single-administration studies	Same as single-administration studies	Eastman Kodak (Rochester, NY); Fisher Scientific Co. (St. Louis, MO)
CHEMICAL/VEHICLE			
Preparation			
Chemical was dissolved in 80% ethanol; solutions were mixed in screwcapped test tubes and hand shaken	Same as single-administration studies	Same as single-administration studies	Appropriate amounts of 2-chloroethanol were added to prelabeled, clean, and dry 100-ml graduated cylinders with stoppers; solutions were adjusted with 70% ethanol to final volumes of 75 ml and mixed by inversion until uniform
Maximum Storage Time			
2 d	2 wk	Rats--1 wk; mice--2 wk	2 wk
Storage Conditions			
Room temp within dosing hood in animal room	Same as single-administration studies	Same as single-administration studies	Room temp

Source and Specifications of Test Animals

The male and female F344/N rats used in these studies were produced under strict barrier conditions at Charles River Breeding Laboratories (Portage, Michigan) under a contract to the Carcinogenesis Program. Breeding starts for the foundation colony at the production facility originated at the National Institutes of Health Repository. Animals shipped for testing were progeny of defined microflora-associated parents that were transferred from isolators to barrier-maintained rooms. The male and female Crl:CD®-1(ICR)BR Swiss mice used in these studies were obtained from Charles River Breeding Laboratories, Portage, Michigan, from their cesarean-originated, barrier-sustained production colony. Rats were shipped to the testing laboratory at 5 weeks of age, and mice at 3 weeks. The rats were quarantined at the testing facility for 2 weeks, and the mice for 3 weeks. Thereafter, a complete necropsy was performed on five animals of each sex and species to assess their health status. The rats were placed on study at 7 weeks of age, and the mice at 6 weeks. The health of the animals was monitored during the course of the study according to the protocols of the NTP Sentinel Animal Program (Appendix K).

Animal Maintenance

Rats and mice were housed five per cage in polycarbonate cages. Feed and water (acidified with hydrochloric acid to pH 2.5 for bacterial control) were available ad libitum. Details of animal maintenance are summarized in Table 4.

Clinical Examinations and Pathology

All animals were observed two times. Clinical signs were recorded once per month. Body weights by cage were recorded once per week for the first 13 weeks of the study and once per month thereafter. Mean body weights were calculated for each group. Moribund animals were killed, as were animals that survived to the end of the study. Necropsies were performed on all animals, including those found dead unless they were excessively autolyzed or cannibalized. Thus, the number of animals from which particular organs or tissues were examined microscopically varies and is not necessarily equal to number of animals that were placed on study in each group.

Examinations for grossly visible lesions were performed on major tissues or organs. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. Tissues examined microscopically are listed in Table 4.

When the pathology examination was completed, the slides, individual animal data records, and summary tables were sent to an independent quality assurance laboratory. Individual animal records and tables were compared for accuracy, slides and tissue counts were verified, and histotechnique was evaluated. All tumor diagnoses, all target tissues, and all tissues from a randomly selected 10% of the animals were evaluated by a quality assurance pathologist. Slides of all target tissues and those about which the original and quality assurance pathologists disagreed were submitted to the Chairperson of the Pathology Working Group (PWG) for evaluation. Representative coded slides selected by the Chairperson were reviewed by PWG pathologists, who reached a consensus and compared their findings with the original and quality assurance diagnoses. When diagnostic differences were found, the PWG sent the appropriate slides and comments to the original pathologist for review. This procedure has been described, in part, by Maronpot and Boorman (1982) and Boorman et al. (1985). The final diagnoses represent a consensus of contractor pathologists and the NTP Pathology Working Group.

Nonneoplastic lesions are not examined routinely by the quality assurance pathologist or the PWG. Certain nonneoplastic findings are reviewed by the quality assurance pathologist and the PWG if they are considered part of the toxic response to a chemical or if they are deemed of special interest.

Statistical Methods

Data Recording: Data on this experiment were recorded in the Carcinogenesis Bioassay Data System (Linhart et al., 1974). The data elements

include descriptive information on the chemicals, animals, experimental design, survival, body weight, and individual pathologic results, as recommended by the International Union Against Cancer (Berenblum, 1969).

Survival Analyses: The probability of survival was estimated by the product-limit procedure of Kaplan and Meier (1958) and is presented in the form of graphs. Animals were censored from the survival analyses at the time they were found dead of other than natural causes or were found to be missing; animals dying from natural causes were not censored. Statistical analyses for a possible dose-related effect on survival used the method of Cox (1972) for testing two groups for equality and Tarone's (1975) life table test for a dose-related trend. All reported P values for the survival analysis are two-sided.

Calculation of Incidence: The incidence of neoplastic or nonneoplastic lesions is given as the ratio of the number of animals bearing such lesions at a specific anatomic site to the number of animals in which that site was examined. In most instances, the denominators include only those animals for which the site was examined histologically. However, when macroscopic examination was required to detect lesions (e.g., skin or mammary tumors) prior to histologic sampling, or when lesions could have appeared at multiple sites (e.g., lymphomas), the denominators consist of the number of animals on which necropsies were performed.

Analysis of Tumor Incidence: Three statistical methods are used to analyze tumor incidence data. The two that adjust for intercurrent mortality employ the classical method for combining contingency tables developed by Mantel and Haenszel (1959). Tests of significance included pairwise comparisons of high dose and low dose groups with vehicle controls and tests for overall dose-response trends.

For studies in which compound administration has little effect on survival, the results of the three alternative analyses will generally be similar. When differing results are obtained by the three methods, the final interpretation of the data will depend on the extent to which the tumor under consideration is regarded as being the cause of death. All reported P values for tumor analyses are one-sided.

Life Table Analyses--The first method of analysis assumed that all tumors of a given type observed in animals dying before the end of the study were "fatal"; i.e., they either directly or indirectly caused the death of the animal. According to this approach, the proportions of tumor-bearing animals in the dosed and vehicle control groups were compared at each point in time at which an animal died with a tumor of interest. The denominators of these proportions were the total number of animals at risk in each group. These results, including the data from animals killed at the end of the study, were then combined by the Mantel-Haenszel method to obtain an overall P value. This method of adjusting for intercurrent mortality is the life table method of Cox (1972) and of Tarone (1975).

Incidental Tumor Analyses--The second method of analysis assumed that all tumors of a given type observed in animals that died before the end of the study were "incidental"; i.e., they were merely observed at necropsy in animals dying of an unrelated cause. According to this approach, the proportions of tumor-bearing animals in dosed and vehicle control groups were compared in each of five time intervals: weeks 0-52, weeks 53-78, weeks 79-92, week 93 to the week before the terminal-kill period, and the terminal-kill period. The denominators of these proportions were the number of animals on which necropsies were actually performed during the time interval. The individual time interval comparisons were then combined by the previously described method to obtain a single overall result. (See Haseman, 1984, for the computational details of both methods.)

Unadjusted Analyses--Primarily, survival-adjusted methods are used to evaluate tumor incidence. In addition, the results of the Fisher exact test for pairwise comparisons and the Cochran-Armitage linear trend test (Armitage, 1971; Gart et al., 1979) are given in the appendix containing the analyses of primary tumor incidence. These two tests are based on the overall proportion of tumor-bearing animals and do not adjust for survival differences.

III. RESULTS

RATS

SINGLE-ADMINISTRATION STUDIES
FOURTEEN-DAY STUDIES
THIRTEEN-WEEK STUDIES
TWO-YEAR STUDIES
Body Weights and Clinical Signs
Survival
Pathology and Statistical Analyses of Results

MICE

SINGLE-ADMINISTRATION STUDIES
FOURTEEN-DAY STUDIES
THIRTEEN-WEEK STUDIES
TWO-YEAR STUDIES
Body Weights and Clinical Signs
Survival
Pathology and Statistical Analyses of Results

SINGLE-ADMINISTRATION STUDIES

All male rats that received 80 mg or more and all female rats that received 239 mg or more were dead within 4 hours (Table 5). All deaths in other groups also occurred within 4 hours of dosing. For female rats, the LD_{50} value (14-day) was estimated to be 58.6 mg/rat (probit analysis; Finney, 1964). For male rats, the steepness of the dose-response curve did not permit a formal LD_{50} value (14-day) estimate; the value is between 60 mg/rat (no deaths) and 80 mg/rat (100% mortality).

TABLE 5. SURVIVAL AND MEAN BODY WEIGHTS OF RATS IN THE SINGLE-ADMINISTRATION DERMAL STUDIES OF 2-CHLOROETHANOL

Dose		Survival	Mean Body Weights (grams)		
mg	mg/kg (a)	(b)	Initial	Day 14	Change
MALE					
7.5	38	2/2	198	240	+ 42
15	96	2/2	156	200	+ 44
20	118	5/5	170	183	+ 13
30	180	2/2	167	212	+ 45
40	235	5/5	170	178	+ 8
60	331	8/8	181	190	+ 9
80	473	0/5	169	--	--
100	588	0/5	170	--	--
119	856	0/2	139	--	--
239	1,552	0/2	154	--	--
479	2,957	0/2	162	--	--
FEMALE					
7.5	55	2/2	136	158	+ 22
15	103	2/2	145	167	+ 22
20	139	5/5	144	157	+ 13
30	222	2/2	135	160	+ 25
40	284	2/5	141	154	+ 13
60	426	5/9	141	154	+ 13
80	563	2/5	142	130	- 12
100	704	1/5	142	167	+ 25
239	1,853	0/2	129	--	--
479	3,713	0/2	129	--	--

(a) Day 1 dose based on initial group mean body weight
(b) Number surviving/number initially in the group. All deaths occurred within 4 hours of dosing.

FOURTEEN-DAY STUDIES

Three rats died: a male that received 80 mg and two females that received 60 mg (Table 6). One of the females that died had cranial blood clots. In both the male and female rat studies, body weights for vehicle control and dosed animals were comparable at the end of the 14-day dosing period. Doses for the 13-week studies were set on the basis of mortality observed in the single-administration and 14-day studies. For the 13-week studies, doses were based on milligrams per kilogram (Table 7) rather than on milligrams per animal; the doses shown in Tables 5 and 6 are shown both as milligrams per animal (actual doses) and as milligrams per kilogram for comparative purposes.

TABLE 6. SURVIVAL AND MEAN BODY WEIGHTS OF RATS IN THE FOURTEEN-DAY DERMAL STUDIES OF 2-CHLOROETHANOL

Dose		Survival	Mean Body Weights (grams)			Relative Weight	Relative Weight Change
mg	mg/kg (a)	(b)	Initial (c)	Final	Change	(percent)	(percent)
MALE							
(d) 0	0	5/5	172.6 ± 6.8	215.2 ± 8.4	+42.6 ± 4.0	--	--
20	114	5/5	175.2 ± 5.8	216.4 ± 5.9	+41.2 ± 4.3	100.5	96.7
30	172	5/5	173.8 ± 7.8	216.2 ± 9.7	+42.4 ± 12.2	100.5	99.5
40	226	5/5	177.2 ± 11.0	213.2 ± 9.8	+36.0 ± 6.6	99.1	84.5
60	339	5/5	177.2 ± 10.4	217.4 ± 10.3	+40.2 ± 7.7	100.9	94.4
80	442	(e) 4/5	181.0 ± 6.0	221.3 ± 11.5	+40.3 ± 5.5	102.8	94.6
FEMALE							
(f) 0	0	5/5	127.8 ± 2.5	145.8 ± 4.8	+18.0 ± 7.0	--	--
20	147	5/5	136.6 ± 6.6	149.6 ± 5.4	+14.0 ± 4.4	102.7	77.8
30	222	5/5	135.0 ± 5.5	145.2 ± 2.9	+10.2 ± 3.0	99.3	56.7
40	313	5/5	127.6 ± 4.6	144.2 ± 3.8	+16.6 ± 4.5	98.6	92.2
60	451	(f) 3/5	133.4 ± 4.5	144.0 ± 4.6	+10.6 ± 4.2	98.6	58.9
80	611	5/5	131.2 ± 4.0	144.6 ± 4.0	+13.4 ± 1.5	99.3	74.4

(a) Day 1 dose based on initial mean body weight
(b) Number surviving/number per group
(c) Initial body weight based on all animals in group. Subsequent calculations are based on those animals surviving to the end of the study.
(d) Vehicle control
(e) Day of death: 1
(f) Day of death: 1, 3

THIRTEEN-WEEK STUDIES

All rats of each sex that received 1,000 mg/kg died (Table 7). One male and three female rats that received 250 mg/kg and 8/10 males and 8/10 females that received 500 mg/kg also died. Most of the compound-related deaths occurred during the first week of dosing. There were no dose-related trends in body weight changes during the studies.

The incidences of pancreatic acinar cell vacuolar change and pulmonary congestion were dose related (Table 8). Pulmonary congestion and edema occurred exclusively in animals that died or that were killed when moribund.

Dose Selection Rationale: Based on mortality as well as on the incidences of pancreatic changes in the 250-1,000 mg/kg groups, the doses selected for the rats for the 2-year studies were 50 and 100 mg/kg.

TABLE 7. SURVIVAL AND MEAN BODY WEIGHTS OF RATS IN THE THIRTEEN-WEEK DERMAL STUDIES OF 2-CHLOROETHANOL

Dose (mg/kg)	Survival (a)	Mean Body Weights (grams)			Final Weight Relative to Vehicle Controls (percent)
		Initial	Final	Change	
MALE					
(b) 0	10/10	139	287	148	--
62	10/10	138	291	153	101.4
125	10/10	139	282	143	98.3
250	(c) 9/10	138	300	162	104.5
500	(d) 2/10	139	265	126	92.3
1,000	(e) 0/10	136	--	--	--
FEMALE					
(b) 0	10/10	105	172	67	--
62	10/10	106	172	66	100
125	10/10	106	169	63	98.3
250	(f) 7/10	106	173	67	100.6
500	(f) 2/10	105	171	66	99.4
1,000	(f) 0/10	105	--	--	--

(a) Number surviving/number in group
(b) Vehicle control
(c) Week of death: 1
(d) Week of death: 1, 1, 1, 1, 1, 4, 5, 10
(e) Week of death: 1, 1, 1, 1, 1, 1, 1, 3, 3, 4
(f) Week of death for all: 1

TABLE 8. INCIDENCES OF PANCREATIC ACINAR CELL VACUOLAR CHANGE AND PULMONARY CONGESTION IN RATS IN THE THIRTEEN-WEEK DERMAL STUDIES OF 2-CHLOROETHANOL

Dose (mg/kg)	Acinar Cell Change	Pulmonary Congestion
MALE		
0	0/10	0/10
62	0/10	0/10
125	0/10	0/10
250	1/10	1/10
500	8/10	7/10
1,000	8/10	7/10
FEMALE		
0	0/10	0/10
62	0/10	0/10
125	1/10	0/10
250	2/10	1/10
500	7/10	7/10
1,000	9/10	7/10

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Throughout the studies, mean body weights of dosed and vehicle control rats of each sex were comparable (Table 9 and Figure 1). An unexplained deviation from the anticipated growth pattern occurred in all groups of male rats from approximately week 30 to week 45. Examination of original weight data, balance calibration records, clinical observation records, and murine virus antibody patterns provided no adequate explanation of this weight gain pattern. No compound-related clinical signs were observed.

Serologic analysis of blood samples from the sentinel animals showed evidence of Sendai virus infection (Appendix K). Animal room environment records (temperature and relative humidity) during the 2-year studies are summarized in Appendix M.

TABLE 9. MEAN BODY WEIGHTS AND SURVIVAL OF RATS IN THE TWO-YEAR DERMAL STUDIES OF 2-CHLOROETHANOL

Weeks on Study	Vehicle Control		50 mg/kg			100 mg/kg		
	Av. Wt. (grams)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of veh controls)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of veh controls)	No. of Survivors
MALE								
0	170	50	171	101	50	169	99	50
1	200	50	199	100	50	196	98	50
2	209	50	212	101	50	207	99	50
3	243	50	236	97	50	217	89	50
4	241	50	236	98	50	224	93	50
5	260	50	251	97	50	241	93	50
6	268	50	262	98	50	251	94	50
7	287	50	285	99	50	277	97	50
8	298	50	294	99	50	290	97	50
9	308	50	324	105	50	302	98	50
10	316	50	313	99	50	310	98	50
11	326	50	323	99	50	319	98	50
12	333	50	329	99	50	330	99	50
13	338	50	335	99	50	335	99	50
16	353	50	348	99	50	347	98	50
20	367	50	366	100	50	363	99	50
24	378	50	374	99	50	372	98	50
28	377	50	379	101	50	378	100	50
32	380	50	383	101	50	379	100	50
36	373	50	382	102	50	377	101	50
40	360	50	365	101	50	364	101	49
44	400	50	402	101	50	410	103	49
48	421	50	423	100	50	435	103	49
52	432	50	440	102	50	441	102	49
56	451	50	454	101	50	457	101	49
60	464	50	465	100	50	466	100	49
64	469	50	471	100	49	471	100	49
68	473	50	475	100	49	475	100	49
72	473	50	482	102	48	477	101	49
76	477	50	486	102	48	482	101	49
80	474	46	485	102	48	479	101	48
84	467	45	483	103	45	473	101	48
88	448	44	482	108	43	478	107	47
92	476	41	478	100	42	481	101	44
96	474	39	472	100	40	470	99	42
100	469	38	466	99	38	463	99	38
104	466	33	459	98	37	457	98	36
FEMALE								
0	118	50	121	103	50	122	103	50
1	133	50	136	102	50	139	105	50
2	143	50	146	102	50	150	105	50
3	153	50	144	94	50	154	101	50
4	159	50	165	104	50	166	104	50
5	170	50	171	101	50	175	103	50
6	175	50	179	102	50	181	103	50
7	174	50	183	105	50	185	106	50
8	184	50	190	103	50	194	105	50
9	186	50	190	102	50	191	103	50
10	188	50	192	102	50	194	103	50
11	195	50	198	102	50	199	102	50
12	199	50	201	101	50	201	101	50
13	200	50	203	102	50	204	102	50
16	210	50	213	101	50	214	102	50
20	216	50	217	100	50	219	101	50
24	226	50	227	100	50	230	102	50
28	235	50	233	99	50	239	102	50
32	239	50	240	100	50	242	101	50
36	243	50	244	100	50	246	101	50
40	247	50	246	100	50	246	100	50
44	255	50	256	100	50	257	101	50
48	260	50	259	100	50	265	102	50
52	260	50	263	101	50	259	100	50
56	267	50	271	101	50	273	102	50
60	276	50	278	101	50	282	102	50
64	283	50	280	99	50	288	102	50
68	291	50	290	100	50	297	102	50
72	304	50	299	98	48	307	101	49
76	309	50	310	100	46	310	100	47
80	314	50	316	101	45	319	102	45
84	320	49	318	99	45	323	101	45
88	324	49	325	100	45	326	101	45
92	324	48	325	100	45	325	100	43
96	325	44	326	100	44	325	100	43
100	330	43	327	99	41	326	99	42
104	329	42	329	100	39	327	99	38

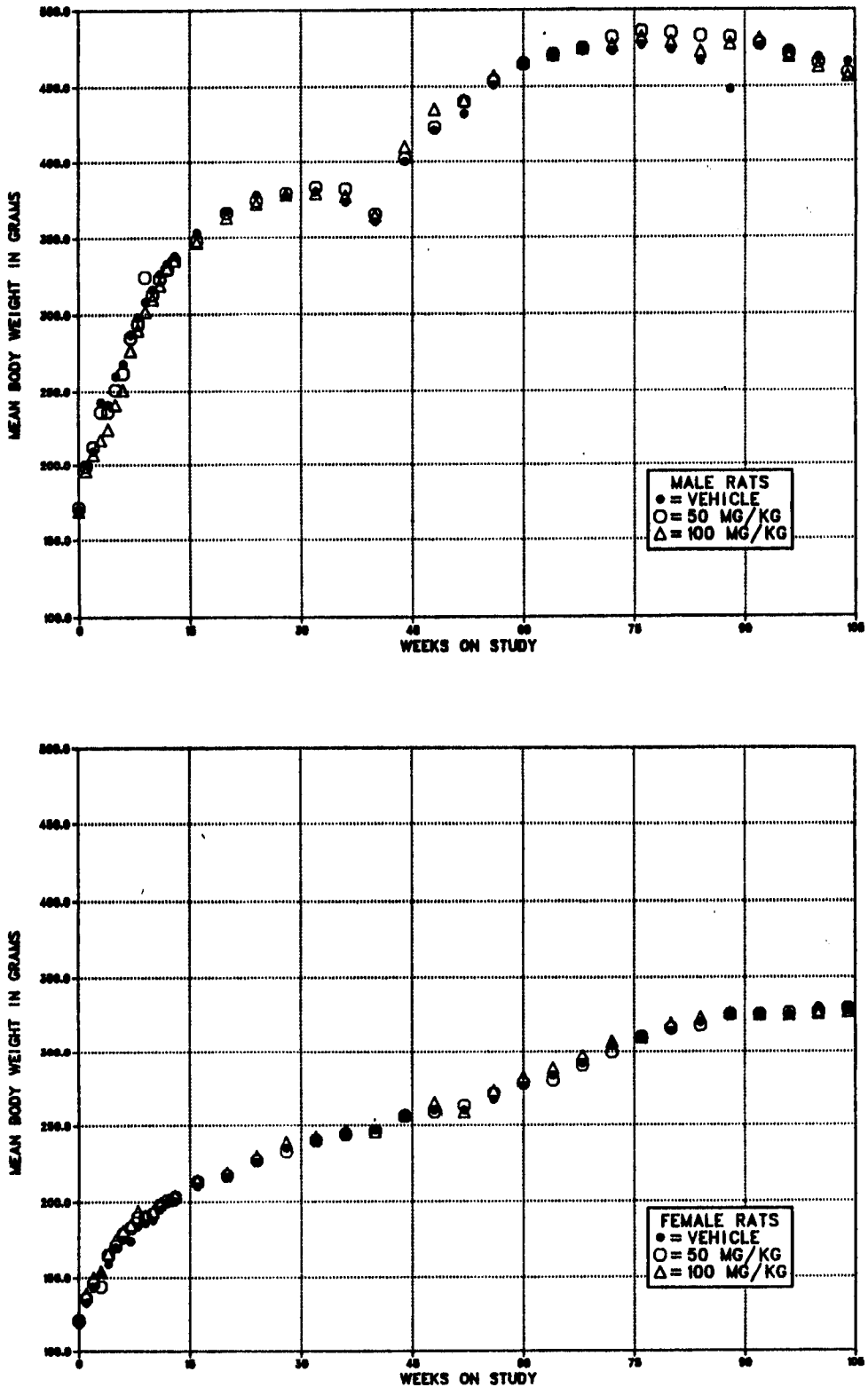


FIGURE 1. GROWTH CURVES FOR RATS ADMINISTERED 2-CHLOROETHANOL BY DERMAL APPLICATION FOR TWO YEARS

Survival

Estimates of the probabilities of the survival of male and female rats administered 2-chloroethanol at the doses of these studies and those of the vehicle controls are shown by the Kaplan and Meier curves in Figure 2. No significant differences in survival were observed between any groups of either sex (Table 10).

Pathology and Statistical Analyses of Results

This section describes significant or noteworthy changes in the incidences of rats with neoplastic or nonneoplastic lesions of skin, pituitary gland, and eye. Histopathologic findings on neoplasms in rats are summarized in Appendix A (Tables A1 and A2); Appendix A (Tables A3 and A4) also gives the survival and tumor status for individual male and female rats. Findings on nonneoplastic lesions are summarized in Appendix C (Tables C1 and C2). Appendix E (Tables E1 and E2) contains the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in one of the three groups. The statistical analyses used are discussed in Chapter II (Statistical Methods) and Appendix E (footnotes).

TABLE 10. SURVIVAL OF RATS IN THE TWO-YEAR DERMAL STUDIES OF 2-CHLOROETHANOL

	Vehicle Control	50 mg/kg	100 mg/kg
MALE (a)			
Animals initially in study	50	50	50
Nonaccidental deaths before termination (b)	16	13	13
Killed at termination	33	37	36
Died during termination period	1	0	1
Survival P values (c)	0.555	0.694	0.626
FEMALE (a)			
Animals initially in study	50	50	50
Nonaccidental deaths before termination (b)	8	11	11
Killed at termination	42	39	38
Died during termination period	0	0	1
Survival P values (c)	0.494	0.583	0.548

(a) Terminal kill period: weeks 104-105
(b) Includes animals killed in a moribund condition
(c) The result of the life table trend test is in the vehicle control column, and the results of the life table pairwise comparisons with the vehicle controls are in the dosed columns.

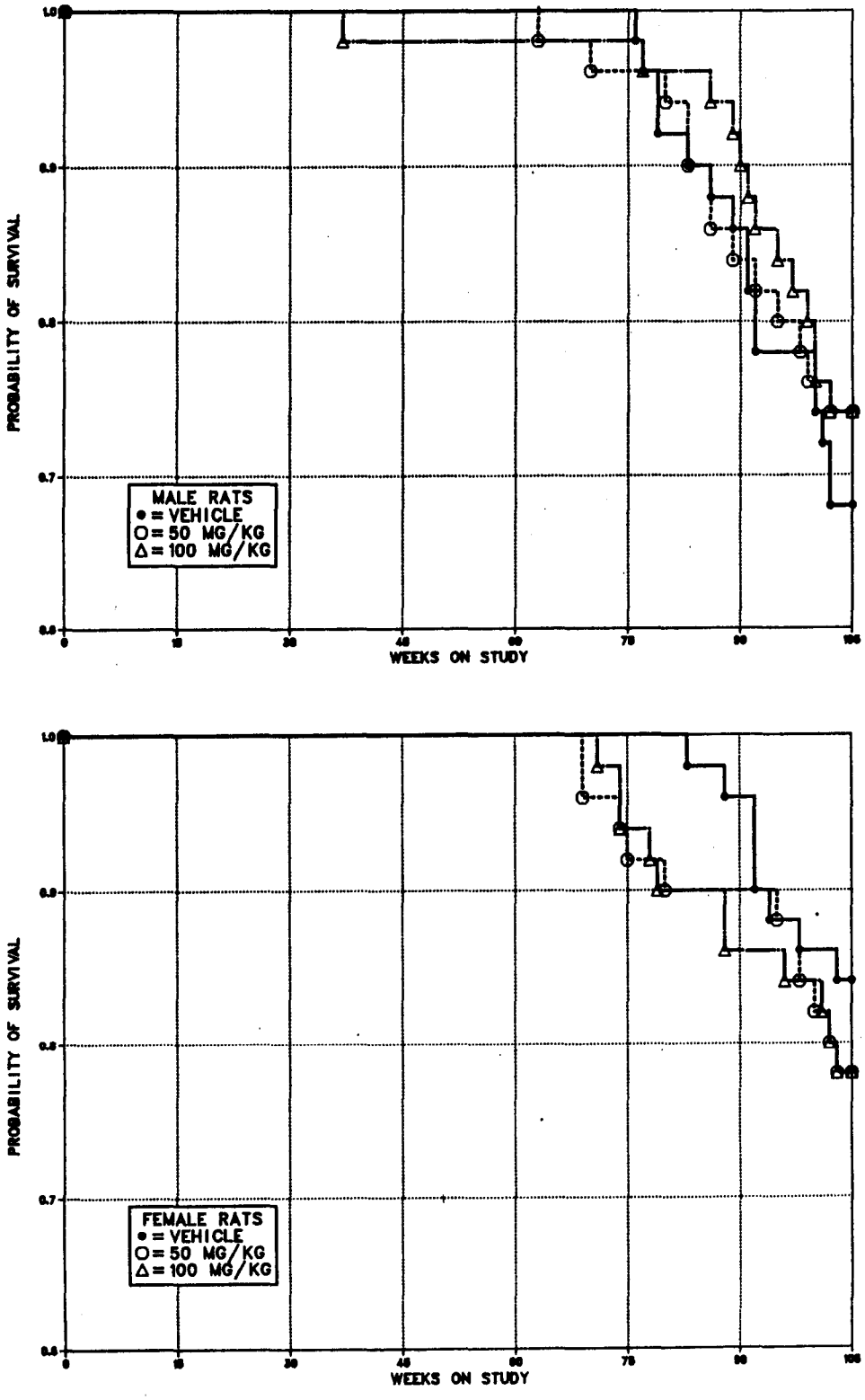


FIGURE 2. KAPLAN-MEIER SURVIVAL CURVES FOR RATS ADMINISTERED 2-CHLOROETHANOL BY DERMAL APPLICATION FOR TWO YEARS

Skin: The incidence of male rats with papillomas (squamous cell or unspecified) of the skin was significant by the trend tests, but the incidences in the dosed groups were not significantly greater than that in the vehicle controls, and the combined incidence of male rats with either papillomas or carcinomas was not statistically significant (Table 11). None of these papillomas appeared at the site of dermal application. Papillomas were not diagnosed in female rats. These papillomas were not life threatening; all the affected animals survived at least until week 102 of the studies. The earliest time to tumor in the high dose male rat group was for a nasal skin lesion noted at month 15. This lesion later was diagnosed as a papilloma.

TABLE 11. ANALYSIS OF SKIN TUMORS IN MALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (a)

	Vehicle Control	50 mg/kg	100 mg/kg
Papilloma			
Overall Rates	1/50 (2%)	0/50 (0%)	6/50 (12%)
Adjusted Rates	2.9%	0.0%	15.8%
Terminal Rates	1/34 (3%)	0/37 (0%)	5/37 (14%)
Life Table Tests	P=0.020	P=0.483N	P=0.073
Incidental Tumor Tests	P=0.022	P=0.483N	P=0.077
Carcinoma			
Overall Rates	2/50 (4%)	1/50 (2%)	0/50 (0%)
Papilloma or Carcinoma			
Overall Rates	3/50 (6%)	1/50 (2%)	6/50 (12%)
Adjusted Rates	8.3%	2.7%	15.8%
Terminal Rates	2/34 (6%)	1/37 (3%)	5/37 (14%)
Life Table Tests	P=0.184	P=0.287N	P=0.283
Incidental Tumor Tests	P=0.196	P=0.303N	P=0.297

(a) The statistical analyses used are discussed in Chapter II (Statistical Methods) and Appendix E (footnotes).

Pituitary Gland: Adenomas and adenomas or carcinomas (combined) of the pituitary gland occurred in female rats with significant positive trends by life table analysis (Table 12). The incidence of adenomas in the high dose group was significantly greater than that in the vehicle controls (life table analysis); the incidence of adenomas or carcinomas (combined) in the dosed groups was not significantly greater than that in the vehicle controls. The majority of these adenomas and carcinomas were found at terminal kill. All but one of the vehicle control animals in which these tumors were found lived to terminal kill; the earliest time to tumor in the dosed animals was reduced (low dose, 69 weeks; high dose, 71 weeks).

NTP has no adequate historical control animal tumor data base for F344/N rats receiving a test compound by dermal application. For all laboratories in the NTP, as of March 1983, the following historical data are available for pituitary gland adenomas in female F344/N rats:

Corn oil gavage controls:
382/1,042 (37%); range: 17%-55%
Untreated controls:
995/2,262 (44%); range: 18%-70%

At Litton Bionetics, Inc., the historical incidence of this tumor was the following:

Corn oil gavage controls:
66/149 (44%); range: 36%-50%
Untreated controls:
111/245 (45%); range: 42%-52%

TABLE 12. ANALYSIS OF PITUITARY GLAND LESIONS IN FEMALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL

	Vehicle Control	50 mg/kg	100 mg/kg
Focal Hyperplasia			
Overall Rates	7/50 (14%)	5/49 (10%)	7/50 (14%)
Adenoma			
Overall Rates	19/50 (38%)	24/49 (49%)	29/50 (58%)
Adjusted Rates	44.2%	52.9%	61.4%
Terminal Rates	18/42 (43%)	18/39 (46%)	21/39 (54%)
Life Table Tests	P=0.022	P=0.148	P=0.025
Incidental Tumor Tests	P=0.084	P=0.416	P=0.103
Carcinoma			
Overall Rates	4/50 (8%)	1/49 (2%)	1/50 (2%)
Adjusted Rates	9.5%	2.3%	2.6%
Terminal Rates	4/42 (10%)	0/39 (0%)	1/39 (3%)
Life Table Tests	P=0.117N	P=0.200N	P=0.202N
Incidental Tumor Tests	P=0.104N	P=0.158N	P=0.202N
Adenoma or Carcinoma (a)			
Overall Rates	22/50 (44%)	25/49 (51%)	30/50 (60%)
Adjusted Rates	51.2%	54.0%	63.6%
Terminal Rates	21/42 (50%)	18/39 (46%)	22/39 (56%)
Life Table Tests	P=0.049	P=0.252	P=0.052
Incidental Tumor Tests	P=0.167	P=0.565N	P=0.188

(a) In the male rats, the corresponding overall rates for vehicle control and dosed animals were: 15/50 (30%), 13/48 (26%), 16/49 (33%).

Eye: The incidences of cataracts and atrophy in vehicle control male and female rats were notably greater than those in the dosed groups (Table 13). Both the male and female vehicle controls were on the top two rows of the rack for the entire test period. Light intensity in the study room was not measured.

TABLE 13. ANALYSIS OF OCULAR LESIONS IN RATS IN THE TWO-YEAR DERMAL STUDIES OF 2-CHLOROETHANOL

	Vehicle Control	50 mg/kg	100 mg/kg
MALE			
Cataracts	15/50(39%)	2/50 (4%)	2/50 (4%)
Atrophy	21/50(42%)	3/50 (6%)	5/50 (10%)
FEMALE			
Cataracts	13/50(26%)	2/50 (4%)	3/50 (6%)
Atrophy	17/50(34%)	3/50 (6%)	3/50 (6%)

SINGLE-ADMINISTRATION STUDIES

All mice that received 68.1 mg died. Other deaths are tabulated in Table 14. The LD_{50} (14-day) value was estimated to be 33.1 mg for males and 41.3 mg for females by probit analysis (Finney, 1964). There was a dose-related reduction in body weight gains for both male and female mice.

TABLE 14. SURVIVAL AND MEAN BODY WEIGHTS OF MICE IN THE SINGLE-ADMINISTRATION DERMAL STUDIES OF 2-CHLOROETHANOL

Dose		Survival	Mean Body Weights (grams)		
mg	mg/kg (a)	(b)	Initial	Day 14	Change
MALE					
10.0	410	5/5	24.4	29.0	+4.6
14.7	544	5/5	27.0	29.0	+2.0
21.5	808	5/5	26.6	28.4	+1.8
31.6	1,239	(c) 2/5	25.5	27.5	+2.0
46.4	1,785	(d) 1/5	26.0	27.0	+1.0
68.1	--	(e) 0/5	--	--	--
FEMALE					
10.0	439	5/5	22.8	25.0	+2.2
14.7	634	5/5	23.2	25.6	+2.4
21.5	995	5/5	21.6	23.4	+1.8
31.6	1,417	(f) 3/5	22.3	24.0	+1.7
46.4	2,178	(g) 3/5	21.3	22.7	+1.4
68.1	--	(e) 0/5	--	--	--

(a) Day 1 dose based on initial group average body weight
(b) Number surviving/number initially in the group
(c) Day of death: 1, 1, 2
(d) Day of death: 1, 1, 1, 2
(e) Day of death of all: 1
(f) Day of death: 1, 4
(g) Day of death: 1, 3

FOURTEEN-DAY STUDIES

All the mice that received 60 mg died (Table 15). Three of five males and 3/5 females that received 45 mg also died. All deaths occurred during the first 2 days of dosing. Final mean body weights of dosed and vehicle control mice were comparable; however, the male mice that received 45 mg lost weight. No compound-related effects were observed at necropsy.

TABLE 15. SURVIVAL AND MEAN BODY WEIGHTS OF MICE IN THE FOURTEEN-DAY DERMAL STUDIES OF 2-CHLOROETHANOL

Dose		Survival	Mean Body Weights (grams)			Final Weight Relative to Vehicle Controls
mg	mg/kg (a)	(b)	Initial (c)	Final	Change	(percent)
MALE						
(d) 0	0	5/5	27.5 ± 1.9	29.5 ± 2.5	+2.0 ± 0.7	--
2.5	92	5/5	27.1 ± 2.0	28.1 ± 2.2	+1.0 ± 0.6	95.3
5.0	174	5/5	28.6 ± 2.0	31.1 ± 2.1	+2.5 ± 1.0	105.4
10	377	5/5	26.5 ± 1.2	29.0 ± 1.7	+2.5 ± 0.7	98.3
20	741	5/5	27.0 ± 1.5	29.3 ± 1.1	+2.3 ± 0.4	99.3
30	1,095	5/5	27.4 ± 1.9	30.0 ± 1.6	+2.6 ± 1.2	101.7
(e) 45	1,411	(f) 2/5	31.9 ± 3.9	30.6 ± 1.4	−1.3 ± 1.2	--
(e) 60	--	(g) 0/5	27.5 ± 2.1	--	--	--
FEMALE						
(d) 0	0	5/5	22.8 ± 2.3	23.4 ± 2.1	+0.6 ± 0.5	--
2.5	109	5/5	22.9 ± 1.4	23.2 ± 2.0	+0.3 ± 1.1	99.1
5.0	225	5/5	22.2 ± 1.4	23.2 ± 1.3	+1.0 ± 0.4	99.1
10	435	5/5	23.0 ± 2.7	23.6 ± 2.9	+0.6 ± 0.5	100.9
20	847	5/5	23.6 ± 0.8	23.6 ± 1.2	0.0 ± 1.2	100.9
30	1,376	5/5	21.8 ± 1.7	23.9 ± 1.9	+2.1 ± 0.6	102.1
(e) 45	1,875	(h) 2/5	23.7 ± 3.3	24.3 ± 0.2	+0.6 ± 2.5	103.8
(e) 60	--	(g) 0/5	22.2 ± 1.8	--	--	--

(a) Day 1 dose based on initial average body weight
(b) Number surviving/number per group
(c) Based on all animals initially in the group. Subsequent calculations are based on those animals surviving to the end of the study.
(d) Vehicle control
(e) Groups tested without matched controls after studies with lower dose groups were completed.
(f) Day of death: 1, 2, 2
(g) Day of death for all: 1
(h) Day of death: 2, 2, 2

THIRTEEN-WEEK STUDIES

All the male mice that received 30 or 45 mg and 1/10 male mice that received 20 mg died (Table 16). Nine of 10 female mice that received 30 or 45 mg and 3/10 that received 20 mg died. All these mice died within 3 days of the start of the studies. Mean body weights of dosed mice were greater than those of the vehicle controls.

Acute nephrosis was diagnosed in 1/1 male and 1/3 female mice examined in the 30-mg groups and in 1/9 males in the 20-mg group. Pancreatic acinar cell necrosis was diagnosed in 2/3 female mice that received 30 mg. Hepatocellular fatty change was diagnosed in 1/1 male and in 2/3 female mice that received 30 mg.

Dose Selection Rationale: Based on mortality in the 30- and 45-mg groups and on the incidences of kidney, pancreatic, and liver lesions found in the 20- and 30-mg groups, doses selected for mice for the 2-year studies were 7.5 and 15 mg per application per mouse.

TWO-YEAR STUDIES

Body Weights and Clinical Signs

Mean body weights of dosed male and female mice were somewhat lower than those of the vehicle controls throughout most of the study (Tables 17 and 18 and Figure 3). No compound-related clinical signs were observed.

Serologic analysis of blood samples from the sentinel animals showed evidence of Sendai virus, minute virus of mice (MVM), and mouse hepatitis virus (MHV) (Appendix K). Animal room environment records (temperature and relative humidity) during the 2-year studies are summarized in Appendix M.

TABLE 16. SURVIVAL AND MEAN BODY WEIGHTS OF MICE IN THE THIRTEEN-WEEK DERMAL STUDIES OF 2-CHLOROETHANOL

Dose		Survival	Mean Body Weights (grams)			Final Weight Relative to Vehicle Controls
mg	mg/kg (a)	(b)	Initial	Final	Change	(percent)
MALE						
(c) 0	--	10/10	26	35	+ 9	--
5	192	10/10	26	37	+11	105.7
10	385	10/10	26	38	+12	108.6
20	769	(d) 9/10	26	34	+ 8	97.1
30	1,154	(d) 0/10	--	--	--	--
45	1,731	(d) 0/10	--	--	--	--
FEMALE						
(c) 0	--	10/10	22	28	+ 6	--
5	227	10/10	22	28	+ 6	0
10	455	10/10	22	29	+ 7	103.6
20	909	(d) 7/10	22	30	+ 8	107.1
30	1,304	(d) 1/10	23	31	+ 8	110.7
45	1,957	(d) 1/10	23	40	+17	142.9

(a) Based on initial mean body weight
(b) Number surviving/number in group
(c) Vehicle control
(d) Week of death: 1

TABLE 17. MEAN BODY WEIGHTS AND SURVIVAL OF MALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL

Weeks on Study	Control		7.5 mg			15 mg		
	Av. Wt. (grams)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of controls) (a)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of controls) (a)	No. of Survivors
	UNTREATED							
0	28.8	50	29.7	103	50	29.2	101	50
1	30.7	50	30.6	100	50	30.0	98	43
2	32.6	50	31.5	97	50	29.4	90	43
3	34.1	50	32.9	96	50	33.1	97	43
4	34.7	50	33.6	97	50	33.6	97	43
5	35.4	50	34.3	97	50	34.5	97	43
6	36.2	50	35.0	97	50	35.3	98	43
7	36.5	50	35.4	97	50	35.8	98	43
8	36.7	50	35.8	98	50	36.0	98	43
9	37.1	50	36.5	98	50	37.5	101	43
10	38.5	50	37.4	97	50	37.7	98	43
11	39.0	50	38.1	98	50	38.2	98	43
12	38.7	49	37.8	98	50	38.1	98	43
13	39.4	49	39.0	99	50	39.2	99	43
16	40.3	49	39.4	98	50	39.6	98	43
20	41.6	49	41.4	100	49	40.8	98	43
24	43.3	49	42.3	98	49	42.3	98	43
28	43.2	49	41.7	97	49	41.5	96	43
32	43.9	49	42.0	96	49	42.6	97	42
36	44.8	49	42.7	95	49	43.0	96	42
40	44.9	49	43.6	97	47	43.8	98	42
44	45.1	49	43.7	97	47	42.7	95	40
48	42.9	49	43.2	101	46	41.7	97	40
52	45.3	48	45.0	99	46	45.4	100	38
56	44.7	47	44.0	98	45	45.2	101	38
60	43.0	45	43.7	102	45	45.3	105	38
64	44.5	44	44.1	99	45	45.0	101	38
68	45.6	40	45.0	99	43	45.7	100	37
72	45.3	39	45.8	101	41	46.0	102	36
76	46.8	36	45.9	98	35	45.3	97	32
80	47.3	35	45.6	96	33	46.1	97	30
84	46.8	31	45.4	97	32	43.5	93	28
88	46.8	30	45.3	97	30	45.4	97	27
92	45.9	28	44.7	97	25	44.3	97	25
96	45.0	27	43.5	97	23	43.2	96	21
100	44.3	25	43.3	98	20	41.5	94	20
104	44.0	24	43.3	98	16	42.0	95	12
	VEHICLE							
0	29.2	50	29.7	102	50	29.2	100	50
1	30.3	50	30.6	101	50	30.0	99	43
2	31.3	50	31.5	101	50	29.4	94	43
3	31.5	50	32.9	104	50	33.1	105	43
4	33.5	50	33.6	100	50	33.6	100	43
5	34.5	50	34.3	99	50	34.5	100	43
6	35.5	50	35.0	99	50	35.3	99	43
7	35.8	50	35.4	99	50	35.8	100	43
8	36.4	50	35.8	98	50	36.0	99	43
9	36.9	50	36.5	99	50	37.5	102	43
10	37.9	50	37.4	99	50	37.7	99	43
11	38.4	50	38.1	99	50	38.2	99	43
12	38.5	50	37.8	98	50	38.1	99	43
13	39.5	50	39.0	99	50	39.2	99	43
16	40.5	50	39.4	97	50	39.6	98	43
20	42.1	50	41.4	98	49	40.8	97	43
24	43.7	50	42.3	97	49	42.3	97	43
28	43.2	50	41.7	97	49	41.5	96	43
32	44.3	50	42.0	95	49	42.6	96	42
36	44.6	50	42.7	96	49	43.0	96	42
40	45.3	50	43.6	96	47	43.8	97	42
44	46.8	49	43.7	93	47	42.7	91	40
48	44.2	48	43.2	98	46	41.7	94	40
52	46.7	48	45.0	96	46	45.4	97	38
56	45.8	48	44.0	96	45	45.2	99	38
60	45.5	47	43.7	96	45	45.3	100	38
64	45.9	47	44.1	96	45	45.0	98	38
68	46.7	46	45.0	96	43	45.7	98	37
72	47.0	46	45.8	97	41	46.0	98	36
76	47.5	44	45.9	97	35	45.3	95	32
80	47.4	41	45.6	96	33	46.1	97	30
84	47.5	38	45.4	96	32	43.5	92	28
88	46.5	37	45.3	97	30	45.4	98	27
92	45.9	33	44.7	97	25	44.3	97	25
96	44.3	32	43.5	98	23	43.2	98	21
100	43.6	31	43.3	99	20	41.5	95	20
104	43.6	28	43.3	99	16	42.0	96	12

(a) Mean body weights of dosed groups are compared with untreated control or vehicle control mice.

TABLE 18. MEAN BODY WEIGHTS AND SURVIVAL OF FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL

Weeks on Study	Control		7.5 mg			15 mg		
	Av. Wt. (grams)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of controls) (a)	No. of Survivors	Av. Wt. (grams)	Wt. (percent of controls) (a)	No. of Survivors
	UNTREATED							
0	24.0	50	24.3	101	50	23.8	99	50
1	24.4	50	23.8	98	50	23.7	97	49
2	25.7	50	24.9	97	50	24.8	96	49
3	26.8	50	25.7	96	50	25.5	95	49
4	27.0	50	26.1	97	50	25.6	95	49
5	27.8	50	30.0	108	50	26.7	96	49
6	28.2	50	27.5	98	50	28.0	99	49
7	29.6	50	27.6	93	50	28.1	95	48
8	29.5	50	28.0	95	50	29.2	99	48
9	30.1	50	28.9	96	50	28.3	94	48
10	30.6	50	29.6	97	50	29.5	96	48
11	31.4	50	29.5	94	50	29.7	95	48
12	31.0	50	29.9	96	50	29.7	96	48
13	31.8	50	30.3	95	50	31.0	97	48
16	32.7	50	31.6	97	50	31.7	97	48
20	35.0	50	33.9	97	49	32.7	93	48
24	36.3	50	33.7	93	49	34.0	94	48
28	35.7	50	33.3	93	49	33.0	92	47
32	37.7	50	34.3	91	48	34.3	91	47
36	38.1	50	34.6	91	48	35.2	92	47
40	39.0	49	35.5	91	48	36.4	93	47
44	39.6	48	36.4	92	47	36.6	92	47
48	39.0	48	37.1	95	46	37.3	96	46
52	41.0	47	37.8	92	45	38.5	94	46
56	41.1	45	38.0	92	45	38.3	93	45
60	41.0	45	38.1	93	45	38.4	94	45
64	41.5	45	38.3	92	43	38.8	93	45
68	41.9	45	38.4	92	42	38.8	93	42
72	42.5	45	39.2	92	42	39.7	93	40
76	44.0	44	39.7	90	41	40.5	92	37
80	43.9	43	40.0	91	38	40.0	91	34
84	43.8	38	40.4	92	36	39.8	91	33
88	44.3	33	38.9	88	32	39.9	90	31
92	43.6	32	38.0	87	31	39.0	89	30
96	43.4	30	37.2	86	28	38.3	88	26
100	42.0	30	35.3	84	21	36.5	87	22
104	41.3	25	36.4	88	20	36.1	87	20
	VEHICLE							
0	24.1	50	24.3	101	50	23.8	99	50
1	23.9	50	23.8	100	50	23.7	99	49
2	25.0	50	24.9	100	50	24.8	99	49
3	25.8	50	25.7	100	50	25.5	99	49
4	25.8	50	26.1	101	50	25.6	99	49
5	27.0	50	30.0	111	50	26.7	99	49
6	27.7	50	27.5	99	50	28.0	101	49
7	27.8	50	27.6	99	50	28.1	101	48
8	28.4	50	28.0	99	50	29.2	103	48
9	28.5	50	28.9	101	50	28.3	99	48
10	29.6	50	29.6	100	50	29.5	100	48
11	29.9	50	29.5	99	50	29.7	99	48
12	30.2	50	29.9	99	50	29.7	98	48
13	31.1	50	30.3	97	50	31.0	100	48
16	31.8	50	31.6	99	50	31.7	100	48
20	33.4	50	33.9	101	49	32.7	98	48
24	35.4	49	33.7	95	49	34.0	96	48
28	34.4	48	33.3	97	49	33.0	96	47
32	35.7	47	34.3	96	48	34.3	96	47
36	38.4	47	34.6	90	48	35.2	92	47
40	38.2	47	35.5	93	48	36.4	95	47
44	38.8	47	36.4	94	47	36.6	94	47
48	38.4	46	37.1	97	46	37.3	97	46
52	39.8	43	37.8	95	45	38.5	97	46
56	39.4	43	38.0	96	45	38.3	97	45
60	40.1	43	38.1	95	45	38.4	96	45
64	40.5	43	38.3	95	43	38.8	96	45
68	41.6	40	38.4	92	42	38.8	93	42
72	41.5	39	39.2	94	42	39.7	96	40
76	42.9	39	39.7	93	41	40.5	94	37
80	42.5	37	40.0	94	38	40.0	94	34
84	42.8	35	40.4	94	36	39.8	93	33
88	42.1	35	38.9	92	32	39.9	95	31
92	41.2	33	38.0	92	31	39.0	95	30
96	40.0	31	37.2	93	28	38.3	96	26
100	39.3	29	35.3	90	21	36.5	93	22
104	37.9	26	36.4	96	20	36.1	95	20

(a) Mean body weights of dosed groups are compared with untreated control or vehicle control mice.

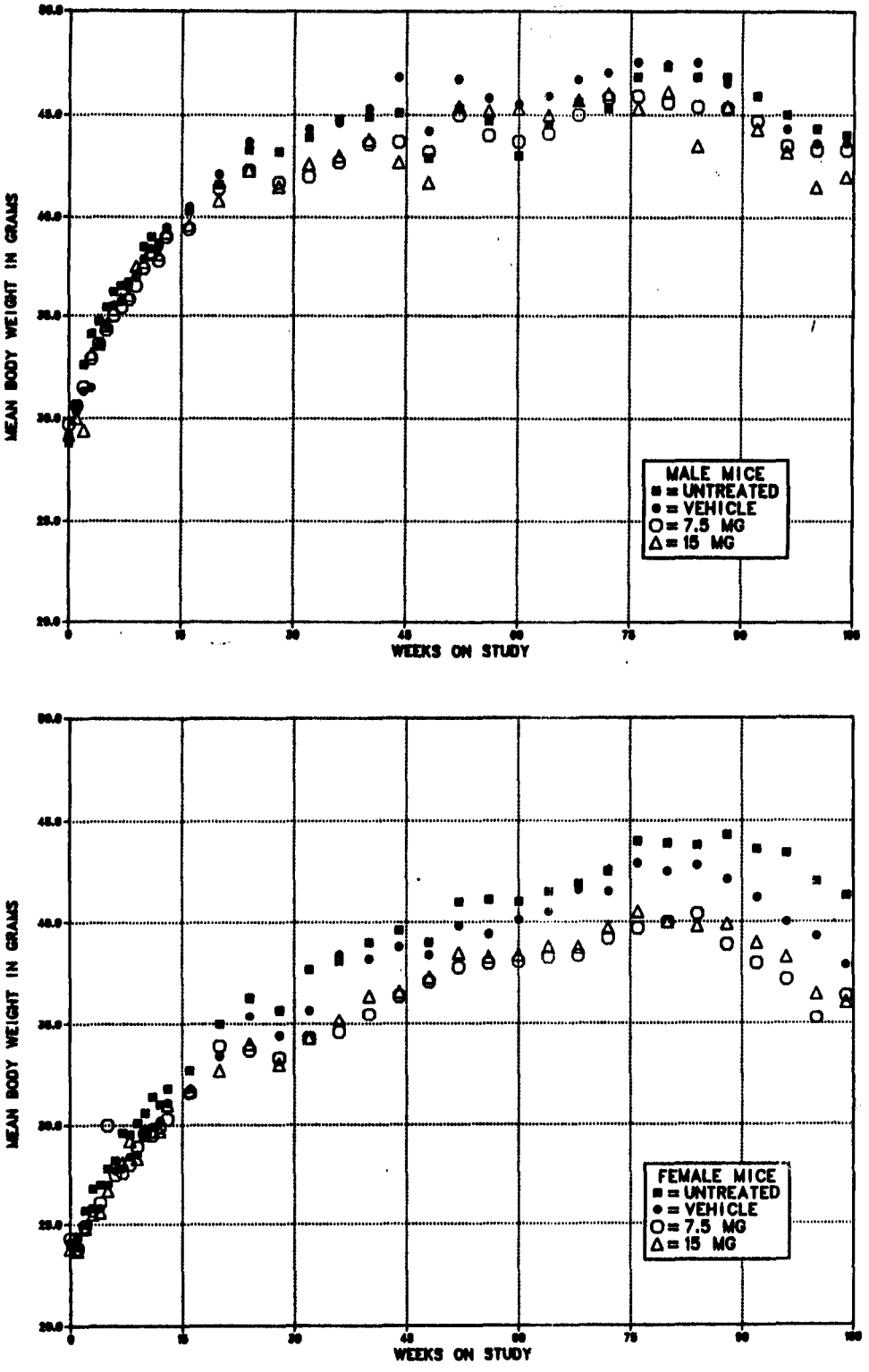


FIGURE 3. GROWTH CURVES FOR MICE ADMINISTERED 2-CHLOROETHANOL BY DERMAL APPLICATION FOR TWO YEARS

Survival

Estimates of the probabilities of survival of male and female mice administered 2-chloroethanol by dermal application at the doses of these studies are shown by the Kaplan and Meier curves in Figures 4 and 5. The survival of the low dose group of male mice was marginally lower than that of the vehicle controls (P = 0.062). The survival of the high dose group of male mice was significantly lower than that of the vehicle controls (P = 0.002; P = 0.023 if seven high dose male mice that died in week 1 are censored) (Table 19). Figure 5 shows the estimates of the probabilities of survival of male mice (Kaplan and Meier curves) if these early-death animals are censored. All seven of these high dose male mice had inflammation at the site of dermal application; five also had ulceration at the site of dermal application, and five had lung congestion, inflammation, or hemorrhage. As this was a toxic response and the early-death animals were not at risk, *only the 43 survivors following week 1 have been used for the statistical analysis of lesions in the high dose male mice.*

Pathology and Statistical Analyses of Results

This section describes significant or noteworthy changes in the incidences of mice with neoplastic or nonneoplastic lesions in lung, hematopoietic system, integumentary system, and adrenal cortex. Histopathologic findings on neoplasms in mice are summarized in Appendix B (Tables B1 and B2); Appendix B (Tables B3 and B4) also gives the survival and tumor status for individual male and female mice. Findings on nonneoplastic lesions are summarized in Appendix D (Tables D1 and D2). Appendix E (Tables E3 and E4) contains the statistical analyses of those primary tumors that occurred with an incidence of at least 5% in the vehicle controls or in either dosed group. The statistical analyses used are discussed in Chapter II (Statistical Methods) and Appendix E (footnotes).

TABLE 19. SURVIVAL OF MICE IN THE TWO-YEAR DERMAL STUDIES OF 2-CHLOROETHANOL

	Control		7.5 mg	15 mg
	Untreated	Vehicle		
MALE (a)				
Animals initially in study	50	50	50	50
Nonaccidental deaths before termination (b)	25	24	32	38
Accidentally killed	1	0	2	0
Killed at termination	24	26	16	12
Survival P values (c)	--	0.022	0.062	0.023
FEMALE (a)				
Animals initially in study	50	50	50	50
Nonaccidental deaths before termination (b)	26	24	30	30
Killed at termination	24	26	20	20
Survival P values (c)	--	0.302	0.397	0.356

(a) Terminal kill period: week 105
(b) Includes animals killed in a moribund condition
(c) The result of the life table trend test is in the vehicle control column, and the results of the life table pairwise comparisons with the vehicle controls are in the dosed columns. The P values given for male mice were obtained with the seven high dose deaths in week 1 censored.

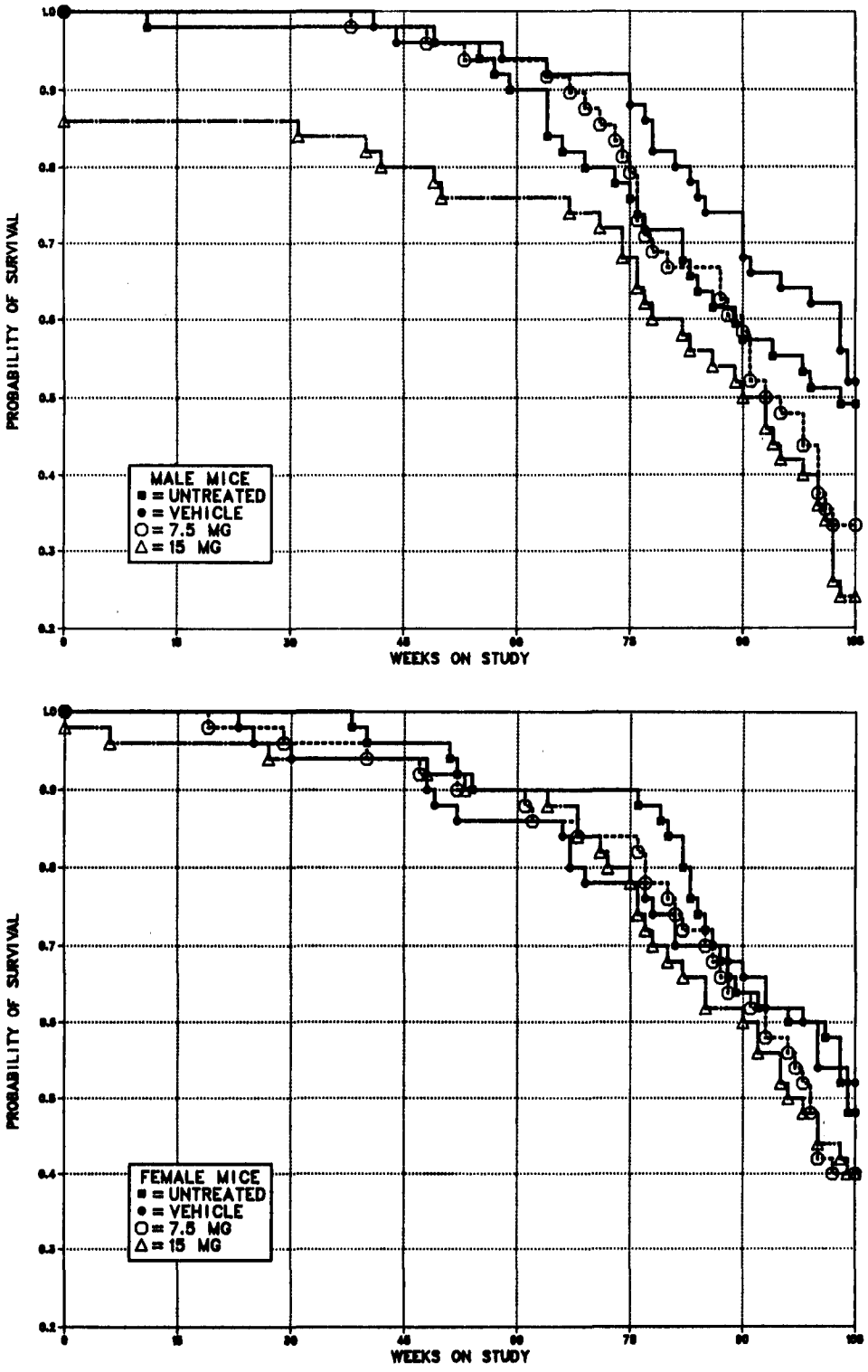


FIGURE 4. KAPLAN-MEIER SURVIVAL CURVES FOR MICE ADMINISTERED 2-CHLOROETHANOL BY DERMAL APPLICATION FOR TWO YEARS

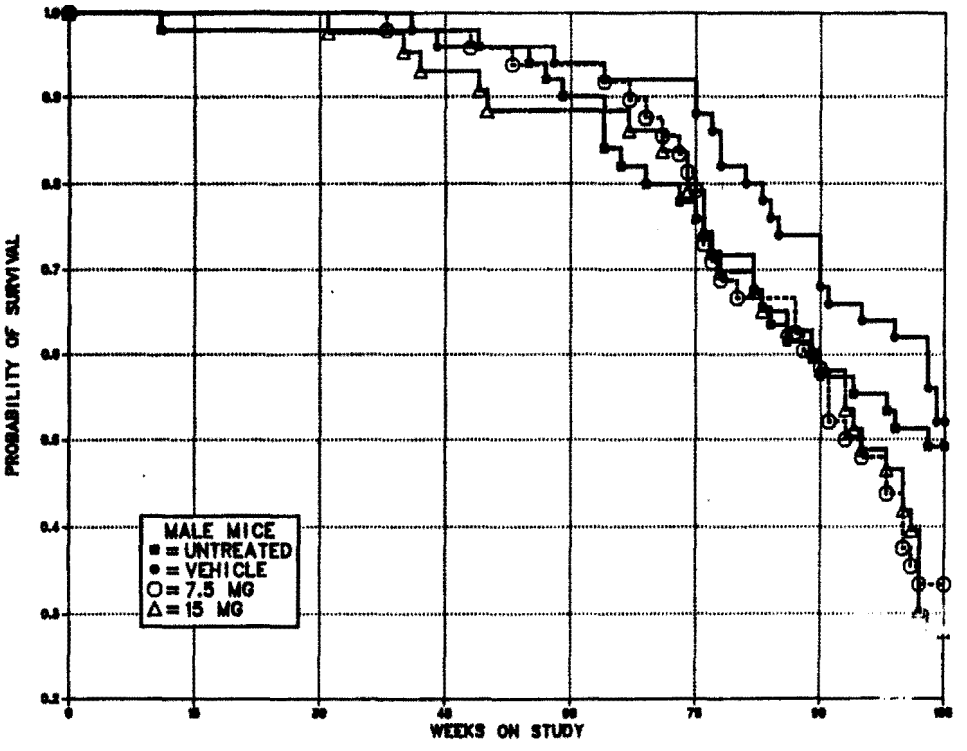


FIGURE 5. KAPLAN-MEIER SURVIVAL CURVES FOR MALE MICE ADMINISTERED 2-CHLOROETHANOL BY DERMAL APPLICATION FOR TWO YEARS WITH WEEK-ONE DEATHS CENSORED

Lung: The incidence of low dose male mice with either alveolar/bronchiolar adenomas or carcinomas (combined) was significantly greater than that of the vehicle controls by the life table test; the incidence of these lesions was not dose related (Table 20). Dosing of female mice with 2-chloroethanol did not significantly alter the incidence of animals with alveolar/bronchiolar adenomas or carcinomas (combined). Ten of the 18 low dose males with these neoplasms were animals that died before the end of the study. The remainder of the neoplasms were found at terminal kill.

TABLE 20. ANALYSIS OF LUNG LESIONS IN MICE IN THE TWO-YEAR DERMAL STUDIES OF 2-CHLOROETHANOL (a)

	Untreated Control	Vehicle Control	7.5 mg	15 mg
MALE				
Alveolar Epithelial Hyperplasia				
Overall Rates	2/50 (4%)	4/50 (8%)	1/50 (2%)	2/43 (5%)
Alveolar/Bronchiolar Adenoma				
Overall Rates	6/50 (12%)	8/50 (16%)	10/50 (20%)	9/43 (21%)
Adjusted Rates	25.0%	26.0%	43.0%	46.0%
Terminal Rates	6/24 (25%)	4/26 (15%)	4/16 (25%)	4/12 (33%)
Life Table Tests		P=0.062	P=0.105	P=0.078
Incidental Tumor Tests		P=0.282	P=0.294	P=0.279
Alveolar/Bronchiolar Carcinoma				
Overall Rates	4/50 (8%)	6/50 (12%)	9/50 (18%)	3/43 (7%)
Adjusted Rates	13.7%	18.1%	38.1%	16.6%
Terminal Rates	2/24 (8%)	3/26 (12%)	4/16 (25%)	1/12 (8%)
Life Table Tests		P=0.501	P=0.095	P=0.587N
Incidental Tumor Tests		P=0.383N	P=0.249	P=0.355N
Alveolar/Bronchiolar Adenoma or Carcinoma				
Overall Rates	10/50 (20%)	14/50 (28%)	18/50 (36%)	11/43 (26%)
Adjusted Rates	37.2%	40.9%	67.1%	55.7%
Terminal Rates	8/24 (33%)	7/26 (27%)	8/16 (50%)	5/12 (42%)
Life Table Tests		P=0.132	P=0.029	P=0.196
Incidental Tumor Tests		P=0.528	P=0.155	P=0.579N
FEMALE				
Alveolar/Bronchiolar Adenoma or Carcinoma				
Overall Rates	10/50 (20%)	9/50 (18%)	10/49 (20%)	9/50 (18%)

(a) The statistical analyses used are discussed in Chapter II (Statistical Methods) and Appendix E (footnotes).

Hematopoietic System: The incidences of low dose male mice with either lymphomas or with lymphomas or leukemia (combined) were significantly greater than those of the vehicle controls by life table analysis (Table 21); these increases were not dose related. The incidences of dosed female mice with lymphomas or leukemia (combined) were not significantly increased. With one exception, the lymphomas or leukemias were found in vehicle control and low dose animals that died or were killed before the terminal kill.

TABLE 21. ANALYSIS OF HEMATOPOIETIC SYSTEM TUMORS IN MICE IN THE TWO-YEAR DERMAL STUDIES OF 2-CHLOROETHANOL

	Untreated Control	Vehicle Control	7.5 mg	15 mg
MALE				
Lymphoma				
Overall Rates	3/50 (6%)	4/50 (8%)	10/50 (20%)	2/43 (5%)
Adjusted Rates	6.6%	11.2%	24.7%	5.0%
Terminal Rates	0/24 (0%)	1/26 (4%)	0/16 (0%)	0/12 (0%)
Life Table Tests		P=0.525N	P=0.044	P=0.538N
Incidental Tumor Tests		P=0.104N	P=0.233	P=0.153N
Leukemia				
Overall Rates	3/50 (6%)	2/50 (4%)	4/50 (8%)	2/43 (5%)
Lymphoma or Leukemia				
Overall Rates	6/50 (12%)	6/50 (12%)	14/50 (28%)	4/43 (9%)
Adjusted Rates	14.0%	14.9%	34.9%	9.9%
Terminal Rates	0/24 (0%)	1/26 (4%)	0/16 (0%)	0/12 (0%)
Life Table Tests		P=0.505	P=0.022	P=0.583N
Incidental Tumor Tests		P=0.086N	P=0.196	P=0.121N
FEMALE				
Lymphoma or Leukemia				
Overall Rates	12/50 (24%)	9/50 (18%)	15/50 (30%)	13/50 (26%)

Integumentary System: Fibromas, fibrosarcomas, or neurofibrosarcomas (combined) in male mice (vehicle control, 3/50; low dose, 0/50; high dose, 0/43) occurred with a significant negative trend (P=0.027, incidental tumor test); but the incidences in the dosed groups were not significantly different from that in the vehicle controls in pairwise comparisons. For the purpose of these analyses, "skin" is considered to be a combination of samples taken at the site at which 2-chloroethanol was administered and from other locations on the same animal.

In male mice, dose-related increases were observed in the incidences of inflammation at the site of dermal application (vehicle control, 7/50; low dose, 12/50; high dose, 18/50). The incidence of ulceration also increased in dosed male mice (vehicle control, 1/50; low dose, 3/50; high dose, 8/50); all these ulcers occurred in male mice with inflammation at the site of dermal application. All seven males that died in the 1st week of the study had inflammation at the site of application, and five also had ulceration.

Adrenal Cortex: Adrenal cortical adenomas in male mice occurred with a significant positive trend; the incidence in the high dose group was significantly greater than that in the vehicle controls (Table 22) but was similar to that observed in the untreated controls. An adrenal cortical adenoma was observed in 1/49 untreated female mice; none was seen in any other group of female mice. All adrenal cortical neoplasms were found at terminal kill.

TABLE 22. ANALYSIS OF ADRENAL CORTICAL LESIONS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL

	Untreated Control	Vehicle Control	7.5 mg	15 mg
Hyperplasia				
Overall Rates	4/48 (8%)	2/48 (4%)	3/49 (6%)	2/43 (4%)
Adenoma				
Overall Rates	4/48 (8%)	0/48 (0%)	2/49 (4%)	3/43 (7%)
Adjusted Rates	8.3%	0.0%	12.5%	25.0%
Terminal Rates	4/24 (17%)	0/26 (0%)	2/16 (13%)	3/12 (25%)
Life Table Tests		P=0.013	P=0.138	P=0.024
Incidental Tumor Tests		P=0.013	P=0.138	P=0.024

IV. DISCUSSION AND CONCLUSIONS

Genetic Toxicology
Toxicity and Carcinogenicity
Conclusions

IV. DISCUSSION AND CONCLUSIONS

The toxicologic and carcinogenic potential of 2-chloroethanol was studied in F344/N rats and Swiss CD-1 mice by dermal application of the test chemical under the following conditions: (1) single-administration studies (14 days' observation): rats, 38-3,713 mg/kg; mice, 410-2,178 mg/kg; (2) 14-day studies: rats, 0-611 mg/kg; mice, 0-1,875 mg/kg; (3) 13-week studies (five doses per week): rats, 0, 62-1,000 mg/kg; mice, 0, 5-45 mg per animal (192-1,957 mg/kg at week 1); (4) 2-year studies (five doses per week): rats, 0, 50, or 100 mg/kg; mice, 0, 7.5, or 15 mg per animal (253-630 mg/kg at week 1, 188-411 mg/kg at week 100).

In all studies, dose-related mortality usually occurred within the 1st week. In the 2-year studies, survival of dosed and vehicle control rats and of dosed and vehicle control female mice were comparable. The survival of high dose male mice was significantly ($P<0.005$) lower than that of the vehicle controls; 7/50 (14%) of these animals died during the first 3 days on study. All seven of these male mice had inflammation at the site of dermal application; five also had ulcers at the site of dermal application, and five had lung congestion, inflammation, or hemorrhage. When the animals that died during week 1 are censored from the analysis, the survival of the high dose group of male mice remains significantly ($P<0.05$) lower than that of the vehicle controls (Figures 4 and 5).

Body weights of rats in the 13-week and 2-year studies and of mice in the 13-week studies were not affected by administration of 2-chloroethanol. Mean body weights of dosed male and female mice were somewhat lower than those of the vehicle controls throughout most of the 2-year studies.

The survival and weight gain data suggest that both male and female F344/N rats could have tolerated a higher dose of 2-chloroethanol in the 2-year studies. The dose-related increased mortality in male mice suggests that the maximum effective dose was probably administered; female mice might have tolerated a higher dose of 2-chloroethanol. Overall survival in all groups of mice was poor (Table 19).

The lethal effects of 2-chloroethanol may be associated with a reduction from the steady-state concentration of hepatic glutathione (GSH) resulting from the conjugation of GSH with 2-chloroacetaldehyde, the enzymatic oxidation product of 2-chloroethanol. A single nonlethal (50% of the LD_{50} value) dose of 2-chloroethanol lowered the GSH content of female rat liver by about 80% after 2 hours (Johnson, 1965).

Genetic Toxicology

2-Chloroacetaldehyde alkylates DNA (Oesch and Doerjer, 1982), causes errors during in vitro DNA synthesis (Hall et al., 1981), and is mutagenic in bacterial virus (Garro and Phillips, 1980) and bacterial DNA transformation systems (Phillips et al., 1980). 2-Chloroacetaldehyde is weakly mutagenic and recombinogenic in yeast (Loprieno et al., 1977), is mutagenic in the fungus *Aspergillus nidulans* (Bignami et al., 1980a,b) as well as in mammalian cell cultures (Huberman et al., 1975), and inhibits interferon induction when mouse embryo fibroblasts are challenged with Newcastle disease virus (Sonnenfeld et al., 1980). 2-Chloroacetaldehyde is more mutagenic in Salmonella than is the parent compound, 2-chloroethanol. The addition of liver S9 reduces the mutagenicity of 2-chloroacetaldehyde, possibly by oxidation to chloroacetic acid, which is not mutagenic in Salmonella (McCann et al., 1975; Bartsch et al., 1980; Bignami et al., 1980b), *E. coli* (Mamber et al., 1983), or mammalian cells (Huberman et al., 1975). Amacher and Turner (1982) reported, however, that chloroacetic acid may be weakly mutagenic in the mouse lymphoma assay in the presence of liver S9.

In vivo studies in rats (Green and Hathway, 1977; Rannug and Beije, 1979) showed that 2-chloroacetaldehyde is conjugated with glutathione by a glutathione S-epoxide transferase to produce a series of S-containing metabolites that are not mutagenic in Salmonella. Taken together, these results suggest that 2-chloroethanol is a weak mutagen that is metabolized to 2-chloroacetaldehyde, a potent mutagen and alkylating agent. This metabolite then can be converted to 2-chloroacetic acid, which is not

mutagenic, or conjugated to glutathione to form a series of nonmutagenic S-conjugates. The detoxification of 2-chloroacetaldehyde could prevent the realization of any carcinogenic potential of 2-chloroethanol. The short-term test results for 2-chloroethanol (i.e., positive in bacteria but negative in a variety of eukaryotes, including fungi, Drosophila, mammalian cells, and rodents) support this view.

Toxicity and Carcinogenicity

No compound-related signs of skin irritation were noted at the site of dermal application in rats or mice in the short-term studies. In the 2-year studies, there were dose-related increases in the incidences of inflammation and ulceration at the site of application in male mice; all the ulcers were accompanied by inflammation. No similar effects were noted at the site of application in female mice or in male and female rats, and no significant differences in incidences of neoplastic lesions were noted at the site of application for rats or mice. Although the sensitivity of mouse skin to carcinogens varies with the stage of the hair growth cycle (Andreasen and Engelbreth-Holm, 1953; Berenblum et al., 1958; Borum, 1954), no information was found concerning the permeability of the skin to chemicals as a function of the hair cycle. Species differences in the dermal absorption of chemicals have been discussed by Bock (1963, 1983).

Male and female rats in the 13-week studies showed dose-related pancreatic acinar cell vacuolar changes at doses above 250 mg/kg; similar changes were seen in female mice that survived to the end of the 13-week studies. Acute nephrosis and hepatocellular fatty changes were noted in dosed male and female mice surviving to the end of the 13-week studies. Possible effects on the pancreas in rats and on the pancreas, kidney, and liver in mice were considered when doses for the 2-year studies were set. None of these sites was affected in rats or mice in the 2-year studies.

Mason et al. (1971) had reported an increased incidence of pituitary gland adenomas (7/100 across all dose groups vs 1/50 for control animals) in female Fischer 344 rats given 2-chloroethanol (0.3-10 mg/kg) by subcutaneous injection. In the present studies, pituitary gland adenomas occurred at an increased incidence in high dose female rats (Table 12). When adenomas and carcinomas were combined, a marginally significant ($P=0.049$) trend remained, and the incidence in the high dose group showed a borderline ($P=0.052$) increase when compared with the vehicle controls by life table analysis. Although results in this report lend support to the conclusion of Mason et al. that 2-chloroethanol may affect the female F344 rat pituitary gland, the results in themselves are considered to be inconclusive for the following reasons: (1) No dose-related pituitary gland hyperplastic response was seen (Appendix C, Table C2); (b) these tumors are considered to be a continuum of neoplastic lesions from adenomas to carcinomas and are therefore properly combined for interpretation purposes; and (c) these tumors are not considered as life threatening and the use of the incidental tumor test is accordingly more appropriate than the life table test. No other increase in neoplasms was observed in rats.

The incidence of alveolar/bronchiolar adenomas or carcinomas (combined) was significantly increased ($P=0.029$, life table test only) in low dose male mice. Considered separately, the incidences of either alveolar/bronchiolar adenomas or carcinomas were not significantly increased. Doses employed in the present study (7.5 and 15 mg per animal, dermal, 5 days per week) were considerably higher than those used by Homburger (1968) (1.2 mg per animal, by intravenous injection, one time per month for 7 months); Homburger reported an increase in the incidence of alveolar/bronchiolar adenomas in female CF-1 mice (5/18 vs a control rate of 2/18). The incidence of alveolar/bronchiolar adenomas or carcinomas (separate or combined) in male mice was similar in the high dose, vehicle control, and untreated control animals. In all groups of male mice, these tumors were found in both early-death animals and in terminal-kill animals.

Lymphomas occurred with a marginally increased incidence in low dose (but not high dose) male mice when compared with vehicle ($P=0.044$) or untreated ($P=0.048$) controls by the life table test. The high dose animals had fewer lymphomas or leukemias than did the

vehicle and untreated controls. Almost all lymphomas and leukemias were found in animals of all groups that died during the course of the 2-year studies (Table 20).

Adrenal cortical adenomas appeared in high dose male mice with a significantly increased incidence when compared with the vehicle controls (0/48 vs 3/43) but not when compared with the untreated controls (4/48 vs 3/43).

There were no statistically significant differences in tumor incidence between the vehicle and untreated control groups for male mice or for female mice. Consequently, these control groups were combined by sex and additional analyses carried out. When statistical comparisons were made relative to the pooled control groups, (1) the increased incidences of alveolar/bronchiolar tumors and of malignant lymphoma in low dose male mice remained significant ($P<0.05$), whereas both of the corresponding high dose effects remained not significant; (2) the increased incidence of cortical adenoma of the adrenal gland in high dose male mice was no longer significant; and (3) combining the control groups revealed no other effects that influenced the overall interpretation of the data.

The increased incidences of alveolar/bronchiolar tumors and malignant lymphoma in low dose male mice are suggestive of a possible response to dermal application of 2-chloroethanol; however, there was no dose-related trend for these tumor incidences (the low dose effects were significant only by a life table test), and supporting evidence was not seen in female mice or in male and female rats. Thus, these increases were not considered to be compound related.

Conclusions: Under the conditions of these 2-year dermal studies, there was *no evidence of carcinogenicity** of 2-chloroethanol for male and female F344/N rats given 50 or 100 mg/kg per day or for male and female Swiss CD-1 mice given 7.5 or 15 mg per animal per day.

*Categories of evidence of carcinogenicity are defined in the Note to the Reader on page 2.

V. REFERENCES

V. REFERENCES

1. Abrahamson, S.; Lewis, E. (1971) The detection of mutations in *Drosophila melanogaster*. Hollaender, A., Ed.: Chemical Mutagens: Principles and Methods for Their Detection, Vol. 2. New York: Plenum Press, pp. 461-487.

2. Adler, N. (1965) Residual ethylene oxide and ethylene glycol in ethylene oxide sterilized pharmaceuticals. J. Pharm. Sci. 54:735-742.

3. Amacher, D.; Turner, G. (1982) Mutagenic evaluation of carcinogens and non-carcinogens in the L5178Y/TK assay utilizing postmitochondrial fractions (S9) from normal rat liver. Mutat. Res. 97:49-65.

4. Ambrose, A. (1950) Toxicological studies of compounds investigated for use as inhibitors of biological processes. II. Toxicity of ethylene chlorohydrin. Arch. Ind. Hyg. Occup. Med. 2:591-597.

5. Andreasen, E.; Engelbreth-Holm, J. (1953) On the significance of the mouse hair cycle in experimental carcinogenesis. Acta Pathol. Scand. 32:165-169.

6. Armitage, P. (1971) Statistical Methods in Medical Research. New York: John Wiley & Sons, Inc., pp. 362-365.

7. Balazs, T. (1976) Toxicity of ethylene oxide and chloroethanol. FDA By-Lines 7:150-155.

8. Ballotta, F.; Bertagni, P.; Troisi, F. (1953) Acute poisoning caused by ingestion of ethylene chlorohydrin. Br. J. Ind. Med. 10:161-163.

9. Barale, R.; Presciuttini, S.; Rossi, A. (1979) *Schizosaccharomyces pombe*--mutazione genica in avanti. Environ. Mutagen Meth. Anal. 1:105-121.

10. Barthelmess, A.; Elkabarity, A. (1962) Chemisch Induzieite Multipolare Mitosen, III. Protoplasma 54:455-475.

11. Bartsch, H.; Malaveille, C.; Montesano, R. (1975) Human, rat and mouse liver-mediated mutagenicity of vinyl chloride in *S. typhimurium* strains. Int. J. Cancer 15:429-437.

12. Bartsch, H.; Malaveille, C.; Camus, A.-M.; Martel-Planche, G.; Brun, G.; Hautefeuille, A.; Sabadie, N.; Barbin, A.; Kuroki, T.; Drevon, C.; Piccoli, C.; Montesano, R. (1980) Validation and comparative studies on 180 chemicals with *S. typhimurium* strains and V79 Chinese hamster cells in the presence of various metabolizing systems. Mutat. Res. 76:1-50.

13. Berenblum, I., Ed. (1969) Carcinogenicity Testing: A Report of the Panel on Carcinogenicity of the Cancer Research Commission of UICC, Vol. 2. Geneva: International Union Against Cancer.

14. Berenblum, I.; Haran-Ghera, N.; Trainin, N. (1958) An experimental analysis of the "hair cycle effect" in mouse skin carcinogenesis. Br. J. Cancer 12:402-413.

15. Bignami, M.; Conti, G.; Conti, L.; Crebelli, R.; Misuraca, F.; Puglia, A.; Randazzo, R.; Sciandrello, G.; Carere, A. (1980a) Mutagenicity of halogenated aliphatic hydrocarbons in *Salmonella typhimurium*, *Streptomyces coelicolor* and *Aspergillus nidulans*. Chem. Biol. Interact. 30:9-23.

16. Bignami, M.; Crebelli, R.; Conti, G.; Conti, L.; Misuraca, F.; Puglia, A.; Randazzo, R.; Sciandrello, G.; Carere, A. (1980b) *In vitro* mutagenicity studies with halogenated aliphatic hydrocarbons. Mutat. Res. 200:73-74.

17. Blackford, J. (1976) Ethylene oxide. Chemical Economics Handbook. Menlo Park, CA: Stanford Research Institute.

18. Blair, A.; Vallee, B. (1966) Some catalytic properties of human liver alcohol dehydrogenase. Biochemistry 5:2026-2034.

19. Bock, F. (1963) Species difference in penetration and absorption of chemical carcinogens. Natl. Cancer Inst. Monogr. 10:361-375.

20. Bock, F. (1983) Comparative anatomy and function of skin as related to experimental carcinogenesis. Homburger, F., Ed.: Progress in Experimental Tumor Research. Basel: S. Karker, pp. 5-17.

21. Boorman, G.; Montgomery, C., Jr.; Hardisty, J.; Eustis, S.; Wolfe, M., McConnell, E. (1985) Quality assurance in pathology for rodent toxicology and carcinogenicity tests. Milman, H.; Weisburger, E., Eds.: Handbook of Carcinogen Testing. Park Ridge, NJ: Noyes Publications.

22. Borum, K. (1954) The role of the mouse hair cycle in epidermal carcinogenesis. Acta Pathol. Scand. 34:542-552.

23. Brown, D. (1970) Determination of ethylene oxide and ethylene chlorohydrin in plastic and rubber surgical equipment sterilized with ethylene oxide. J. Assoc. Off. Anal. Chem. 53:263-267.

24. Bush, A.; Abrams, H., Brown, H. (1949) Fatality and illness caused by ethylene chlorohydrin in an agricultural operation. J. Ind. Hyg. Toxicol. 31:352-358.

25. Carpenter, C.; Smyth, H.; Pozzani, U. (1949) The assay of acute vapor toxicity, and the grading and interpretation of results on 96 chemical compounds. J. Ind. Hyg. Toxicol. 31:343-346.

26. Castro, C.; Bartnicki, E. (1968) Biodehalogenation. Epoxidation of halohydrins, epoxide opening, and transhalogenation by a *Flavobacterium* sp. Biochemistry 7:3213-3218.

27. Conan, L.; Foucault, B.; Siou, G.; Chaigneau, M.; Le Moan, G. (1979) Contribution a la recherche d'une action mutagene des residus d'oxyde d'ethylene, d'ethylene glycol et de chloro-2-ethanol dans le materiel plastique sterilise par l'oxide d'ethylene. Ann. Fals. Exp. Chim. 773:141-151.

28. Cox, D. (1972) Regression models and life tables. J. R. Stat. Soc. B34:187-220.

29. Dunkelberg, H. (1983) Carcinogenic activity of ethylene oxide and its reaction products 2-chloroethanol, 2-bromoethanol, ethylene glycol and diethylene glycol. II. Testing of 2-chloroethanol and 2-bromoethanol for carcinogenicity. Zbl. Bakt. Hyg., I. Abt. Orig. B 177:269-281.

30. Elmore, J.; Wong, J.; Laumbach, A.; Streips, U. (1976) Vinyl chloride mutagenicity via the metabolites chlorooxirane and chloroacetaldehyde monomer hydrate. Biochim. Biophys. Acta 442:405-419.

31. Epstein, S.; Arnold, E.; Andrea, J.; Bass, W.; Bishop, Y. (1972) Detection of chemical mutagens by the dominant lethal assay in the mouse. Toxicol. Appl. Pharmacol. 23:288-325.

32. Finney, D. (1964) Statistical Methods in Biological Assay. New York: Hadner Publishing Co., pp. 451-500.

33. Fishbein, L. (1969) Degradation and residues of alkylating agents. Ann. N.Y. Acad. Sci. 163:869-894.

34. Fishbein, L. (1976) Potential hazards of fumigant residues. Environ. Health Perspect. 14:39-45.

35. Food and Drug Administration (FDA) (1978) Ethylene oxide, ethylene chlorohydrin and ethylene glycol. Fed. Reg. 43:27474-27483.

36. Garro, A.; Phillips, R. (1980) Detection of mutagen-induced lesions in isolated DNA by marker rescue of Bacillus subtilis phage PH105. Mutat. Res. 73:1-13.

37. Gart, J.; Chu, K.; Tarone, R. (1979) Statistical issues in interpretation of chronic bioassay tests for carcinogenicity. J. Natl. Cancer Inst. 62(4):957-974.

38. Generoso, W.; Cain, K.; Krishna, M.; Sheu, C.; Gryder, R. (1981) Heritable translocation and dominant lethal mutation induced with ethylene oxide in mice. Mutat. Res. 73:133-142.

39. Glaser, Z. (1979) Ethylene oxide--Toxicology review and field study results of hospital use. J. Environ. Pathol. Toxicol. 2:173-208.

40. Gleason, M.; Gosselin, R.; Hodge, H.; Smith, R. (1969) Clinical Toxicology of Commercial Products. Baltimore: Williams and Wilkins, p. 66.

V. REFERENCES

41. Goldblatt, M.; Chiesman, W. (1944) Toxic effects of ethylene chlorohydrin. Part I. Clinical. Br. J. Ind. Med. 1:207-223.

42. Green, T.; Hathway, D. (1975) The biological fate in rats of vinyl chloride in relation to its oncogenicity. Chem. Biol. Interact. 11:545-562.

43. Green, T.; Hathway, D. (1977) The chemistry and biogenesis of the S-containing metabolites of vinyl chloride in rats. Chem. Biol. Interact. 17:137-150.

44. Grigorescu, I.; Toba, G. (1966) Clorura divinil. Aspecte de toxicologie industriala. Rev. Chim. Rem. 17:499-501.

45. Grunow, W.; Altmann, H.-J. (1982) Toxicokinetics of chloroethanol in the rat after single oral administration. Arch. Toxicol. 49:275-284.

46. Guess, W. (1970) Tissue reactions to 2-chloroethanol in rabbits. Toxicol. Appl. Pharmacol. 16:382-390.

47. Gunther, D. (1974a) Safety of ethylene oxide gas residuals. Part i. Am. J. Hosp. Pharmacol. 31:558-561.

48. Gunther, D. (1974b) Safety of ethylene oxide gas residuals. Part ii. Am. J. Hosp. Pharmacol. 31:684-686.

49. Hall, J.; Saffhill, R.; Green, T.; Hathway, D. (1981) The induction of errors during in vitro DNA synthesis following chloroacetaldehyde-treatment of poly(dA-dT) and poly(dC-dG) templates. Carcinogenesis (London) 2:141-146.

50. Haseman, J. (1984) Statistical issues in the design, analysis and interpretation of animal carcinogenicity studies. Environ. Health Perspect. 58:385-392.

51. Haworth, S.; Lawlor, T.; Mortelmans, K.; Speck, W.; Zeiger, E. (1983) Salmonella mutagenicity test results for 250 chemicals. Environ. Mutagen. Suppl. 1:3-142.

52. Hogstedt, C.; Malmqvist, N.; Wadman, B. (1979a) Leukemia in workers exposed to ethylene oxide. J. Am. Med. Assoc. 241:1132-1133.

53. Hogstedt, C.; Rohlen, O.; Berndtsson, B.; Axelson, O.; Ehrenberg, L. (1979b) A cohort study of mortality and cancer incidence in ethylene oxide production workers. Br. J. Ind. Med. 36:276-280.

54. Holmgren, A.; Diding, N. (1969) Ethylene oxide treatment of crude drugs. Part V. Formation of ethylene chlorohydrin. Acta Pharm. Succica 6:33-36.

55. Homburger, F. (1968) Final Report. Contract PH-43-67-677, Project C-173. Springfield, VA: National Technical Information Service.

56. Huberman, E.; Bartsch, H.; Sachs, L. (1975) Mutation induction in Chinese hamster V79 cells by two vinyl chloride metabolites, chloroethylene oxide and 2-chloroacetaldehyde. Int. J. Cancer 16:639-644.

57. International Agency for Research on Cancer (IARC) (1976) Ethylene oxide. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man, Vol. 11. Lyon, France: IARC, World Health Organization, pp. 157-167.

58. International Agency for Research on Cancer (IARC) (1984) Some Allyl Compounds, Aldehydes, Epoxides, and Peroxides. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, Vol. 36. Lyon, France: IARC, World Health Organization (in press).

59. Isakova, G.; Ekshtat, B.; Kerkis, Y. (1971) On studies of the mutagenic properties of chemical substances in the establishment of hygienic standards. Hyg. Sanit. (USSR) 36:178-184. Translated from Gig. Sanit. 36:9-13, 1971.

60. Johnson, M. (1965) The influence of some aliphatic compounds on rat liver glutathione levels. Biochem. Pharmacol. 14:1383-1385.

61. Johnson, M. (1967) Metabolism of chloroethanol in the rat. Biochem. Pharmacol. 16:185-199.

62. Jones, B.; Hathway, D. (1978) The biological fate of vinylidene chloride in rats. Chem. Biol. Interact. 20:27-41.

63. Joyner, R. (1964) Chronic toxicity of ethylene oxide. Arch. Environ. Health 8:700-710.

64. Kaplan, E.; Meier, P. (1958) Nonparametric estimation of incomplete observations. J. Am. Stat. Assoc. 53:457-481.

65. Kimmel, C.; LaBorde, J. (1979) Teratogenic potential of ethylene oxide. Teratology 19:34A-35A.

66. Knaap, A.; Voogd, C.; Kramers, P. (1982) Comparison of the mutagenic potency of 2-chloroethanol, 2-bromoethanol, 1,2-epoxybutane, epichlorohydrin and glycidaldehyde in *Klebsiella pneumoniae, Drosophila melanogaster* and L5178Y mouse lymphoma cells. Mutat. Res. 101:199-208.

67. Koelsch, F. (1927) Die Giftigkeit des Aethylenchlorohydrins. Zentralbl. Gewerbehyg. 4:312-316.

68. Kozlenchkov, Y.; Medvedev, O. (1975) Early diagnosis and treatment of glycol poisoning. Voen. Med. Zh. 10:30-40.

69. Kronevi, T.; Wahlberg, J.; Holmberg, B. (1979) Histopathology of skin, liver, and kidney after epicutaneous administration of five industrial solvents to guinea pigs. Environ. Res. 19:56-69.

70. LaBorde, J.; Kimmel, C. (1980) The teratogenicity of ethylene oxide administered intravenously to mice. Toxicol. Appl. Pharmacol. 56:16-22.

71. Laumbach, A.; Lee, S.; Wong, J.; Streips, U. (1977) Studies on the Mutagenicity of Vinyl Chloride Metabolites and Related Chemicals. Proceedings of the Third International Symposium on Detection and Prevention of Cancer, Vol. 1, pp. 155-170.

72. Lawrence, W.; Turner, J.; Autian, J. (1971) Toxicity of ethylene chlorohydrin. I. Acute toxicity studies. J. Pharm. Sci. 60:568-571.

73. Linhart, M.; Cooper, J.; Martin, R.; Page, N.; Peters, J. (1974): Carcinogenesis bioassay data system. Comp. Biomed. Res. 7:230-248.

74. Lofroth, G. (1978) The mutagenicity of dichloroacetaldehyde. Z. Naturforsch. 33:783-785.

75. Loprieno, N.; Barale, R.; Baroncelli, S.; Bartsch, H.; Bronzetti, G.; Cammellini, A.; Corsi, C.; Frezza, D.; Nieri, R.; Leporini, C.; Rosellini, D.; Rossi, A. (1977) Induction of gene mutations and gene conversions by vinyl chloride metabolites in yeast. Cancer Res. 36:253-257.

76. Malaveille, C.; Bartsch, H.; Barbin, A.; Camus, A.; Montesano, R.; Croisy, A.; Jacquignon, P. (1975) Mutagenicity of vinyl chloride, chloroethylene oxide, chloroaceldehyde and chloroethanol. Biochem. Biophys. Res. Com. 63:363-370.

77. Mamber, S.; Bryson, V.; Katz, S. (1983) The *Escherichia coli* WP2/WP100 rec assay for detection of potential carcinogens. Mutat. Res. 119:135-144.

78. Mantel, N.; Haenszel, W. (1959) Statistical aspects of the analysis of data from retrospective studies of disease. J. Natl. Cancer Inst. 22:719-748.

79. Maronpot, R.; Boorman, G. (1982) Interpretation of rodent hepatocellular proliferative alterations and hepatocellular tumors in chemical safety assessment. Toxicol. Pathol. 10:71-80.

80. Mason, M.; Cate, C.; Baker, J. (1971) Toxicology and carcinogenesis of various chemicals used in the preparation of vaccines. Clin. Toxicol. 4:185-204.

81. McCann, J.; Simmon, V.; Streitwieser, D.; Ames, B. (1975) Mutagenicity of chloroacetaldehyde, a possible metabolic product of 1,2-dichloroethane (ethylene dichloride), chloroethanol (ethylene chlorohydrin), vinyl chloride, and cyclophosphamide. Proc. Natl. Acad. Sci. 72:3190-3193.

V. REFERENCES

82. McGunnigle, R.; Renner, J.; Remano, S.; Abodeely, R., Jr. (1975) Residual ethylene oxide--Levels in medical grade tubing and effects on an *in vitro* biologic system. J. Biomed. Mater. Res. 9:273-283.

83. Merck Index (1968) Stecher, P., Ed. Rahway, NJ: Merck and Company, Inc., p. 434.

84. Nakamura, A.; Tateno, N.; Kojima, S.; Kaniwa, M.; Kawamura, T. (1979) The mutagenicity of halogenated alkanols and their phosphoric acid esters for *Salmonella typhimurium*. Mutat. Res. 66:373-380.

85. National Cancer Institute (NCI) (1976) Guidelines for Carcinogen Bioassay in Small Rodents. NCI Carcinogenesis Technical Report Series No. 1. U.S. Department of Health, Education, and Welfare, Public Health Service, National Institutes of Health.

86. National Institute for Occupational Safety and Health (NIOSH) (1975)

87. National Institute for Occupational Safety and Health (NIOSH) (1977) NIOSH Registry of Toxic Effects of Chemical Substances, Vol. II. U.S. Department of Health, Education, and Welfare, National Institute for Occupational Safety and Health, Rockville, MD.

88. National Institute for Occupational Safety and Health (NIOSH) (1983) Study. Preliminary results presented by T. Lewis at the Subcommittee on Environmental Mutagenesis, Bethesda, MD.

89. National Institutes of Health (NIH) (1978) NIH Specification, NIH-11-133f, November 1.

90. Neely, W.; Branson, D.; Blau, G. (1974) Partition coefficient to measure bioconcentration potential of organic chemicals in fish. Environ. Sci. Technol. 8:1113-1115.

91. Norpoth, K.; Reisch, A.; Heinecke, A. (1980) Biostatistics of Ames test data. Norpoth, K.; Garner, R., Eds: Short-Term Test Systems for Detecting Carcinogens. New York: Springer-Verlag, pp. 312-322.

92. Occupational Safety and Health Administration (OSHA) (1982) Occupational exposure to ethylene oxide. Fed. Reg. 47:3566-3570.

93. Occupational Safety and Health Administration (OSHA) (1983) Occupational exposure to ethylene oxide. Fed. Reg. 48:17284-17319.

94. Oesch, F.; Doerjer, G. (1982) Detection of N^2,3-ethenoguanine in DNA after treatment with chloroacetaldehyde in vitro. Carcinogenesis (London) 3:663-665.

95. O'Leary, R.; Guess, W. (1968) The toxicogenic potential of medical plastics sterilized with ethylene oxide vapors. J. Biomed. Mater. Res. 2:297-311.

96. Oser, B.; Morgareidge, K.; Cox, G.; Carson, S. (1975) Short-term toxicity of ethylene chlorohydrin (ECH) in rats, dogs and monkeys. Food Cosmet. Toxicol. 13:313-315.

97. Painter, R.; Howard, R. (1982) The HeLa DNA-synthesis inhibition test as a rapid screen for mutagenic carcinogens. Mutat. Res. 92:427-437.

98. Pfeiffer, E.; Dunkelberg, H. (1980) Mutagenicity of ethylene oxide and propylene oxide and of the glycols and halohydrins formed from them during the fumigation of foodstuffs. Food Cosmet. Toxicol. 18:115-118.

99. Phillips, R.; Zahler, S.; Garro, A. (1980) Detection of mutagen-induced lesions in isolated DNA using a new Bacillus subtilis transformation-based assay. Mutat. Res. 74:267-281.

100. Ragelis, E.; Fisher, B.; Klimeck, B. (1966) Note on determination of chlorohydrins in foods fumigated with ethylene oxide and with propylene oxide. J. Assoc. Off. Anal. Chem. 49:963-965.

101. Ragelis, E.; Fisher, B.; Klimeck, B.; Johnson, C. (1968) Isolation and determination of chlorohydrins in foods fumigated with ethylene oxide or with propylene oxide. J. Assoc. Off. Anal. Chem. 51:709-715.

102. Rannug, U.; Beije, B. (1979) The mutagenic effect of 1,2-dichloroethane on *Salmonella typhimurium*. II. Activation by the isolated perfused rat liver. Chem.-Biol. Interact. 24:265-285.

103. Rannug, U.; Goethe, R.; Wachtneister, C. (1976) The mutagenicity of chloroethylene oxide, chloroacetaldehyde, 2-chloroethanol, and chloroacetic acid, conceivable metabolites of vinyl chloride. Chem.-Biol. Interact. 12:251-263.

104. Research Triangle Institute (RTI) (1983a) Teratologic Evaluation of Ethylene Chlorohyrin (CAS No. 107-07-3) in CD-1 Mice. Final Report, Contract No. NO1-ES-6-2127, National Institute of Environmental Health Sciences.

105. Research Triangle Institute (RTI) (1983b) Teratologic Evaluation of Ethylene Chlorohyrin (CAS No. 107-07-3) in New Zealand White Rabbits. Final Report, Contract No. NO1-ES-6-2127, National Institute of Environmental Health Sciences.

106. Riesser, G. (1979) Chlorohydrins. Kirk-Othmer Encyclopedia of Chemical Technology, 3rd ed. New York: John Wiley and Sons. 6:848-864.

107. Rosenkranz, H.; Wlodkowski, T. (1974) Mutagenicity of ethylene chlorohydrin. A degradation product present in foodstuffs exposed to ethylene oxide. J. Agr. Food Chem. 22:407-409.

108. Rosenkranz, S.; Carr, H.; Rosenkranz, H. (1974) 2-Haloethanols--Mutagenicity and reactivity with DNA. Mutat. Res. 26:367-370.

109. Sadtler Standard Spectra, IR No. 73, NMR No. 10320. Philadelphia: Sadtler Research Laboratories.

110. Saitanov, A.; Konanova, A. (1976) Acute ethylene chlorohydrin poisoning. Gig. Tr. Prof. Zabol., pp. 49-50.

111. Schultze, H. (1965) Ethylene oxide. Kirk-Othmer Encyclopedia of Chemical Technology, 2nd ed. New York: John Wiley and Sons. 8:253-558.

112. Sheu, C.; Cain, K.; Gryder, R.; Generoso, W. (1983) Heritable translocations test with ethylene chlorohydrin in male mice. J. Am. Col. Toxicol. 2:221-223.

113. Snellings, W.; Zelenak, J.; Weil, C. (1982) Effects on reproduction in Fischer 344 rats exposed to ethylene oxide by inhalation for one generation. Toxicol. Appl. Pharmacol. 63:382-388.

114. Sonnenfeld, G.; Barnes, M.; Schooler, J.; Streips, U. (1980) Inhibition of interferon induction as a screen for the carcinogenic potential of chemicals. Khan, A.; Hill, N.; Dorn, G., Eds.: Interferon: Properties and Clinical Uses. Proceedings of the International Symposium on Interferon, Wadley Institute of Molecular Biology, Dallas, TX, 1979. Dallas: Leland Fisk Foundation Press, pp. 589-596.

115. Stich, H.; San, R.; Lam, P.; Koropatnick, D. (1976) The Detection of Naturally Occurring and Man-made Carcinogens and Mutagens by the DNA Repair Assay. Second Joint U.S./USSR Symposium on the Comprehensive Analysis of the Environment, pp. 85-88.

116. Stolzenberg, S.; Hine, C. (1980) Mutagenicity of 2- and 3-carbon halogenated compounds in the Salmonella/mammalian-microsome test. Environ. Mutagenesis 2:59-66.

117. Strusevich, E.; Ekshtat, B. (1973) Effect of ethylene chlorohydrin on liver and pancreatic enzymes in a subacute experiment. Uch. Zap-Mosk. Nauchno-Issled Inst. Gig. 20:71-74.

118. Tarone, R. (1975) Tests for trend in life table analysis. Biometrika 62:679-682.

119. U.S. Environmental Protection Agency (USEPA) (1978) Notice of rebuttable presumption against registration and continued registration of pesticide products containing ethylene oxide. Fed. Reg. 43:3801-3812.

120. U.S. Environmental Protection Agency (USEPA) (1984) Ethylene oxide; revised labeling for pesticide products containing ethylene oxide which are registered for the sterilization of equipment and supplies in hospitals and health care facilities. Fed. Reg. 49:15268-15273.

121. Verrett, M. (1974) Investigation of the toxic teratogenic effects of 2-chloroethanol to the developing chick embryo. Memorandum to L. Friedman, Food and Drug Administration, 8 pp. Cited in Fed. Reg. 43:3812.

122. Vig, B. (1975) Soybean (*Glycine max*): A new test system for study of genetic parameters as affected by environmental mutagens. Mutat. Res. 31:49-56.

123. Voogd, C. (1973) Mutagenic action of epoxy compounds and several alcohols. Mutat. Res. 21:52-53.

124. Voogd, C.; van der Vet, P. (1969) Mutagenic action of ethylene halogenhydrins. Experientia 25:85-86.

125. Voogd, C.; Jacobs, J.; van der Stel, J. (1972) On the mutagenic action of dichlorvos. Mutat. Res. 16:413-416.

126. Wahlberg, J.; Boman, A. (1978) 2-Chloroethanol--Percutaneous toxicity of a solvent. Dermatologica 156:299-302.

127. Watanabe, P.; McGowan, G.; Gehring, P. (1976) Fate of [^{14}C] vinyl chloride after single oral administration in rats. Toxicol. Appl. Pharmacol. 36:339-352.

128. Wesley, F.; Rourke, B.; Darbishire, O. (1965) The formation of persistent toxic chlorohydrins in foodstuffs by fumigation with ethylene oxide and with propylene oxide. J. Food Sci. 30:1037-1042.

129. Yllner, S. (1971) Metabolism of 1,2-dichloroethane-^{14}C in the mouse. Acta Pharmacol. Toxicol. 30:257-265.

APPENDIX A

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN RATS IN THE TWO-YEAR DERMAL STUDIES OF 2-CHLOROETHANOL

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
#SKIN PAINT SITE	(48)	(49)	(49)
SQUAMOUS CELL CARCINOMA	1 (2%)		
KERATOACANTHOMA			1 (2%)
*SKIN	(50)	(50)	(50)
PAPILLOMA, NOS	1 (2%)		4 (8%)
SQUAMOUS CELL PAPILLOMA			2 (4%)
SQUAMOUS CELL CARCINOMA	1 (2%)	1 (2%)	
BASAL-CELL TUMOR	1 (2%)		
KERATOACANTHOMA	1 (2%)	3 (6%)	1 (2%)
*SUBCUT TISSUE	(50)	(50)	(50)
FIBROMA	2 (4%)	6 (12%)	1 (2%)
FIBROSARCOMA	1 (2%)	2 (4%)	
RESPIRATORY SYSTEM			
#LUNG	(49)	(50)	(50)
SQUAMOUS CELL CARCINOMA, METASTA	1 (2%)		
ALVEOLAR/BRONCHIOLAR ADENOMA	1 (2%)		
ALVEOLAR/BRONCHIOLAR CARCINOMA		4 (8%)	1 (2%)
PHEOCHROMOCYTOMA, METASTATIC	1 (2%)		
CARCINOSARCOMA, METASTATIC	1 (2%)		
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIG. LYMPHOMA, LYMPHOCYTIC TYPE	1 (2%)		
LEUKEMIA,MONONUCLEAR CELL	11 (22%)	7 (14%)	12 (24%)
#SPLEEN	(50)	(50)	(50)
SARCOMA, NOS		2 (4%)	
#MANDIBULAR L. NODE	(49)	(50)	(49)
CARCINOSARCOMA, METASTATIC	1 (2%)		
CIRCULATORY SYSTEM			
*PULMONARY ARTERY	(50)	(50)	(50)
C-CELL CARCINOMA, METASTATIC		1 (2%)	
#SALIVARY GLAND	(50)	(49)	(50)
ANGIOSARCOMA	1 (2%)		
DIGESTIVE SYSTEM			
#LIVER	(50)	(50)	(50)
NEOPLASTIC NODULE		3 (6%)	3 (6%)
PHEOCHROMOCYTOMA, METASTATIC	1 (2%)		
#DUODENUM	(50)	(47)	(49)
ADENOCARCINOMA, NOS			1 (2%)
#JEJUNUM	(50)	(47)	(49)
LEIOMYOSARCOMA	1 (2%)		
URINARY SYSTEM			
#URINARY BLADDER	(49)	(50)	(48)
TRANSITIONAL-CELL CARCINOMA		1 (2%)	

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM			
#PITUITARY	(50)	(48)	(49)
CARCINOMA, NOS	3 (6%)	2 (4%)	1 (2%)
ADENOMA, NOS	12 (24%)	11 (23%)	15 (31%)
#ADRENAL	(50)	(50)	(50)
CORTICAL ADENOMA	1 (2%)	3 (6%)	1 (2%)
PHEOCHROMOCYTOMA	7 (14%)	11 (22%)	9 (18%)
PHEOCHROMOCYTOMA, MALIGNANT	1 (2%)		2 (4%)
#ADRENAL MEDULLA	(50)	(50)	(50)
PHEOCHROMOCYTOMA	1 (2%)	2 (4%)	1 (2%)
#THYROID	(49)	(49)	(49)
FOLLICULAR-CELL ADENOMA		1 (2%)	
FOLLICULAR-CELL CARCINOMA	2 (4%)	1 (2%)	1 (2%)
C-CELL ADENOMA	6 (12%)	4 (8%)	3 (6%)
C-CELL CARCINOMA		1 (2%)	1 (2%)
#PANCREATIC ISLETS	(50)	(50)	(49)
ISLET-CELL ADENOMA	3 (6%)	3 (6%)	
ISLET-CELL CARCINOMA	1 (2%)	1 (2%)	
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
PAPILLARY ADENOMA		1 (2%)	
FIBROADENOMA	1 (2%)	1 (2%)	1 (2%)
*PREPUTIAL GLAND	(50)	(50)	(50)
CARCINOMA, NOS	1 (2%)	1 (2%)	2 (4%)
ADENOMA, NOS	2 (4%)	2 (4%)	1 (2%)
#PROSTATE	(49)	(49)	(48)
ADENOMA, NOS	1 (2%)		
#TESTIS	(50)	(50)	(50)
INTERSTITIAL-CELL TUMOR	45 (90%)	41 (82%)	44 (88%)
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
*EAR CANAL	(50)	(50)	(50)
CARCINOSARCOMA	1 (2%)		
*ZYMBAL GLAND	(50)	(50)	(50)
CARCINOMA, NOS	1 (2%)		1 (2%)
ADENOMA, NOS			1 (2%)
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*PERITONEUM	(50)	(50)	(50)
MESOTHELIOMA, MALIGNANT	1 (2%)		
*MESENTERY	(50)	(50)	(50)
MESOTHELIOMA, NOS	1 (2%)		
*TUNICA VAGINALIS	(50)	(50)	(50)
MESOTHELIOMA, NOS	1 (2%)		1 (2%)

TABLE A1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)		(50) (50)
MESOTHELIOMA, NOS			1 (2%)
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH	2	4	2
MORIBUND SACRIFICE	15	9	12
SCHEDULED SACRIFICE			
TERMINAL SACRIFICE	33	37	36
DOSING ACCIDENT			
ACCIDENTALLY KILLED, NDA			
ACCIDENTALLY KILLED, NOS			
ANIMAL MISSING			
ANIMAL MISSEXED			
OTHER CASES			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS**	50	49	48
TOTAL PRIMARY TUMORS	115	115	112
TOTAL ANIMALS WITH BENIGN TUMORS	49	48	48
TOTAL BENIGN TUMORS	85	89	85
TOTAL ANIMALS WITH MALIGNANT TUMORS	23	21	20
TOTAL MALIGNANT TUMORS	28	23	22
TOTAL ANIMALS WITH SECONDARY TUMORS##	3	1	
TOTAL SECONDARY TUMORS	5	1	
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	1	3	4
TOTAL UNCERTAIN TUMORS	2	3	5
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

* NUMBER OF ANIMALS NECROPSIED
** PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE A2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
TRICHOEPITHELIOMA		1 (2%)	
KERATOACANTHOMA	1 (2%)		
*SUBCUT TISSUE	(50)	(50)	(50)
SARCOMA, NOS		1 (2%)	
FIBROMA			2 (4%)
RESPIRATORY SYSTEM			
#LUNG	(50)	(50)	(48)
ALVEOLAR/BRONCHIOLAR CARCINOMA	1 (2%)	1 (2%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
LEUKEMIA,MONONUCLEAR CELL	7 (14%)	7 (14%)	6 (12%)
#SPLEEN	(50)	(48)	(50)
LEUKEMIA,MONONUCLEAR CELL	1 (2%)		
CIRCULATORY SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
ANGIOSARCOMA		1 (2%)	
DIGESTIVE SYSTEM			
*TONGUE	(50)	(50)	(50)
SQUAMOUS CELL CARCINOMA		1 (2%)	
#LIVER	(50)	(50)	(50)
NEOPLASTIC NODULE	1 (2%)	2 (4%)	
URINARY SYSTEM			
NONE			
ENDOCRINE SYSTEM			
#PITUITARY	(50)	(49)	(50)
CARCINOMA, NOS	4 (8%)	1 (2%)	1 (2%)
ADENOMA, NOS	19 (38%)	24 (49%)	29 (58%)
#ADRENAL	(49)	(50)	(50)
CORTICAL ADENOMA	1 (2%)	2 (4%)	2 (4%)
PHEOCHROMOCYTOMA	3 (6%)	3 (6%)	3 (6%)
PHEOCHROMOCYTOMA, MALIGNANT		1 (2%)	1 (2%)
PHEOCHROMOCYTOMA, METASTATIC			1 (2%)
GANGLIONEUROMA		1 (2%)	
#THYROID	(49)	(50)	(49)
FOLLICULAR-CELL ADENOMA		1 (2%)	
FOLLICULAR-CELL CARCINOMA		1 (2%)	
C-CELL ADENOMA	2 (4%)	3 (6%)	4 (8%)
C-CELL CARCINOMA	1 (2%)		1 (2%)
#PANCREATIC ISLETS	(49)	(49)	(50)
ISLET-CELL ADENOMA	1 (2%)	3 (6%)	1 (2%)
ISLET-CELL CARCINOMA			1 (2%)

TABLE A2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
ADENOCARCINOMA, NOS		2 (4%)	
PAPILLARY ADENOMA			1 (2%)
CYSTADENOMA, NOS	3 (6%)	3 (6%)	3 (6%)
FIBROADENOMA	13 (26%)	7 (14%)	11 (22%)
*CLITORAL GLAND	(50)	(50)	(50)
CARCINOMA, NOS	1 (2%)		
ADENOMA, NOS			1 (2%)
#UTERUS	(50)	(50)	(50)
ENDOMETRIAL STROMAL POLYP	7 (14%)	4 (8%)	7 (14%)
ENDOMETRIAL STROMAL SARCOMA	1 (2%)		1 (2%)
#CERVIX UTERI	(50)	(50)	(50)
FIBROMA	1 (2%)		
#UTERUS/ENDOMETRIUM	(50)	(50)	(50)
CARCINOMA, NOS		1 (2%)	
#OVARY	(49)	(50)	(50)
GRANULOSA-CELL TUMOR			1 (2%)
NERVOUS SYSTEM			
#BRAIN	(49)	(50)	(50)
CARCINOMA, NOS, INVASIVE		1 (2%)	
ASTROCYTOMA	1 (2%)		
SPECIAL SENSE ORGANS			
*ZYMBAL GLAND	(50)	(50)	(50)
CARCINOMA, NOS	1 (2%)		
ADENOMA, NOS		1 (2%)	
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
NONE			
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
PHEOCHROMOCYTOMA, METASTATIC		1 (2%)	
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH	1	3	2
MORIBUND SACRIFICE	7	8	10
SCHEDULED SACRIFICE			
TERMINAL SACRIFICE	42	39	38
DOSING ACCIDENT			
ACCIDENTALLY KILLED, NDA			
ACCIDENTALLY KILLED, NOS			
ANIMAL MISSING			
ANIMAL MISSEXED			
OTHER CASES			

TABLE A2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS**	38	43	43
TOTAL PRIMARY TUMORS	70	72	76
TOTAL ANIMALS WITH BENIGN TUMORS	32	35	40
TOTAL BENIGN TUMORS	51	53	64
TOTAL ANIMALS WITH MALIGNANT TUMORS	16	16	10
TOTAL MALIGNANT TUMORS	18	17	11
TOTAL ANIMALS WITH SECONDARY TUMORS##		2	1
TOTAL SECONDARY TUMORS		2	1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	1	2	1
TOTAL UNCERTAIN TUMORS	1	2	1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

• NUMBER OF ANIMALS NECROPSIED
** PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL: VEHICLE CONTROL

ANIMAL NUMBER	021	005	004	006	016	010	020	040	043	019	032	011	018	029	036	045	001	002	003	007	008	009	012	013	014
WEEKS ON STUDY	076	077	079	079	083	086	089	091	091	092	092	100	100	101	102	102	104	104	104	104	104	104	104	104	104
INTEGUMENTARY SYSTEM																									
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma, NOS																									
Squamous cell carcinoma												X													
Basal cell tumor																								X	
Keratoacanthoma	X																								
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroma																X									
Fibrosarcoma																				X					
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+
Squamous cell carcinoma, metastatic												X													
Alveolar/bronchiolar adenoma																									
Pheochromocytoma, metastatic						X																			
Carcinosarcoma, metastatic			X																						
Trachea	+	+	+	+	+	−	+	+	−	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+
Carcinosarcoma, metastatic			X																						
Thymus	+	+	+	−	+	+	+	+	+	+	+	−	−	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Angiosarcoma																				X					
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Pheochromocytoma, metastatic						X																			
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyosarcoma																									
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Adenoma, NOS	X			X	X	X	X						X	X			X			X		X			
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																									
Pheochromocytoma														X				X							
Pheochromocytoma, malignant						X																			
Thyroid	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell carcinoma					X														X						
C-cell adenoma																		X		X					
Parathyroid	+	+	+	+	+	−	+	+	+	+	+	+	+	+	−	−	+	+	−	+	+	+	−	+	+
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																									
Islet cell carcinoma									X																
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	N	N	+	+	+
Fibroadenoma																									
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Interstitial cell tumor	X	X	X			X	X	X		X	X	X	X	X	X	X	X		X	X	X	X	X	X	X
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+
Adenoma, NOS																								X	
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																									
Adenoma, NOS																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
Ear	N	N	+	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinosarcoma			X																						
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS									X																
BODY CAVITIES																									
Peritoneum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mesothelioma, malignant											X														
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesothelioma, NOS								X																	
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mesothelioma, NOS								X																	
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Malignant lymphoma, lymphocytic type															X										
Leukemia, mononuclear cell	X	X							X	X		X		X						X			X		

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: VEHICLE CONTROL (Continued)

ANIMAL NUMBER	017	018	022	023	024	025	026	027	028	030	031	033	034	035	037	038	039	041	042	044	046	047	048	049	050	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	
INTEGUMENTARY SYSTEM																										
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	48
Squamous cell carcinoma																								X		1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	*50
Papilloma, NOS																					X					1
Squamous cell carcinoma																										1
Basal cell tumor																										1
Keratoacanthoma																										1
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	*50
Fibroma			X																							2
Fibrosarcoma																										1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Squamous cell carcinoma, metastatic																										1
Alveolar/bronchiolar adenoma											X															1
Pheochromocytoma, metastatic																										1
Carcinosarcoma, metastatic																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	46
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinosarcoma, metastatic																										1
Thymus	+	+	+	+	+	+	–	+	+	–	–	–	+	–	+	+	+	–	–	+	–	–	+	–	+	37
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Angiosarcoma																										1
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Pheochromocytoma, metastatic																										1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leiomyosarcoma			X																							1
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, NOS							X											X			X					3
Adenoma, NOS		X			X																					12
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cortical adenoma																			X							1
Pheochromocytoma						X							X	X		X							X	X		8
Pheochromocytoma, malignant																										1
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Follicular cell carcinoma																										2
C-cell adenoma	X												X							X			X			6
Parathyroid	+	+	+	–	–	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	–	+	+	–	–	39
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islet cell adenoma				X		X														X						3
Islet cell carcinoma																										1
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	*50
Fibroadenoma																			X							1
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Interstitial cell tumor	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	45
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenoma, NOS																										1
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS	X																									1
Adenoma, NOS										X					X											2
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
Ear	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	*50
Carcinosarcoma																										1
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS																										1
BODY CAVITIES																										
Peritoneum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Mesothelioma, malignant																										1
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Mesothelioma, NOS																										1
Mesentery	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Mesothelioma, NOS																										1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Malignant lymphoma, lymphocytic type																										1
Leukemia, mononuclear cell	X												X	X												11

* Animals necropsied

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL: LOW DOSE

ANIMAL NUMBER	014	026	023	025	034	017	049	016	012	022	028	031	043	041	033	044	047	048	049	010	011	013	015	018	019
WEEKS ON STUDY	063	070	080	083	083	086	088	089	092	093	092	092	102	104	104	104	104	104	104	104	104	104	104	105	105
INTEGUMENTARY SYSTEM																									
Skin paint site	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Squamous cell carcinoma																			X						
Keratoacanthoma						X		X						X											
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroma				X			X	X																	
Fibrosarcoma					X																				
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma																							X	X	
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS						X						X													
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	–	–	+	+	+	–	+	+	+	–	+	+	+	–	–	–	–	+	+	+	+	–	–	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Blood vessels	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
C-cell carcinoma, metastatic																							X		
DIGESTIVE SYSTEM																									
Salivary gland	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule																								X	
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	–	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Transitional cell carcinoma																									
ENDOCRINE SYSTEM																									
Pituitary	+	+	–	+	M	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS													X												
Adenoma, NOS		X					X	X												X			X		
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma														X		X									
Pheochromocytoma		X		X						X					X		X				X				
Thyroid	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma													X												
Follicular cell carcinoma																									
C-cell adenoma																					X				
C-cell carcinoma																							X		
Parathyroid	–	–	+	–	+	+	+	+	+	+	+	+	+	+	+	+	–	+	–	–	+	+	–	+	+
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma								X									X								
Islet cell carcinoma		X																							
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	+	N	+	+	+	+	+	+	+	+	N	+	+	+	+	N	+	+	+	+	+
Papillary adenoma										X															
Fibroadenoma																									
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Interstitial cell tumor			X		X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																	X								
Adenoma, NOS																X									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Leukemia, mononuclear cell	X		X						X		X														

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: LOW DOSE (Continued)

ANIMAL NUMBER	020	021	022	024	025	027	028	029	030	032	033	035	036	037	038	039	040	041	042	044	045	046	047	048	050	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	
INTEGUMENTARY SYSTEM																										
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Skin	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	*50
Squamous cell carcinoma																										1
Keratoacanthoma																										3
Subcutaneous tissue	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	*50
Fibroma	X							X	X																	6
Fibrosarcoma																		X								2
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma												X							X							4
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma, NOS																										2
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thymus	−	+	+	−	+	+	+	+	+	+	+	+	+	+	+	−	+	−	+	−	+	−	−	+	+	33
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Blood vessels	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
C-cell carcinoma, metastatic																										1
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Neoplastic nodule																X					X					3
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	49
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Small intestine	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Transitional cell carcinoma																				X						1
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Carcinoma, NOS																			X							2
Adenoma, NOS							X		X			X			X			X			X					11
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cortical adenoma							X																			3
Pheochromocytoma			X		X				X	X	X													X	X	13
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Follicular cell adenoma																										1
Follicular cell carcinoma			X																							1
C-cell adenoma	X											X					X									4
C-cell carcinoma																										1
Parathyroid	+	+	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	−	+	+	39
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islet cell adenoma												X														3
Islet cell carcinoma																										1
REPRODUCTIVE SYSTEM																										
Mammary gland	+	N	+	+	N	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Papillary adenoma															X											1
Fibroadenoma																										1
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Interstitial cell tumor	X	X	X	X	X	X		X	X	X	X	X				X	X		X	X	X	X	X	X	X	41
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	49
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS																										1
Adenoma, NOS														X												2
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Leukemia, mononuclear cell					X							X													X	7

* Animals necropsied

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL: HIGH DOSE

ANIMAL NUMBER	020	013	001	008	017	032	036	050	028	024	027	048	016	002	003	004	005	006	007	009	010	025	011	012	014
WEEKS ON STUDY	032	077	086	089	090	091	092	095	097	099	100	100	102	104	104	104	104	104	104	104	104	104	105	105	105
INTEGUMENTARY SYSTEM																									
Skin paint site	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma																									
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	.+	+	+	+	+
Papilloma, NOS																							X		
Squamous cell papilloma													X												
Keratoacanthoma																							X		
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroma																		X							
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma																									
Trachea	+	+	+	+	+	+	−	+	+	+	+	−	+	+	+	+	−	+	+	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	−	−	+	+	−	+	+	+	+	+	−	−	+	+	+	+	+	+	+	+	+	+	−
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS									X																
Large intestine	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+
Carcinoma, NOS										X															
Adenoma, NOS		X			X	X							X	X				X	X					X	X
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																									
Pheochromocytoma						X						X				X				X					
Pheochromocytoma, malignant																		X				X			
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell carcinoma											X														
C-cell adenoma																									
C-cell carcinoma																									
Parathyroid	+	−	+	+	+	+	+	+	+	−	+	+	+	+	−	+	+	+	−	−	+	−	−	−	−
REPRODUCTIVE SYSTEM																									
Mammary gland	N	+	+	+	+	+	+	+	N	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroadenoma																									
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Interstitial cell tumor			X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X
Prostate	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS									X																
Adenoma, NOS																			X						
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
SPECIAL SENSE ORGANS																									
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS								X																	
Adenoma, NOS																						X			
BODY CAVITIES																									
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mesothelioma, NOS																									
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Mesothelioma, NOS							X																		
Leukemia, mononuclear cell		X	X			X					X	X	X						X				X		X

+: Tissue examined microscopically
−: Required tissue not examined microscopically
X: Tumor incidence
N: Necropsy, no autolysis, no microscopic examination
S: Animal missexed
: No tissue information submitted
C: Necropsy, no histology due to protocol
A: Autolysis
M: Animal missing
B: No necropsy performed

TABLE A3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE RATS: HIGH DOSE (Continued)

ANIMAL NUMBER	015	018	019	021	022	023	026	029	030	031	033	034	035	037	038	039	040	041	042	043	044	045	046	047	049	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	
INTEGUMENTARY SYSTEM																										
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Keratoacanthoma									X																	1
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Papilloma, NOS					X						X								X							4
Squamous cell papilloma																						X				2
Keratoacanthoma																										1
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Fibroma																										1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma										X																1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	49
Thymus	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Neoplastic nodule				X									X					X								3
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Pancreas	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenocarcinoma, NOS																										1
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma, NOS																										1
Adenoma, NOS						X			X				X					X			X				X	15
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cortical adenoma						X																				1
Pheochromocytoma	X		X	X						X			X		X											10
Pheochromocytoma, malignant																										2
Thyroid	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Follicular cell carcinoma																										1
C-cell adenoma			X		X				X																	3
C-cell carcinoma												X														1
Parathyroid	+	+	–	+	+	+	+	+	–	–	–	+	+	+	+	+	+	+	+	+	+	–	–	+	+	35
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Fibroadenoma																			X							1
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Interstitial cell tumor	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X		X	44
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS													X													2
Adenoma, NOS																										1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
SPECIAL SENSE ORGANS																										
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS																										1
Adenoma, NOS																										1
BODY CAVITIES																										
Tunica vaginalis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Mesothelioma, NOS													X													1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Mesothelioma, NOS																										1
Leukemia, mononuclear cell													X				X				X					12

* Animals necropsied

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL: VEHICLE CONTROL

ANIMAL NUMBER	011	032	030	042	046	033	039	025	001	002	003	004	005	006	007	008	009	010	012	013	014	015	016	017	018
WEEKS ON STUDY	083	088	092	092	092	094	098	103	104	104	104	104	104	104	104	104	104	104	105	105	105	105	105	105	105
INTEGUMENTARY SYSTEM																									
Skin paint site	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Keratoacanthoma											X														
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma											X														
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia, mononuclear cell																									
Lymph nodes	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	−	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	−	+	−
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pancreas	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS													X		X										X
Adenoma, NOS								X					X	X				X	X	X				X	
Adrenal	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma															X										
Pheochromocytoma																		X							
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+
C-cell adenoma							X																		
C-cell carcinoma																									
Parathyroid	+	+	−	−	+	+	−	+	−	+	+	+	+	+	+	−	+	+	+	+	+	+	+	−	+
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cystadenoma, NOS																			X						
Fibroadenoma					X			X						X					X		X				X
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroma																									
Endometrial stromal polyp	X					X								X											
Endometrial stromal sarcoma																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Astrocytoma																									
SPECIAL SENSE ORGANS																									
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinoma, NOS																									
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Leukemia, mononuclear cell															X								X		

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: VEHICLE CONTROL (Continued)

ANIMAL NUMBER	019	020	021	022	023	024	026	027	028	029	031	034	035	036	037	038	040	041	043	044	045	047	048	049	050	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	
INTEGUMENTARY SYSTEM																										
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	*50
Keratoacanthoma																										1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma																										1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leukemia, mononuclear cell											X															1
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Thymus	-	-	+	+	+	-	+	+	+	-	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	40
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Neoplastic nodule																									X	1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	47
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, NOS																								X		4
Adenoma, NOS	X			X	X			X	X	X		X			X		X		X	X			X			19
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Cortical adenoma																										1
Pheochromocytoma				X																X						3
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
C-cell adenoma			X														X									2
C-cell carcinoma																										1
Parathyroid	+	-	+	-	+	+	+	+	+	+	-	+	+	+	+	-	-	+	+	+	+	+	+	-	+	38
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Islet cell adenoma																			X							1
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	N	N	+	+	+	+	+	+	+	+	+	+	+	*50
Cystadenoma, NOS												X												X		3
Fibroadenoma	X					X				X	X						X			X			X			13
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS											X															1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibroma																									X	1
Endometrial stromal polyp				X											X	X								X		7
Endometrial stromal sarcoma		X																								1
Ovary	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Astrocytoma									X																	1
SPECIAL SENSE ORGANS																										
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinoma, NOS																					X					1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Leukemia, mononuclear cell					X																				X	7

* Animals necropsied

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL: LOW DOSE

ANIMAL NUMBER	035	047	046	023	049	038	027	030	045	041	031	001	002	003	004	005	006	007	008	009	010	011	012	013	014
WEEKS ON STUDY	069	069	074	075	080	095	098	098	100	102	103	104	104	104	104	104	104	104	104	104	105	105	105	105	105
INTEGUMENTARY SYSTEM																									
Skin paint site	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trichoepithelioma																									
Subcutaneous tissue	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS						X																			
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar carcinoma																									
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	−
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−
Lymph nodes	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	−	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	−	+	−	−	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Oral cavity	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Squamous cell carcinoma				X																					
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Neoplastic nodule						X																			
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	−	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	−	−	+	+	+	+	+	+	+	+	−	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS							X																		
Adenoma, NOS	X		X	X		X		X		X		X	X					X		X			X		X
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																								X	
Pheochromocytoma								X																	
Pheochromocytoma, malignant		X																							
Ganglioneuroma																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Follicular cell adenoma																									
Follicular cell carcinoma																									
C-cell adenoma												X													
Parathyroid	+	−	+	+	−	+	+	+	+	+	+	+	+	−	−	+	+	+	+	+	+	−	+	+	+
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−
Islet cell adenoma						X												X							
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	N	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS			X																						
Cystadenoma, NOS												X	X												
Fibroadenoma								X									X					X	X		
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Endometrial stromal polyp																						X			X
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS, invasive							X																		
SPECIAL SENSE ORGANS																									
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenoma, NOS																								X	
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pheochromocytoma, metastatic		X																							
Angiosarcoma											X														
Leukemia, mononuclear cell					X			X								X								X	

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: LOW DOSE (Continued)

ANIMAL NUMBER	015	016	017	018	019	020	021	022	024	025	026	028	029	032	033	034	036	037	039	040	042	043	044	048	050	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	
INTEGUMENTARY SYSTEM																										
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Skin	+	N	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Trichoepithelioma													X													1
Subcutaneous tissue	+	N	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Sarcoma, NOS																										1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar carcinoma														X												1
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	48
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	44
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Oral cavity	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Squamous cell carcinoma																										1
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Neoplastic nodule																								X		2
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	45
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Carcinoma, NOS																										1
Adenoma, NOS				X	X	X	X		X	X				X	X					X		X	X		X	24
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cortical adenoma											X															2
Pheochromocytoma						X								X												3
Pheochromocytoma, malignant																										1
Ganglioneuroma																							X			1
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Follicular cell adenoma																	X									1
Follicular cell carcinoma								X																		1
C-cell adenoma	X																				X					3
Parathyroid	+	+	+	+	+	+	+	+	+	+	+	-	-	-	-	+	+	-	+	-	+	-	-	+	+	37
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Islet cell adenoma												X														3
REPRODUCTIVE SYSTEM																										
Mammary gland	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Adenocarcinoma, NOS														X												2
Cystadenoma, NOS																			X							3
Fibroadenoma				X		X					X															7
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, NOS			X																							1
Endometrial stromal polyp		X															X									4
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, NOS, invasive																										1
SPECIAL SENSE ORGANS																										
Zymbal gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Adenoma, NOS																										1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Pheochromocytoma, metastatic																										1
Angiosarcoma																										1
Leukemia, mononuclear cell	X						X			X																7

* Animals necropsied

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL: HIGH DOSE

ANIMAL NUMBER	013	028	037	032	017	020	022	049	021	039	011	001	002	003	004	005	006	007	008	009	010	012	019	038	014
WEEKS ON STUDY	071	074	074	078	079	088	088	096	101	102	103	104	104	104	104	104	104	104	104	104	104	104	104	104	105
INTEGUMENTARY SYSTEM																									
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+
Fibroma			X																				X		
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	−	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trachea	+	+	+	+	+	−	+	+	−	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	−	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	−	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																									
Adenoma, NOS	X	X	X	X	X				X	X	X	X	X	X				X	X	X	X		X	X	
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																									
Pheochromocytoma																					X				
Pheochromocytoma, malignant									X																
Pheochromocytoma, metastatic									X																
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
C-cell adenoma																X							X		
C-cell carcinoma																									
Parathyroid	−	+	+	−	+	+	+	+	+	+	−	+	−	−	+	−	+	−	+	+	−	+	−	+	+
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Islet cell adenoma																X									
Islet cell carcinoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland	N	+	+	N	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+
Papillary adenoma																								X	
Cystadenoma, NOS																								X	
Fibroadenoma							X				X				X		X			X					
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Adenoma, NOS																									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Endometrial stromal polyp			X												X										X
Endometrial stromal sarcoma																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Granulosa cell tumor																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Leukemia, mononuclear cell						X	X	X	X														X		

+: Tissue examined microscopically
−: Required tissue not examined microscopically
X: Tumor incidence
N: Necropsy, no autolysis, no microscopic examination
S: Animal missexed
: No tissue information submitted
C: Necropsy, no histology due to protocol
A: Autolysis
M: Animal missing
B: No necropsy performed

TABLE A4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE RATS: HIGH DOSE (Continued)

ANIMAL NUMBER	0 1 5	0 1 6	0 1 8	0 2 3	0 2 4	0 2 5	0 2 6	0 2 7	0 2 9	0 3 0	0 3 1	0 3 3	0 3 4	0 3 5	0 3 6	0 4 0	0 4 1	0 4 2	0 4 3	0 4 4	0 4 5	0 4 6	0 4 7	0 4 8	0 5 0	TOTAL:
WEEKS ON STUDY	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	TISSUES / TUMORS
INTEGUMENTARY SYSTEM																										
Skin paint site	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Fibroma																										2
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Trachea	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph nodes	+	−	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	−	+	+	+	48
Thymus	+	+	+	−	+	+	+	+	+	+	+	+	+	+	−	+	+	+	−	+	+	+	+	+	+	45
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	49
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	49
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, NOS																							X			1
Adenoma, NOS			X	X	X		X		X				X	X			X		X		X	X			X	29
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cortical adenoma																	X								X	2
Pheochromocytoma								X					X													3
Pheochromocytoma, malignant																										1
Pheochromocytoma, metastatic																										1
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	49
C-cell adenoma									X					X												4
C-cell carcinoma																X										1
Parathyroid	−	−	−	+	−	+	−	−	+	+	−	−	−	−	+	+	+	−	+	+	+	−	+	−	−	27
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Islet cell adenoma																										1
Islet cell carcinoma																							X			1
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	*50
Papillary adenoma																										1
Cystadenoma, NOS					X									X												3
Fibroadenoma	X			X														X		X			X		X	11
Preputial/clitoral gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Adenoma, NOS				X																						1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Endometrial stromal polyp								X		X						X	X									7
Endometrial stromal sarcoma							X																			1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Granulosa cell tumor																							X			1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Leukemia, mononuclear cell																					X					6

* Animals necropsied

APPENDIX B

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MICE IN THE TWO-YEAR DERMAL STUDIES OF 2-CHLOROETHANOL

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL

	CONTROL (UNTR)	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50	50
ANIMALS NECROPSIED	50	50	50	50
ANIMALS EXAMINED HISTOPATH	50	50	50	50
INTEGUMENTARY SYSTEM				
#SKIN PAINT SITE	(44)	(50)	(49)	(50)
FIBROMA		1 (2%)		
*SUBCUT TISSUE	(50)	(50)	(50)	(50)
SARCOMA, NOS		4 (8%)	4 (8%)	1 (2%)
FIBROSARCOMA	2 (4%)	1 (2%)		
NEUROFIBROSARCOMA		1 (2%)		
RESPIRATORY SYSTEM				
#LUNG	(50)	(50)	(50)	(50)
ALVEOLAR/BRONCHIOLAR ADEN	6 (12%)	8 (16%)	10 (20%)	9 (18%)
ALVEOLAR/BRONCHIOLAR CARCIN	4 (8%)	6 (12%)	9 (18%)	3 (6%)
HEMATOPOIETIC SYSTEM				
*MULTIPLE ORGANS	(50)	(50)	(50)	(50)
MALIGNANT LYMPHOMA, NOS	3 (6%)	3 (6%)	10 (20%)	2 (4%)
MALIG. LYMPHOMA, HISTIOCYTIC TYPE		1 (2%)		
GRANULOCYTIC LEUKEMIA	3 (6%)	2 (4%)	4 (8%)	2 (4%)
#AXILLARY LYMPH NODE	(27)	(32)	(37)	(35)
FIBROSARCOMA, METASTATIC	1 (4%)			
CIRCULATORY SYSTEM				
#SPLEEN	(44)	(49)	(50)	(50)
HEMANGIOSARCOMA		1 (2%)		
#LIVER	(50)	(49)	(50)	(50)
HEMANGIOSARCOMA		1 (2%)		
DIGESTIVE SYSTEM				
#LIVER	(50)	(49)	(50)	(50)
BILE DUCT CARCINOMA		1 (2%)		
HEPATOCELLULAR ADENOMA	1 (2%)	2 (4%)	3 (6%)	1 (2%)
HEPATOCELLULAR CARCINOMA	6 (12%)	9 (18%)	6 (12%)	4 (8%)
HEPATOBLASTOMA				1 (2%)
#PANCREAS	(46)	(49)	(50)	(50)
ACINAR-CELL CARCINOMA			1 (2%)	
#STOMACH	(45)	(50)	(49)	(49)
ADENOCARCINOMA, NOS		1 (2%)	1 (2%)	
ADENOMATOUS POLYP, NOS				1 (2%)
*ANUS	(50)	(50)	(50)	(50)
LEIOMYOSARCOMA			1 (2%)	
URINARY SYSTEM				
#KIDNEY	(50)	(50)	(50)	(50)
TUBULAR-CELL ADENOCARCINOMA			1 (2%)	1 (2%)
#URINARY BLADDER	(44)	(50)	(50)	(47)
TRANSITIONAL-CELL CARCINOMA			1 (2%)	

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (UNTR)	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ENDOCRINE SYSTEM				
#ADRENAL	(48)	(48)	(49)	(50)
CORTICAL ADENOMA	3 (6%)		2 (4%)	1 (2%)
PHEOCHROMOCYTOMA		1 (2%)		
#ADRENAL CORTEX	(48)	(48)	(49)	(50)
ADENOMA, NOS	1 (2%)			2 (4%)
#THYROID	(47)	(47)	(44)	(46)
FOLLICULAR-CELL ADENOMA			1 (2%)	
REPRODUCTIVE SYSTEM				
*PREPUCE	(50)	(50)	(50)	(50)
PAPILLOMA, NOS				1 (2%)
*SEMINAL VESICLE	(50)	(50)	(50)	(50)
CARCINOMA, NOS			1 (2%)	
#TESTIS	(49)	(50)	(50)	(50)
INTERSTITIAL-CELL TUMOR	1 (2%)			
NERVOUS SYSTEM				
NONE				
SPECIAL SENSE ORGANS				
NONE				
MUSCULOSKELETAL SYSTEM				
*HUMERUS	(50)	(50)	(50)	(50)
OSTEOSARCOMA			1 (2%)	
BODY CAVITIES				
*ABDOMINAL CAVITY	(50)	(50)	(50)	(50)
SARCOMA, NOS				1 (2%)
ALL OTHER SYSTEMS				
*MULTIPLE ORGANS	(50)	(50)	(50)	(50)
BILE DUCT CARCINOMA, METASTATIC		1 (2%)		
ALVEOLAR/BRONCHIOLAR CA, INVASIVE		2 (4%)		
SARCOMA, NOS, UNC PRIM OR META				1 (2%)
HEPATOBLASTOMA, METASTATIC				1 (2%)
ANIMAL DISPOSITION SUMMARY				
ANIMALS INITIALLY IN STUDY	50	50	50	50
NATURAL DEATH	19	13	11	19
MORIBUND SACRIFICE	6	11	21	19
SCHEDULED SACRIFICE				
TERMINAL SACRIFICE	24	26	16	12
DOSING ACCIDENT				
ACCIDENTALLY KILLED, NDA				
ACCIDENTALLY KILLED, NOS	1		2	
ANIMAL MISSING				
ANIMAL MISSEXED				
OTHER CASES				

TABLE B1. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (UNTR)	CONTROL (VEH)	LOW DOSE	HIGH DOSE
TUMOR SUMMARY				
TOTAL ANIMALS WITH PRIMARY TUM**	23	29	39	21
TOTAL PRIMARY TUMORS	30	43	56	31
TOTAL ANIMALS WITH BENIGN TUMORS	7	11	14	12
TOTAL BENIGN TUMORS	12	12	16	15
TOTAL ANIMALS WITH MALIGNANT TUM	17	25	32	14
TOTAL MALIGNANT TUMORS	18	31	40	15
TOTAL ANIMALS WITH SECONDARY TUM##	1	3		1
TOTAL SECONDARY TUMORS	1	3		1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT				
TOTAL UNCERTAIN TUMORS				
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC				1
TOTAL UNCERTAIN TUMORS				1

• NUMBER OF ANIMALS NECROPSIED
** PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE B2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL

	CONTROL (UNTR)	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50	50
ANIMALS NECROPSIED	50	50	50	50
ANIMALS EXAMINED HISTOPATH	50	50	50	50
INTEGUMENTARY SYSTEM				
#SKIN PAINT SITE	(48)	(49)	(48)	(47)
SARCOMA, NOS, INVASIVE				1 (2%)
*SKIN	(50)	(50)	(50)	(50)
PAPILLOMA, NOS			1 (2%)	
TRICHOEPITHELIOMA		1 (2%)		
*SUBCUT TISSUE	(50)	(50)	(50)	(50)
BASAL-CELL CARCINOMA	1 (2%)			
TRICHOEPITHELIOMA	1 (2%)			
SARCOMA, NOS	1 (2%)	1 (2%)		2 (4%)
MYXOMA		1 (2%)		
LIPOSARCOMA	1 (2%)			
CARCINOSARCOMA			1 (2%)	
RESPIRATORY SYSTEM				
#LUNG	(50)	(50)	(49)	(50)
ALVEOLAR/BRONCHIOLAR ADEN	7 (14%)	7 (14%)	6 (12%)	6 (12%)
ALVEOLAR/BRONCHIOLAR CARCIN	3 (6%)	2 (4%)	5 (10%)	3 (6%)
SARCOMA, NOS, METASTATIC				1 (2%)
CARCINOSARCOMA, METASTATIC			1 (2%)	
HEMATOPOIETIC SYSTEM				
*MULTIPLE SITES	(50)	(50)	(50)	(50)
MALIGNANT LYMPHOMA, NOS	1 (2%)			
*MULTIPLE ORGANS	(50)	(50)	(50)	(50)
MALIGNANT LYMPHOMA, NOS	9 (18%)	8 (16%)	8 (16%)	9 (18%)
MALIG. LYMPHOMA, HISTIOCYTIC TYPE	1 (2%)		2 (4%)	1 (2%)
GRANULOCYTIC LEUKEMIA		1 (2%)	4 (8%)	3 (6%)
#SPLEEN	(47)	(49)	(48)	(49)
MALIG. LYMPHOMA, HISTIOCYTIC TYPE			1 (2%)	
#MESENTERIC L. NODE	(38)	(33)	(36)	(44)
MALIGNANT LYMPHOMA, NOS	1 (3%)			
CIRCULATORY SYSTEM				
*SUBCUT TISSUE	(50)	(50)	(50)	(50)
HEMANGIOSARCOMA, METASTATIC			1 (2%)	
#SPLEEN	(47)	(49)	(48)	(49)
HEMANGIOSARCOMA			2 (4%)	
#HEART	(50)	(50)	(50)	(50)
HEMANGIOSARCOMA, METASTATIC			1 (2%)	
#UTERUS	(50)	(49)	(49)	(50)
HEMANGIOMA		1 (2%)		
HEMANGIOSARCOMA			1 (2%)	
#OVARY	(50)	(50)	(49)	(48)
HEMANGIOMA	1 (2%)	2 (4%)	2 (4%)	
DIGESTIVE SYSTEM				
#LIVER	(50)	(50)	(49)	(50)
ADENOCARCINOMA, NOS, META	1 (2%)			
HEPATOCELLULAR ADENOMA	1 (2%)	2 (4%)		
HEPATOCELLULAR CARCINOMA		1 (2%)		1 (2%)
*GALLBLADDER	(50)	(50)	(50)	(50)
PAPILLARY ADENOMA				1 (2%)

TABLE B2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (UNTR)	CONTROL (VEH)	LOW DOSE	HIGH DOSE
URINARY SYSTEM				
#KIDNEY	(50)	(50)	(50)	(50)
SARCOMA, NOS, UNC PRIM OR META	1 (2%)			
ENDOCRINE SYSTEM				
#PITUITARY	(46)	(48)	(49)	(47)
CHROMOPHOBE ADENOMA	4 (9%)	2 (4%)	2 (4%)	3 (6%)
ACIDOPHIL ADENOMA	1 (2%)			
#ADRENAL	(49)	(50)	(50)	(49)
CORTICAL ADENOMA	1 (2%)			
PHEOCHROMOCYTOMA	1 (2%)			
#ADRENAL/CAPSULE	(49)	(50)	(50)	(49)
ADENOMA, NOS			1 (2%)	
#PANCREATIC ISLETS	(48)	(50)	(47)	(50)
ISLET-CELL ADENOMA			1 (2%)	
REPRODUCTIVE SYSTEM				
*MAMMARY GLAND	(50)	(50)	(50)	(50)
ADENOMA, NOS			1 (2%)	
ADENOCARCINOMA, NOS	4 (8%)	2 (4%)	2 (4%)	5 (10%)
ADENOSQUAMOUS CARCINOMA			1 (2%)	
CARCINOSARCOMA			1 (2%)	2 (4%)
#UTERUS	(50)	(49)	(49)	(50)
LEIOMYOMA		1 (2%)	1 (2%)	2 (4%)
LEIOMYOSARCOMA	1 (2%)	2 (4%)	1 (2%)	1 (2%)
ENDOMETRIAL STROMAL POLYP	2 (4%)			
ENDOMETRIAL STROMAL SARCOMA			1 (2%)	
#UTERUS/ENDOMETRIUM	(50)	(49)	(49)	(50)
CARCINOMA, NOS				1 (2%)
#OVARY	(50)	(50)	(49)	(48)
CYSTADENOMA, NOS		1 (2%)		
PAPILLARY CYSTADENOMA, NOS		1 (2%)		
LUTEOMA	1 (2%)	1 (2%)		
GRANULOSA-CELL TUMOR			1 (2%)	
NERVOUS SYSTEM				
#BRAIN	(50)	(50)	(50)	(50)
ASTROCYTOMA	1 (2%)			
SPECIAL SENSE ORGANS				
NONE				
MUSCULOSKELETAL SYSTEM				
*SKELETAL MUSCLE	(50)	(50)	(50)	(50)
LEIOMYOSARCOMA, INVASIVE				1 (2%)
BODY CAVITIES				
NONE				

TABLE B2. SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (UNTR)	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ALL OTHER SYSTEMS				
*MULTIPLE ORGANS	(50)	(50)	(50)	(50)
ADENOCARCINOMA, NOS, META				1 (2%)
ALVEOLAR/BRONCHIOLAR CA, INVASIVE	1 (2%)			
CARCINOSARCOMA, METASTATIC			1 (2%)	
ANIMAL DISPOSITION SUMMARY				
ANIMALS INITIALLY IN STUDY	50	50	50	50
NATURAL DEATH	12	12	5	10
MORIBUND SACRIFICE	14	12	25	20
SCHEDULED SACRIFICE				
TERMINAL SACRIFICE	24	26	20	20
DOSING ACCIDENT				
ACCIDENTALLY KILLED, NDA				
ACCIDENTALLY KILLED, NOS				
ANIMAL MISSING				
ANIMAL MISSEXED				
OTHER CASES				
TUMOR SUMMARY				
TOTAL ANIMALS WITH PRIMARY TUM**	36	27	32	32
TOTAL PRIMARY TUMORS	45	37	46	40
TOTAL ANIMALS WITH BENIGN TUMORS	19	15	11	10
TOTAL BENIGN TUMORS	20	20	15	12
TOTAL ANIMALS WITH MALIGNANT TUM	22	16	26	25
TOTAL MALIGNANT TUMORS	24	17	30	28
TOTAL ANIMALS WITH SEC TUM##	2		4	4
TOTAL SECONDARY TUMORS	2		4	4
TOTAL ANIMALS WITH TUM UNCERTAIN-BENIGN OR MALIGNANT			1	
TOTAL UNCERTAIN TUMORS			1	
TOTAL ANIMALS WITH TUM UNCERTAIN-PRIMARY OR METASTATIC	1			
TOTAL UNCERTAIN TUMORS	1			

* NUMBER OF ANIMALS NECROPSIED
** PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL: UNTREATED CONTROL

ANIMAL NUMBER	097	029	031	093	016	018	028	035	020	095	048	004	040	014	033	092	009	012	027	008	049	013	015	001	019
WEEKS ON STUDY	011	049	055	057	059	064	064	064	065	066	068	073	075	076	077	082	082	083	084	086	089	090	094	098	099
INTEGUMENTARY SYSTEM																									
Skin paint site	−	+	−	+	+	−	+	+	−	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibrosarcoma														X	X										
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																X		X							
Alveolar/bronchiolar carcinoma																									
Trachea	+	+	−	−	+	−	−	−	−	+	+	−	+	+	+	−	+	+	−	−	−	−	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	−	−	−	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	−	−	+	+	+	−	−	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	−	+	+	+	+	−	−	−	+	+	−	+	+	−	+	+	+	+	+	+	+	−	+	−
Fibrosarcoma, metastatic														X											
Thymus	+	−	+	−	+	−	+	+	+	−	+	−	+	+	−	+	−	+	+	+	−	+	−	−	−
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																					X				
Hepatocellular carcinoma																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	+	N	N	N	N	+	N	+	N	+	N	+	N	N	+	N	N	+	+	+	+	+
Pancreas	−	−	+	+	+	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	−	−	+	+	+	−	−	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	−	−	−	+	+	−	−	−	+	−	+	+	+	+	+	+	+	+	−	−	−	+	+	−	+
Large intestine	−	+	+	+	+	−	−	−	+	+	+	+	+	+	+	+	+	−	+	+	+	+	−	+	
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	−	+	+	+	+	+	−	−	+	−	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	−	+	−	+	+	−	+	+	+	+	+	−	−	+	+	+	+	+	+	+	+	+	−	−	+
Adrenal	−	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Cortical adenoma																									
Thyroid	−	+	+	+	+	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid	−	−	−	−	−	−	−	−	−	−	−	−	+	−	−	−	+	−	−	−	−	−	−	−	−
REPRODUCTIVE SYSTEM																									
Mammary gland	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+
Interstitial cell tumor																									
Prostate	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Malignant lymphoma, NOS			X			X				X															
Granulocytic leukemia				X									X								X				

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: UNTREATED CONTROL (Continued)

ANIMAL NUMBER	017	008	010	011	021	022	023	024	025	026	030	032	034	036	037	038	039	041	042	043	044	045	046	047	050	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	103	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	
INTEGUMENTARY SYSTEM																										
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	44
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Fibrosarcoma																										2
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma							X			X				X				X		X					X	6
Alveolar/bronchiolar carcinoma						X						X														4
Trachea	–	–	+	–	–	–	+	–	–	+	+	–	+	–	+	+	+	+	–	–	–	+	–	–	–	23
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	–	+	+	+	–	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	43
Spleen	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Lymph nodes	+	+	–	+	–	+	–	–	–	–	+	–	+	–	+	+	–	+	–	–	+	–	–	–	–	27
Fibrosarcoma, metastatic																										1
Thymus	–	+	+	+	+	+	–	–	+	–	+	+	+	–	+	–	+	–	+	–	+	+	–	+	+	30
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	47
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma																									X	1
Hepatocellular carcinoma	X									X			X		X							X				6
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Esophagus	+	+	+	+	+	+	–	+	+	+	+	+	+	+	–	+	+	+	–	+	+	+	+	+	+	46
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	39
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
ENDOCRINE SYSTEM																										
Pituitary	+	–	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	41
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Adenoma, NOS																				X						1
Cortical adenoma							X	X		X																3
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Parathyroid	–	+	+	–	+	–	–	+	–	+	–	–	–	–	+	–	–	–	+	–	–	+	–	+	+	12
REPRODUCTIVE SYSTEM																										
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	*50
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Interstitial cell tumor																				X						1
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Malignant lymphoma, NOS																										3
Granulocytic leukemia																										3

* Animals necropsied

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL: VEHICLE CONTROL

ANIMAL NUMBER	04 07	04 09	04 12	04 28	04 02	04 08	04 36	04 15	04 27	04 22	04 13	04 20	04 07	04 35	04 37	04 40	04 38	04 34	04 16	04 05	04 11	04 19	04 42	04 43	04 01
WEEKS ON STUDY	04 41	04 44	05 58	06 04	07 05	07 05	07 07	07 08	07 08	08 01	08 03	08 04	08 05	09 00	09 00	09 00	09 01	09 05	09 09	10 03	10 03	10 03	10 04	10 04	10 05
INTEGUMENTARY SYSTEM																									
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Fibroma																							X		
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS																							X	X	
Fibrosarcoma																									
Neurofibrosarcoma																								X	
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																X				X			X	X	
Alveolar/bronchiolar carcinoma					X	X															X				
Trachea	–	–	–	–	+	–	–	–	+	–	–	–	+	–	+	–	+	–	–	–	–	+	+	–	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+
Spleen	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Lymph nodes	+	+	+	+	–	+	+	+	–	+	+	+	+	+	–	+	–	–	+	–	+	+	+	+	–
Thymus	+	–	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	–	+	–	+	+	–	–	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bile duct carcinoma																		X							
Hepatocellular adenoma																									
Hepatocellular carcinoma								X											X						
Hemangiosarcoma																					X				
Bile duct	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	+	N	+	+	+	N	+	N	+	+	N	+	+	N	N	+	+	N	+	+	+
Pancreas	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	–	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	–	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
Small intestine	–	–	+	–	+	–	+	+	+	–	+	–	+	+	–	+	+	+	+	+	+	+	+	+	+
Large intestine	+	–	+	–	+	+	+	+	+	–	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	–	–	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
Pheochromocytoma																									
Thyroid	+	–	+	+	+	+	+	+	+	–	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid	–	–	–	–	–	+	–	–	+	–	–	–	–	–	–	–	+	–	–	–	–	–	+	–	+
REPRODUCTIVE SYSTEM																									
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Bile duct carcinoma, metastatic																		X							
Alveolar/bronchiolar carcinoma, invasive					X	X																			
Malignant lymphoma, NOS	X																			X				X	
Malignant lymphoma, histiocytic type													X												
Granulocytic leukemia			X	X																					

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: VEHICLE CONTROL (Continued)

ANIMAL NUMBER	0 0 3	0 0 4	0 0 6	0 1 0	0 1 4	0 1 7	0 1 8	0 2 1	0 2 3	0 2 4	0 2 5	0 2 6	0 2 9	0 3 0	0 3 1	0 3 2	0 3 3	0 3 9	0 4 1	0 4 4	0 4 5	0 4 8	0 4 9	0 5 0	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	1 0 5	
INTEGUMENTARY SYSTEM																									
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Fibroma																									1
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Sarcoma, NOS										X						X									4
Fibrosarcoma																					X				1
Neurofibrosarcoma																									1
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma											X				X			X					X		8
Alveolar/bronchiolar carcinoma		X				X										X									6
Trachea	–	+	+	–	–	+	+	–	–	–	–	+	–	–	–	–	+	–	–	–	+	+	+	–	–	17
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Hemangiosarcoma								X																	1
Lymph nodes	+	+	+	–	–	–	–	–	+	–	+	+	+	+	–	+	–	–	+	+	–	–	+	+	32
Thymus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	43
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Bile duct carcinoma																									1
Hepatocellular adenoma			X			X																			2
Hepatocellular carcinoma										X	X			X			X				X		X	X	9
Hemangiosarcoma																									1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Gallbladder & common bile duct	+	+	+	+	+	+	+	+	+	N	N	+	+	+	+	N	+	+	+	+	+	+	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Esophagus	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	–	+	+	–	+	+	44
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, NOS		X																							1
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	42
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ENDOCRINE SYSTEM																									
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Pheochromocytoma																X									1
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Parathyroid	+	–	+	–	–	+	–	–	–	–	+	–	–	–	+	–	+	–	–	+	+	–	+	–	+	15
REPRODUCTIVE SYSTEM																									
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Bile duct carcinoma, metastatic																									1
Alveolar/bronchiolar carcinoma, invasive																									2
Malignant lymphoma, NOS																									3
Malignant lymphoma, histiocytic type																									1
Granulocytic leukemia																									2

* Animals necropsied

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL: LOW DOSE

ANIMAL NUMBER	034	038	017	055	019	037	059	039	049	049	018	014	044	021	043	048	047	025	035	046	032	033	036	013	022
WEEKS ON STUDY	092	052	082	042	052	084	067	052	071	072	074	075	078	078	078	077	078	080	087	087	088	090	091	091	091
INTEGUMENTARY SYSTEM																									
Skin paint site	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS		X																			X				
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																						X			
Alveolar/bronchiolar carcinoma													X							X	X				
Trachea	−	+	−	−	+	−	+	+	−	−	+	+	−	−	−	+	+	−	−	−	+	+	+	−	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	−
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	−	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	+	−	+	+	+	+	−	−	−	+	+	+	−	+	+	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																									
Hepatocellular carcinoma																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	+	+	+	N	+	+	N	N	+	+	N	+	+	+	+	+	N	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Acinar cell carcinoma																									
Esophagus	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+
Stomach	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS																									
Small intestine	+	−	+	+	+	+	+	−	+	+	+	−	+	+	+	+	+	−	−	+	+	+	+	+	+
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Rectum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Leiomyosarcoma																									
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tubular cell adenocarcinoma																									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Transitional cell carcinoma																									
ENDOCRINE SYSTEM																									
Pituitary	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+
Adrenal	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																									
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	−	−	−	+	+	+	+	+
Follicular cell adenoma																									
Parathyroid	−	+	−	−	+	−	−	+	−	−	−	−	+	−	−	−	+	−	−	−	+	−	+	−	+
REPRODUCTIVE SYSTEM																									
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Seminal vesicle	N	N	N	N	+	N	N	N	N	N	N	+	N	N	N	N	N	N	+	N	+	N	+	N	+
Carcinoma, NOS																									
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MUSCULOSKELETAL SYSTEM																									
Bone	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Osteosarcoma																			X						
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Malignant lymphoma, NOS				X	X		X	X	X	X	X														X
Granulocytic leukemia																X	X							X	

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: LOW DOSE (Continued)

ANIMAL NUMBER	027	024	019	039	025	041	047	026	002	001	008	011	012	015	018	020	028	029	031	033	036	042	044	045	050	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	093	095	098	098	100	100	100	101	102	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	
INTEGUMENTARY SYSTEM																										
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Sarcoma, NOS			X																	X						4
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma		X	X	X	X			X						X									X	X	X	10
Alveolar/bronchiolar carcinoma					X		X				X					X	X			X						9
Trachea	+	–	–	–	–	+	+	–	+	+	+	+	+	–	–	–	–	+	–	+	+	+	+	–	–	25
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	–	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph nodes	+	+	–	+	+	+	+	–	+	+	–	–	+	–	+	–	+	–	–	+	+	–	–	–	+	37
Thymus	+	–	+	+	–	+	+	–	+	+	+	–	+	+	–	+	+	–	+	–	+	+	+	+	+	38
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma						X						X							X							3
Hepatocellular carcinoma			X						X	X			X							X					X	6
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	+	+	N	N	+	+	+	N	+	+	+	+	+	N	+	N	+	+	+	+	N	+	+	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Acinar cell carcinoma							X																			1
Esophagus	+	+	+	+	+	+	+	+	+	+	–	+	–	+	+	+	+	+	+	+	+	+	+	+	+	46
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenocarcinoma, NOS						X																				1
Small intestine	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Large intestine	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Rectum	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Leiomyosarcoma								X																		1
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tubular cell adenocarcinoma																						X				1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Transitional cell carcinoma									X																	1
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Cortical adenoma																						X	X			2
Thyroid	–	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Follicular cell adenoma					X																					1
Parathyroid	–	–	–	+	–	–	–	–	–	–	+	–	+	+	–	+	–	–	–	–	+	–	–	–	–	14
REPRODUCTIVE SYSTEM																										
Mammary gland	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	N	N	+	N	N	N	*50
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Seminal vesicle	N	N	N	+	+	+	N	N	+	+	N	+	N	N	+	+	N	N	N	+	+	N	+	N	N	*50
Carcinoma, NOS						X																				1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
MUSCULOSKELETAL SYSTEM																										
Bone	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Osteosarcoma																										1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Malignant lymphoma, NOS	X	X																								10
Granulocytic leukemia							X																			4

* Animals necropsied

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL: HIGH DOSE

ANIMAL NUMBER	0041	0168	0204	0235	0341	0448	0096	0122	0211	0447	0444	0267	0171	0289	0499	0097	0321	0144	0233	0199	0455	0155	0433	0008
WEEKS ON STUDY	0000	0000	0000	0000	0000	0000	0000	0310	0402	0490	0500	0867	0711	0744	0744	0766	0768	0777	0788	0822	0883	0886	0889	0900
INTEGUMENTARY SYSTEM																								
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS																								
RESPIRATORY SYSTEM																								
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																		X		X		X		
Alveolar/bronchiolar carcinoma																				X				
Trachea	−	−	−	−	−	−	−	−	−	−	+	−	+	+	−	+	+	+	+	+	+	+	−	−
HEMATOPOIETIC SYSTEM																								
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	−	+	+	+	−	−	+	+	+	+	+	+	+	−	+	+	+	+	+	+
Thymus	+	+	+	+	+	+	+	−	+	+	−	−	−	+	+	+	+	−	+	+	−	+	+	+
CIRCULATORY SYSTEM																								
Heart	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																								
Salivary gland	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																								
Hepatocellular carcinoma																		X						
Hepatoblastoma																				X				
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	+	N	N	N	N	N	N	+	N	+	+	+	+	+	N	+	+	N	+	N	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenomatous polyp, NOS												X												
Small intestine	−	+	+	+	−	+	−	+	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+
Large intestine	+	+	+	+	−	+	+	+	+	+	+	+	−	−	+	+	+	−	+	+	+	+	+	+
URINARY SYSTEM																								
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Tubular cell adenocarcinoma															X									
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+
ENDOCRINE SYSTEM																								
Pituitary	+	+	+	−	+	−	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																								
Cortical adenoma																								
Thyroid	+	+	+	+	+	+	+	−	+	−	+	+	+	+	+	+	+	+	−	+	+	+	+	+
Parathyroid	−	+	−	+	−	−	+	−	+	−	−	−	−	−	−	+	+	−	+	+	−	−	−	−
REPRODUCTIVE SYSTEM																								
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Prostate	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Penis	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Papilloma, NOS																X								
NERVOUS SYSTEM																								
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
BODY CAVITIES																								
Peritoneum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Sarcoma, NOS																								
ALL OTHER SYSTEMS																								
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Sarcoma, NOS, unclear primary or metastatic																								
Hepatoblastoma, metastatic																				X				
Malignant lymphoma, NOS								X						X										
Granulocytic leukemia										X			X											

+: Tissue examined microscopically
−: Required tissue not examined microscopically
X: Tumor incidence
N: Necropsy, no autolysis, no microscopic examination
S: Animal missexed
: No tissue information submitted
C: Necropsy, no histology due to protocol
A: Autolysis
M: Animal missing
B: No necropsy performed

TABLE B3. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF MALE MICE: HIGH DOSE (Continued)

ANIMAL NUMBER	037	038	013	028	005	001	036	034	002	026	031	033	010	003	009	011	018	022	025	030	039	040	042	046	050	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	093	093	094	095	098	100	100	101	102	102	102	102	103	105	105	105	105	105	105	105	105	105	105	105	105	
INTEGUMENTARY SYSTEM																										
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Sarcoma, NOS													X													1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma					X					X				X						X		X	X			9
Alveolar/bronchiolar carcinoma												X			X											3
Trachea	−	+	+	−	+	+	−	−	+	+	+	−	−	−	+	−	−	+	−	+	+	−	−	−	−	22
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Lymph nodes	+	+	−	+	+	+	+	−	+	+	+	+	−	−	−	+	−	−	+	−	+	+	−	+	−	35
Thymus	−	−	−	+	+	+	−	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	39
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma															X											1
Hepatocellular carcinoma			X							X										X						4
Hepatoblastoma																										1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	49
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Adenomatous polyp, NOS																										1
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Tubular cell adenocarcinoma																										1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	−	+	+	+	+	+	47
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma, NOS																				X		X				2
Cortical adenoma													X													1
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	46
Parathyroid	−	−	+	−	−	−	−	−	+	+	+	+	−	+	−	−	−	−	+	−	−	+	+	+	+	19
REPRODUCTIVE SYSTEM																										
Mammary gland	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	+	N	N	N	N	N	N	N	N	*50
Testis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Prostate	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	48
Penis	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Papilloma, NOS																										1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
BODY CAVITIES																										
Peritoneum	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Sarcoma, NOS					X																					1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Sarcoma, NOS, unclear primary or meta			X																							1
Hepatoblastoma, metastatic																										1
Malignant lymphoma, NOS																										2
Granulocytic leukemia																										2

* Animals necropsied

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL: UNTREATED CONTROL

ANIMAL NUMBER	0034	0046	0023	0013	0039	0003	0031	0042	0029	0048	0017	0019	0021	0008	0028	0040	0043	0050	0035	0007	0005	0002	0006	0011	0022
WEEKS ON STUDY	038	040	051	052	054	076	079	080	082	082	083	083	084	085	086	087	088	089	092	096	101	103	103	103	104
INTEGUMENTARY SYSTEM																									
Skin paint site	+	+	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Basal cell carcinoma									X																
Trichoepithelioma																					X				
Sarcoma, NOS																					X				
Liposarcoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma														X				X		X					
Alveolar/bronchiolar carcinoma										X													X		
Trachea	−	+	−	−	−	−	+	+	−	+	−	+	+	+	−	+	−	−	−	−	−	+	+	+	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	−	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Malignant lymphoma, NOS																									
Thymus	+	−	+	+	−	+	+	+	+	+	−	+	+	+	−	+	+	+	−	−	+	−	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS, metastatic																						X			
Hepatocellular adenoma																						X			
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	+	N	N	+	N	+	N	+	N	N	+	+	+	N	N	+	+	+	+	+	+	+	+	+	N
Pancreas	+	+	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+
Stomach	+	−	−	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	−	−	+	−	+	−	+	+	+	+	+	+	−	−	+	+	+	+	+	+	+	+	+	+
Large intestine	−	−	−	+	−	+	−	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS, unclear primary or metastatic																									
Urinary bladder	+	+	−	+	−	+	+	+	+	+	+	+	+	+	−	+	+	−	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	−	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	−
Chromophobe adenoma																	X								
Acidophil adenoma																									
Adrenal	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cortical adenoma																									
Pheochromocytoma																									
Thyroid	+	−	−	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid	−	−	−	−	−	−	+	−	−	+	+	−	−	+	+	−	−	−	−	+	−	+	−	−	+
REPRODUCTIVE SYSTEM																									
Mammary gland	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS										X					X	X						X			
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyosarcoma																									
Endometrial stromal polyp																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Luteoma																									
Hemangioma																							X		
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Astrocytoma																			X						
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Alveolar/bronchiolar carcinoma, invasive										X															
Malignant lymphoma, NOS	X		X			X		X				X		X				X					X		X
Malignant lymphoma, histiocytic type																				X					

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: UNTREATED CONTROL (Continued)

ANIMAL NUMBER	045	091	094	099	010	012	014	015	016	018	020	024	025	026	027	030	032	033	036	037	038	041	044	047	049	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	104	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	
INTEGUMENTARY SYSTEM																										
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	*50
Basal cell carcinoma																										1
Trichoepithelioma																										1
Sarcoma, NOS																										1
Liposarcoma	X																									1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma										X						X	X							X		7
Alveolar/bronchiolar carcinoma												X														3
Trachea	+	−	+	−	+	+	−	+	+	−	+	−	+	−	−	−	−	−	−	−	+	−	+	−	−	22
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Lymph nodes	+	+	−	+	−	+	+	−	+	−	+	+	+	−	−	−	−	+	+	+	+	−	+	−	−	38
Malignant lymphoma, NOS																				X						1
Thymus	−	+	+	+	+	+	+	+	−	+	+	+	+	+	−	+	+	+	−	+	+	+	+	+	+	39
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	−	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenocarcinoma, NOS, metastatic																										1
Hepatocellular adenoma																										1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	48
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	44
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	43
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Sarcoma, NOS, unclear primary or meta									X																	1
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Chromophobe adenoma						X															X		X			4
Acidophil adenoma			X																							1
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Cortical adenoma														X												1
Pheochromocytoma																		X								1
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	−	+	+	+	+	+	+	45
Parathyroid	+	−	+	−	−	+	−	+	−	−	−	−	+	+	−	−	+	−	−	−	−	−	+	−	+	17
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Adenocarcinoma, NOS																										4
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Leiomyosarcoma					X																					1
Endometrial stromal polyp		X																		X						2
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Luteoma																						X				1
Hemangioma																										1
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Astrocytoma																										1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Alveolar/bronchiolar carcinoma, invasi																										1
Malignant lymphoma, NOS	X																									10
Malig. lymphoma, histiocytic type																										1

* Animals necropsied

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL: VEHICLE CONTROL

ANIMAL NUMBER	018	020	026	028	037	038	042	052	054	013	042	037	043	053	011	042	017	014	050	016	021	025	034	011	003
WEEKS ON STUDY	092	092	090	092	092	092	092	092	087	087	092	077	078	091	091	092	092	092	092	092	092	090	092	094	105
INTEGUMENTARY SYSTEM																									
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Trichoepithelioma																									
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS												X													
Myxoma																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																X					X	X		X	
Alveolar/bronchiolar carcinoma																									
Trachea	–	–	–	–	+	–	–	–	+	–	–	+	–	+	–	–	–	+	–	–	+	–	–	–	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	–	–	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	–	–	+	–
Thymus	+	+	+	+	+	+	–	+	+	+	+	+	+	+	–	–	+	+	–	+	+	+	+	+	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																			X						
Hepatocellular carcinoma																									
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	N	N	+	+	+	N	+	+	N	+	+	N	N	+	+	+	+	N	+	+	+	+
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	–	–	–	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	–	+	+	+	+
Large intestine	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	–	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Chromophobe adenoma																				X					
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
Parathyroid	–	–	–	+	–	–	–	–	+	–	+	+	+	–	–	–	–	+	+	–	–	–	–	–	+
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	+	+	N	+	+	+	+	+	+	N	N	+	+	+	+	+	+	+	+	+	+	+	+
Adenocarcinoma, NOS														X		X									
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+
Leiomyoma																									
Leiomyosarcoma																									
Hemangioma																									
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cystadenoma, NOS																									
Papillary cystadenoma, NOS																									
Luteoma																									
Hemangioma																			X						
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Malignant lymphoma, NOS						X		X		X						X	X				X	X			
Granulocytic leukemia									X																

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: VEHICLE CONTROL (Continued)

ANIMAL NUMBER	095	096	097	099	110	112	115	119	120	121	122	124	128	129	131	132	133	135	136	138	139	144	145	147	148	TOTAL:
WEEKS ON STUDY	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	TISSUES TUMORS
INTEGUMENTARY SYSTEM																										
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Trichoepithelioma	X																									1
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Sarcoma, NOS																										1
Myxoma															X											1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma							X					X			X		X									7
Alveolar/bronchiolar carcinoma											X															2
Trachea	+	+	+	–	+	+	+	+	+	+	+	+	+	+	–	+	+	–	–	+	–	+	+	–	+	26
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph nodes	+	–	–	–	+	+	–	–	+	–	–	+	–	+	+	–	+	–	+	+	+	+	+	+	–	33
Thymus	+	+	+	+	+	+	+	–	+	+	+	+	+	+	–	+	+	–	+	–	+	+	+	+	+	42
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular adenoma										X																2
Hepatocellular carcinoma																X										1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Esophagus	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	47
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	45
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	49
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Chromophobe adenoma										X																2
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Thyroid	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Parathyroid	+	–	+	–	+	+	–	+	–	–	+	–	–	+	–	+	–	–	–	+	+	–	+	–	–	19
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Adenocarcinoma, NOS																										2
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leiomyoma																								X		1
Leiomyosarcoma																				X					X	2
Hemangioma										X																1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Cystadenoma, NOS	X																									1
Papillary cystadenoma, NOS																								X		1
Luteoma					X																					1
Hemangioma																							X			2
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Malignant lymphoma, NOS												X														8
Granulocytic leukemia																										1

* Animals necropsied

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL: LOW DOSE

ANIMAL NUMBER	0 0 9	0 1 6	0 4 1	0 4 4	0 1 3	0 2 4	0 0 7	0 2 5	0 2 2	0 1 2	0 1 7	0 2 1	0 2 3	0 2 9	0 4 9	0 2 2	0 4 3	0 1 4	0 2 3	0 0 5	0 1 0	0 0 1	0 2 7	0 2 0	0 1 7
WEEKS ON STUDY	0 1 9	0 2 9	0 4 0	0 4 7	0 5 2	0 6 1	0 6 2	0 6 8	0 7 6	0 7 7	0 7 7	0 8 0	0 8 1	0 8 2	0 8 5	0 8 8	0 8 7	0 8 8	0 9 1	0 9 3	0 9 3	0 9 6	0 9 7	0 9 8	0 9 9
INTEGUMENTARY SYSTEM																									
Skin paint site	–	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Skin	N	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papilloma, NOS																									
Subcutaneous tissue	N	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinosarcoma																			X						
Hemangiosarcoma, metastatic																									
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma								X																	
Alveolar/bronchiolar carcinoma																			X		X				
Carcinosarcoma, metastatic													X												
Trachea	–	–	–	–	–	–	–	+	–	–	+	–	+	+	+	+	–	+	–	+	+	–	+	–	–
HEMATOPOIETIC SYSTEM																									
Bone marrow	–	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–
Spleen	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma																									
Malignant lymphoma, histiocytic type																									
Lymph nodes	+	+	+	–	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	–	+	+	+	–	+
Thymus	+	–	–	–	+	+	+	+	+	–	–	+	+	+	+	+	+	–	+	+	+	–	–	–	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemangiosarcoma, metastatic																									
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Bile duct	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	+	N	+	N	+	+	+	+	+	+	+	N	+	+	+	N	+	+	+	+	+	+	+
Pancreas	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+
Esophagus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	–	+	–	–	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Large intestine	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Chromophobe adenoma																X									
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																									
Thyroid	+	+	+	+	–	–	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	–	+
Parathyroid	–	+	–	–	–	–	–	–	–	+	–	–	+	+	+	–	–	+	+	+	+	–	–	–	–
Pancreatic islets	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+
Islet cell adenoma																									
REPRODUCTIVE SYSTEM																									
Mammary gland	N	N	N	N	+	N	+	+	+	+	+	+	+	N	+	+	+	+	+	+	+	+	+	+	+
Adenoma, NOS																					X				
Adenocarcinoma, NOS									X																
Adenosquamous carcinoma																									
Carcinosarcoma													X												
Uterus	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leiomyoma																									
Leiomyosarcoma																									
Endometrial stromal sarcoma							X																		
Hemangiosarcoma															X										
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+
Granulosa cell tumor																X									
Hemangioma																					X		X		
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
ALL OTHER SYSTEMS																									
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Carcinosarcoma, metastatic																			X						
Malignant lymphoma, NOS	X					X		X			X			X											
Malignant lymphoma, histiocytic type					X																				
Granulocytic leukemia		X							X													X			X

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: LOW DOSE (Continued)

ANIMAL NUMBER	0031	0155	0288	0455	0111	0092	0093	0094	0096	0099	0118	0119	0120	0222	0224	0225	0226	0333	0336	0400	0422	0446	0447	0448	0450	TOTAL:
WEEKS ON STUDY	099	100	100	100	102	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	TISSUES / TUMORS
INTEGUMENTARY SYSTEM																										
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Papilloma, NOS																X										1
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Carcinosarcoma																										1
Hemangiosarcoma, metastatic																				X						1
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	49
Alveolar/bronchiolar adenoma			X					X				X										X			X	6
Alveolar/bronchiolar carcinoma			X		X																		X			5
Carcinosarcoma, metastatic																										1
Trachea	+	−	+	+	+	+	+	+	−	+	−	+	+	+	+	+	−	+	+	+	+	+	+	+	−	29
HEMATOPOIETIC SYSTEM																										
Bone marrow	+	+	+	−	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	−	+	+	+	44
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	48
Hemangiosarcoma														X						X						2
Malig. lymphoma, histiocytic type	X																									1
Lymph nodes	−	+	+	+	+	−	+	−	+	+	+	+	−	−	−	+	−	−	−	+	+	+	+	+	−	36
Thymus	+	+	+	−	−	+	+	+	+	+	+	+	+	−	+	−	+	+	+	+	+	+	+	−	+	36
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hemangiosarcoma, metastatic														X												1
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Gallbladder & common bile duct	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	N	N	+	+	+	*50
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	47
Esophagus	+	+	+	+	−	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	−	+	+	+	46
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Small intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Chromophobe adenoma												X														2
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Adenoma, NOS								X																		1
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Parathyroid	−	+	−	−	−	−	+	−	+	−	+	−	+	+	−	−	−	−	−	−	+	−	+	−	−	17
Pancreatic islets	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	47
Islet cell adenoma												X														1
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Adenoma, NOS																										1
Adenocarcinoma, NOS												X														2
Adenosquamous carcinoma			X																							1
Carcinosarcoma																										1
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Leiomyoma															X											1
Leiomyosarcoma													X													1
Endometrial stromal sarcoma																										1
Hemangiosarcoma																										1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Granulosa cell tumor																										1
Hemangioma																										2
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Carcinosarcoma, metastatic																										1
Malignant lymphoma, NOS			X	X											X										8
Malignant lymphoma, histiocytic type		X																								2
Granulocytic leukemia																										4

* Animals necropsied

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL: HIGH DOSE

ANIMAL NUMBER	040	038	052	028	025	021	019	047	017	029	030	010	043	049	006	050	023	012	014	001	038	044	039	048	037
WEEKS ON STUDY	000	026	027	048	053	064	068	068	071	072	075	076	076	077	078	080	082	085	085	090	092	092	095	095	096
INTEGUMENTARY SYSTEM																									
Skin paint site	−	−	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS, invasive											X														
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma, NOS											X														
RESPIRATORY SYSTEM																									
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Alveolar/bronchiolar adenoma																								X	
Alveolar/bronchiolar carcinoma																					X				
Sarcoma, NOS, metastatic											X														
Trachea	−	−	−	+	+	−	+	−	−	−	+	−	−	−	+	+	−	−	+	−	−	−	−	−	+
HEMATOPOIETIC SYSTEM																									
Bone marrow	+	+	−	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Spleen	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Lymph nodes	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thymus	+	+	+	−	+	+	+	−	+	−	+	+	−	+	+	−	+	−	+	+	+	+	+	−	+
CIRCULATORY SYSTEM																									
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
DIGESTIVE SYSTEM																									
Salivary gland	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular carcinoma																				X					
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gallbladder & common bile duct	N	N	N	+	N	N	N	+	+	N	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Papillary adenoma																									
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Esophagus	+	+	−	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Small intestine	+	+	−	+	−	+	+	+	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+
Large intestine	+	+	−	+	+	−	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
URINARY SYSTEM																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Urinary bladder	+	+	+	+	+	+	+	+	+	−	+	+	+	+	−	+	+	+	−	+	+	+	+	+	+
ENDOCRINE SYSTEM																									
Pituitary	+	−	+	−	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Chromophobe adenoma																									
Adrenal	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Thyroid	+	+	−	−	+	+	+	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+
Parathyroid	−	−	−	−	−	−	−	−	+	+	+	−	+	−	+	+	−	−	+	+	−	+	+	+	+
REPRODUCTIVE SYSTEM																									
Mammary gland	+	+	N	N	N	+	+	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	N	+	+
Adenocarcinoma, NOS										X														X	X
Carcinosarcoma							X										X								
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, NOS																					X				
Leiomyoma								X																	
Leiomyosarcoma																									
Ovary	+	+	−	+	+	+	+	−	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
NERVOUS SYSTEM																									
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
MUSCULOSKELETAL SYSTEM																									
Muscle	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Leiomyosarcoma, invasive																									
ALL OTHER SYSTEMS																									
Multiple organs, NOS	*N*	*N*	*N*	*N*	*N*	*N*	*N*	*N*	*N*	*N*	*N*	*N*	*N*	*N*	*N*	*N*	*N*	*N*	*N*	*N*	*N*	*N*	*N*	*N*	*N*
Adenocarcinoma, NOS, metastatic										X															
Malignant lymphoma, NOS				X				X														X	X	X	
Malignant lymphoma, histiocytic type																									
Granulocytic leukemia			X			X													X						

+: Tissue examined microscopically
−: Required tissue not examined microscopically
X: Tumor incidence
N: Necropsy, no autolysis, no microscopic examination
S: Animal missexed
: No tissue information submitted
C: Necropsy, no histology due to protocol
A: Autolysis
M: Animal missing
B: No necropsy performed

TABLE B4. INDIVIDUAL ANIMAL TUMOR PATHOLOGY OF FEMALE MICE: HIGH DOSE (Continued)

ANIMAL NUMBER	034	011	022	013	007	003	004	005	008	009	015	016	018	020	024	026	027	031	032	033	035	041	042	045	046	TOTAL: TISSUES TUMORS
WEEKS ON STUDY	098	100	103	103	104	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	105	
INTEGUMENTARY SYSTEM																										
Skin paint site	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Sarcoma, NOS, invasive																	X									1
Subcutaneous tissue	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Sarcoma, NOS																	X									2
RESPIRATORY SYSTEM																										
Lungs and bronchi	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Alveolar/bronchiolar adenoma								X		X										X		X		X		6
Alveolar/bronchiolar carcinoma					X														X							3
Sarcoma, NOS, metastatic																										1
Trachea	–	+	+	–	–	–	–	–	–	–	+	–	–	–	–	–	+	+	–	–	–	–	+	+	–	15
HEMATOPOIETIC SYSTEM																										
Bone marrow	–	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	46
Spleen	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Lymph nodes	+	–	+	+	+	+	+	–	+	+	+	+	+	–	+	+	–	+	+	+	+	+	+	–	+	44
Thymus	+	–	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	41
CIRCULATORY SYSTEM																										
Heart	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
DIGESTIVE SYSTEM																										
Salivary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Hepatocellular carcinoma																										1
Bile duct	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Gallbladder & common bile duct	N	+	+	+	N	N	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Papillary adenoma																						X				1
Pancreas	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Esophagus	+	+	+	+	+	+	+	–	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	45
Stomach	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Small intestine	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	45
Large intestine	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
URINARY SYSTEM																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Urinary bladder	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	–	45
ENDOCRINE SYSTEM																										
Pituitary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	47
Chromophobe adenoma									X		X									X						3
Adrenal	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	49
Thyroid	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	46
Parathyroid	–	–	+	–	+	–	–	–	–	–	+	–	–	–	–	+	+	+	–	+	+	+	–	–	–	21
REPRODUCTIVE SYSTEM																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	*50
Adenocarcinoma, NOS		X	X																							5
Carcinosarcoma																										2
Uterus	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
Carcinoma, NOS																										1
Leiomyoma														X												2
Leiomyosarcoma																						X				1
Ovary	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	48
NERVOUS SYSTEM																										
Brain	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	50
MUSCULOSKELETAL SYSTEM																										
Muscle	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Leiomyosarcoma, invasive																						X				1
ALL OTHER SYSTEMS																										
Multiple organs, NOS	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	*50
Adenocarcinoma, NOS, metastatic																										1
Malignant lymphoma, NOS	X		X										X					X								9
Malignant lymphoma, histiocytic type				X																						1
Granulocytic leukemia																										3

* Animals necropsied

APPENDIX C

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN RATS IN THE TWO-YEAR DERMAL STUDIES OF 2-CHLOROETHANOL

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
#SKIN PAINT SITE	(48)	(49)	(49)
EPIDERMAL INCLUSION CYST		1 (2%)	
EDEMA, NOS		1 (2%)	
*SKIN	(50)	(50)	(50)
HYPERKERATOSIS		1 (2%)	
ACANTHOSIS			1 (2%)
*SUBCUT TISSUE	(50)	(50)	(50)
HEMORRHAGE		1 (2%)	
ABSCESS, NOS			1 (2%)
GRANULOMA, NOS			1 (2%)
RESPIRATORY SYSTEM			
#TRACHEA	(46)	(50)	(47)
INFLAMMATION, SUPPURATIVE			2 (4%)
#LUNG/BRONCHUS	(49)	(50)	(50)
LYMPHOCYTIC INFLAMMATORY INFILTR		1 (2%)	
#LUNG	(49)	(50)	(50)
ATELECTASIS	1 (2%)		
CONGESTION, NOS	1 (2%)	2 (4%)	2 (4%)
INFLAMMATION, INTERSTITIAL	1 (2%)		1 (2%)
PNEUMONIA, ASPIRATION			1 (2%)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
INFLAMMATION, CHRONIC FOCAL	1 (2%)	3 (6%)	2 (4%)
FIBROSIS, FOCAL	1 (2%)		
HYPERPLASIA, ADENOMATOUS	2 (4%)		1 (2%)
#LUNG/ALVEOLI	(49)	(50)	(50)
HISTIOCYTOSIS	3 (6%)	1 (2%)	2 (4%)
HEMATOPOIETIC SYSTEM			
#BONE MARROW	(49)	(49)	(49)
HYPOPLASIA, NOS		1 (2%)	
HYPERPLASIA, NOS			1 (2%)
MYELOFIBROSIS	1 (2%)		
#SPLEEN	(50)	(50)	(50)
INFLAMMATION, FOCAL GRANULOMATOUS			1 (2%)
FIBROSIS	1 (2%)		
FIBROSIS, FOCAL	2 (4%)	2 (4%)	4 (8%)
NECROSIS, FOCAL	1 (2%)		
HEMOSIDEROSIS	7 (14%)	4 (8%)	3 (6%)
HEMATOPOIESIS	6 (12%)	3 (6%)	1 (2%)
#MANDIBULAR L. NODE	(49)	(50)	(49)
EDEMA, NOS		1 (2%)	
HYPERPLASIA, NOS	1 (2%)		
PLASMACYTOSIS		1 (2%)	
#MEDIASTINAL L. NODE	(49)	(50)	(49)
INFLAMMATION, FOCAL GRANULOMATOUS			1 (2%)
HEMOSIDEROSIS	2 (4%)		
#HEPATIC LYMPH NODE	(49)	(50)	(49)
INFLAMMATION, GRANULOMATOUS		1 (2%)	
HYPERPLASIA, NOS		1 (2%)	
#PANCREATIC L. NODE	(49)	(50)	(49)
HEMORRHAGE		1 (2%)	
#LUMBAR LYMPH NODE	(49)	(50)	(49)
HEMOSIDEROSIS		1 (2%)	

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
HEMATOPOIETIC SYSTEM (Continued)			
#RENAL LYMPH NODE	(49)	(50)	(49)
EDEMA, NOS			1 (2%)
#LIVER	(50)	(50)	(50)
HEMATOPOIESIS	1 (2%)		1 (2%)
#THYMUS	(37)	(33)	(43)
HEMORRHAGE		1 (3%)	
CIRCULATORY SYSTEM			
#LUNG	(49)	(50)	(50)
PERIVASCULITIS	1 (2%)		
#HEART/ATRIUM	(50)	(50)	(50)
THROMBOSIS, NOS		1 (2%)	
#MYOCARDIUM	(50)	(50)	(50)
DEGENERATION, NOS	39 (78%)	46 (92%)	44 (88%)
*PULMONARY ARTERY	(50)	(50)	(50)
MINERALIZATION	7 (14%)	6 (12%)	7 (14%)
LYMPHOCYTIC INFLAMMATORY INFILTR	1 (2%)		
*PANCREATIC ARTERY	(50)	(50)	(50)
DEGENERATION, MUCOID	1 (2%)		
*VEIN	(50)	(50)	(50)
DILATATION, NOS		1 (2%)	
#LIVER	(50)	(50)	(50)
THROMBOSIS, NOS	1 (2%)		
THROMBUS, ORGANIZED			1 (2%)
#ADRENAL	(50)	(50)	(50)
THROMBOSIS, NOS		1 (2%)	
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(50)	(49)	(50)
ATROPHY, FOCAL	1 (2%)		
#LIVER	(50)	(50)	(50)
INFLAMMATION, FOCAL GRANULOMATOUS	5 (10%)	4 (8%)	4 (8%)
DEGENERATION, CYSTIC	1 (2%)	1 (2%)	3 (6%)
DEGENERATION, HYDROPIC		1 (2%)	
NECROSIS, FOCAL		2 (4%)	1 (2%)
NECROSIS, COAGULATIVE	1 (2%)	1 (2%)	1 (2%)
LIPOIDOSIS	6 (12%)	1 (2%)	2 (4%)
BASOPHILIC CYTO CHANGE	2 (4%)	2 (4%)	1 (2%)
GROUND-GLASS CYTO CHANGE	1 (2%)	4 (8%)	3 (6%)
FOCAL CELLULAR CHANGE	1 (2%)		
CLEAR-CELL CHANGE	1 (2%)		
ANGIECTASIS	2 (4%)		1 (2%)
#PORTAL TRACT	(50)	(50)	(50)
INFLAMMATION, CHRONIC	2 (4%)		
#LIVER/CENTRILOBULAR	(50)	(50)	(50)
NECROSIS, NOS	1 (2%)		
LIPOIDOSIS	1 (2%)		
#BILE DUCT	(50)	(50)	(50)
HYPERPLASIA, NOS	38 (76%)	45 (90%)	40 (80%)
#PANCREAS	(50)	(50)	(49)
ACCESSORY STRUCTURE			1 (2%)
DILATATION/DUCTS	1 (2%)		
#PANCREATIC ACINUS	(50)	(50)	(49)
ATROPHY, NOS	7 (14%)	10 (20%)	15 (31%)
ATROPHY, FOCAL	4 (8%)	1 (2%)	3 (6%)
#ESOPHAGUS	(48)	(49)	(49)
INFLAMMATION, SUPPURATIVE			1 (2%)
#GASTRIC SUBMUCOSA	(50)	(50)	(49)
EDEMA, NOS			1 (2%)

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM (Continued)			
#FORESTOMACH	(50)	(50)	(49)
ULCER, NOS	1 (2%)		
EOSINOPHILIC INFILTRATE			1 (2%)
REACTION, FOREIGN BODY	1 (2%)		
HYPERPLASIA, BASAL CELL			1 (2%)
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
CYST, NOS	1 (2%)	1 (2%)	
LYMPHOCYTIC INFLAMMATORY INFILTR			1 (2%)
ABSCESS, NOS			1 (2%)
NEPHROPATHY	47 (94%)	46 (92%)	48 (96%)
#KIDNEY/CORTEX	(50)	(50)	(50)
ABSCESS, NOS			1 (2%)
FIBROSIS	1 (2%)		
#KIDNEY/TUBULE	(50)	(50)	(50)
ABSCESS, NOS	1 (2%)		
PIGMENTATION, NOS	44 (88%)	47 (94%)	42 (84%)
#KIDNEY/PELVIS	(50)	(50)	(50)
HYPERPLASIA, EPITHELIAL	1 (2%)		
#URINARY BLADDER	(49)	(50)	(48)
INFLAMMATION, CHRONIC	1 (2%)		
*URETHRA	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE	1 (2%)		
ENDOCRINE SYSTEM			
#PITUITARY	(50)	(48)	(49)
CYST, NOS	4 (8%)	3 (6%)	2 (4%)
HEMORRHAGIC CYST	1 (2%)		
FOCAL CELLULAR CHANGE	1 (2%)		
HYPERPLASIA, FOCAL	5 (10%)	9 (19%)	7 (14%)
ANGIECTASIS			1 (2%)
#ADRENAL	(50)	(50)	(50)
CONGESTION, NOS	1 (2%)		
DEGENERATION, LIPOID			1 (2%)
ATROPHY, DIFFUSE		1 (2%)	
HYPERPLASIA, FOCAL		1 (2%)	
ANGIECTASIS		2 (4%)	
#ADRENAL CORTEX	(50)	(50)	(50)
CYST, NOS			1 (2%)
DEGENERATION, LIPOID	5 (10%)	6 (12%)	1 (2%)
HYPERPLASIA, FOCAL	1 (2%)	2 (4%)	4 (8%)
ANGIECTASIS	1 (2%)		
#ADRENAL MEDULLA	(50)	(50)	(50)
HYPERPLASIA, NOS		3 (6%)	
HYPERPLASIA, FOCAL	3 (6%)	7 (14%)	5 (10%)
#THYROID	(49)	(49)	(49)
FOLLICULAR CYST, NOS		1 (2%)	1 (2%)
ATROPHY, FOCAL	1 (2%)		
HYPERPLASIA, C-CELL	4 (8%)	5 (10%)	3 (6%)
#PARATHYROID	(39)	(39)	(35)
HYPERPLASIA, FOCAL	1 (3%)		

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
GALACTOCELE		1 (2%)	1 (2%)
INFLAMMATION, SUPPURATIVE	1 (2%)		
INFLAMMATION, GRANULOMATOUS	1 (2%)		
LACTATION	12 (24%)	12 (24%)	11 (22%)
*MAMMARY DUCT	(50)	(50)	(50)
HYPERPLASIA, NOS	1 (2%)	1 (2%)	
*MAMMARY LOBULE	(50)	(50)	(50)
HYPERPLASIA, NOS	6 (12%)	2 (4%)	
*PREPUTIAL GLAND	(50)	(50)	(50)
DILATATION, NOS	1 (2%)		
DILATATION/DUCTS	1 (2%)		
INFLAMMATION, SUPPURATIVE	1 (2%)		
INFLAMMATION, CHRONIC	1 (2%)		
HYPERPLASIA, NOS	1 (2%)		
#PROSTATE	(49)	(49)	(48)
INFLAMMATION, SUPPURATIVE	1 (2%)		
INFLAMMATION, CHRONIC	2 (4%)	1 (2%)	1 (2%)
INFLAMMATION, CHRONIC FOCAL	1 (2%)		2 (4%)
INFLAMMATION, CHRONIC SUPPURATIVE	2 (4%)		
INFLAMMATION, FOCAL GRANULOMATOUS			1 (2%)
NECROSIS, FOCAL	1 (2%)		
ATROPHY, NOS	1 (2%)		
HYPERPLASIA, EPITHELIAL	2 (4%)		
HYPERPLASIA, FOCAL	2 (4%)	4 (8%)	8 (17%)
#TESTIS	(50)	(50)	(50)
MINERALIZATION	1 (2%)		
ATROPHY, NOS	4 (8%)	1 (2%)	1 (2%)
HYPERPLASIA, INTERSTITIAL CELL	1 (2%)	2 (4%)	3 (6%)
#TESTIS/TUBULE	(50)	(50)	(50)
MINERALIZATION	1 (2%)		1 (2%)
*EPIDIDYMIS	(50)	(50)	(50)
DILATATION, NOS	1 (2%)		
HYPERPLASIA, EPITHELIAL		1 (2%)	
NERVOUS SYSTEM			
#LATERAL VENTRICLE	(50)	(50)	(50)
DILATATION, NOS		1 (2%)	
*CHOROID PLEXUS	(50)	(50)	(50)
LYMPHOCYTIC INFLAMMATORY INFILTR			1 (2%)
#BRAIN	(50)	(50)	(50)
HEMORRHAGE		2 (4%)	
SPECIAL SENSE ORGANS			
*EYE	(50)	(50)	(50)
CATARACT	15 (30%)	2 (4%)	2 (4%)
*SCLERA	(50)	(50)	(50)
MINERALIZATION		2 (4%)	
METAPLASIA, OSSEOUS	3 (6%)	1 (2%)	2 (4%)
*EYE/RETINA	(50)	(50)	(50)
ATROPHY, NOS	21 (42%)	3 (6%)	5 (10%)
*EAR	(50)	(50)	(50)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
MUSCULOSKELETAL SYSTEM			
*JOINT	(50)	(50)	(50)
INFLAMMATION PROLIFERATIVE			1 (2%)

TABLE C1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
BODY CAVITIES			
*ABDOMINAL CAVITY	(50)	(50)	(50)
NECROSIS, FAT	2 (4%)	1 (2%)	
*MESENTERY	(50)	(50)	(50)
NECROSIS, FAT	1 (2%)		
ALL OTHER SYSTEMS			
ADIPOSE TISSUE			
NECROSIS, FAT		3	1
SPECIAL MORPHOLOGY SUMMARY			
NONE			

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
EPIDERMAL INCLUSION CYST	1 (2%)		
INFLAMMATION, ACUTE NECROTIZING		1 (2%)	
ABSCESS, NOS			1 (2%)
FIBROSIS, FOCAL	1 (2%)		
*SUBCUT TISSUE	(50)	(50)	(50)
ABSCESS, NOS			1 (2%)
RESPIRATORY SYSTEM			
*NASAL CAVITY	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE		1 (2%)	
#LUNG	(50)	(50)	(48)
ATELECTASIS		2 (4%)	
CONGESTION, NOS		1 (2%)	
BRONCHOPNEUMONIA, ACUTE		1 (2%)	
INFLAMMATION, CHRONIC FOCAL	2 (4%)	1 (2%)	1 (2%)
PIGMENTATION, NOS			1 (2%)
HYPERPLASIA, ADENOMATOUS	1 (2%)		
#LUNG/ALVEOLI	(50)	(50)	(48)
HISTIOCYTOSIS	2 (4%)	1 (2%)	1 (2%)
HEMATOPOIETIC SYSTEM			
#BONE MARROW	(49)	(50)	(49)
INFLAMMATION, FOCAL GRANULOMATOUS		1 (2%)	1 (2%)
HYPOPLASIA, NOS	1 (2%)		
MYELOFIBROSIS	1 (2%)		
#SPLEEN	(50)	(48)	(50)
INFLAMMATION, GRANULOMATOUS		1 (2%)	
GRANULOMA, NOS			1 (2%)
INFLAMMATION, FOCAL GRANULOMATOUS		2 (4%)	1 (2%)
INFARCT, NOS	1 (2%)		
HEMOSIDEROSIS	26 (52%)	21 (44%)	29 (58%)
LYMPHOID DEPLETION	1 (2%)		
HEMATOPOIESIS	10 (20%)	3 (6%)	18 (36%)
#SPLENIC CAPSULE	(50)	(48)	(50)
HYPERPLASIA, NOS	1 (2%)		
#LYMPH NODE	(49)	(48)	(45)
HYPERPLASIA, LYMPHOID	1 (2%)		
#MANDIBULAR L. NODE	(49)	(48)	(45)
HEMOSIDEROSIS		1 (2%)	
#MEDIASTINAL L. NODE	(49)	(48)	(45)
HEMOSIDEROSIS		1 (2%)	
#LIVER	(50)	(50)	(50)
HEMATOPOIESIS			1 (2%)
#THYMUS	(40)	(44)	(45)
CYST, NOS	1 (3%)		
HYPERPLASIA, EPITHELIAL		1 (2%)	
CIRCULATORY SYSTEM			
#MANDIBULAR L. NODE	(49)	(48)	(45)
LYMPHANGIECTASIS		1 (2%)	
#LUNG	(50)	(50)	(48)
PERIVASCULITIS	1 (2%)		

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
CIRCULATORY SYSTEM (Continued)			
#MYOCARDIUM	(50)	(50)	(49)
MINERALIZATION		1 (2%)	
DEGENERATION, NOS	28 (56%)	22 (44%)	36 (73%)
*CORONARY ARTERY	(50)	(50)	(50)
MINERALIZATION		1 (2%)	
*PULMONARY ARTERY	(50)	(50)	(50)
MINERALIZATION	2 (4%)	9 (18%)	6 (12%)
*MENINGEAL ARTERY	(50)	(50)	(50)
MINERALIZATION		1 (2%)	
DIGESTIVE SYSTEM			
#LIVER	(50)	(50)	(50)
HEMORRHAGIC CYST	1 (2%)		
INFLAMMATION, CHRONIC FOCAL	5 (10%)	2 (4%)	3 (6%)
INFLAMMATION, GRANULOMATOUS		1 (2%)	1 (2%)
INFLAMMATION, FOCAL GRANULOMATOUS	12 (24%)	10 (20%)	15 (30%)
NECROSIS, FOCAL			1 (2%)
LIPOIDOSIS	1 (2%)	3 (6%)	1 (2%)
BASOPHILIC CYTO CHANGE	4 (8%)		6 (12%)
GROUND-GLASS CYTO CHANGE	1 (2%)	2 (4%)	6 (12%)
FOCAL CELLULAR CHANGE	1 (2%)		1 (2%)
EOSINOPHILIC CYTO CHANGE		1 (2%)	
CLEAR-CELL CHANGE	1 (2%)	1 (2%)	1 (2%)
HEPATOCYTOMEGALY			1 (2%)
HYPERTROPHY, FOCAL	2 (4%)		
ANGIECTASIS			1 (2%)
#HEPATIC CAPSULE	(50)	(50)	(50)
INFLAMMATION, CHRONIC	1 (2%)		
#PORTAL TRACT	(50)	(50)	(50)
INFLAMMATION, ACUTE/CHRONIC		1 (2%)	
#LIVER/CENTRILOBULAR	(50)	(50)	(50)
NECROSIS, NOS	1 (2%)		
NECROSIS, COAGULATIVE			1 (2%)
LIPOIDOSIS		1 (2%)	
#LIVER/PERIPORTAL	(50)	(50)	(50)
LIPOIDOSIS	1 (2%)		2 (4%)
#LIVER/HEPATOCYTES	(50)	(50)	(50)
HYPERTROPHY, FOCAL		1 (2%)	1 (2%)
#BILE DUCT	(50)	(50)	(50)
HYPERPLASIA, NOS	12 (24%)	21 (42%)	13 (26%)
#PANCREATIC DUCT	(49)	(49)	(50)
HYPERPLASIA, FOCAL			1 (2%)
#PANCREATIC ACINUS	(49)	(49)	(50)
ATROPHY, NOS	11 (22%)	6 (12%)	9 (18%)
ATROPHY, FOCAL		1 (2%)	1 (2%)
ATROPHY, DIFFUSE	1 (2%)		
#STOMACH	(50)	(50)	(50)
ULCER, NOS		1 (2%)	
#GASTRIC MUCOSA	(50)	(50)	(50)
CYST, NOS	1 (2%)		
#GASTRIC SUBMUCOSA	(50)	(50)	(50)
EDEMA, NOS		1 (2%)	
#FORESTOMACH	(50)	(50)	(50)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		1 (2%)
HYPERPLASIA, BASAL CELL		1 (2%)	
#DUODENAL MUCOSA	(49)	(48)	(50)
NECROSIS, FOCAL	1 (2%)		
#JEJUNUM	(49)	(48)	(50)
EOSINOPHILIC GRANULOMA	1 (2%)		

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM (Continued)			
#COLON	(50)	(50)	(50)
PARASITISM		1 (2%)	
#COLONIC CRYPT OF LIEBERKÜHN	(50)	(50)	(50)
CYST, NOS	1 (2%)		
#CECUM	(50)	(50)	(50)
INFLAMMATION, CHRONIC			1 (2%)
HYPERPLASIA, EPITHELIAL			1 (2%)
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
MINERALIZATION	1 (2%)	6 (12%)	4 (8%)
LYMPHOCYTIC INFLAMMATORY INFILTR		1 (2%)	
NEPHROPATHY	24 (48%)	28 (56%)	33 (66%)
#KIDNEY/CORTEX	(50)	(50)	(50)
MINERALIZATION	1 (2%)		
CALCIFICATION, FOCAL	1 (2%)		
#KIDNEY/TUBULE	(50)	(50)	(50)
MINERALIZATION		1 (2%)	1 (2%)
NEPHROSIS, NOS		2 (4%)	
PIGMENTATION, NOS	48 (96%)	48 (96%)	48 (96%)
#KIDNEY/PELVIS	(50)	(50)	(50)
CALCULUS,MICROSCOPIC EXAMINATION			2 (4%)
MINERALIZATION	1 (2%)		
HYPERPLASIA, EPITHELIAL	1 (2%)		1 (2%)
#URINARY BLADDER	(50)	(45)	(49)
INFLAMMATION, ACUTE/CHRONIC		1 (2%)	
HYPERPLASIA, EPITHELIAL		1 (2%)	
ENDOCRINE SYSTEM			
#PITUITARY	(50)	(49)	(50)
CYST, NOS	15 (30%)	14 (29%)	19 (38%)
CYTOPLASMIC VACUOLIZATION			1 (2%)
HYPERPLASIA, FOCAL	7 (14%)	5 (10%)	7 (14%)
ANGIECTASIS	3 (6%)	4 (8%)	3 (6%)
#ADRENAL	(49)	(50)	(50)
ACCESSORY STRUCTURE		1 (2%)	
CYST, NOS			1 (2%)
ANGIECTASIS		1 (2%)	1 (2%)
#ADRENAL CORTEX	(49)	(50)	(50)
DEGENERATION, NOS	1 (2%)		
DEGENERATION, LIPOID	7 (14%)	10 (20%)	7 (14%)
FOCAL CELLULAR CHANGE		1 (2%)	1 (2%)
ATROPHY, NOS		1 (2%)	
HYPERTROPHY, FOCAL	1 (2%)		
HYPERPLASIA, FOCAL	4 (8%)	1 (2%)	2 (4%)
ANGIECTASIS		1 (2%)	
#ADRENAL MEDULLA	(49)	(50)	(50)
CYST, NOS		1 (2%)	
FIBROSIS	1 (2%)		
ATROPHY, NOS	1 (2%)		
HYPERPLASIA, NOS	1 (2%)		
HYPERPLASIA, FOCAL	2 (4%)		1 (2%)
#THYROID	(49)	(50)	(49)
HYPERPLASIA, C-CELL	6 (12%)	6 (12%)	7 (14%)

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
GALACTOCELE	1 (2%)	6 (12%)	1 (2%)
CYST, NOS		1 (2%)	1 (2%)
INFLAMMATION, CHRONIC	1 (2%)		
HYPERPLASIA, FOCAL		1 (2%)	
LACTATION	34 (68%)	32 (64%)	38 (76%)
*MAMMARY DUCT	(50)	(50)	(50)
HYPERPLASIA, NOS		2 (4%)	
HYPERPLASIA, FOCAL		2 (4%)	
*MAMMARY LOBULE	(50)	(50)	(50)
HYPERPLASIA, NOS	1 (2%)	2 (4%)	4 (8%)
*CLITORAL GLAND	(50)	(50)	(50)
DILATATION, NOS		1 (2%)	
INFLAMMATION, ACUTE/CHRONIC	1 (2%)		
HYPERPLASIA, NOS	1 (2%)	1 (2%)	
#UTERUS/ENDOMETRIUM	(50)	(50)	(50)
FIBROSIS		2 (4%)	3 (6%)
HYPERPLASIA, CYSTIC			1 (2%)
#OVARY	(49)	(50)	(50)
CYST, NOS	1 (2%)	2 (4%)	2 (4%)
INFLAMMATION, CHRONIC		1 (2%)	
INFLAMMATION, GRANULOMATOUS	1 (2%)		
NERVOUS SYSTEM			
#LATERAL VENTRICLE	(49)	(50)	(50)
DILATATION, NOS		1 (2%)	
*CHOROID PLEXUS	(50)	(50)	(50)
MINERALIZATION		1 (2%)	
SPECIAL SENSE ORGANS			
*EYE	(50)	(50)	(50)
CATARACT	13 (26%)	2 (4%)	3 (6%)
*SCLERA	(50)	(50)	(50)
METAPLASIA, OSSEOUS	1 (2%)		
*EYE/CORNEA	(50)	(50)	(50)
INFLAMMATION, SUPPURATIVE		1 (2%)	
*EYE/CHOROID	(50)	(50)	(50)
INFLAMMATION, ACUTE/CHRONIC			1 (2%)
*EYE/RETINA	(50)	(50)	(50)
ATROPHY, NOS	17 (34%)	3 (6%)	3 (6%)
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*ABDOMINAL CAVITY	(50)	(50)	(50)
NECROSIS, FAT	2 (4%)	4 (8%)	1 (2%)
*PELVIC PERITONEUM	(50)	(50)	(50)
NECROSIS, FAT		1 (2%)	
*PLEURA	(50)	(50)	(50)
INFLAMMATION, CHRONIC	1 (2%)		
*MESENTERY	(50)	(50)	(50)
NECROSIS, FAT	1 (2%)		

TABLE C2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ALL OTHER SYSTEMS			
NONE			
SPECIAL MORPHOLOGY SUMMARY			
NONE			

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
• NUMBER OF ANIMALS NECROPSIED

APPENDIX D

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MICE IN THE TWO-YEAR DERMAL STUDIES OF 2-CHLOROETHANOL

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL

	CONTROL (UNTR)	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50	50
ANIMALS NECROPSIED	50	50	50	50
ANIMALS EXAMINED HISTOPATH	50	50	50	50
INTEGUMENTARY SYSTEM				
#SKIN PAINT SITE	(44)	(50)	(49)	(50)
EDEMA, NOS		1 (2%)	1 (2%)	
ULCER, NOS	1 (2%)	1 (2%)	3 (6%)	8 (16%)
INFLAMMATION, ACUTE	1 (2%)	1 (2%)	1 (2%)	8 (16%)
ULCER, ACUTE	1 (2%)			
INFLAMMATION, ACUTE FOCAL			1 (2%)	
INFLAMMATION, ACUTE/CHRONIC	1 (2%)	3 (6%)	3 (6%)	5 (10%)
INFLAMMATION, CHRONIC		3 (6%)	7 (14%)	4 (8%)
INFLAMMATION, CHRONIC FOCAL	1 (2%)			
INFLAMMATION, GRANULOMATOUS				1 (2%)
SCLEROSIS				1 (2%)
HYPERKERATOSIS	1 (2%)		1 (2%)	
ACANTHOSIS		1 (2%)	2 (4%)	
*SKIN	(50)	(50)	(50)	(50)
DILATATION/DUCTS			1 (2%)	
EDEMA, NOS			1 (2%)	
ULCER, NOS			1 (2%)	2 (4%)
INFLAMMATION, ACUTE			1 (2%)	1 (2%)
INFLAMMATION, ACUTE FOCAL			1 (2%)	
ABSCESS, NOS		1 (2%)		
INFLAMMATION, ACUTE/CHRONIC		2 (4%)	2 (4%)	1 (2%)
INFLAMMATION, CHRONIC	1 (2%)	2 (4%)		1 (2%)
ABSCESS, CHRONIC	1 (2%)			
HYPERPLASIA, NOS		1 (2%)		
HYPERPLASIA, EPITHELIAL		1 (2%)		
ACANTHOSIS				1 (2%)
*SUBCUT TISSUE	(50)	(50)	(50)	(50)
EPIDERMAL INCLUSION CYST		1 (2%)		
EDEMA, NOS				1 (2%)
INFLAMMATION, GRANULOMATOUS				1 (2%)
RESPIRATORY SYSTEM				
#TRACHEA	(23)	(17)	(25)	(22)
CYST, NOS			1 (4%)	
#TRACHEAL GLAND	(23)	(17)	(25)	(22)
DILATATION, NOS	1 (4%)	2 (12%)		
#BRONCHIAL GLAND	(50)	(50)	(50)	(50)
DILATATION, NOS	1 (2%)		1 (2%)	
#LUNG	(50)	(50)	(50)	(50)
MINERALIZATION	1 (2%)		1 (2%)	
ATELECTASIS			1 (2%)	
CONGESTION, NOS	3 (6%)	2 (4%)		5 (10%)
EDEMA, NOS		1 (2%)		2 (4%)
HEMORRHAGE	3 (6%)	2 (4%)	3 (6%)	1 (2%)
LYMPHOCYTIC INFLAMMATORY INFILTR				1 (2%)
INFLAMMATION, INTERSTITIAL		1 (2%)		1 (2%)
PNEUMONIA, ASPIRATION	1 (2%)			
BRONCHOPNEUMONIA, ACUTE				1 (2%)
INFLAMMATION, ACUTE				1 (2%)
INFLAMMATION, GRANULOMATOUS				2 (4%)
CRYSTALS, NOS	1 (2%)			
HYPERPLASIA, ALVEOLAR EPITHELIUM	2 (4%)	4 (8%)	1 (2%)	2 (4%)
HISTIOCYTOSIS	4 (8%)	4 (8%)	9 (18%)	7 (14%)

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (UNTR)	CONTROL (VEH)	LOW DOSE	HIGH DOSE
HEMATOPOIETIC SYSTEM				
*MULTIPLE ORGANS	(50)	(50)	(50)	(50)
LEUKEMOID REACTION	1 (2%)		1 (2%)	
PLASMACYTOSIS	1 (2%)	1 (2%)		
HYPERPLASIA, LYMPHOID	2 (4%)	1 (2%)	1 (2%)	1 (2%)
HEMATOPOIESIS	1 (2%)	1 (2%)	2 (4%)	3 (6%)
#BONE MARROW	(43)	(47)	(45)	(49)
HYPERPLASIA, GRANULOCYTIC	1 (2%)	1 (2%)	2 (4%)	1 (2%)
#SPLEEN	(44)	(49)	(50)	(50)
HEMOSIDEROSIS	1 (2%)	3 (6%)		1 (2%)
HYPERPLASIA, LYMPHOID			1 (2%)	
HEMATOPOIESIS	2 (5%)	5 (10%)	6 (12%)	6 (12%)
#LYMPH NODE	(27)	(32)	(37)	(35)
INFLAMMATION, GRANULOMATOUS				1 (3%)
SCLEROSIS			1 (3%)	
PLASMACYTOSIS				1 (3%)
HYPERPLASIA, LYMPHOID			1 (3%)	2 (6%)
#MANDIBULAR L. NODE	(27)	(32)	(37)	(35)
INFLAMMATION, ACUTE		1 (3%)		
HEMOSIDEROSIS				1 (3%)
PLASMACYTOSIS			2 (5%)	
HYPERPLASIA, LYMPHOID				1 (3%)
MASTOCYTOSIS				1 (3%)
#MEDIASTINAL L. NODE	(27)	(32)	(37)	(35)
HEMORRHAGE		1 (3%)	2 (5%)	1 (3%)
INFLAMMATION, ACUTE			1 (3%)	
#PANCREATIC L. NODE	(27)	(32)	(37)	(35)
HYPERPLASIA, LYMPHOID			1 (3%)	
#LUMBAR LYMPH NODE	(27)	(32)	(37)	(35)
PLASMACYTOSIS				1 (3%)
#MESENTERIC L. NODE	(27)	(32)	(37)	(35)
EDEMA, NOS		1 (3%)		
HEMORRHAGE	1 (4%)	1 (3%)	2 (5%)	1 (3%)
INFLAMMATION, ACUTE				1 (3%)
PIGMENTATION, NOS	1 (4%)			
PLASMACYTOSIS			1 (3%)	
HYPERPLASIA, LYMPHOID				1 (3%)
HEMATOPOIESIS	1 (4%)	2 (6%)	1 (3%)	
#INGUINAL LYMPH NODE	(27)	(32)	(37)	(35)
CYST, NOS		1 (3%)		
HEMORRHAGE				1 (3%)
HYPERPLASIA, LYMPHOID	1 (4%)	1 (3%)		
#KIDNEY	(50)	(50)	(50)	(50)
HEMATOPOIESIS		1 (2%)		
#THYMUS	(30)	(43)	(38)	(39)
ACCESSORY STRUCTURE			1 (3%)	
CYST, NOS	2 (7%)	6 (14%)	11 (29%)	9 (23%)
INFLAMMATION, CHRONIC			1 (3%)	
HYPERPLASIA, LYMPHOID		1 (2%)		
#THYMIC LYMPHOCYTES	(30)	(43)	(38)	(39)
NECROSIS, NOS	1 (3%)			

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (UNTR)	CONTROL (VEH)	LOW DOSE	HIGH DOSE
CIRCULATORY SYSTEM				
*MULTIPLE ORGANS	(50)	(50)	(50)	(50)
THROMBOSIS, NOS	1 (2%)			
*SKIN	(50)	(50)	(50)	(50)
LYMPHANGIECTASIS				1 (2%)
#INGUINAL LYMPH NODE	(27)	(32)	(37)	(35)
THROMBOSIS, NOS				1 (3%)
#HEART	(50)	(49)	(50)	(49)
THROMBOSIS, NOS	1 (2%)		3 (6%)	4 (8%)
EDEMA, NOS		1 (2%)		
INFLAMMATION, ACUTE				1 (2%)
INFLAMMATION, ACUTE/CHRONIC	1 (2%)	1 (2%)		
INFLAMMATION, CHRONIC	1 (2%)	1 (2%)	1 (2%)	
FIBROSIS	5 (10%)	6 (12%)	12 (24%)	8 (16%)
DEGENERATION, NOS				1 (2%)
ATHEROSCLEROSIS		1 (2%)		
*BLOOD VESSEL	(50)	(50)	(50)	(50)
INFLAMMATION, ACUTE/CHRONIC		1 (2%)		1 (2%)
*CORONARY ARTERY	(50)	(50)	(50)	(50)
INFLAMMATION, ACUTE/CHRONIC		1 (2%)		
*PULMONARY ARTERY	(50)	(50)	(50)	(50)
MINERALIZATION	1 (2%)			
THROMBOSIS, NOS				1 (2%)
*THYMIC ARTERY	(50)	(50)	(50)	(50)
INFLAMMATION, FIBRINOID			1 (2%)	
*RENAL ARTERY	(50)	(50)	(50)	(50)
INFLAMMATION, FIBRINOID	1 (2%)			
#TESTIS	(49)	(50)	(50)	(50)
THROMBOSIS, NOS	1 (2%)			
#ADRENAL MEDULLA	(48)	(48)	(49)	(50)
THROMBOSIS, NOS			1 (2%)	
DIGESTIVE SYSTEM				
#SALIVARY GLAND	(47)	(50)	(50)	(49)
INFLAMMATION, NECROTIZING				1 (2%)
#LIVER	(50)	(49)	(50)	(50)
MINERALIZATION				1 (2%)
CONGESTION, NOS			1 (2%)	
LYMPHOCYTIC INFLAMMATORY INFILTR			1 (2%)	
INFLAMMATION, ACUTE		3 (6%)	2 (4%)	4 (8%)
INFLAMMATION, ACUTE NECROTIZING	1 (2%)	1 (2%)	2 (4%)	
INFLAMMATION, GRANULOMATOUS				1 (2%)
GRANULOMA, NOS			2 (4%)	1 (2%)
NECROSIS, NOS	1 (2%)	4 (8%)	1 (2%)	3 (6%)
NUCLEAR-SIZE ALTERATION			1 (2%)	
NUCLEAR-SHAPE ALTERATION	1 (2%)			
CYTOPLASMIC VACUOLIZATION	1 (2%)	4 (8%)	2 (4%)	4 (8%)
BASOPHILIC CYTO CHANGE	3 (6%)	2 (4%)	1 (2%)	5 (10%)
EOSINOPHILIC CYTO CHANGE			1 (2%)	1 (2%)
CLEAR-CELL CHANGE	1 (2%)		2 (4%)	
HEPATOCYTOMEGALY	22 (44%)	26 (53%)	24 (48%)	23 (46%)
ANGIECTASIS		1 (2%)		
#LIVER/CENTRILOBULAR	(50)	(49)	(50)	(50)
HEPATOCYTOMEGALY		3 (6%)		1 (2%)
#LIVER/KUPFFER CELL	(50)	(49)	(50)	(50)
HYPERPLASIA, NOS		1 (2%)		1 (2%)

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (UNTR)	CONTROL (VEH)	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM (Continued)				
#LIVER/HEPATOCYTES	(50)	(49)	(50)	(50)
HEPATOCYTOMEGALY	2 (4%)			
*GALLBLADDER	(50)	(50)	(50)	(50)
INFLAMMATION, CHRONIC	1 (2%)			
#BILE DUCT	(50)	(49)	(50)	(50)
INFLAMMATION, ACUTE/CHRONIC		1 (2%)		
HYPERPLASIA, NOS	1 (2%)	1 (2%)		
#PANCREAS	(46)	(49)	(50)	(50)
EDEMA, NOS			1 (2%)	
#PANCREATIC ACINUS	(46)	(49)	(50)	(50)
EDEMA, NOS	1 (2%)			
CYTOPLASMIC VACUOLIZATION			1 (2%)	1 (2%)
ATROPHY, NOS		1 (2%)	1 (2%)	
HYPERPLASIA, NODULAR			1 (2%)	
#STOMACH	(45)	(50)	(49)	(49)
MINERALIZATION	5 (11%)	7 (14%)	2 (4%)	3 (6%)
CYST, NOS			1 (2%)	
ULCER, NOS		1 (2%)		
INFLAMMATION, ACUTE/CHRONIC	6 (13%)	5 (10%)	6 (12%)	5 (10%)
INFLAMMATION, CHRONIC	1 (2%)		1 (2%)	1 (2%)
INFLAMMATION, GRANULOMATOUS	1 (2%)			
HYPERPLASIA, EPITHELIAL	14 (31%)	6 (12%)	9 (18%)	13 (27%)
HYPERPLASIA, ADENOMATOUS		1 (2%)		
ADENOMYOSIS	5 (11%)	2 (4%)		4 (8%)
#GASTRIC MUCOSA	(45)	(50)	(49)	(49)
DILATATION, NOS	3 (7%)	3 (6%)	1 (2%)	
#GASTRIC FUNDAL GLAND	(45)	(50)	(49)	(49)
DILATATION, NOS	1 (2%)			
#GASTRIC SEROSA	(45)	(50)	(49)	(49)
CYST, NOS				1 (2%)
#STOMACH WALL	(45)	(50)	(49)	(49)
CYST, NOS				1 (2%)
#DUODENUM	(39)	(42)	(44)	(45)
FIBROSIS			1 (2%)	
URINARY SYSTEM				
#KIDNEY	(50)	(50)	(50)	(50)
MINERALIZATION	6 (12%)	3 (6%)	5 (10%)	11 (22%)
HYDRONEPHROSIS	3 (6%)	1 (2%)	4 (8%)	3 (6%)
CYST, NOS	6 (12%)	3 (6%)	6 (12%)	4 (8%)
MULTIPLE CYSTS		1 (2%)	1 (2%)	
GLOMERULONEPHRITIS, NOS	4 (8%)	8 (16%)	2 (4%)	1 (2%)
LYMPHOCYTIC INFLAMMATORY INFIL	10 (20%)	5 (10%)	12 (24%)	12 (24%)
INFLAMMATION, INTERSTITIAL	1 (2%)			
PYELONEPHRITIS, ACUTE		1 (2%)		1 (2%)
INFLAMMATION, ACUTE/CHRONIC		1 (2%)		
INFLAMMATION, CHRONIC		1 (2%)		
GLOMERULONEPHRITIS, CHRONIC	1 (2%)			
GRANULOMA, NOS	1 (2%)			1 (2%)
SCLEROSIS		1 (2%)		
NEPHROSIS, NOS	11 (22%)	12 (24%)	14 (28%)	8 (16%)
INFARCT, NOS	1 (2%)	3 (6%)	2 (4%)	2 (4%)
AMYLOIDOSIS	1 (2%)		1 (2%)	1 (2%)
PIGMENTATION, NOS	1 (2%)	1 (2%)		
METAPLASIA, OSSEOUS		2 (4%)	1 (2%)	

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (UNTR)	CONTROL (VEH)	LOW DOSE	HIGH DOSE
URINARY SYSTEM (Continued)				
#KIDNEY/GLOMERULUS	(50)	(50)	(50)	(50)
DILATATION, NOS			1 (2%)	1 (2%)
AMYLOIDOSIS				1 (2%)
#KIDNEY/TUBULE	(50)	(50)	(50)	(50)
DILATATION, NOS				2 (4%)
#URINARY BLADDER	(44)	(50)	(50)	(47)
CALCULUS,GROSS OBSERV ONLY	3 (7%)	1 (2%)		1 (2%)
MINERALIZATION			1 (2%)	
DILATATION, NOS			1 (2%)	2 (4%)
CONGESTION, NOS			1 (2%)	
HEMORRHAGE	1 (2%)	2 (4%)	2 (4%)	2 (4%)
INFLAMMATION, ACUTE	1 (2%)	2 (4%)	1 (2%)	
INFLAMMATION, ACUTE/CHRONIC				1 (2%)
#U. BLADDER/SEROSA	(44)	(50)	(50)	(47)
INFLAMMATION, ACUTE				1 (2%)
*URETHRA	(50)	(50)	(50)	(50)
DILATATION, NOS	1 (2%)			
IMPACTION, NOS				1 (2%)
HEMORRHAGE	2 (4%)			
ENDOCRINE SYSTEM				
#PITUITARY	(41)	(47)	(47)	(47)
CYST, NOS		2 (4%)	1 (2%)	5 (11%)
FIBROSIS				1 (2%)
HYPERPLASIA, CHROMOPHOBE-CELL		1 (2%)		
#ADRENAL	(48)	(48)	(49)	(50)
FOCAL CELLULAR CHANGE	1 (2%)			
ATROPHY, BROWN	1 (2%)	2 (4%)	5 (10%)	
#ADRENAL CORTEX	(48)	(48)	(49)	(50)
DEGENERATION, CYSTIC	1 (2%)			
CYTOPLASMIC VACUOLIZATION		1 (2%)	1 (2%)	
FOCAL CELLULAR CHANGE	3 (6%)	6 (13%)	5 (10%)	2 (4%)
EOSINOPHILIC CYTO CHANGE				1 (2%)
ATROPHY, NOS	1 (2%)			2 (4%)
ATROPHY, BROWN	17 (35%)	21 (44%)	19 (39%)	14 (28%)
HYPERPLASIA, NOS	4 (8%)		3 (6%)	2 (4%)
HYPERPLASIA, FOCAL		2 (4%)		
#ADRENAL MEDULLA	(48)	(48)	(49)	(50)
HYPERPLASIA, NOS	1 (2%)	6 (13%)	5 (10%)	6 (12%)
#PERIADRENAL TISSUE	(48)	(48)	(49)	(50)
INFLAMMATION, GRANULOMATOUS		1 (2%)		
#THYROID	(47)	(47)	(44)	(46)
MINERALIZATION		1 (2%)		
CYST, NOS		1 (2%)		
FOLLICULAR CYST, NOS	23 (49%)	16 (34%)	16 (36%)	16 (35%)
HYPERPLASIA, ADENOMATOUS				1 (2%)
HYPERPLASIA, FOLLICULAR-CELL	1 (2%)	1 (2%)		
#PARATHYROID	(12)	(15)	(14)	(19)
CYST, NOS				1 (5%)
#PANCREATIC ISLETS	(46)	(49)	(50)	(50)
HYPERPLASIA, NOS	1 (2%)	1 (2%)		

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (UNTR)	CONTROL (VEH)	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM				
*PENIS	(50)	(50)	(50)	(50)
HEMORRHAGE			1 (2%)	
INFLAMMATION, ACUTE		1 (2%)		
*PREPUCE	(50)	(50)	(50)	(50)
IMPACTION, NOS			1 (2%)	
INFLAMMATION, ACUTE			1 (2%)	
INFLAMMATION, ACUTE/CHRONIC			1 (2%)	1 (2%)
HYPERKERATOSIS			1 (2%)	
*PREPUTIAL GLAND	(50)	(50)	(50)	(50)
DILATATION, NOS			1 (2%)	2 (4%)
DILATATION/DUCTS	6 (12%)	7 (14%)	2 (4%)	1 (2%)
IMPACTION, NOS	2 (4%)			
ABSCESS, NOS		2 (4%)		
INFLAMMATION, ACUTE/CHRONIC		4 (8%)	1 (2%)	
#PROSTATE	(49)	(50)	(50)	(48)
INFLAMMATION, ACUTE	3 (6%)	2 (4%)	2 (4%)	1 (2%)
INFLAMMATION, ACUTE/CHRONIC		1 (2%)	1 (2%)	2 (4%)
*SEMINAL VESICLE	(50)	(50)	(50)	(50)
MINERALIZATION			1 (2%)	
DILATATION, NOS	8 (16%)	7 (14%)	13 (26%)	9 (18%)
INFLAMMATION, ACUTE	1 (2%)		3 (6%)	1 (2%)
INFLAMMATION, ACUTE/CHRONIC				1 (2%)
PIGMENTATION, NOS	1 (2%)			
HYPERPLASIA, EPITHELIAL			1 (2%)	
*COAGULATING GLAND	(50)	(50)	(50)	(50)
DILATATION, NOS	2 (4%)			
#TESTIS	(49)	(50)	(50)	(50)
MINERALIZATION	11 (22%)	12 (24%)	13 (26%)	14 (28%)
SPERMATOCELE			1 (2%)	
INFLAMMATION, ACUTE		1 (2%)		
GRANULOMA, SPERMATIC			1 (2%)	
ATROPHY, NOS	4 (8%)	6 (12%)	2 (4%)	5 (10%)
HYPERPLASIA, INTERSTITIAL CELL	6 (12%)	9 (18%)	8 (16%)	7 (14%)
#TESTIS/TUBULE	(49)	(50)	(50)	(50)
DILATATION, NOS				1 (2%)
MULTINUCLEATE GIANT-CELL	1 (2%)			
HYPERPLASIA, CYSTIC		1 (2%)		
*EPIDIDYMIS	(50)	(50)	(50)	(50)
SPERMATOCELE			1 (2%)	2 (4%)
GRANULOMA, SPERMATIC				1 (2%)
NERVOUS SYSTEM				
#BRAIN/MENINGES	(50)	(50)	(50)	(50)
FIBROSIS				1 (2%)
#BRAIN	(50)	(50)	(50)	(50)
MINERALIZATION		1 (2%)	1 (2%)	3 (6%)
EDEMA, NOS	1 (2%)			1 (2%)
HEMORRHAGE			1 (2%)	
CYTOPLASMIC VACUOLIZATION	1 (2%)			

TABLE D1. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (UNTR)	CONTROL (VEH)	LOW DOSE	HIGH DOSE
SPECIAL SENSE ORGANS				
*EYE	(50)	(50)	(50)	(50)
MINERALIZATION			1 (2%)	
RETINOPATHY	3 (6%)	2 (4%)	4 (8%)	4 (8%)
CATARACT	2 (4%)		2 (4%)	3 (6%)
*EYE/CORNEA	(50)	(50)	(50)	(50)
MINERALIZATION		1 (2%)		
ULCER, NOS		1 (2%)		
INFLAMMATION, ACUTE			1 (2%)	
*EYE/CRYSTALLINE LENS	(50)	(50)	(50)	(50)
RUPTURE				1 (2%)
*EYELID	(50)	(50)	(50)	(50)
INFLAMMATION, ACUTE		1 (2%)		
MUSCULOSKELETAL SYSTEM				
*SKELETAL MUSCLE	(50)	(50)	(50)	(50)
INFLAMMATION, CHRONIC		1 (2%)		1 (2%)
BODY CAVITIES				
*MEDIASTINUM	(50)	(50)	(50)	(50)
CYST, NOS		1 (2%)		
HEMORRHAGE		1 (2%)		
*PELVIC PERITONEAL CAVITY	(50)	(50)	(50)	(50)
CYST, NOS				1 (2%)
*EPICARDIUM	(50)	(50)	(50)	(50)
INFLAMMATION, ACUTE			1 (2%)	
INFLAMMATION, ACUTE/CHRONIC		1 (2%)		
ALL OTHER SYSTEMS				
*MULTIPLE ORGANS	(50)	(50)	(50)	(50)
MINERALIZATION	1 (2%)		1 (2%)	1 (2%)
CONGESTION, NOS	2 (4%)			
LYMPHOCYTIC INFLAMMATORY INFIL	18 (36%)	32 (64%)	14 (28%)	19 (38%)
INFLAMMATION, ACUTE				1 (2%)
INFLAMMATION, GRANULOMATOUS				2 (4%)
BACTERIAL SEPTICEMIA		1 (2%)		
NECROSIS, NOS				2 (4%)
NECROSIS, ISCHEMIC			1 (2%)	
AMYLOIDOSIS	1 (2%)	10 (20%)	6 (12%)	4 (8%)
SPECIAL MORPHOLOGY SUMMARY				
AUTO/NECROPSY/HISTO PERF	1			

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL

	CONTROL (UNTR)	CONTROL (VEH)	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50	50
ANIMALS NECROPSIED	50	50	50	50
ANIMALS EXAMINED HISTOPATHOL	50	50	50	50
INTEGUMENTARY SYSTEM				
#SKIN PAINT SITE	(48)	(49)	(48)	(47)
INFLAMMATION, ACUTE	1 (2%)		1 (2%)	1 (2%)
INFLAMMATION, ACUTE/CHRONIC	2 (4%)		1 (2%)	1 (2%)
INFLAMMATION, CHRONIC		4 (8%)	2 (4%)	2 (4%)
FIBROSIS		1 (2%)		2 (4%)
ACANTHOSIS	1 (2%)			2 (4%)
*SKIN	(50)	(50)	(50)	(50)
EDEMA, NOS		1 (2%)		
ULCER, NOS				1 (2%)
INFLAMMATION, ACUTE/CHRONIC		1 (2%)		2 (4%)
HYPERPLASIA, NOS			1 (2%)	
ACANTHOSIS				1 (2%)
RESPIRATORY SYSTEM				
*LARYNX	(50)	(50)	(50)	(50)
INFLAMMATION, ACUTE	1 (2%)			
#BRONCHIAL GLAND	(50)	(50)	(49)	(50)
DILATATION, NOS	1 (2%)	1 (2%)	1 (2%)	
#LUNG	(50)	(50)	(49)	(50)
MINERALIZATION	1 (2%)	1 (2%)	1 (2%)	
CONGESTION, NOS	1 (2%)		1 (2%)	1 (2%)
EDEMA, NOS			1 (2%)	
HEMORRHAGE	1 (2%)	3 (6%)	3 (6%)	2 (4%)
LYMPHOCYTIC INFLAM INFILTR	1 (2%)		1 (2%)	
PNEUMONIA, ASPIRATION	1 (2%)			
HYPERPLASIA, ALVEOLAR EPITHELIUM	1 (2%)	1 (2%)	1 (2%)	
HISTIOCYTOSIS	4 (8%)	6 (12%)	8 (16%)	6 (12%)
HEMATOPOIETIC SYSTEM				
*MULTIPLE ORGANS	(50)	(50)	(50)	(50)
LEUKEMOID REACTION	2 (4%)		1 (2%)	3 (6%)
PLASMACYTOSIS				1 (2%)
HYPERPLASIA, LYMPHOID	3 (6%)	4 (8%)	4 (8%)	2 (4%)
HEMATOPOIESIS	1 (2%)		6 (12%)	4 (8%)
#BONE MARROW	(50)	(49)	(44)	(46)
MYELOSCLEROSIS		1 (2%)		1 (2%)
HYPERPLASIA, GRANULOCYTIC			1 (2%)	2 (4%)
#SPLEEN	(47)	(49)	(48)	(49)
HEMOSIDEROSIS	9 (19%)	4 (8%)	4 (8%)	4 (8%)
HYPERPLASIA, LYMPHOID		1 (2%)	1 (2%)	
HEMATOPOIESIS	12 (26%)	4 (8%)	3 (6%)	2 (4%)
#MANDIBULAR L. NODE	(38)	(33)	(36)	(44)
HEMORRHAGE	3 (8%)	1 (3%)		2 (5%)
INFLAMMATION, ACUTE				1 (2%)
INFLAMMATION, GRANULOMATOUS				1 (2%)
PLASMACYTOSIS				1 (2%)
HYPERPLASIA, LYMPHOID			1 (3%)	
#MEDIASTINAL L. NODE	(38)	(33)	(36)	(44)
HEMORRHAGE			5 (14%)	
PIGMENTATION, NOS				1 (2%)
HYPERPLASIA, LYMPHOID		1 (3%)		
#HEPATIC LYMPH NODE	(38)	(33)	(36)	(44)
HYPERPLASIA, LYMPHOID	1 (3%)			

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (UNTR)	CONTROL (VEH)	LOW DOSE	HIGH DOSE
HEMATOPOIETIC SYSTEM (Continued)				
#LUMBAR LYMPH NODE	(38)	(33)	(36)	(44)
NECROSIS, NOS	1 (3%)			
#MESENTERIC L. NODE	(38)	(33)	(36)	(44)
HEMORRHAGE	1 (3%)	3 (9%)		3 (7%)
HYPERPLASIA, LYMPHOID	1 (3%)	1 (3%)	2 (6%)	
#RENAL LYMPH NODE	(38)	(33)	(36)	(44)
HEMORRHAGE		1 (3%)		
PLASMACYTOSIS		1 (3%)		
#LIVER	(50)	(50)	(49)	(50)
LEUKEMOID REACTION	1 (2%)			
#PEYER'S PATCH	(44)	(45)	(46)	(45)
HYPERPLASIA, LYMPHOID		1 (2%)		
#PITUITARY	(46)	(48)	(49)	(47)
HYPERPLASIA, EOSINOPHILIC			1 (2%)	1 (2%)
#THYMUS	(39)	(42)	(36)	(41)
CYST, NOS	3 (8%)	3 (7%)	1 (3%)	3 (7%)
HEMORRHAGE		1 (2%)		
INFLAMMATION, PYOGRANULOMATOUS			1 (3%)	
NECROSIS, NOS			1 (3%)	
HYPERPLASIA, LYMPHOID	6 (15%)	8 (19%)	12 (33%)	12 (29%)
CIRCULATORY SYSTEM				
*MULTIPLE ORGANS	(50)	(50)	(50)	(50)
ARTERIOSCLEROSIS, NOS		1 (2%)		
#MEDIASTINAL L. NODE	(38)	(33)	(36)	(44)
THROMBOSIS, NOS	1 (3%)			
#LUNG	(50)	(50)	(49)	(50)
THROMBOSIS, NOS				1 (2%)
#HEART	(50)	(50)	(50)	(50)
MINERALIZATION	2 (4%)			
THROMBOSIS, NOS			1 (2%)	
INFLAMMATION, CHRONIC	1 (2%)			
FIBROSIS	5 (10%)	3 (6%)		1 (2%)
DEGENERATION, NOS			1 (2%)	2 (4%)
DEGENERATION, HYALINE		1 (2%)		
#MYOCARDIUM	(50)	(50)	(50)	(50)
DEGENERATION, NOS	1 (2%)			
*BLOOD VESSEL	(50)	(50)	(50)	(50)
INFLAMMATION, ACUTE/CHRONIC				1 (2%)
*CORONARY ARTERY	(50)	(50)	(50)	(50)
DEGENERATION, MUCOID		1 (2%)		
*THYMIC ARTERY	(50)	(50)	(50)	(50)
INFLAMMATION, FIBRINOID	1 (2%)		1 (2%)	2 (4%)
*UTERINE ARTERY	(50)	(50)	(50)	(50)
INFLAMMATION, FIBRINOID				1 (2%)
NECROSIS, FIBRINOID				1 (2%)
*OVARIAN ARTERY	(50)	(50)	(50)	(50)
INFLAMMATION, FIBRINOID			2 (4%)	1 (2%)
#UTERUS	(50)	(49)	(49)	(50)
THROMBOSIS, NOS		1 (2%)		
#OVARY	(50)	(50)	(49)	(48)
THROMBOSIS, NOS			1 (2%)	1 (2%)
DIGESTIVE SYSTEM				
#SALIVARY GLAND	(48)	(50)	(50)	(49)
HEMORRHAGE	1 (2%)			
INFLAMMATION, ACUTE			1 (2%)	
FIBROSIS		1 (2%)		
ATROPHY, NOS			1 (2%)	

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (UNTR)	CONTROL (VEH)	LOW DOSE	HIGH DOSE
DIGESTIVE SYSTEM				
#LIVER	(50)	(50)	(49)	(50)
CYST, NOS			1 (2%)	
LYMPHOCYTIC INFLAM INFILTR			1 (2%)	
INFLAMMATION, ACUTE	2 (4%)	3 (6%)		1 (2%)
INFLAMMATION, ACUTE NECROTIZING	2 (4%)	1 (2%)	1 (2%)	
GRANULOMA, NOS	1 (2%)	4 (8%)	2 (4%)	
NECROSIS, NOS	1 (2%)	3 (6%)		4 (8%)
INFARCT, NOS			1 (2%)	
NUCLEAR-SIZE ALTERATION			1 (2%)	
CYTOPLASMIC VACUOLIZATION	6 (12%)	4 (8%)	1 (2%)	2 (4%)
FOCAL CELLULAR CHANGE			1 (2%)	
EOSINOPHILIC CYTO CHANGE				1 (2%)
CLEAR-CELL CHANGE	4 (8%)	2 (4%)	1 (2%)	2 (4%)
HEPATOCYTOMEGALY	2 (4%)	2 (4%)	2 (4%)	3 (6%)
ANGIECTASIS	1 (2%)			
#LIVER/CAUDATE LOBE	(50)	(50)	(49)	(50)
HEMORRHAGE			1 (2%)	
NECROSIS, NOS			1 (2%)	
INFARCT, NOS				1 (2%)
#LIVER/KUPFFER CELL	(50)	(50)	(49)	(50)
HYPERPLASIA, NOS			2 (4%)	
*GALLBLADDER	(50)	(50)	(50)	(50)
HYPERPLASIA, EPITHELIAL			1 (2%)	
#BILE DUCT	(50)	(50)	(49)	(50)
HYPERPLASIA, NOS	1 (2%)	1 (2%)		1 (2%)
#PANCREAS	(48)	(50)	(47)	(50)
EDEMA, NOS			2 (4%)	1 (2%)
NECROSIS, FAT	1 (2%)			
#PANCREATIC ACINUS	(48)	(50)	(47)	(50)
CYTOPLASMIC VACUOLIZATION	2 (4%)	1 (2%)	2 (4%)	
ATROPHY, NOS		1 (2%)		
ATROPHY, EXHAUSTION	1 (2%)			
HYPERPLASIA, NOS		3 (6%)	1 (2%)	
#ESOPHAGUS	(48)	(47)	(46)	(45)
GRANULOMA, NOS		1 (2%)		
#STOMACH	(47)	(50)	(50)	(50)
MINERALIZATION	2 (4%)	2 (4%)	4 (8%)	3 (6%)
INFLAMMATION, ACUTE	1 (2%)	1 (2%)	1 (2%)	
INFLAMMATION, ACUTE/CHRONIC	5 (11%)	4 (8%)	4 (8%)	2 (4%)
INFLAMMATION, CHRONIC		2 (4%)	1 (2%)	
FIBROSIS			1 (2%)	
NECROSIS, NOS			1 (2%)	
HYPERPLASIA, EPITHELIAL	9 (19%)	12 (24%)	9 (18%)	5 (10%)
HYPERKERATOSIS				1 (2%)
ACANTHOSIS				1 (2%)
ADENOMYOSIS		1 (2%)		1 (2%)
URINARY SYSTEM				
#KIDNEY	(50)	(50)	(50)	(50)
MINERALIZATION	1 (2%)	1 (2%)	1 (2%)	2 (4%)
HYDRONEPHROSIS	2 (4%)	1 (2%)	3 (6%)	4 (8%)
CYST, NOS	3 (6%)			
CONGESTION, NOS	1 (2%)			
GLOMERULONEPHRITIS, NOS	8 (16%)	5 (10%)	9 (18%)	8 (16%)
LYMPHOCYTIC INFLAMMATORY INFILTR	5 (10%)	10 (20%)	3 (6%)	6 (12%)
INFLAMMATION, ACUTE/CHRONIC				1 (2%)
GLOMERULONEPHRITIS, CHRONIC	1 (2%)			
NEPHROSIS, NOS	8 (16%)	6 (12%)	5 (10%)	4 (8%)
INFARCT, NOS		1 (2%)		1 (2%)
AMYLOIDOSIS			1 (2%)	2 (4%)
PIGMENTATION, NOS	1 (2%)	1 (2%)		

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (UNTR)	CONTROL (VEH)	LOW DOSE	HIGH DOSE
URINARY SYSTEM				
#KIDNEY (Continued)	(50)	(50)	(50)	(50)
CYTOPLASMIC VACUOLIZATION	1 (2%)			
METAPLASIA, OSSEOUS		2 (4%)		
#KIDNEY/GLOMERULUS	(50)	(50)	(50)	(50)
DILATATION, NOS				1 (2%)
#URINARY BLADDER	(46)	(49)	(48)	(45)
CALCULUS,MICROSCOPIC EXAM	1 (2%)			
INFLAMMATION, ACUTE/CHRONIC	1 (2%)			
HYPERPLASIA, EPITHELIAL	1 (2%)			
#U. BLADDER/SEROSA	(46)	(49)	(48)	(45)
INFLAMMATION, CHRONIC			1 (2%)	
ENDOCRINE SYSTEM				
#PITUITARY	(46)	(48)	(49)	(47)
CYST, NOS			1 (2%)	
CONGESTION, NOS		1 (2%)		
PIGMENTATION, NOS	1 (2%)			
HYPERPLASIA, CHROMOPHOBE-CELL	2 (4%)	1 (2%)	3 (6%)	1 (2%)
ANGIECTASIS		1 (2%)		
#ADRENAL	(49)	(50)	(50)	(49)
ACCESSORY STRUCTURE		1 (2%)		
CONGESTION, NOS	1 (2%)	2 (4%)	1 (2%)	
ATROPHY, BROWN	1 (2%)	1 (2%)	1 (2%)	2 (4%)
ANGIECTASIS		1 (2%)		
#ADRENAL CORTEX	(49)	(50)	(50)	(49)
ACCESSORY STRUCTURE			1 (2%)	
MINERALIZATION	1 (2%)			
DEGENERATION, BALLOONING		1 (2%)		
CYTOPLASMIC VACUOLIZATION	1 (2%)	1 (2%)	2 (4%)	
FOCAL CELLULAR CHANGE				1 (2%)
ATROPHY, BROWN	14 (29%)	18 (36%)	12 (24%)	8 (16%)
HYPERPLASIA, NOS	1 (2%)		1 (2%)	1 (2%)
HYPERPLASIA, FOCAL		1 (2%)		
#ADRENAL MEDULLA	(49)	(50)	(50)	(49)
HYPERPLASIA, NOS	1 (2%)	2 (4%)	5 (10%)	1 (2%)
ANGIECTASIS		1 (2%)		1 (2%)
#THYROID	(45)	(48)	(46)	(46)
FOLLICULAR CYST, NOS	15 (33%)	12 (25%)	17 (37%)	17 (37%)
LYMPHOCYTIC INFLAM INFILTR	1 (2%)			
HYPERPLASIA, C-CELL		1 (2%)	1 (2%)	
HYPERPLASIA, FOLLICULAR-CELL	1 (2%)		2 (4%)	1 (2%)
#PARATHYROID	(17)	(19)	(17)	(21)
HYPERPLASIA, NOS		1 (5%)		
REPRODUCTIVE SYSTEM				
*MAMMARY GLAND	(50)	(50)	(50)	(50)
DILATATION/DUCTS	2 (4%)	1 (2%)	3 (6%)	4 (8%)
GALACTOCELE	1 (2%)			
FIBROSIS	1 (2%)			
HYPERPLASIA, NOS	6 (12%)	3 (6%)	2 (4%)	2 (4%)
LACTATION	1 (2%)	1 (2%)		1 (2%)
#UTERUS	(50)	(49)	(49)	(50)
MINERALIZATION			1 (2%)	
HEMATOMA, NOS		1 (2%)		
INFLAM, FOCAL GRANULOMATOUS			1 (2%)	
ADENOMYOSIS	5 (10%)	5 (10%)	2 (4%)	1 (2%)
#CERVIX UTERI	(50)	(49)	(49)	(50)
MINERALIZATION			1 (2%)	
FIBROUS DYSPLASIA			1 (2%)	

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (UNTR)	CONTROL (VEH)	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM				
#UTERUS/ENDOMETRIUM	(50)	(49)	(49)	(50)
CYST, NOS	13 (26%)	13 (27%)	12 (24%)	22 (44%)
HEMATOMA, NOS			1 (2%)	
INFLAMMATION, ACUTE	1 (2%)	1 (2%)		
INFLAMMATION, ACUTE/CHRONIC		1 (2%)		
HYPERPLASIA, NOS	1 (2%)	1 (2%)	1 (2%)	1 (2%)
HYPERPLASIA, EPITHELIAL		1 (2%)		
HYPERPLASIA, CYSTIC	22 (44%)	16 (33%)	16 (33%)	11 (22%)
HYPERPLASIA, STROMAL	1 (2%)			
ANGIECTASIS			3 (6%)	
#OVARY/PAROVARIAN	(50)	(50)	(49)	(48)
HEMATOMA, NOS			1 (2%)	
INFLAMMATION, GRANULOMATOUS	1 (2%)			
#OVARY	(50)	(50)	(49)	(48)
MINERALIZATION		1 (2%)		
CYST, NOS	30 (60%)	36 (72%)	30 (61%)	31 (65%)
HEMORRHAGE	2 (4%)	2 (4%)	1 (2%)	2 (4%)
HEMATOCELE				1 (2%)
INFLAMMATION, CHRONIC	1 (2%)			
DEPOSIT, NOS	1 (2%)			
ATROPHY, NOS		2 (4%)		
ANGIECTASIS		1 (2%)	1 (2%)	2 (4%)
NERVOUS SYSTEM				
*CHOROID PLEXUS	(50)	(50)	(50)	(50)
LYMPHOCYTIC INFLAM INFILTR			1 (2%)	
#BRAIN	(50)	(50)	(50)	(50)
MINERALIZATION	1 (2%)	4 (8%)	3 (6%)	1 (2%)
HYDROCEPHALUS, NOS	1 (2%)		1 (2%)	
EDEMA, NOS	3 (6%)	2 (4%)	1 (2%)	3 (6%)
HEMORRHAGE	1 (2%)		1 (2%)	
LYMPHOCYTIC INFLAM INFILTR	1 (2%)			
MALACIA		1 (2%)		1 (2%)
#BRAIN STEM	(50)	(50)	(50)	(50)
MALACIA		1 (2%)		
SPECIAL SENSE ORGANS				
*EYE	(50)	(50)	(50)	(50)
MINERALIZATION				1 (2%)
INFLAMMATION, ACUTE				1 (2%)
RETINOPATHY	3 (6%)	1 (2%)	8 (16%)	2 (4%)
CATARACT		3 (6%)	5 (10%)	
*EYE/CORNEA	(50)	(50)	(50)	(50)
INFLAMMATION, CHRONIC		1 (2%)		
MUSCULOSKELETAL SYSTEM				
*BONE/PERIOSTEUM	(50)	(50)	(50)	(50)
INFLAMMATION, ACUTE/CHRONIC			1 (2%)	

TABLE D2. SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	CONTROL (UNTR)	CONTROL (VEH)	LOW DOSE	HIGH DOSE
BODY CAVITIES				
*MEDIASTINUM	(50)	(50)	(50)	(50)
THYROGLOSSAL DUCT CYST				1 (2%)
INFLAMMATION, GRANULOMATOUS				1 (2%)
*EPICARDIUM	(50)	(50)	(50)	(50)
INFLAMMATION, FIBRINOUS	1 (2%)			
PIGMENTATION, NOS		1 (2%)		
ALL OTHER SYSTEMS				
*MULTIPLE ORGANS	(50)	(50)	(50)	(50)
CONGESTION, NOS	1 (2%)	4 (8%)		1 (2%)
EDEMA, NOS				1 (2%)
HEMORRHAGE				2 (4%)
LYMPHOCYTIC INFLAM INFILTR	25 (50%)	26 (52%)	22 (44%)	25 (50%)
INFLAMMATION, ACUTE/CHRONIC		1 (2%)	1 (2%)	
INFLAMMATION, GRANULOMATOUS	1 (2%)	1 (2%)		1 (2%)
INFLAMMATION, PYOGRANULOMATOUS				1 (2%)
NECROSIS, NOS			1 (2%)	1 (2%)
AMYLOIDOSIS	1 (2%)	12 (24%)	6 (12%)	4 (8%)
PIGMENTATION, NOS				1 (2%)
HEMOSIDEROSIS	1 (2%)		1 (2%)	
CYTOPLASMIC VACUOLIZATION		1 (2%)		
ANGIECTASIS				1 (2%)
ADIPOSE TISSUE				
INFLAMMATION, ACUTE/CHRONIC	1			
OMENTUM				
HEMORRHAGE				1
UTERINE LIGAMENT				
NECROSIS, FAT		1	1	
SPECIAL MORPHOLOGY SUMMARY				
NONE				

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

APPENDIX E

ANALYSES OF PRIMARY TUMORS IN RATS AND MICE IN THE TWO-YEAR DERMAL STUDIES OF 2-CHLOROETHANOL

TABLE E1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL

	Vehicle Control	50 mg/kg	100 mg/kg
Skin: Papilloma			
Overall Rates (a)	1/50 (2%)	0/50 (0%)	6/50 (12%)
Adjusted Rates (b)	2.9%	0.0%	15.8%
Terminal Rates (c)	1/34 (3%)	0/37 (0%)	5/37 (14%)
Life Table Tests (d)	P=0.020	P=0.483N	P=0.073
Incidental Tumor Tests (d)	P=0.022	P=0.483N	P=0.077
Cochran-Armitage Trend Test (d)	P=0.016		
Fisher Exact Test		P=0.500N	P=0.056
Skin: Papilloma or Carcinoma			
Overall Rates (a)	3/50 (6%)	1/50 (2%)	6/50 (12%)
Adjusted Rates (b)	8.3%	2.7%	15.8%
Terminal Rates (c)	2/34 (6%)	1/37 (3%)	5/37 (14%)
Life Table Tests (d)	P=0.184	P=0.287N	P=0.283
Incidental Tumor Tests (d)	P=0.196	P=0.303N	P=0.297
Cochran-Armitage Trend Test (d)	P=0.158		
Fisher Exact Test		P=0.309N	P=0.243
Skin: Keratoacanthoma			
Overall Rates (a)	1/50 (2%)	3/50 (6%)	2/50 (4%)
Adjusted Rates (b)	2.0%	7.1%	5.4%
Terminal Rates (c)	0/34 (0%)	1/37 (3%)	2/37 (5%)
Life Table Tests (d)	P=0.424	P=0.310	P=0.517
Incidental Tumor Tests (d)	P=0.302	P=0.269	P=0.441
Cochran-Armitage Trend Test (d)	P=0.399		
Fisher Exact Test		P=0.309	P=0.500
Subcutaneous Tissue: Fibroma			
Overall Rates (a)	2/50 (4%)	6/50 (12%)	1/50 (2%)
Adjusted Rates (b)	5.6%	14.1%	2.7%
Terminal Rates (c)	1/34 (3%)	3/37 (8%)	1/37 (3%)
Life Table Tests (d)	P=0.384N	P=0.158	P=0.474N
Incidental Tumor Tests (d)	P=0.477N	P=0.111	P=0.459N
Cochran-Armitage Trend Test (d)	P=0.417N		
Fisher Exact Test		P=0.134	P=0.500N
Subcutaneous Tissue: Fibroma or Fibrosarcoma			
Overall Rates (a)	3/50 (6%)	8/50 (16%)	1/50 (2%)
Adjusted Rates (b)	8.5%	18.4%	2.7%
Terminal Rates (c)	2/34 (6%)	4/37 (11%)	1/37 (3%)
Life Table Tests (d)	P=0.260N	P=0.127	P=0.280N
Incidental Tumor Tests (d)	P=0.355N	P=0.081	P=0.269N
Cochran-Armitage Trend Test (d)	P=0.290N		
Fisher Exact Test		P=0.100	P=0.309N
Lung: Alveolar/Bronchiolar Carcinoma			
Overall Rates (a)	0/49 (0%)	4/50 (8%)	1/50 (2%)
Adjusted Rates (b)	0.0%	10.8%	2.7%
Terminal Rates (c)	0/33 (0%)	4/37 (11%)	1/37 (3%)
Life Table Tests (d)	P=0.430	P=0.078	P=0.523
Incidental Tumor Tests (d)	P=0.430	P=0.078	P=0.523
Cochran-Armitage Trend Test (d)	P=0.397		
Fisher Exact Test		P=0.061	P=0.505
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma			
Overall Rates (a)	1/49 (2%)	4/50 (8%)	1/50 (2%)
Adjusted Rates (b)	3.0%	10.8%	2.7%
Terminal Rates (c)	1/33 (3%)	4/37 (11%)	1/37 (3%)
Life Table Tests (d)	P=0.557N	P=0.214	P=0.736N
Incidental Tumor Tests (d)	P=0.557N	P=0.214	P=0.736N
Cochran-Armitage Trend Test (d)	P=0.593N		
Fisher Exact Test		P=0.187	P=0.747N

TABLE E1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	Vehicle Control	50 mg/kg	100 mg/kg
Hematopoietic System: Mononuclear Cell Leukemia			
Overall Rates (a)	11/50 (22%)	7/50 (14%)	12/50 (24%)
Adjusted Rates (b)	26.0%	16.1%	27.3%
Terminal Rates (c)	5/34 (15%)	3/37 (8%)	6/37 (16%)
Life Table Tests (d)	P=0.505	P=0.209N	P=0.556
Incidental Tumor Tests (d)	P=0.331	P=0.248N	P=0.377
Cochran-Armitage Trend Test (d)	P=0.450		
Fisher Exact Test		P=0.218N	P=0.500
Liver: Neoplastic Nodule			
Overall Rates (a)	0/50 (0%)	3/50 (6%)	3/50 (6%)
Adjusted Rates (b)	0.0%	8.1%	8.1%
Terminal Rates (c)	0/34 (0%)	3/37 (8%)	3/37 (8%)
Life Table Tests (d)	P=0.114	P=0.136	P=0.136
Incidental Tumor Tests (d)	P=0.114	P=0.136	P=0.136
Cochran-Armitage Trend Test (d)	P=0.101		
Fisher Exact Test		P=0.121	P=0.121
Pituitary: Adenoma			
Overall Rates (a)	12/50 (24%)	11/48 (23%)	15/49 (31%)
Adjusted Rates (b)	27.5%	26.7%	36.6%
Terminal Rates (c)	5/34 (15%)	8/37 (22%)	11/36 (31%)
Life Table Tests (d)	P=0.342	P=0.456N	P=0.390
Incidental Tumor Tests (d)	P=0.174	P=0.581	P=0.202
Cochran-Armitage Trend Test (d)	P=0.263		
Fisher Exact Test		P=0.545N	P=0.304
Pituitary: Carcinoma			
Overall Rates (a)	3/50 (6%)	2/48 (4%)	1/49 (2%)
Adjusted Rates (b)	8.8%	5.3%	2.4%
Terminal Rates (c)	3/34 (9%)	1/37 (3%)	0/36 (0%)
Life Table Tests (d)	P=0.207N	P=0.464N	P=0.287N
Incidental Tumor Tests (d)	P=0.195N	P=0.515N	P=0.276N
Cochran-Armitage Trend Test (d)	P=0.229N		
Fisher Exact Test		P=0.520N	P=0.316N
Pituitary: Adenoma or Carcinoma			
Overall Rates (a)	15/50 (30%)	13/48 (27%)	16/49 (33%)
Adjusted Rates (b)	35.0%	31.1%	38.2%
Terminal Rates (c)	8/34 (24%)	9/37 (24%)	11/36 (31%)
Life Table Tests (d)	P=0.518	P=0.364N	P=0.559
Incidental Tumor Tests (d)	P=0.344	P=0.521N	P=0.374
Cochran-Armitage Trend Test (d)	P=0.430		
Fisher Exact Test		P=0.462N	P=0.473
Adrenal: Cortical Adenoma			
Overall Rates (a)	1/50 (2%)	3/50 (6%)	1/50 (2%)
Adjusted Rates (b)	2.9%	8.1%	2.7%
Terminal Rates (c)	1/34 (3%)	3/37 (8%)	1/37 (3%)
Life Table Tests (d)	P=0.580N	P=0.335	P=0.743N
Incidental Tumor Tests (d)	P=0.580N	P=0.335	P=0.743N
Cochran-Armitage Trend Test (d)	P=0.610		
Fisher Exact Test		P=0.309	P=0.753
Adrenal: Pheochromocytoma			
Overall Rates (a)	8/50 (16%)	13/50 (26%)	10/50 (20%)
Adjusted Rates (b)	22.7%	31.7%	25.3%
Terminal Rates (c)	7/34 (21%)	10/37 (27%)	8/37 (22%)
Life Table Tests (d)	P=0.429	P=0.216	P=0.467
Incidental Tumor Tests (d)	P=0.385	P=0.188	P=0.451
Cochran-Armitage Trend Test (d)	P=0.356		
Fisher Exact Test		P=0.163	P=0.397

TABLE E1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	Vehicle Control	50 mg/kg	100 mg/kg
Adrenal: Pheochromocytoma or Pheochromocytoma, Malignant			
Overall Rates (a)	9/50 (18%)	13/50 (26%)	12/50 (24%)
Adjusted Rates (b)	24.5%	31.7%	30.4%
Terminal Rates (c)	7/34 (21%)	10/37 (27%)	10/37 (27%)
Life Table Tests (d)	P=0.349	P=0.299	P=0.386
Incidental Tumor Tests (d)	P=0.290	P=0.256	P=0.341
Cochran-Armitage Trend Test (d)	P=0.275		
Fisher Exact Test		P=0.235	P=0.312
Thyroid: C-Cell Adenoma			
Overall Rates (a)	6/49 (12%)	4/49 (8%)	3/49 (6%)
Adjusted Rates (b)	17.6%	10.8%	8.3%
Terminal Rates (c)	6/34 (18%)	4/37 (11%)	3/36 (8%)
Life Table Tests (d)	P=0.159N	P=0.315N	P=0.212N
Incidental Tumor Tests (d)	P=0.159N	P=0.315N	P=0.212N
Cochran-Armitage Trend Test (d)	P=0.187N		
Fisher Exact Test		P=0.370N	P=0.243N
Thyroid: C-Cell Adenoma or Carcinoma			
Overall Rates (a)	6/49 (12%)	5/49 (10%)	4/49 (8%)
Adjusted Rates (b)	17.6%	13.5%	11.1%
Terminal Rates (c)	6/34 (18%)	5/37 (14%)	4/36 (11%)
Life Table Tests (d)	P=0.271N	P=0.440N	P=0.331N
Incidental Tumor Tests (d)	P=0.271N	P=0.440N	P=0.331N
Cochran-Armitage Trend Test (d)	P=0.308N		
Fisher Exact Test		P=0.500N	P=0.370N
Pancreatic Islets: Islet Cell Adenoma			
Overall Rates (a)	3/50 (6%)	3/50 (6%)	0/49 (0%)
Adjusted Rates (b)	8.8%	7.6%	0.0%
Terminal Rates (c)	3/34 (9%)	2/37 (5%)	0/36 (0%)
Life Table Tests (d)	P=0.091N	P=0.631N	P=0.111N
Incidental Tumor Tests (d)	P=0.108N	P=0.649N	P=0.111N
Cochran-Armitage Trend Test (d)	P=0.104N		
Fisher Exact Test		P=0.661	P=0.125N
Pancreatic Islets: Islet Cell Adenoma or Carcinoma			
Overall Rates (a)	4/50 (8%)	4/50 (8%)	0/49 (0%)
Adjusted Rates (b)	10.9%	9.5%	0.0%
Terminal Rates (c)	3/34 (9%)	2/37 (5%)	0/36 (0%)
Life Table Tests (d)	P=0.055N	P=0.616N	P=0.058N
Incidental Tumor Tests (d)	P=0.087N	P=0.637	P=0.076N
Cochran-Armitage Trend Test (d)	P=0.062N		
Fisher Exact Test		P=0.643	P=0.061N
Preputial Gland: Adenoma or Carcinoma			
Overall Rates (a)	3/50 (6%)	3/50 (6%)	3/50 (6%)
Adjusted Rates (b)	8.8%	8.1%	7.7%
Terminal Rates (c)	3/34 (9%)	3/37 (8%)	2/37 (5%)
Life Table Tests (d)	P=0.543N	P=0.624N	P=0.624N
Incidental Tumor Tests (d)	P=0.535N	P=0.624N	P=0.615N
Cochran-Armitage Trend Test (d)	P=0.583		
Fisher Exact Test		P=0.661	P=0.661
Testis: Interstitial Cell Tumor			
Overall Rates (a)	45/50 (90%)	41/50 (82%)	44/50 (88%)
Adjusted Rates (b)	95.7%	89.1%	93.6%
Terminal Rates (c)	32/34 (94%)	32/37 (86%)	34/37 (92%)
Life Table Tests (d)	P=0.235N	P=0.138N	P=0.262N
Incidental Tumor Tests (d)	P=0.412N	P=0.168N	P=0.464N
Cochran-Armitage Trend Test (d)	P=0.442N		
Fisher Exact Test		P=0.195N	P=0.500N

TABLE E1. ANALYSIS OF PRIMARY TUMORS IN MALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

(a) Number of tumor-bearing animals/number of animals examined at the site
(b) Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality
(c) Observed tumor incidence at terminal kill
(d) Beneath the vehicle control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between that dosed group and the vehicle controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group is indicated by (N).

TABLE E2. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL

	Vehicle Control	50 mg/kg	100 mg/kg
Hematopoietic System: Mononuclear Cell Leukemia			
Overall Rates (a)	8/50 (16%)	7/50 (14%)	6/50 (12%)
Adjusted Rates (b)	17.1%	16.7%	13.6%
Terminal Rates (c)	4/42 (10%)	5/39 (13%)	2/39 (5%)
Life Table Tests (d)	P=0.392N	P=0.548N	P=0.443N
Incidental Tumor Tests (d)	P=0.439N	P=0.579	P=0.455N
Cochran-Armitage Trend Test (d)	P=0.333N		
Fisher Exact Test		P=0.500N	P=0.387N
Pituitary: Adenoma			
Overall Rates (a)	19/50 (38%)	24/49 (49%)	29/50 (58%)
Adjusted Rates (b)	44.2%	52.9%	61.4%
Terminal Rates (c)	18/42 (43%)	18/39 (46%)	21/39 (54%)
Life Table Tests (d)	P=0.022	P=0.148	P=0.025
Incidental Tumor Tests (d)	P=0.084	P=0.416	P=0.103
Cochran-Armitage Trend Test (d)	P=0.029		
Fisher Exact Test		P=0.184	P=0.036
Pituitary: Carcinoma			
Overall Rates (a)	4/50 (8%)	1/49 (2%)	1/50 (2%)
Adjusted Rates (b)	9.5%	2.3%	2.6%
Terminal Rates (c)	4/42 (10%)	0/39 (0%)	1/39 (3%)
Life Table Tests (d)	P=0.117N	P=0.200N	P=0.202N
Incidental Tumor Tests (d)	P=0.104N	P=0.158N	P=0.202N
Cochran-Armitage Trend Test (d)	P=0.102N		
Fisher Exact Test		P=0.188N	P=0.181N
Pituitary: Adenoma or Carcinoma			
Overall Rates (a)	22/50 (44%)	25/49 (51%)	30/50 (60%)
Adjusted Rates (b)	51.2%	54.0%	63.6%
Terminal Rates (c)	21/42 (50%)	18/39 (46%)	22/39 (56%)
Life Table Tests (d)	P=0.049	P=0.252	P=0.052
Incidental Tumor Tests (d)	P=0.167	P=0.565N	P=0.188
Cochran-Armitage Trend Test (d)	P=0.067		
Fisher Exact Test		P=0.309	P=0.080
Adrenal: Pheochromocytoma			
Overall Rates (a)	3/49 (6%)	3/50 (6%)	3/50 (6%)
Adjusted Rates (b)	7.1%	7.3%	7.7%
Terminal Rates (c)	3/42 (7%)	2/39 (5%)	3/39 (8%)
Life Table Tests (d)	P=0.547	P=0.633	P=0.629
Incidental Tumor Tests (d)	P=0.563	P=0.640N	P=0.629
Cochran-Armitage Trend Test (d)	P=0.574N		
Fisher Exact Test		P=0.651N	P=0.651N
Adrenal: Pheochromocytoma or Pheochromocytoma, Malignant			
Overall Rates (a)	3/49 (6%)	4/50 (8%)	4/50 (8%)
Adjusted Rates (b)	7.1%	9.1%	9.9%
Terminal Rates (c)	3/42 (7%)	2/39 (5%)	3/39 (8%)
Life Table Tests (d)	P=0.392	P=0.472	P=0.462
Incidental Tumor Tests (d)	P=0.493	P=0.640N	P=0.488
Cochran-Armitage Trend Test (d)	P=0.435		
Fisher Exact Test		P=0.511	P=0.511
Thyroid: C-Cell Adenoma			
Overall Rates (a)	2/49 (4%)	3/50 (6%)	4/49 (8%)
Adjusted Rates (b)	4.9%	7.7%	10.5%
Terminal Rates (c)	2/41 (5%)	3/39 (8%)	4/38 (11%)
Life Table Tests (d)	P=0.233	P=0.477	P=0.302
Incidental Tumor Tests (d)	P=0.233	P=0.477	P=0.302
Cochran-Armitage Trend Test (d)	P=0.263		
Fisher Exact Test		P=0.510	P=0.339

TABLE E2. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	Vehicle Control	50 mg/kg	100 mg/kg
Thyroid: C-Cell Adenoma or Carcinoma			
Overall Rates (a)	3/49 (6%)	3/50 (6%)	5/49 (10%)
Adjusted Rates (b)	7.0%	7.7%	13.2%
Terminal Rates (c)	2/41 (5%)	3/39 (8%)	5/38 (13%)
Life Table Tests (d)	P=0.249	P=0.642	P=0.318
Incidental Tumor Tests (d)	P=0.259	P=0.631N	P=0.340
Cochran-Armitage Trend Test (d)	P=0.282		
Fisher Exact Test		P=0.651N	P=0.357
Pancreatic Islets: Islet Cell Adenoma			
Overall Rates (a)	1/49 (2%)	3/49 (6%)	1/50 (2%)
Adjusted Rates (b)	2.4%	7.4%	2.6%
Terminal Rates (c)	1/41 (2%)	2/38 (5%)	1/39 (3%)
Life Table Tests (d)	P=0.592	P=0.289	P=0.751
Incidental Tumor Tests (d)	P=0.609N	P=0.345	P=0.751
Cochran-Armitage Trend Test (d)	P=0.602N		
Fisher Exact Test		P=0.309	P=0.747N
Pancreatic Islets: Islet Cell Adenoma or Carcinoma			
Overall Rates (a)	1/49 (2%)	3/49 (6%)	2/50 (4%)
Adjusted Rates (b)	2.4%	7.4%	5.1%
Terminal Rates (c)	1/41 (2%)	2/38 (5%)	2/39 (5%)
Life Table Tests (d)	P=0.383	P=0.289	P=0.483
Incidental Tumor Tests (d)	P=0.397	P=0.345	P=0.483
Cochran-Armitage Trend Test (d)	P=0.407		
Fisher Exact Test		P=0.309	P=0.508
Mammary Gland: Cystadenoma			
Overall Rates (a)	3/50 (6%)	3/50 (6%)	(f) 3/50 (6%)
Adjusted Rates (b)	7.1%	7.7%	7.7%
Terminal Rates (c)	3/42 (7%)	3/39 (8%)	3/39 (8%)
Life Table Tests (d)	P=0.546	P=0.629	P=0.629
Incidental Tumor Tests (d)	P=0.546	P=0.629	P=0.629
Cochran-Armitage Trend Test (d)	P=0.583		
Fisher Exact Test		P=0.661	P=0.661
Mammary Gland: Adenoma or Adenocarcinoma			
Overall Rates (a)	3/50 (6%)	5/50 (10%)	3/50 (6%)
Adjusted Rates (b)	7.1%	12.1%	7.7%
Terminal Rates (c)	3/42 (7%)	4/39 (10%)	3/39 (8%)
Life Table Tests (d)	P=0.537	P=0.320	P=0.629
Incidental Tumor Tests (d)	P=0.539N	P=0.459	P=0.629
Cochran-Armitage Trend Test (d)	P=0.576		
Fisher Exact Test		P=0.357	P=0.661
Mammary Gland: Fibroadenoma			
Overall Rates (a)	13/50 (26%)	7/50 (14%)	11/50 (22%)
Adjusted Rates (b)	29.4%	17.3%	26.7%
Terminal Rates (c)	11/42 (26%)	6/39 (15%)	9/39 (23%)
Life Table Tests (d)	P=0.431N	P=0.145N	P=0.492N
Incidental Tumor Tests (d)	P=0.438N	P=0.135N	P=0.496N
Cochran-Armitage Trend Test (d)	P=0.356N		
Fisher Exact Test		P=0.106N	P=0.408N
Uterus: Endometrial Stromal Polyp			
Overall Rates (a)	7/50 (14%)	4/50 (8%)	7/50 (14%)
Adjusted Rates (b)	15.6%	10.3%	17.1%
Terminal Rates (c)	5/42 (12%)	4/39 (10%)	6/39 (15%)
Life Table Tests (d)	P=0.508	P=0.306N	P=0.557
Incidental Tumor Tests (d)	P=0.559	P=0.333N	P=0.560N
Cochran-Armitage Trend Test (d)	P=0.561		
Fisher Exact Test		P=0.263N	P=0.613N

TABLE E2. ANALYSIS OF PRIMARY TUMORS IN FEMALE RATS IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	Vehicle Control	50 mg/kg	100 mg/kg
Uterus: Endometrial Stromal Polyp or Sarcoma			
Overall Rates (a)	8/50 (16%)	4/50 (8%)	8/50 (16%)
Adjusted Rates (b)	17.9%	10.3%	19.6%
Terminal Rates (c)	6/42 (14%)	4/39 (10%)	7/39 (18%)
Life Table Tests (d)	P=0.502	P=0.217N	P=0.546
Incidental Tumor Tests (d)	P=0.550	P=0.237N	P=0.565N
Cochran-Armitage Trend Test (d)	P=0.558		
Fisher Exact Test		P=0.179N	P=0.607N

(a) Number of tumor-bearing animals/number of animals examined at the site
(b) Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality
(c) Observed tumor incidence at terminal kill
(d) Beneath the vehicle control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between that dosed group and the vehicle controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group is indicated by (N).
(e) No values are presented because no tumors were observed in 50 mg/kg and vehicle control groups.
(f) One animal had a cystadenoma and a papillary adenoma.

TABLE E3. ANALYSIS OF PRIMARY TUMORS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL

	Untreated Control	Vehicle Control	7.5 mg	15 mg
Integumentary System: Fibroma, Fibrosarcoma, or Neurofibrosarcoma				
Overall Rates (a)	2/50 (4%)	3/50 (6%)	0/50 (0%)	0/43 (0%)
Adjusted Rates (b)	5.4%	10.7%	0.0%	0.0%
Terminal Rates (c)	0/24 (0%)	1/26 (4%)	0/16 (0%)	0/12 (0%)
Life Table Tests (d)		P=0.112N	P=0.232N	P=0.300N
Incidental Tumor Tests (d)		P=0.027N	P=0.114N	P=0.083N
Cochran-Armitage Trend Test (d)		P=0.044N		
Fisher Exact Test			P=0.121N	P=0.151N
Subcutaneous Tissue: Sarcomas				
Overall Rates (a)	2/50 (4%)	(e) 5/50 (10%)	4/50 (8%)	1/43 (2%)
Adjusted Rates (b)	5.4%	17.9%	15.1%	7.7%
Terminal Rates (c)	0/24 (0%)	3/26 (12%)	1/16 (6%)	0/12 (0%)
Life Table Tests (d)		P=0.304N	P=0.531	P=0.379N
Incidental Tumor Tests (d)		P=0.062N	P=0.534N	P=0.103N
Cochran-Armitage Trend Test (d)		P=0.111N		
Fisher Exact Test			P=0.500N	P=0.140N
Lung: Alveolar/Bronchiolar Adenoma				
Overall Rates (a)	6/50 (12%)	8/50 (16%)	10/50 (20%)	9/43 (21%)
Adjusted Rates (b)	25.0%	26.0%	43.0%	46.0%
Terminal Rates (c)	6/24 (25%)	4/26 (15%)	4/16 (25%)	4/12 (33%)
Life Table Tests (d)		P=0.062	P=0.105	P=0.078
Incidental Tumor Tests (d)		P=0.282	P=0.294	P=0.279
Cochran-Armitage Trend Test (d)		P=0.314		
Fisher Exact Test			P=0.397	P=0.364
Lung: Alveolar/Bronchiolar Carcinoma				
Overall Rates (a)	4/50 (8%)	6/50 (12%)	9/50 (18%)	3/43 (7%)
Adjusted Rates (b)	13.7%	18.1%	38.1%	16.6%
Terminal Rates (c)	2/24 (8%)	3/26 (12%)	4/16 (25%)	1/12 (8%)
Life Table Tests (d)		P=0.501	P=0.095	P=0.587N
Incidental Tumor Tests (d)		P=0.383N	P=0.249	P=0.355N
Cochran-Armitage Trend Test (d)		P=0.306N		
Fisher Exact Test			P=0.288	P=0.324N
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma				
Overall Rates (a)	10/50 (20%)	14/50 (28%)	18/50 (36%)	11/43 (26%)
Adjusted Rates (b)	37.2%	40.9%	67.1%	55.7%
Terminal Rates (c)	8/24 (33%)	7/26 (27%)	8/16 (50%)	5/12 (42%)
Life Table Tests (d)		P=0.132	P=0.029	P=0.196
Incidental Tumor Tests (d)		P=0.528	P=0.155	P=0.579N
Cochran-Armitage Trend Test (d)		P=0.464N		
Fisher Exact Test			P=0.260	P=0.490N
Hematopoietic System: Granulocytic Leukemia				
Overall Rates (a)	3/50 (6%)	2/50 (4%)	4/50 (8%)	2/43 (5%)
Adjusted Rates (b)	7.9%	4.2%	13.4%	5.1%
Terminal Rates (c)	0/24 (0%)	0/26 (0%)	0/16 (0%)	0/12 (0%)
Life Table Tests (d)		P=0.456	P=0.259	P=0.614
Incidental Tumor Tests (d)		P=0.441N	P=0.557	P=0.580N
Cochran-Armitage Trend Test (d)		P=0.520		
Fisher Exact Test			P=0.339	P=0.632N
Hematopoietic System: Lymphoma				
Overall Rates (a)	3/50 (6%)	4/50 (8%)	10/50 (20%)	2/43 (5%)
Adjusted Rates (b)	6.6%	11.2%	24.7%	5.0%
Terminal Rates (c)	0/24 (0%)	1/26 (4%)	0/16 (0%)	0/12 (0%)
Life Table Tests (d)		P=0.525N	P=0.044	P=0.538N
Incidental Tumor Tests (d)		P=0.104N	P=0.233	P=0.235N
Cochran-Armitage Trend Test (d)		P=0.407N		
Fisher Exact Test			P=0.074	P=0.413N

TABLE E3. ANALYSIS OF PRIMARY TUMORS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	Untreated Control	Vehicle Control	7.5 mg	15 mg
Hematopoietic System: Lymphoma or Leukemia				
Overall Rates (a)	6/50 (12%)	6/50 (12%)	14/50 (28%)	4/43 (9%)
Adjusted Rates (b)	14.0%	14.9%	34.9%	9.9%
Terminal Rates (c)	0/24 (0%)	1/26 (4%)	0/16 (0%)	0/12 (0%)
Life Table Tests (d)		P=0.505	P=0.022	P=0.583N
Incidental Tumor Tests (d)		P=0.086N	P=0.196	P=0.205N
Cochran-Armitage Trend Test (d)		P=0.464N		
Fisher Exact Test			P=0.039	P=0.470N
Liver: Adenoma				
Overall Rates (a)	1/50 (2%)	2/49 (4%)	3/50 (6%)	1/43 (2%)
Adjusted Rates (b)	4.2%	7.7%	16.7%	8.3%
Terminal Rates (c)	1/24 (4%)	2/26 (8%)	2/16 (13%)	1/12 (8%)
Life Table Tests (d)		P=0.511	P=0.294	P=0.716
Incidental Tumor Tests (d)		P=0.586	P=0.348	P=0.716
Cochran-Armitage Trend Test (d)		P=0.449N		
Fisher Exact Test			P=0.510	P=0.549N
Liver: Carcinoma				
Overall Rates (a)	6/50 (12%)	9/49 (18%)	6/50 (12%)	4/43 (9%)
Adjusted Rates (b)	22.7%	30.9%	32.5%	20.1%
Terminal Rates (c)	4/24 (17%)	7/26 (27%)	4/16 (25%)	1/12 (8%)
Life Table Tests (d)		P=0.463N	P=0.570	P=0.496N
Incidental Tumor Tests (d)		P=0.206N	P=0.485N	P=0.238N
Cochran-Armitage Trend Test (d)		P=0.128N		
Fisher Exact Test			P=0.274N	P=0.173N
Liver: Carcinoma or Hepatoblastoma				
Overall Rates (a)	6/50 (12%)	9/49 (18%)	6/50 (12%)	5/43 (12%)
Adjusted Rates (b)	22.7%	30.9%	32.5%	22.7%
Terminal Rates (c)	4/24 (17%)	7/26 (27%)	4/16 (25%)	1/12 (8%)
Life Table Tests (d)		P=0.524	P=0.570	P=0.604
Incidental Tumor Tests (d)		P=0.329N	P=0.485N	P=0.380N
Cochran-Armitage Trend Test (d)		P=0.214N		
Fisher Exact Test			P=0.274N	P=0.274N
Liver: Adenoma, Carcinoma, or Hepatoblastoma				
Overall Rates (a)	7/50 (14%)	11/49 (22%)	9/50 (18%)	6/43 (14%)
Adjusted Rates (b)	26.5%	38.1%	46.4%	29.7%
Terminal Rates (c)	5/24 (21%)	9/26 (35%)	6/16 (38%)	2/12 (17%)
Life Table Tests (d)		P=0.474	P=0.341	P=0.587
Incidental Tumor Tests (d)		P=0.351N	P=0.532	P=0.398N
Cochran-Armitage Trend Test (d)		P=0.180N		
Fisher Exact Test			P=0.382N	P=0.219N
Adrenal Cortex: Adenoma				
Overall Rates (a)	4/48 (8%)	0/48 (0%)	2/49 (4%)	3/43 (7%)
Adjusted Rates (b)	8.3%	0.0%	12.5%	25.0%
Terminal Rates (c)	4/24 (17%)	0/26 (0%)	2/16 (13%)	3/12 (25%)
Life Table Tests (d)		P=0.013	P=0.138	P=0.024
Incidental Tumor Tests (d)		P=0.013	P=0.138	P=0.024
Cochran-Armitage Trend Test (d)		P=0.066		
Fisher Exact Test			P=0.253	P=0.102

TABLE E3. ANALYSIS OF PRIMARY TUMORS IN MALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

(a) Number of tumor-bearing animals/number of animals examined at the site
(b) Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality
(c) Observed tumor incidence at terminal kill
(d) Beneath the vehicle control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between that dosed group and the vehicle controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group is indicated by (N).
(e) A skin fibroma was also present in one animal.

TABLE E4. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL

	Untreated Control	Vehicle Control	7.5 mg	15 mg
Lung: Alveolar/Bronchiolar Adenoma				
Overall Rates (a)	7/50 (14%)	7/50 (14%)	6/49 (12%)	6/50 (12%)
Adjusted Rates (b)	23.9%	24.0%	26.1%	27.7%
Terminal Rates (c)	4/24 (17%)	4/26 (15%)	4/19 (21%)	5/20 (25%)
Life Table Tests (d)		P=0.497	P=0.537	P=0.551
Incidental Tumor Tests (d)		P=0.536N	P=0.543N	P=0.611N
Cochran-Armitage Trend Test (d)		P=0.440N		
Fisher Exact Test			P=0.516N	P=0.500N
Lung: Alveolar/Bronchiolar Carcinoma				
Overall Rates (a)	3/50 (6%)	2/50 (4%)	5/49 (10%)	3/50 (6%)
Adjusted Rates (b)	9.7%	6.4%	18.9%	12.5%
Terminal Rates (c)	1/24 (4%)	1/26 (4%)	1/19 (5%)	1/20 (5%)
Life Table Tests (d)		P=0.328	P=0.163	P=0.415
Incidental Tumor Tests (d)		P=0.475	P=0.345	P=0.565
Cochran-Armitage Trend Test (d)		P=0.421		
Fisher Exact Test			P=0.210	P=0.500
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma				
Overall Rates (a)	10/50 (20%)	9/50 (18%)	10/49 (20%)	9/50 (18%)
Adjusted Rates (b)	31.9%	29.4%	38.4%	37.9%
Terminal Rates (c)	5/24 (21%)	5/26 (19%)	5/19 (26%)	6/20 (30%)
Life Table Tests (d)		P=0.347	P=0.298	P=0.394
Incidental Tumor Tests (d)		P=0.502	P=0.547	P=0.548
Cochran-Armitage Trend Test (d)		P=0.551		
Fisher Exact Test			P=0.480	P=0.603N
Hematopoietic System: Granulocytic Leukemia				
Overall Rates (a)	0/50 (0%)	1/50 (2%)	4/50 (8%)	3/50 (6%)
Adjusted Rates (b)	0.0%	2.4%	11.2%	7.2%
Terminal Rates (c)	0/24 (0%)	0/26 (0%)	0/20 (0%)	0/20 (0%)
Life Table Tests (d)		P=0.239	P=0.180	P=0.311
Incidental Tumor Tests (d)		P=0.325	P=0.210	P=0.414
Cochran-Armitage Trend Test (d)		P=0.252		
Fisher Exact Test			P=0.181	P=0.309
Hematopoietic System: Malignant Lymphoma, Histiocytic Type				
Overall Rates (a)	1/50 (2%)	0/50 (0%)	3/50 (6%)	1/50 (2%)
Adjusted Rates (b)	3.2%	0.0%	9.9%	4.5%
Terminal Rates (c)	0/24 (0%)	0/26 (0%)	0/20 (0%)	0/20 (0%)
Life Table Tests (d)		P=0.334	P=0.105	P=0.459
Incidental Tumor Tests (d)		P=0.351	P=0.150	P=0.527
Cochran-Armitage Trend Test (d)		P=0.378		
Fisher Exact Test			P=0.121	P=0.500
Hematopoietic System: Lymphoma, All Malignant				
Overall Rates (a)	12/50 (24%)	8/50 (16%)	11/50 (22%)	10/50 (20%)
Adjusted Rates (b)	30.3%	21.1%	30.5%	32.1%
Terminal Rates (c)	1/24 (4%)	1/26 (4%)	1/20 (5%)	2/20 (10%)
Life Table Tests (d)		P=0.274	P=0.258	P=0.309
Incidental Tumor Tests (d)		P=0.472	P=0.454	P=0.525
Cochran-Armitage Trend Test (d)		P=0.352		
Fisher Exact Test			P=0.305	P=0.397
Hematopoietic System: Lymphoma or Leukemia				
Overall Rates (a)	12/50 (24%)	9/50 (18%)	15/50 (30%)	13/50 (26%)
Adjusted Rates (b)	30.3%	23.0%	38.4%	37.0%
Terminal Rates (c)	1/24 (4%)	1/26 (4%)	1/20 (5%)	2/20 (10%)
Life Table Tests (d)		P=0.167	P=0.114	P=0.190
Incidental Tumor Tests (d)		P=0.328	P=0.205	P=0.380
Cochran-Armitage Trend Test (d)		P=0.208		
Fisher Exact Test			P=0.121	P=0.235

TABLE E4. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

	Untreated Control	Vehicle Control	7.5 mg	15 mg
Circulatory System: Hemangioma				
Overall Rates (a)	1/50 (2%)	3/50 (6%)	2/50 (4%)	0/50 (0%)
Adjusted Rates (b)	3.4%	10.5%	6.7%	0.0%
Terminal Rates (c)	0/24 (0%)	2/26 (8%)	0/20 (0%)	0/20 (0%)
Life Table Tests (d)		P=0.120N	P=0.567N	P=0.166N
Incidental Tumor Tests (d)		P=0.078N	P=0.424N	P=0.145N
Cochran-Armitage Trend Test (d)		P=0.082N		
Fisher Exact Test			P=0.500N	P=0.122N
Circulatory System: Hemangiosarcoma				
Overall Rates (a)	0/50 (0%)	0/50 (0%)	3/50 (6%)	0/50 (0%)
Adjusted Rates (b)	0.0%	0.0%	12.5%	0.0%
Terminal Rates (c)	0/24 (0%)	0/26 (0%)	2/20 (10%)	0/20 (0%)
Life Table Tests (d)		P=0.584	P=0.094	(e)
Incidental Tumor Tests (d)		P=0.635N	P=0.125	(e)
Cochran-Armitage Trend Test (d)		P=0.640		
Fisher Exact Test			P=0.121	(e)
Circulatory System: Hemangioma or Hemangiosarcoma				
Overall Rates (a)	1/50 (2%)	3/50 (6%)	5/50 (10%)	0/50 (0%)
Adjusted Rates (b)	3.4%	10.5%	18.3%	0.0%
Terminal Rates (c)	0/24 (0%)	2/26 (8%)	2/20 (10%)	0/20 (0%)
Life Table Tests (d)		P=0.199N	P=0.279	P=0.166N
Incidental Tumor Tests (d)		P=0.135N	P=0.422	P=0.145N
Cochran-Armitage Trend Test (d)		P=0.133N		
Fisher Exact Test			P=0.357	P=0.122N
Liver: Adenoma or Carcinoma				
Overall Rates (a)	1/50 (2%)	3/50 (6%)	0/49 (0%)	1/50 (2%)
Adjusted Rates (b)	3.4%	10.5%	0.0%	3.2%
Terminal Rates (c)	0/24 (0%)	2/26 (8%)	0/20 (0%)	0/20 (0%)
Life Table Tests (d)		P=0.226N	P=0.159N	P=0.379N
Incidental Tumor Tests (d)		P=0.168N	P=0.124N	P=0.291N
Cochran-Armitage Trend Test (d)		P=0.177N		
Fisher Exact Test			P=0.125N	P=0.309N
Pituitary: Chromophobe Adenoma				
Overall Rates (a)	(f) 4/46 (9%)	2/48 (4%)	2/49 (4%)	3/47 (6%)
Adjusted Rates (b)	15.1%	6.9%	7.7%	15.0%
Terminal Rates (c)	3/24 (13%)	1/26 (4%)	1/20 (5%)	3/20 (15%)
Life Table Tests (d)		P=0.309	P=0.633	P=0.385
Incidental Tumor Tests (d)		P=0.358	P=0.642N	P=0.417
Cochran-Armitage Trend Test (d)		P=0.397		
Fisher Exact Test			P=0.684N	P=0.490
Mammary Gland: Adenoma or Adenocarcinoma				
Overall Rates (a)	4/50 (8%)	2/50 (4%)	4/50 (8%)	5/50 (10%)
Adjusted Rates (b)	11.1%	5.5%	14.0%	17.1%
Terminal Rates (c)	0/24 (0%)	0/26 (0%)	1/20 (5%)	0/20 (0%)
Life Table Tests (d)		P=0.132	P=0.304	P=0.177
Incidental Tumor Tests (d)		P=0.252	P=0.497	P=0.354
Cochran-Armitage Trend Test (d)		P=0.169		
Fisher Exact Test			P=0.339	P=0.218
Uterus: Leiomyoma or Leiomyosarcoma				
Overall Rates (a)	1/50 (2%)	3/49 (6%)	2/49 (4%)	3/50 (6%)
Adjusted Rates (b)	2.0%	11.5%	10.0%	12.0%
Terminal Rates (c)	1/24 (4%)	3/26 (12%)	2/20 (10%)	2/20 (10%)
Life Table Tests (d)		P=0.481	P=0.621N	P=0.567
Incidental Tumor Tests (d)		P=0.514	P=0.621N	P=0.609
Cochran-Armitage Trend Test (d)		P=0.579N		
Fisher Exact Test			P=0.500N	P=0.651N

TABLE E4. ANALYSIS OF PRIMARY TUMORS IN FEMALE MICE IN THE TWO-YEAR DERMAL STUDY OF 2-CHLOROETHANOL (Continued)

(a) Number of tumor-bearing animals/number of animals examined at the site
(b) Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality
(c) Observed tumor incidence at terminal kill
(d) Beneath the vehicle control incidence are the P values associated with the trend test. Beneath the dosed group incidence are the P values corresponding to pairwise comparisons between that dosed group and the vehicle controls. The life table analysis regards tumors in animals dying prior to terminal kill as being (directly or indirectly) the cause of death. The incidental tumor test regards these lesions as nonfatal. The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates. A negative trend or lower incidence in a dosed group is indicated by (N).
(e) No values are presented because no tumors were observed in the 15 mg and control groups.
(f) One acidophil adenoma was also present.

APPENDIX F

GENETIC TOXICOLOGY OF 2-CHLOROETHANOL

TABLE F1. MUTAGENICITY OF 2-CHLOROETHANOL IN SALMONELLA

Strain	Dose (µg/plate)	Revertants/plate (a) −S9	+S9 (rat)	+S9 (hamster)
TA100	0	145 ± 4.3	131 ± 5.9	121 ± 3.5
	100	--	122 ± 0.3	--
	333	144 ± 8.1	130 ± 12.0	136 ± 3.3
	1,000	127 ± 3.8	134 ± 8.5	141 ± 3.5
	3,333	138 ± 4.9	143 ± 12.7	150 ± 5.4
	6,667	190 ± 8.7	--	154 ± 6.0
	10,000	249 ± 5.5	157 ± 7.1	181 ± 4.2
TA1535	0	23 ± 2.4	12 ± 0.7	10 ± 0.6
	333	23 ± 3.2	11 ± 1.5	15 ± 0.3
	1,000	21 ± 5.1	17 ± 1.0	13 ± 1.5
	3,333	28 ± 3.5	28 ± 3.9	27 ± 5.3
	6,667	23 ± 1.2	56 ± 8.6	48 ± 3.5
	10,000	38 ± 0.6	63 ± 2.2	66 ± 4.2
TA1537	0	8 ± 0.7	14 ± 2.9	8 ± 0.6
	100	9 ± 1.9	13 ± 1.7	8 ± 1.9
	333	7 ± 1.9	7 ± 1.0	7 ± 0.7
	1,000	7 ± 1.2	9 ± 1.8	9 ± 1.2
	3,333	9 ± 1.2	11 ± 3.2	4 ± 2.0
	10,000	7 ± 0.9	6 ± 0.3	6 ± 1.2
TA98	0	28 ± 2.3	36 ± 6.8	28 ± 2.2
	100	20 ± 3.2	33 ± 1.5	23 ± 5.8
	333	23 ± 3.9	29 ± 1.5	27 ± 1.3
	1,000	23 ± 1.9	37 ± 4.3	29 ± 5.0
	3,333	22 ± 1.3	32 ± 3.4	26 ± 4.2
	10,000	24 ± 3.8	29 ± 2.2	25 ± 3.5

(a) The S9 fractions were prepared from the livers of Aroclor 1254-induced animals (male Sprague-Dawley rats and male Syrian hamsters). Cells and test compound or solvent (water) were incubated for 20 minutes at 37° C in the presence of either S9 or buffer. After the addition of soft agar, the contents of each tube were poured onto minimal medium, and the plates were incubated at 37° C for 48 hours (Haworth et al., 1983). The experiment was performed twice, each in triplicate; because the results were similar, data from only one experiment are shown.

TABLE F2. INDUCTION OF SEX-LINKED RECESSIVE LETHAL MUTATIONS IN DROSOPHILA BY 2-CHLOROETHANOL

Route of Exposure	Dose (ppm)	No. of Lethals/No. of X Chromosomes Tested (a) Mating 1	Mating 2	Mating 3	Total
Inhalation	0	0/881	1/800	2/785	3/2,466
		0/1,115	0/1,135	1/1,042	1/3,292
					4/5,758 (0.07%)
	400	3/954	0/928	0/884	3/2,766
		0/823	2/824	0/778	2/2,425
					5/5,191 (0.10%)

(a) The sex-linked recessive lethal assay was performed essentially as described by Abrahamson and Lewis (1971). Canton-S males (24-h-old) were exposed to an atmosphere of the test compound for 4 h and then allowed to recover for 48 h. Exposed males were mated to three *Basc* females for 3 d and given fresh females at 2-d intervals to produce three broods of 3, 2, and 2 d, after which the parents were discarded. F_1 heterozygous females were crossed to their siblings and placed in individual vials. F_1 daughters from the same parental males were kept together to identify clusters; none was found. After 17 d, presumptive lethals were identified as vials containing no wild-type males; these were retested.

APPENDIX G

CHEMICAL CHARACTERIZATION

OF 2-CHLOROETHANOL

I. Identity and Purity Determinations Performed by the Analytical Chemistry Laboratory

A. Lot No. A3X

1. Physical Properties

a. Appearance: Light yellow liquid

b. Boiling Point:

Determined	Literature Values
124.0°-128.0° C at 751 mm clear liquid distilled, yellow residue (macrodistillation)	128° - 130° C (Merck, 1968)

c. Index of Refraction

Determined	Literature Values
n_D^{20} 1.4421	n_D^{20} 1.4419 (Merck, 1968)

2. Spectral Data

a. Infrared

	Determined	Literature Values
(1) Instrument:	Beckman IR-12	
(2) Cell:	Barnes Engineering liquid cell	
(3) Results:	See Figure 6	Identical to literature spectrum (Sadtler Standard Spectra)

b. Ultraviolet/Visible

	Determined	Literature Values
(1) Instrument:	Cary 118	
(2) Solvent:	95% Ethanol	
(3) Results:	λ_{max} (nm) ε 305 936 ± 0.17 (δ) No absorption 800-350 nm at 0.2 g/ml	No literature reference found. Spectrum consistent with structure.

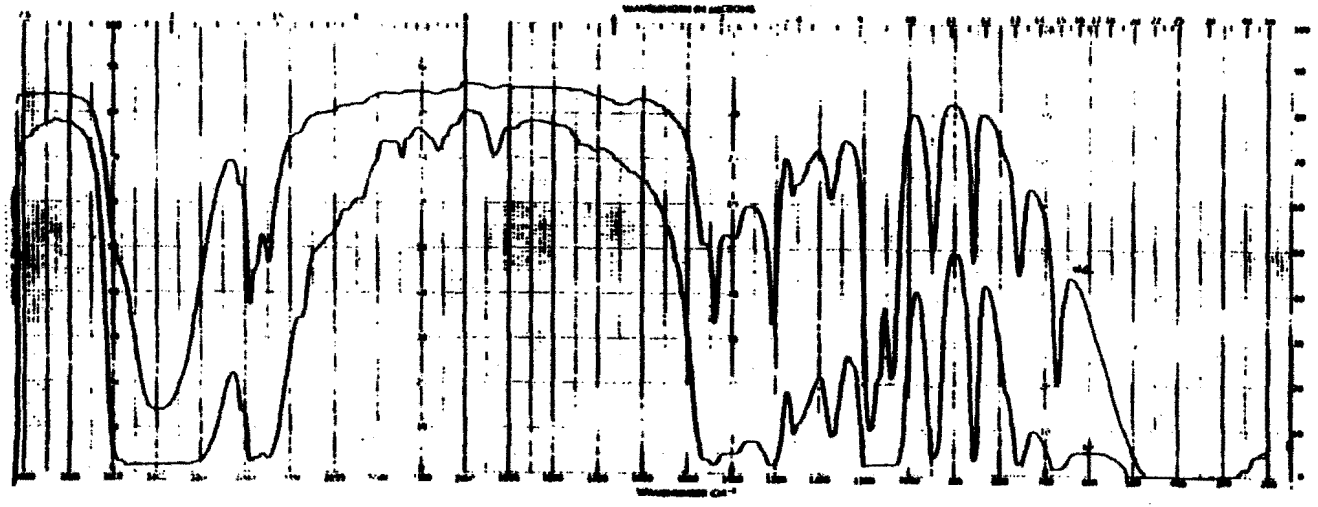


FIGURE 6. INFRARED ABSORPTION SPECTRUM OF 2-CHLOROETHANOL (LOT NO. A3X)

c. Nuclear Magnetic Resonance

	Determined	Literature Values
(1) Instrument:	Varian HA-100	
(2) Solvent:	Neat with internal tetramethylsilane standard	
(3) Assignments:	See Figure 7	Identical to literature spectrum (Sadtler Standard Spectrum)
(4) Chemical Shift (δ):		
a 3.56 ppm b 3.75 ppm c 4.75 ppm	a, b: A_2B_2 pattern	
(5) Integration Ratios:		
a, b	4.10	
c	0.90	

3. **Water Analysis (Karl Fischer):** 0.090% ± 0.003(δ)%

4. **Elemental Analysis:**

Element	C	H	Cl
Theory	29.83	6.26	44.04
Determined	29.68 29.79	6.29 6.18	44.13 43.97

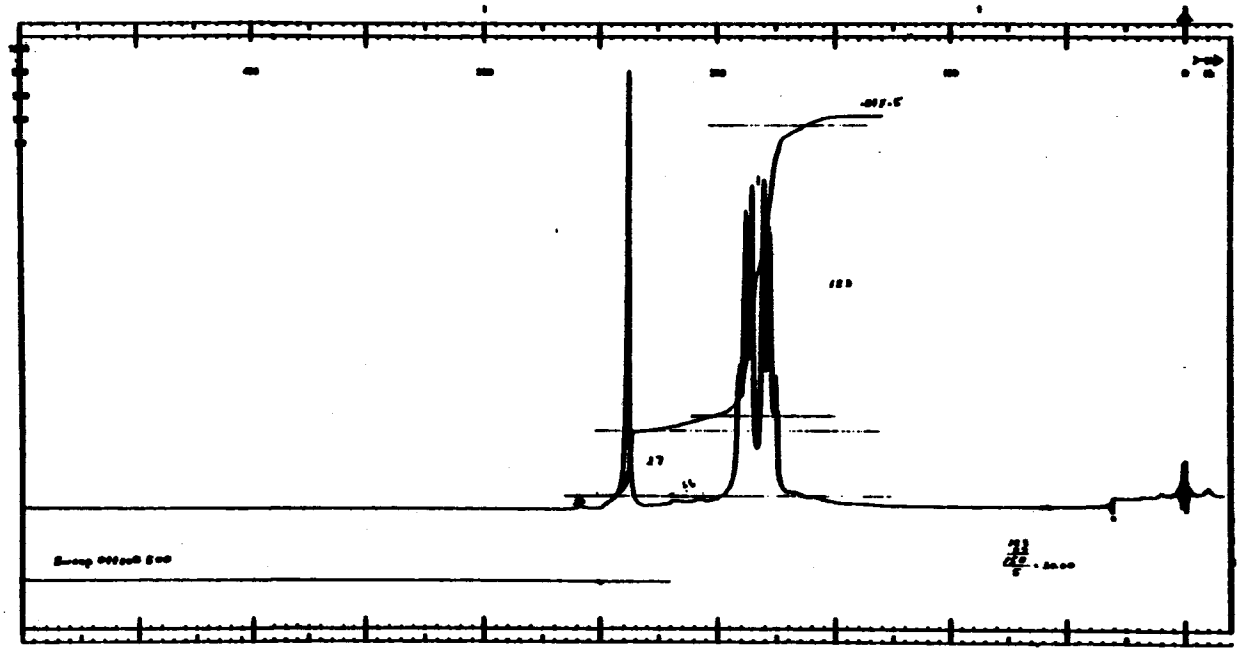


FIGURE 7. NUCLEAR MAGNETIC RESONANCE SPECTRUM OF 2-CHLOROETHANOL (LOT NO. A3X)

5. Chromatographic Analyses

Gas Chromatography:

a. System 1:

(1) Instrument: Tracor MT-220
(2) Column: 3% OV-17 on W(HP) 80/100 mesh, 1.8 m × 4 mm ID
(3) Detector: Flame ionization
(4) Temperature Program: 60°-120° C at 5° C/min

(5) Results: Single homogenous peak at 1.0 min

b. System 2:

(1) Instrument: Bendix 2500
(2) Column: Porapak-Q, 80/100 mesh, 1.8 m × 4 mm ID
(3) Detector: Flame ionization
(4) Temperature Program: 100° C, 1 min; 100°-200° C at 8° C/min; 200° C, 10 min

(5) Results: Major peak and one impurity

Peak No.	Time (min)	Retention Time Relative to Major Peak	Area (percent of major peak)
1	16.3	1.00	100
2	20.3	1.25	0.20

c. System 3:

(1) Instrument: Tracor MT-220
(2) Column: Chromosorb 102, 1.8 m × 2 mm ID
(3) Detector: Flame ionization
(4) Temperature Program: 100°-235° C at 10° C/min

(5) Results: Major peak and two impurities

Peak No.	Retention Time (min)	Retention Time Relative to Major Peak	Area (percent of major peak)
1	6.2	1.00	100
2	7.9	1.28	0.25
3	12.6	2.03	0.14

B. Lot No. C 742

1. Physical Properties--Appearance: Light yellow liquid

2. Spectral Data

a. Infrared	**Determined**	**Literature Values**
(1) Instrument:	Perkin-Elmer 283	
(2) Cell:	Thin film between silver chloride plates	
(3) Results:	See Figure 8	Spectrum consistent with literature spectrum (Sadtler Standard Spectra)

b. Ultraviolet/Visible	**Determined**	**Literature Values**
(1) Instrument:	Cary 219	
(2) Solvent:	95% Ethanol	
(3) Results:	No absorbance from 800 to 350 nm at a concentration of 1% (v/v). No maximum from 350 to 215 nm but a gradual increase in absorbance toward 215 nm at a concentration of 1% (v/v).	No literature reference found. Spectrum consistent with structure.

c. Nuclear Magnetic Resonance	**Determined**	**Literature Values**
(1) Instrument:	Varian EM-360A	
(2) Solvent:	Neat with internal tetramethylsilane standard	
(3) Assignments:	See Figure 9	Spectrum consistent with literature reference (Sadtler Standard Spectra)
(4) Chemical Shift (δ):	a m, 3.65 ppm b m, 3.78 ppm c s, 4.87 ppm	

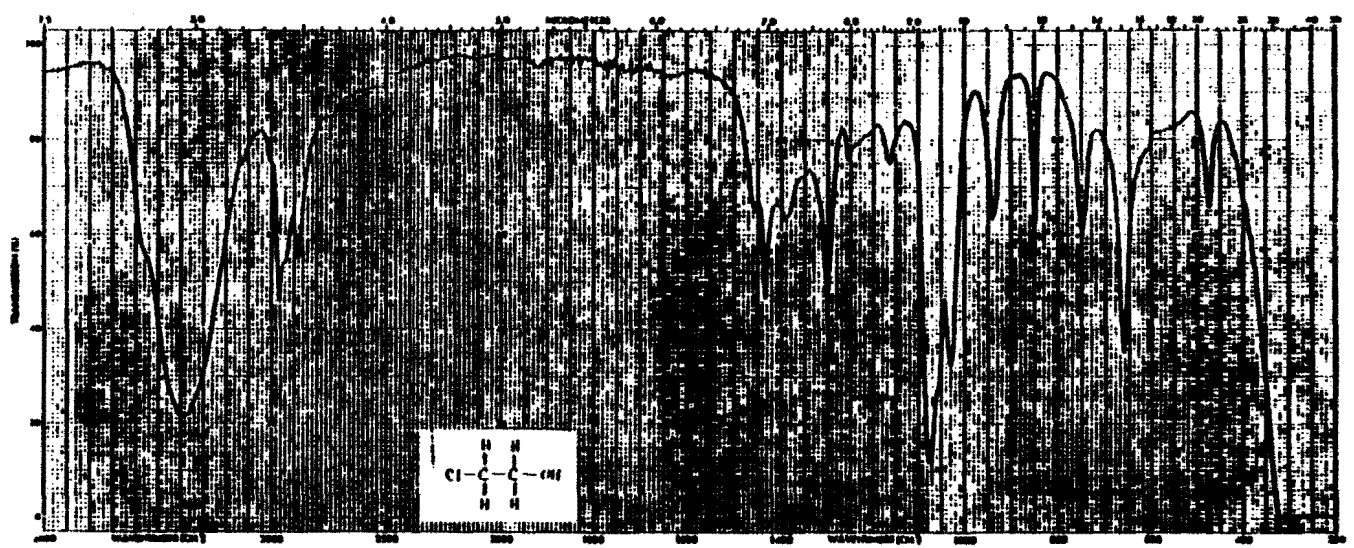


FIGURE 8. INFRARED ABSORPTION SPECTRUM OF 2-CHLOROETHANOL (LOT NO. C742)

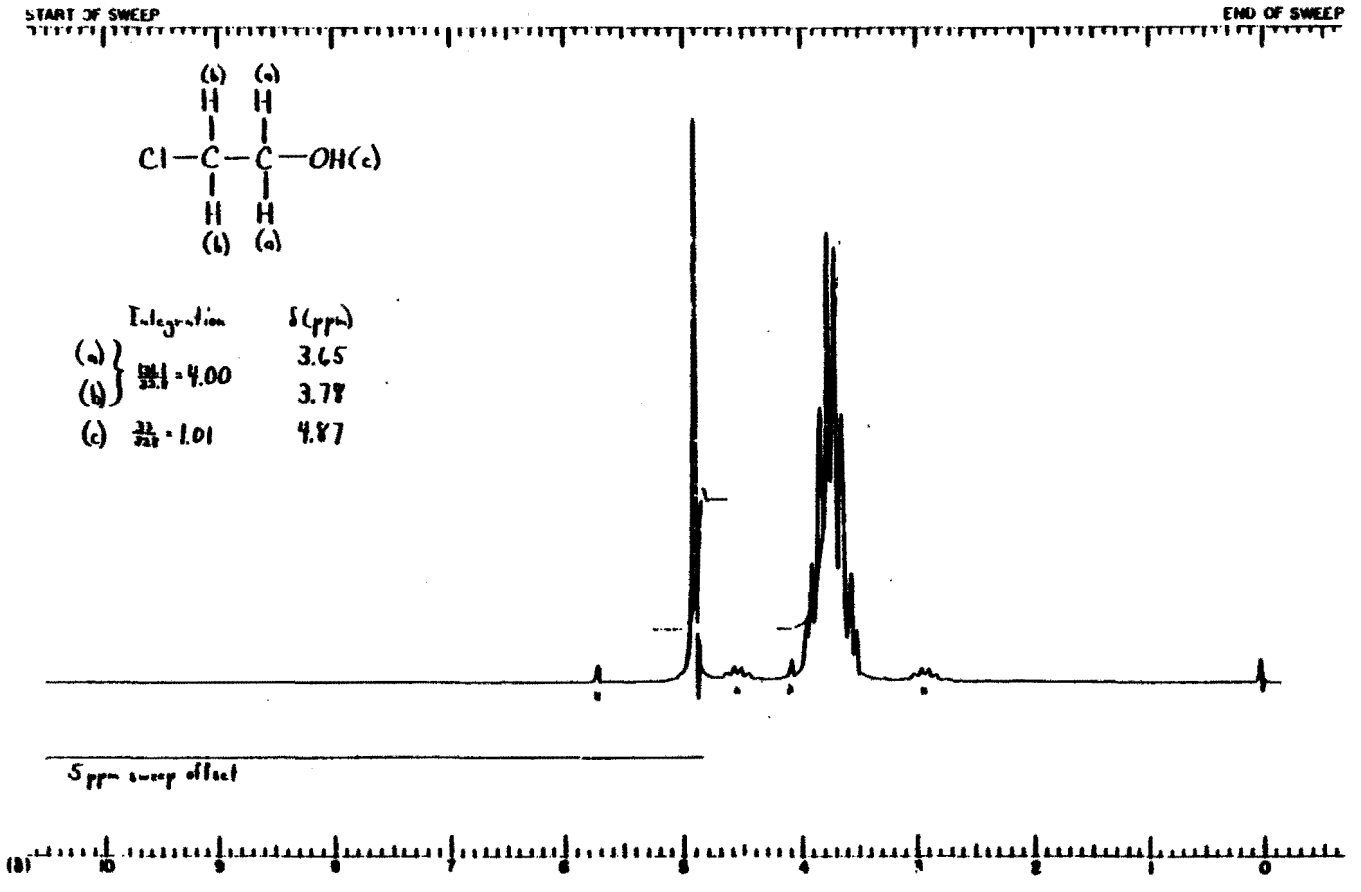


FIGURE 9. NUCLEAR MAGNETIC RESONANCE SPECTRUM OF 2-CHLOROETHANOL (LOT NO. C742)

(5) Integration Ratios:

a, b] 4.00
c 1.01

3. Water Analysis (Karl Fischer): 0.082% ± 0.004(δ)%

4. Elemental Analysis:

Element	C	H	Cl
Theory	29.83	6.26	44.04
Determined	29.78 29.54	6.15 6.25	44.46 44.32

5. Chromatographic Analyses: Gas Chromatography

Instrument: Varian 3700
Detector: Flame ionization
Inlet Temperature: 200° C
Detector Temperature: 250° C
Carrier Gas: Nitrogen
Carrier flow rate: 70 cc/min

a. System 1:

Column: Porapak QS, 80/100 mesh; 1.8 m × 4 mm ID, glass
Oven Temperature Program: 100° C for 1 min, then 100°-200° C at 8° C/min
Samples Injected: Neat liquid (4 µl) and solutions of 1.0% and 0.5% (v/v) 2-chloroethanol in methylene chloride to detect impurities, quantitate the major peak, and check for detector overload.

Results: Major peak and five impurities. Two impurities with a combined area of 0.03% of the major peak that eluted before the major peak. The other three impurities eluted after the major peak and had a combined area of 1.4% that of the major peak. The largest impurity had an area 1.3% of the major peak area.

Peak No.	Retention Time (min)	Retention Time Relative to Major Peak	Area (percent of major peak)
1	4.2	0.32	0.02
2	8.3	0.63	0.01
3	13.1	1.00	100
4	14.7	1.12	0.04
5	16.2	1.24	0.04
6	36.0	2.75	1.3

Note: A sample of the previous lot (lot no. A3X) was run on this system concomitantly with the current batch. The following results were obtained:

Peak No.	Retention Time (min)	Retention Time Relative to Major Peak	Area (percent of major peak)
1	4.2	0.32	0.02
2	13.1	1.00	100
3	14.7	1.12	0.24
4	36.5	2.79	0.14

b. System 2:

Column: 10% Carbowax 20M-TPA on 80/100 Chromosorb W(AW); 1.8 m × 4 mm ID, glass
Oven Temperature Program: 60° C for 6 min, then 60°-200° C at 10° C/min
Samples Injected: Neat liquid (4 µl) and solutions of 1.0% and 0.5% (v/v) 2- chloroethanol in methylene chloride to detect impurities, quantitate the major peak, and check for detector overload.

Results: Major peak and eight impurities. Three of the impurities with a combined area of 0.08% of the major peak area eluted before the major peak. Three of the other five impurities eluted after the major peak and had a combined area of 1.8% of the major peak area. The largest impurity had an area 1.6% of the major peak area.

Peak No.	Retention Time (min)	Retention Time Relative to Major Peak	Area (percent of major peak)
1	0.9	0.07	0.01
2	6.0	0.45	0.06
3	12.1	0.92	0.01
4	13.2	1.00	100
5	15.5	1.17	0.01
6	18.1	1.37	1.60
7	18.5	1.40	0.17
8	18.7	1.42	0.02
9	23.7	1.80	0.01

Note: A sample of the previous lot (lot no. A3X) was run on this system concomitantly with the current batch. The following results were obtained:

Peak No.	Retention Time (min)	Retention Time Relative to Major Peak	Area (percent of major peak)
1	6.0	0.45	0.29
2	13.2	1.00	100
3	18.1	1.37	0.22

II. Test Chemical Stability at the Testing Laboratory

A. Analytical Method:

1. Infrared Spectroscopy:

Instrument: Perkin-Elmer model 283B, 398, or 457
Phase: Neat liquid

Results: All bulk spectra were consistent with those of the reference sample stored at −20° C and with those supplied by the analytical chemistry laboratory.

2. Gas Chromatography:

a. System 1:

Instrument: Varian 2100
Detection: Flame ionization
Column: 1.8 m × 2 mm ID glass packed with 100/120 mesh Chromosorb 102
Oven Temperature Program: 100°-235° C at 10° C/min

b. System 2:

Instrument: Shimadzu GC Mini-2 with C-RIA Data System
Detector: Flame ionization
Inlet Temperature: 225° C
Detector Temperature: 225° C
Carrier Gas: Nitrogen
Carrier flow rate: 70 ml/min
Column: 1.8 m × 2.6 mm ID silanized glass with Porapak QS on 80/100 mesh
Oven Temperature Program: 100° C for 1 min; 100°- 200° C at 8° C/min; 200° C for 10 min.
Samples Injection: 3 µl neat for each sample; 3 µl solutions of 1.0% and 0.5% 2-chloroethanol in methylene chloride to quantitate the major peak and to check for detector overloading.

B. Results:

Date of Analysis	Percent 2-Chloroethanol Bulk	Reference
Lot No. A3X		
01/08/75	99.6	--
(a) 01/31/78	99.6	--
(a) 06/17/78	99.8	(b) 21.9
10/16/79	99.5	99.9
01/18/80	99.4	99.9
05/21/80	99.8	
09/12/80	99.9	99.9
11/24/80	99.9	--
Lot No. C-742		
11/24/80	100.0	--
03/13/81	99.0	99.0
07/16/81	99.0	99.0
02/25/82	99.9	97.5

(a) Analyzed by system 1; subsequent analyses by system 2.
(b) Reference sample believed to have reacted with the storage vial liner. A new reference sample was taken and stored in glass.

C. Conclusion: No notable degradation was observed during the studies.

III. A Special Reanalysis of Lot A3X Performed by the Analytical Chemistry Laboratory in February 1980

A. Analytical Method: Gas Chromatography

Instrument: Varian 3700
Detector: Flame ionization
Inlet Temperature: 200° C
Detector Temperature: 250° C
Carrier Gas: Nitrogen
Carrier flow rate: 70 cc/min
Column: Porapak QS, 80/100 mesh; 1.8 m × 4 mm ID, glass
Oven Temperature Program: 100° C for 1 min, then 100° -200° C at 8° C/min
Samples Injected: Neat liquid (3 µl) and solutions of 1.0% and 0.5% (v/v) 2-chloroethanol in methylene chloride to detect impurities, quantitate the major peak, and check for detector overload.

B. Results: Both the sample and reference chromatograms indicated a major peak followed by two impurities. This chromatogram with Porapak QS was extended to 38 min to observe the small peak previously seen on Chromosorb 102 but not on Porapak because of its long retention time. The chromatogram is tabulated below:

Peak No.	Retention Time (min)	Retention Time Relative to Major Peak	Area (percent of major peak)	
			Bulk	Reference
1	13.1	1.00	100	100
2	15.2	1.16	0.20	0.19
3	38.0	2.90	0.16	0.08

(a) Stored at −20° C

C. Conclusion : No notable differences were observed between this and the original analysis..

APPENDIX H

PREPARATION AND CHARACTERIZATION OF DOSE MIXTURES

APPENDIX H. PREPARATION AND CHARACTERIZATION

I. Sample Preparation

Solutions of 2-chloroethanol in 70% (v/v) ethanol-water were prepared in duplicate on five different days over a 14-day period. The days were chosen so that the solutions, when analyzed on the 14th day, represented samples that had been stored 0, 0 + 3 hours open to air and light, 1, 7, 11, and 14 days at room temperature and 0, 7, and 14 days at 5° C. All samples were stored in the dark after preparation, except the 3-hour stability sample.

The solutions were prepared by dissolving approximately 0.5 g of 2-chloroethanol, weighed to the nearest 0.1 mg, in a few ml of 70% ethanol-water and diluting to 25 ml with the solvent. After thorough mixing, about 7 ml of each solution was sealed in an 8.5-ml septum vial for the stability study. Samples exposed to air and light for 3 hours were prepared in duplicate by dissolving 2 g of 2-chloroethanol, weighed to the nearest milligram, in a few milliliters of solvent and diluting to 100 ml. Approximately 95 ml of this solution was placed in a 125-ml Erlenmeyer flask for the 3-hour study. The concentration of the chemical in the solutions was approximately 20 mg/ml.

II. Analysis Procedure

A 5-ml aliquot of each sample was pipetted into individual 100-ml volumetric flasks containing 5 ml of an internal standard solution (isoamyl alcohol, 10 mg/ml in methanol), and diluted to 100 ml with methanol. The concentration of 2-chloroethanol in the solutions was determined by the gas chromatographic system described below.

Instrument: Varian 3700 equipped with an autosampler and CDS-111 data system
Column: Glass, 6 ft × 2 mm ID, packed with Chromosorb 102, 100 to 120 mesh
Detector: Flame ionization
Temperatures: Injector--190° C
Oven--180 C, isothermal
Detector--230 C
Carrier gas: Nitrogen at 30 ml/min
Injection volume: 4 µl
Retention times: Test chemical--4.4 min
Internal standard--7.9 min

The instrument was calibrated with two independently weighed stock standard solutions of 2-chloroethanol (~ 20 mg/ml in 70% ethanol). Aliquots (3,5, and 6 ml) of the solutions were mixed with 5 ml of internal standard solution and diluted for the samples as described above.

III. Quality Assurance Measures

Analyses were performed by making duplicate injections of sample solutions prepared in duplicate from each stability sample tested in duplicate (determinations), following a randomized order for the standards and samples. All determinations were related to an internal standard incorporated into the solutions. Results were calculated from relative response factors (RRF) computed from peak areas of the calibration standards by the following equations:

$$RRF = \frac{\text{milligrams per milliliter test chemical} \times \text{peak area of internal standard}}{\text{peak area of test chemical} \times \text{milligrams per milliliter of internal standard}}$$

then the milligrams per gram chemical in the vehicle =

$$\frac{RRF \times \text{sample peak area} \times \text{milligrams per milliliter internal standard} \times DF}{\text{peak area internal standard} \times \text{gram of sample}}$$

where DF = dilution factor

The linearity of the gas chromatographic system was evaluated with standard dilutions of 2-chloroethanol in 70% ethanol-water at concentrations of approximately 1.2, 1.0, and 0.6 mg/ml. The correlation coefficient was calculated from the linear regression equation by the standard curve data.

IV. Results

A. Two-week Stability Study

Storage Time (Days)	Storage Temperature	Milligrams 2-Chloroethanol Found/Milliliter 70% Ethanol-water	Target Milligrams/ Milliliter 2-Chloroethanol in 70% Ethanol-water	Percent Recovery (Found/Target x 100)
0		20.2	20.2	100.0
		20.6	20.4	101.0
				Av = 100.5 ± 0.5
0 + 3 h open to air and light	Ambient	20.4	20.0	102.0
		20.2	20.0	101.0
				Av = 101.5 ± 0.5
1	Ambient	19.7	19.9	99.0
		20.1	20.1	100.0
				Av = 100.5 ± 0.5
7	Ambient	20.2	20.2	100.0
		19.9	20.0	99.5
				Av = 99.8 ± 0.3
7	5°C	20.4	20.2	101.0
		19.9	20.0	99.5
				Av = 100.3 ± 0.8
11	Ambient	19.9	19.9	100.0
		19.8	19.8	100.0
				Av = 100.0 ± 0.0
14	Ambient	20.1	20.3	99.0
		19.8	19.9	99.5
				Av = 99.3 ± 0.3
14	5°C	20.3	20.3	100.0
		19.9	19.9	100.0
				Av = 100.0 ± 0.0

B. Evaporation Study

To determine how much of the sample was lost by evaporation during 3-hour exposure to the atmosphere, individual 125-ml Erlenmeyer flasks were filled with approximately 2 ml, 45 ml, and 95 ml of dose mixture, in duplicate, and were placed uncovered in a standard laboratory hood for 3 hours. The flasks were each weighed before and after the exposure period to determine loss by evaporation. The results follow.

Volume in Flask (ml)	Weight Loss (g)	Weight of Solution (g)	Percent Evaporation Loss by Weight
~95	1.2	83.18	1.44
~45	0.63	39.23	1.61
~2	0.19	1.75	12.7

The concentration of 2-chloroethanol in the 3-hour samples was 101.5% of the target concentration and reflects the apparent concentration of 2-chloroethanol caused by evaporation of the vehicle.

V. **Conclusions:** 2-Chloroethanol (2% w/v) in 70% (v/v) ethanol/water was found to be stable for 14 days at room temperature in a covered container.

APPENDIX I

ANALYSIS OF DOSE MIXTURES: METHODS

APPENDIX I. ANALYSIS: METHODS

I. Analytical Chemistry Laboratory

A. Procedure

1. Preparation of Standards: Two standard solutions of 2-chloroethanol were prepared independently in methanol at concentrations of 6.26 and 5.17 mg/ml. These solutions were diluted with methanol to make four additional standards at concentrations of 3.13, 2.59, 1.57, and 1.29 mg/ml. Aliquots (8 ml) of the six standard solutions were pipetted into individual 25-ml volumetric flasks. A blank was prepared by diluting 4 ml of undosed 70% ethanol to 100 ml with methanol and then pipetting an 8-ml aliquot of the diluted blank into a 25-ml volumetric flask. The spiked standards and the blank were used in the analysis procedure described below.

2. Preparation of the Referee Sample: Two portions (4 ml each) of the referee skin paint sample were pipetted into individual 100-ml volumetric flasks and diluted to volume with methanol. After being mixed, an 8-ml aliquot of each sample was pipetted into individual 25-ml volumetric flasks; then the samples were analyzed by the procedure described below.

3. Analysis: A 14-ml volume of internal standard solution (*n*-amyl alcohol in methanol, 1 mg/ml) was added to each standard, blank, and the referee sample flask was prepared as described above and diluted to 25 ml with methanol. After the solutions were mixed, the 2-chloroethanol content was determined by the gas chromatographic system described below:

Instrument: Varian 3700 Gas Chromatograph with Autosampler and Varian CDS 111-C integrator
Column: Chromosorb 102, 100/120 mesh; 1.8 m × 2 mm ID, glass silanized
Detection: Flame ionization
Inlet Temperature 250° C
Detector Temperature: 300° C
Carrier Gas: Nitrogen
Carrier flow rate: 30 cc/min
Oven Temperature Program: 200° C, isothermal
Samples Injected: 3 µl.
Retention Times: 2-Chloroethanol: 3.2 min
n-Amyl alcohol (Internal Standard): 5.9 min

B. Results: The total amount of 2-chloroethanol in the referee skin paint samples was determined from the linear regression equation computed from the standard data, relating the ratio obtained by dividing the peak area of each spiked standard by the peak area of the internal standard, to the amount of chemical in the respective spiked standard.

II. Testing Laboratory

Procedure: Samples were analyzed, as submitted, by gas chromatography. The instrument used was a Varian Model 2100 equipped with flame ionization detectors. A silanized glass column, 1.8 m × 2.6 mm ID, containing 100/120 mesh Chromosorb 102 was used. The column temperature was 170° C, with a nitrogen (carrier) flow rate of 30 ml/min. Suitable aliquots, from 1 to 4 µl, of the samples were injected directly into the chromatograph without prior treatment. Concentrations were determined by reference to a calibration curve obtained by analysis under the same parameters of a standard solution of 2-chloroethanol in 80% ethanol.

APPENDIX J

ANALYSES OF DOSE MIXTURES: DATA

TABLE J1. CONCENTRATIONS OF 2-CHLOROETHANOL IN THE TWO-YEAR DERMAL STUDIES

Date Mixed	Target Concentration (mg/ml)	Actual Concentration	Percent of Target Concentration
12/14/79	25.0	22.6	90.4
	50.3	47.3	94.0
	75.0	71.8	95.7
	150.0	141.0	94.0
1/25/80	150.0	161.0	107.3
	150.0	156.0	104.0
2/01/80	35.0	36.5	104.3
	70.0	68.8	98.3
	75.0	73.4	97.6
	150.0	142.0	94.7
3/28/80	58.0	57.0	98.3
	75.0	75.0	100.0
	116.0	113.0	97.4
	150.0	152.0	101.3
5/27/80	75.0	78.2	104.3
	150.0	156.0	104.0
	67.0	69.2	103.3
	135.0	133.0	98.5
7/18/80	75.0	76.4	101.9
	150.0	154.0	102.7
	72.6	75.3	103.7
	146.0	145.0	99.3
9/12/80	75.0	80.8	107.7
	150.0	159.0	106.0
	76.6	81.8	106.8
	153.0	162.0	105.9
11/07/80	75.0	81.6	108.8
	150.0	154.0	102.7
	77.4	85.8	110.9
	156.0	160.0	102.6
	77.4	75.6	97.7
1/02/81	75.0	70.9	94.5
	150.0	148.0	98.7
	82.2	83.2	101.2
	165.0	165.0	100.0
2/27/81	75.0	84.4	(b) 112.5
	150.0	164.0	109.3
	87.0	94.8	109.0
	174.0	185.0	106.3
3/03/81	75.0	79.6	(c) 106.1
4/24/81	75.0	78.6	104.8
	150.0	144.5	96.3
	93.4	93.9	100.5
	186.0	172.0	92.5
6/19/81	75.0	42.0	(b) 56.0
	150.0	149.5	99.7
	95.8	102.5	107.0
	192.0	192.5	100.3
	75.0	81.7	(c) 108.9
8/14/81	75.0	75.8	101.1
	150.0	148.5	99.0
	99.0	98.2	99.2
	197.9	194.8	98.4
10/7/81	75.0	79.7	106.3
	150.0	160.0	106.7
	99.0	104.0	105.1
	197.9	214.0	108.1
Mean			101.0
Standard deviation			7.90
Coefficient of variation (percent)			7.82
Range			56.1-112.5
Number of samples			55

(a) The data presented are the average of the results of duplicated analyses.
(b) Out of specifications, not used in the study
(c) Remix, not included in the mean

TABLE J2. RESULTS OF REFEREE ANALYSES OF 2-CHLOROETHANOL/ETHANOL MIXTURES IN THE TWO-YEAR DERMAL STUDIES

Date Mixed	Target Concentration (mg/ml)	Determined Concentration	
		Testing Laboratory	Analytical Laboratory
3/28/80	150.0	--	157.0
7/18/80	75.0	76.4	75.8
1/02/81	150.0	148.0	153.0
8/14/81	99.0	98.2	100.2

APPENDIX K

SENTINEL ANIMAL PROGRAM

APPENDIX K. SENTINEL ANIMAL PROGRAM

I. Methods

Rodents used in the Carcinogenesis Program of the National Toxicology Program are produced in optimally clean facilities to eliminate potential pathogens that may affect test results. The Sentinel Animal Program is part of the periodic monitoring of animal health that occurs during the toxicologic evaluation of chemical compounds. Under this program, the disease state of the rodents in the program is monitored via viral serology on sera from extra (sentinel) animals in the test rooms. These animals are untreated, and they and the test animals are both subject to identical environmental conditions. The sentinel animals come from the same production source and weanling groups as the animals used for the studies of chemical compounds.

Fifteen Swiss CD-1 mice of each sex and 15 F344/N rats of each sex are selected at the time of randomization and allocation of the animals to the various study groups. Five animals of each designated sentinel group are killed at 6, 12, and 18 months on study. Data from animals surviving 24 months are collected from 5/50 randomly selected control animals of each sex and species. The blood from each animal is collected and clotted, and the serum is separated. The serum is cooled on ice and shipped to Microbiological Associates' Comprehensive Animal Diagnostic Service for determination of the viral antibody titers. The following tests are performed:

	Hemagglutination Inhibition	Complement Fixation	ELISA
Rats	PVM (pneumonia virus of mice) KRV (Kilham rat virus) H-1 (Toolan's H-1 virus) Sendai (12, 18, 24 mo)	RCV (rat coronavirus) Sendai (6 mo)	
Mice	PVM Reo 3 (reovirus type 3) GDVII (Theiler's encephalomyelitis virus) Poly (polyoma virus) Sendai MVM (minute virus of mice) Ectro (infectious ectromelia)	M.Ad. (mouse adenovirus) LCM (lymphocytic choriomeningitis virus MHV (mouse hepatitis virus) (6, 12, 18 mo)	MHV (mouse hepatitis virus) (24 mo)

II. Results

See Table K1.

TABLE K1. MURINE VIRUS ANTIBODY DETERMINATIONS FOR RATS AND MICE IN THE TWO-YEAR DERMAL STUDIES OF 2-CHLOROETHANOL

Interval (months)	Positive serology/ Number sera tested		Positive Serologic Reaction for
	MALE	FEMALE	
RATS			
6	--	--	--
12	4/4	3/3	Sendai
18	5/5	3/5	Sendai
24	5/5	5/5	Sendai
MICE			
6	3/5	2/5	MVM
	2/5	2/2	MHV
12	3/5	1/4	Sendai
	1/5	2/4	MVM
18	(a)	1/5	Sendai
24	1/5	2/5	MVM
	2/5	2/5	(b) MHV

(a) Not done
(b) 24-month MHV results by ELISA method

APPENDIX L

INGREDIENTS, NUTRIENT COMPOSITION, AND MEASURED CONTAMINANT LEVELS OF THE NIH 07 DIET

Pelleted Diet: December 1979 to January 1982

(Manufactured by Zeigler Bros., Inc.)
(Gardners, PA)

TABLE L1. INGREDIENTS OF THE NIH 07 DIET (a)

Ingredients (b)	Percent by Weight
Ground #2 yellow shelled corn	24.50
Ground hard winter wheat	23.00
Soybean meal (49% protein)	12.00
Fish meal (60% protein)	10.00
Wheat middlings	10.00
Dried skim milk	5.00
Alfalfa meal (dehydrated, 17% protein)	4.00
Corn gluten meal (60% protein)	3.00
Soy oil	2.50
Brewer's dried yeast	2.00
Dry molasses	1.50
Dicalcium phosphate	1.25
Ground limestone	0.50
Salt	0.50
Pre-mixes (vitamin and mineral)	0.25

(a) NIH, 1978; NCI, 1976
(b) Ingredients should be ground to pass through a U.S. Standard Screen #16 before mixing.

TABLE L2. VITAMINS AND MINERALS IN THE NIH 07 DIET (a)

	Amount	Source
Vitamins		
A	5,500,000 IU	Stabilized vitamin A palmitate or acetate
D_3	4,600,000 IU	D activated animal sterol
d-A-tocopheryl acetate	20,000 IU	
Riboflavin	3.4 g	
Thiamine	10.0 g	Thiamine mononitrate
Niacin	30.0 g	
d-Pantothenic acid	18.0 g	d-Calcium pantothenate
Folic acid	2.2 g	
Pyridoxine	1.7 g	Pyridoxine hydrochloride
B_{12}	4,000 µg	
Biotin	140.0 mg	d-biotin
K_3	2.8 g	Menadione activity
Choline	560.0 g	Choline chloride
Minerals		
Iron	120.0 g	Iron sulfate
Manganese	60.0 g	Manganous oxide
Zinc	16.0 g	Zinc oxide
Copper	4.0 g	Copper sulfate
Iodine	1.4 g	Calcium iodate
Cobalt	0.4 g	Cobalt carbonate

(a) Per ton (2,000 lb) of finished product

TABLE L3. NUTRIENT COMPOSITION OF THE NIH 07 DIET (a)

Nutrient	Mean ± Standard Deviation	Range	Number of Samples
Crude protein (percent by weight)	24.29 ± 0.81	22.7 - 26.1	24
Crude fat (percent by weight)	4.81 ± 0.38	4.1 - 5.5	24
Crude fiber (percent by weight)	3.31 ± 0.50	1.4 - 4.3	24
Ash (percent by weight)	6.76 ± 0.44	5.83 - 7.43	24
Vitamins			
Vitamin A (IU/kg)	10,192 ± 2,534	6,700 - 17,000	24
Vitamin D (IU/kg)	6,300		1
A-tocopherol (ppm)	37.6	31.1 - 44.0	2
Thiamine (ppm)	16.2 ± 4.5	7.4 - 27	24
Riboflavin (ppm)	6.9	6.1 - 7.4	2
Niacin (ppm)	75	65 - 85	2
Pantothenic acid (ppm)	30.2	29.8 - 30.5	2
Pyridoxine (ppm)	7.2	5.6 - 8.8	2
Folic acid (ppm)	2.1	1.8 - 2.4	2
Biotin (ppm)	0.24	0.21 - 0.27	2
Vitamin B_{12} (ppb)	12.8	10.6 - 15.0	2
Choline (ppm)	3,315	3,200 - 3,430	2
Minerals			
Calcium (percent)	1.34 ± 0.20	0.81 - 1.69	24
Phosphorous (percent)	1.01 ± 0.08	0.82 - 1.10	24
Potassium (percent)	0.809	0.772 - 0.846	2
Chloride (percent)	0.557	0.479 - 0.635	2
Sodium (percent)	0.304	0.258 - 0.349	2
Magnesium (percent)	0.172	0.166 - 0.177	2
Sulfur (percent)	0.278	0.270 - 0.285	2
Iron (ppm)	418	409 - 426	2
Manganese (ppm)	90.8	86.0 - 95.5	2
Zinc (ppm)	55.1	54.2 - 56.0	2
Copper (ppm)	12.68	9.65 - 15.70	2
Iodine (ppm)	2.58	1.52 - 3.64	2
Chromium (ppm)	1.86	1.79 - 1.93	2
Cobalt (ppm)	0.57	0.49 - 0.65	2
Essential Amino Acids (percent of total diet)			
Arginine	1.260	1.21 - 1.31	2
Cystine	0.395	0.39 - 0.40	2
Glycine	1.175	1.15 - 1.20	2
Histidine	0.553	0.530 - 0.576	2
Isoleucine	0.908	0.881 - 0.934	2
Leucine	1.905	1.85 - 1.96	2
Lysine	1.250	1.20 - 1.30	2
Methionine	0.310	0.306 - 0.314	2
Phenylalanine	0.967	0.960 - 0.974	2
Threonine	0.834	0.840 - 0.827	2
Tryptophan	0.175	0.171 - 0.178	2
Tyrosine	0.587	0.566 - 0.607	2
Valine	1.085	1.05 - 1.12	2
Essential Fatty Acids (percent of total diet)			
Linoleic	2.37		1
Linolenic	0.308		1
Arachidonic	0.008		1

(a) One or two batches of feed analyzed for nutrients reported in this table were done on batches of diet manufactured in January and/or April 1983.

TABLE L4. CONTAMINANT LEVELS OF THE NIH 07 DIET

Contaminant	Mean ± Standard Deviation	Range	Number of Samples
Arsenic (ppm)	0.39 ± 0.23	<0.05 - 1.06	24
Lead (ppm)	0.91 ± 0.51	0.50 - 2.65	24
Mercury (ppm)	(a) <0.05		
Cadmium (ppm)	0.11 ± 0.07	(b) <0.05 - 0.40	24
Selenium (ppm)	0.29 ± 0.09	0.10 - 0.52	24
Aflatoxins (ppb)	(a, c) <10		
Nitrate nitrogen (ppm) (d)	7.00 ± 3.70	(e) <0.1 - 13.0	24
Nitrite nitrogen (ppm) (d)	1.45 ± 1.02	<0.1 - 4.0	24
BHA (ppm) (f)	3.83 ± 3.88	(g) <0.2 - 13.0	24
BHT (ppm) (f)	2.97 ± 1.74	0.8 - 7.6	24
Aerobic plate count (CFU/g)	48,786 ± 32,701	(h) 5,500 - 120,000	22
	70,970 ± 81,410	(i) 5,500 - 320,000	24
Coliform (MPN/g) (j)	39 ± 57	(k) <3 - 240	20
	270 ± 580	(l) <3 - 2400	24
E. coli (MPN/g)	(m) <3		24
Total nitrosamines (ppb)	7.63 ± 6.67	(n, o) 2.2 - 24.5	21
	29.77 ± 64.59	(n, p) 2.2 - 273	24
N-Nitrosodimethylamine (ppb)	5.81 ± 6.30	(n, o) 1.1 - 20.0	21
	27.79 ± 64.31	(n, p) 1.1 - 272	24
N-Nitrosopyrrolidine (ppb)	1.44 ± 0.89	0.5 - 3.5	24
Pesticides (ppm)			
Alpha BHC (q)	(a) <0.01		24
Beta BHC	(a) <0.02		24
Gamma BHC - Lindane	(a) <0.01		24
Delta BHC	(a) <0.01		24
Heptachlor	(a) <0.01		24
Aldrin	(a) <0.01		24
Heptachlor epoxide	(a) <0.01		24
DDE	(a) <0.01		24
DDD	(a) <0.01		24
HCB	(a) <0.01		24
Mirex	(a) <0.01		24
Methoxychlor	(a) <0.05	(r) 0.09 (8/26/81)	24
Dieldrin	(a) <0.01		24
Endrin	(a) <0.01		24
Telodrin	(a) <0.01		24
Chlordane	(a) <0.05		24
Toxaphene	(a) <0.1		24
Estimated PCB's	(a) <0.2		24
Ronnel	(a) <0.01		24
Ethion	(a) <0.02		24
Trithion	(a) <0.05		24
Diazinon	(a) <0.1	(r) 0.2 (4/27/81)	24
Methyl parathion	(a) <0.02		24
Ethyl parathion	(a) <0.02		24
Malathion	<0.10 ± 0.07	(s) <0.05 - 0.27	24
Endosulfan I	(a) <0.01		24
Endosulfan II	(a) <0.01		24
Endosulfan sulfate	(a) <0.03		24

TABLE L4. CONTAMINANT LEVELS OF THE NIH 07 DIET (Continued)

(a) All values were less than the detection limit; the detection limit is given as the mean.
(b) Three batches contained more than 0.1 ppm.
(c) Detection limit reduced from 10 ppb to 5 ppb after 7/81
(d) Source of contamination: alfalfa, grains, and fish meal
(e) Two batches contained less than 0.1 ppm.
(f) Source of contamination: soy oil and fish meal
(g) Six batches contained less than 0.5 ppm.
(h) Excludes two extreme values 300,000 and 320,000 obtained in batches produced 12/21/79 and 2/26/80. CFU = Colony Forming Unit.
(i) Includes two extreme values 300,000 and 320,000 obtained in batches produced 12/21/79 and 2/26/80
(j) MPN = most probable number
(k) Excludes four values in the range 1,100 to 2,400 obtained in batches produced 2/4/80, 2/26/80, 5/29/80 and 12/16/80
(l) Includes four values in the range 1,100 to 2,400 obtained in batches produced 2/4/80, 2/26/80, 5/29/80 and 12/16/80
(m) All values were <3 MPN/g.
(n) All values are corrected for percent recovery.
(o) Excludes three values in the range of 115-280 ppb obtained in batches produced 1/26/81, 2/23/81, and 4/27/81
(p) Includes three values in the range of 115-280 ppb obtained in batches produced 1/26/81, 2/23/81, and 4/27/81
(q) BHC is hexachlorocyclohexane or benzene hexachloride.
(r) One value above the detection limit (noted in the range column) was obtained on this date.
(s) Nine batches contained more than 0.05 ppm.

APPENDIX M

ENVIRONMENTAL CONDITIONS DURING THE TWO-YEAR DERMAL STUDIES OF 2-CHLOROETHANOL

TABLE M1. TEMPERATURE RECORD FOR THE TWO-YEAR DERMAL STUDIES OF 2-CHLOROETHANOL

Room No.	Month/ Year	T av (a) (°F)	SD (b)	n (c)	T max (°F)	T min (°F)	n in Specification	Percent of Readings in Specification	Hours Out of Specification (d) Above	Below
A211E	1/80	74.4	2.0	18	79	71	15	83.3	24	12
	2/80	74.6	2.9	41	80	62	30	73.2	120	12
	3/80	73.4	1.9	42	80	70	37	88.1	24	36
	4/80	73.5	1.5	44	78	71	40	90.9	12	36
	5/80	73.7	1.4	42	78	71	38	90.5	12	36
	6/80	73.1	2.0	42	77	65	36	85.7	12	60
	7/80	74.5	1.4	46	78	72	42	91.3	48	0
	8/80	74.5	1.9	42	80	72	37	88.1	60	0
	9/80	73.8	1.3	42	77	70	40	95.2	12	12
	10/80	74.3	2.2	46	79	69	34	73.9	120	24
	11/80	74.7	2.2	40	82	71	30	75.0	108	12
	12/80	73.9	2.6	46	80	68	33	71.7	108	48
	1/81	74.0	2.1	44	79	71	33	75.0	96	36
	2/81	74.1	2.0	40	80	70	34	85.0	48	24
	3/81	74.6	1.7	44	78	72	37	84.1	84	0
	4/81	74.7	2.1	44	80	72	34	77.3	120	0
	5/81	74.3	1.9	42	82	72	38	90.5	48	0
	6/81	74.7	1.9	44	79	72	35	79.6	108	0
	7/81	74.1	2.0	46	78	69	34	73.9	108	36
	8/81	74.6	1.7	42	77	70	36	85.7	60	12
	9/81	75.0	1.7	44	79	72	34	77.3	120	0
	10/81	74.9	1.5	44	77	71	35	79.6	96	12
	11/81	75.8	2.4	42	85	72	26	61.9	192	0
	12/81	75.7	1.6	45	80	73	32	71.1	156	0
	1/82	76.5	2.1	42	83	72	16	38.1	312	0
	2/82	75.5	1.8	15	79	72	10	66.7	60	0
Study Summary		74.5	1.9	1,069	79.4	70.5	846	79.0	2,268	408

(a) Temperature (T) average; recommended temperature for animal room was 74° ± 2° F (23° ± 1° C).
(b) SD = standard deviation
(c) n = number of readings
(d) Approximation

TABLE M2. RELATIVE HUMIDITY RECORD FOR THE TWO-YEAR DERMAL STUDIES OF 2-CHLOROETHANOL

Room No.	Month/ Year	RH av (a) (percent)	SD (b)	n (c)	RH max (percent)	RH min (percent)	n in Specification	Percent of Readings in Specification	Hours Out of Specification (d) Above	Hours Out of Specification (d) Below
A211E										
	1/80	48.6	6.3	18	62	37	15	83.3	12	24
	2/80	51.2	6.5	41	70	39	37	90.2	36	12
	3/80	55.0	5.8	42	72	43	38	90.5	48	0
	4/80	56.2	7.9	44	73	40	32	72.7	144	0
	5/80	55.9	7.3	42	74	39	32	76.2	108	12
	6/80	59.5	10.4	42	82	39	24	57.1	192	24
	7/80	66.8	9.1	46	86	52	15	32.6	372	0
	8/80	70.7	5.3	42	82	58	1	2.4	492	0
	9/80	68.7	6.7	42	78	44	5	11.9	444	0
	10/80	51.5	14.3	46	86	26	22	47.8	144	144
	11/80	40.8	8.0	40	56	22	22	55.0	0	216
	12/80	42.6	8.6	46	70	30	27	58.7	12	216
	1/81	41.8	7.6	44	65	28	28	63.6	12	180
	2/81	45.3	11.8	40	66	24	19	47.5	60	192
	3/81	47.9	10.1	44	66	24	32	72.7	48	96
	4/81	46.1	10.1	44	70	25	28	63.6	48	144
	5/81	55.9	9.9	42	68	32	22	52.4	192	48
	6/81	61.9	8.8	44	74	40	18	40.9	312	0
	7/81	65.3	7.0	46	80	44	12	26.1	408	0
	8/81	64.0	5.8	42	70	48	11	26.2	372	0
	9/81	58.2	7.4	44	74	42	29	65.9	180	0
	10/81	56.0	9.8	44	75	40	31	70.5	156	0
	11/81	50.0	10.4	42	70	22	31	73.8	72	60
	12/81	47.6	6.7	45	60	26	43	95.6	0	24
	1/82	48.8	8.1	42	66	30	37	88.1	48	12
	2/82	47.7	6.3	15	58	40	15	100.0	0	0
Study Summary		54.0	8.3	1,069	71.3	35.9	626	60.2	3,912	1,404

(a) Relative humidity (RH) average; recommended relative humidity for animal rooms was 50% ± 10%.
(b) SD = Standard deviation
(c) n = number of readings
(d) Approximation

APPENDIX N

DATA AUDIT SUMMARY

APPENDIX N. DATA AUDIT SUMMARY

The experimental data for the Technical Report on the 2-year dermal studies of 2-chloroethanol in F344/N rats and Swiss CD-1 mice conducted at Litton Bionetics, Inc., were audited for completeness, consistency, and accuracy and for consistency of scientific procedures with Good Laboratory Practices. The 2-year studies were initiated by the National Cancer Institute in January 1980, prior to the NTP's requirement for full compliance with Good Laboratory Practices procedures in October 1981. The audit of the experimental data was conducted by ImmuQuest Laboratories, Inc., on February 27-March 9, 1984. Audit team members were Dr. L. Brennecke, Ms. P. Errico, Mr. C. Reese, Dr. K. Whitkin, and Mr. D.C. Haynes.

The complete report of the audit of 2-chloroethanol is on file at the National Toxicology Program, NIEHS. The audit consisted of (a) review of records for the in-life portions of the studies, including clinical observations and body weight data for 10% of the animals and all environmental and mortality records, (b) review of all chemistry data, and (c) review of pathology data consisting of (1) all individual animal pathology records (IADR's), (2) 100% slide/block match for all animals in all dose groups, and (3) wet tissues for 10% of the animals in each group.

The audit identified no outstanding problems with the conduct of the studies or with the collecting or reporting of the experimental data. The analytical chemistry data were considered adequate to support the stated conclusions regarding chemical analyses. Animals were identified by a combination of toe clipping and ear punching. In each of the groups of untreated and vehicle male mice, the identification of two mice did not match the wet tissue bag label identification. Tissue descriptions from the necropsy records confirmed that only the bags were mislabeled. Apparent discrepancies between necropsy gross observations and microscopic diagnoses consisted predominantly of minor tissue alterations with no potential impact on study interpretation. In four mice, lung nodules were undiagnosed (one untreated male, two vehicle control males, and one low dose male); and in rats, three splenic enlargements (one high dose female, one vehicle control male, and one high dose male) and one liver nodule (high dose male) were undiagnosed. These do not alter the interpretative conclusions of the Technical Report. Paraffin blocks for one high dose male mouse and one untreated female mouse were mislabeled (interchanged). The slides for these two mice contained tissues of the appropriate sex for their respective groups. Slides for one high dose female rat were mislabeled with the wrong group letters on the back (VF instead of HF). The front labels were correct, and the slides matched the blocks. These minor pathology discrepancies are not considered to affect the outcome or interpretation of the studies. In conclusion, no data discrepancies were found that would influence the final interpretation of this experiment.