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Office of Toxic Substances
U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

Attn: Section 8(e) Coordinator (CAP Agreement)

Re: CAP Agreement Identification No. 8ECAP-0110

Dear Sir or Madam:

Union Carbide Corporation ("Union Carbide") herewith submits the following reports pursuant to the terms of the TSCA §8(e) Compliance Audit Program and Union Carbide's CAP Agreement dated August 14, 1991 (8ECAP-0110). These reports describe a variety of toxicology studies with ethylene glycol monomethyl ether (CASRN 109-86-4).

(1) "Ethylene Glycol Monomethyl Ether: Inhalation Teratology Study in Mice", Dow Chemical U.S.A., GE-7.0-Ter-Inh-Dow, November 23, 1982.

(2) "Ethylene Glycol Monomethyl Ether: Inhalation Teratology Study in Rats and Rabbits", Dow Chemical U.S.A., G-2.0-Ter-Ihl-Dow, September 20, 1982.

(3) "Ethylene Glycol Monomethyl Ether: Inhalation Reproduction and Dominant Lethal Study in Rats", Dow Chemical U.S.A., GE-TTG-12C, February 10, 1982.

(4) "Ethylene Glycol Monomethyl Ether: 13-Week Vapor Inhalation Study With Rats and Rabbits", Dow Chemical U.S.A., 12/29/81.

(5) "Ethylene Glycol Monomethyl Ether: Inhalation Teratology Probe Study in Rats and Rabbits", Dow Chemical U.S.A., January 29, 1982.

egmono

1/30/95

Complete summaries of these reports are attached.

Previous TSCA Section 8(e) or "FYI" Submission(s) related to this substance are:

(None)

Previous PMN submissions related to this substance are: (None)

This information is submitted in light of EPA's current guidance. Union Carbide does not necessarily agree that this information reasonably supports the conclusion that the subject chemical presents a substantial risk of injury to health or the environment.

In the attached reports the term "CONFIDENTIAL" may appear. This precautionary statement was for internal use at the time of issuance of these reports. Confidentiality is hereby waived for purposes of the needs of the Agency in assessing health and safety information. The Agency is advised, however, that the publication rights to the contained information are the property of Union Carbide.

Yours truly,

William C. Kuryla, Ph.D.
Associate Director
Product Safety
(203/794-5230)

WCK/cr
Attachment (3 copies of cover letter, summaries, and reports)

egmono

SUMMARY

12/29/81

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B-17a

ETHYLENE GLYCOL MONOMETHYL ETHER:
13-WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

R. R. Miller, J. A. Ayres and J. T. Young

Reviewed by:
M. J. McKenna

Toxicology Research Laboratory
Health and Environmental Sciences, U.S.A.
Dow Chemical USA
Midland, Michigan 48640

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ETHYLENE GLYCOL MONOMETHYL ETHER: 13-WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS. R. R. Miller, J. A. Ayres, and J. T. Young.

ABSTRACT

Male and female Sprague-Dawley rats and New Zealand White rabbits were exposed to 0, 30, 100 or 300 ppm ethylene glycol monomethyl ether (EGME) vapors 6 hours per day, 5 days per week, for a total of 13 weeks. There were no mortalities of rats prior to scheduled sacrifice, but 2 of 5 male and 2 of 5 female rabbits in the 300 ppm group as well as 2 of 5 female rabbits in the 100 ppm group died or were sacrificed moribund during the study. The specific cause of death of most of these animals could not be determined.

Body weights as well as thymus gland and testicular weights of animals in the 300 ppm group were reduced as a result of the exposures. Hematologic analyses after 4 weeks, and again after 12 weeks, revealed abnormal depressions of cellular elements in the blood in rats and rabbits exposed to 300 ppm. Concentrations of total protein, albumin and globulins in serum of rats (but not rabbits) in the 300 ppm group were lower than for controls.

Gross pathologic observations attributed to exposure to 300 ppm EGME included decreased size of thymus gland in both sexes, small flaccid testes in males, decreased abdominal fat in some females, and decreased lymphoid tissue in some rabbits. In rabbits, a slight-to-moderate decrease in size of testes was noted in 4 of 5 animals in the 100 ppm group as well as in 2 of 5 animals exposed to 30 ppm.

Microscopic examinations of tissues revealed treatment-related degenerative changes in germinal epithelium of testes in all male rats and rabbits in the 300 ppm group, as well as in 3 of 5 male rabbits and 1 of 5 male rabbits in the 100 and 30 ppm groups, respectively.

The only effects attributed to exposure to 30 ppm EGME in this study were slight microscopic changes in testes of 1 of 5 male rabbits. A follow-up study is currently being conducted with larger group sizes to determine if these observations in testes are reproducible in male rabbits exposed to low concentrations of EGME.

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INTRODUCTION

Ethylene glycol monomethyl ether (DOWANOL* EM; 2-methoxyethanol; EGME) is a volatile, nearly odorless liquid with the following properties:

Structural formula:	CH_3-O-CH_2-CH_2-OH
Molecular weight:	76.09
Boiling Point:	124.6°C @ 760 mmHg
Vapor Pressure:	9.5 mmHg @ 25°C
Solubility:	Miscible with water
Flash Point:	107°F

Rowe and Wolf (1981) have provided a comprehensive review of the available toxicological literature pertaining to EGME. In addition, recent short-term two-week vapor inhalation studies, in which rats, mice and rabbits were exposed to 0, 100, 300 or 1000 ppm (0, 0.31, 0.93 or 3.11 mg/l), resulted in adverse effects on body weight gain, peripheral blood counts, bone marrow, testes, and lymphoid tissues in animals exposed to the high concentration (Miller et al.; 1980, 1981). Similar but less pronounced changes in some of these parameters also occurred in animals exposed to 300 ppm, while 100 ppm had no appreciable adverse effects during the course of the short-term two-week studies.

McGregor et al. (1981) recently reported results of multiple assays for genotoxic potential of EGME. Antifertility effects were seen in a dominanat lethal assay during weeks 3-8 of treatment. Frequencies of mouse sperm abnormalities were increased after 5 weeks of exposure, but not at other time points. There was no evidence of clastogenic potential in bone marrow cells, or for increases in reversion numbers in the Ames assay, or for DNA synthesis induction in the UDS assay.

An additional very recent report by Nagano et al. (1981) described the embryotoxic effects of EGME in mice given daily oral doses of 31.25 to 1000 mg/kg on days 7 through 14 of gestation.

The purpose of the present study was to determine the target organs and spectrum of toxicity in rats and rabbits exposed subchronically to EGME vapors in order to assess the potential hazard to humans, and to provide additional perspective pertaining to guidelines for safe handling.

*Trademark of The Dow Chemical Company

MATERIALS AND METHODS

Chemical

EGME was obtained from the production facilities of Dow Chemical USA, Michigan Division, Midland, MI. Gas chromatographic analysis of the test material (Lot 54, Tank 374) indicated a purity of 99.78-99.93% (Hermann, 1980).

Animals

Male and female Sprague-Dawley rats (6-8 weeks of age) were purchased from Charles River Breeding Laboratories, Portage, MI. Male and female New Zealand White rabbits (6-7 months of age) were purchased from Langshaw Farms, Inc., Augusta, MI. The animals were individually identified with metal ear tags, randomly assigned to control or exposure groups using a computer-assisted randomization procedure, and allowed to acclimate to laboratory conditions prior to initiating exposures. The control and exposure groups each contained 10 rats of each sex and 5 rabbits of each sex at the start of the study. When not in chambers, rabbits were housed in rooms designed to control relative humidity (40-60%) and temperature (approximately 72°F). Rats were housed in the exposure chambers at all times; clean, filtered air was supplied during non-exposure periods. Both rats and rabbits were maintained on a 12 hour light-dark cycle. Rats were housed two per cage, and rabbits were housed singly in stainless steel cages with wire mesh bottoms. Purina Certified Chow (Ralston Purina Co., St. Louis, MO) was available *ad libitum* except during exposure. Rats had access to water at all times; rabbits were not given water during exposure intervals.

The animals in this study were exposed in inhalation chambers simultaneously with animals used for reproduction and dominant lethal studies (Rao, *et al.*, 1981).

Chambers

The exposures were conducted in 14.5 m^3 chambers with stainless steel ceilings, and epoxy resin-coated walls and floors. Air supply to the chambers was controlled by a system designed to maintain temperature at approximately 72°F and relative humidity at approximately 50%. The chambers were operated under dynamic airflow conditions (total chamber airflow of approximately 2500 liters per minute) at a slight negative pressure relative to the surrounding area.

Vapor Generation and Analysis

Animals were exposed to 0, 30, 100 or 300 ppm (0.09, 0.31 or 0.93 mg/l) 6 hours per day, 5 days per week, for a total of 13-weeks. The test atmospheres were generated as described by Miller et al., (1980), with minor modifications. Liquid test material was metered at calculated rates in glass vaporization tubes. Vapors from the tubes were swept into the chamber inlet ducts with compressed air. The compressed air to the vaporization tubes was preheated to the minimal extent necessary (approximately 120°C) to ensure complete vaporization using a compressed air flameless heat torch (Master, Model FHT-4). The nominal concentration (ratio of the amount of EGME vaporized to the total airflow through the chamber) was calculated for each chamber on a daily basis. The actual concentration of EGME in each exposure chamber was measured 1-2 times per hour by infrared spectroscopy using a Miran I infrared gas analyzer at a wavelength of 8.8 μ. Concentrations in the chambers were interpolated from standard curves derived from standards of known concentration, utilizing a microprocessor unit. Standardization of the analytical system was evaluated with at least one standard prior to each day of exposure.

Criteria of Response.

Animals were observed daily for signs of toxicity and changes in appearance and demeanor. Body weights were recorded immediately prior to the first exposure, and weekly thereafter. Moribund animals were removed from the study and sent to pathology if it appeared they would not survive until the next observation period in order to minimize the occurrence of post-mortem autolysis. Records of mortalities were maintained.

Hematologic analyses[1] were performed for each surviving animal after 4 weeks of exposure, and again after 12 weeks of exposure. The hematologic parameters which were evaluated included packed cell volume (PCV), hemoglobin (Hgb), erythrocyte count (RBC), total and differential leucocyte counts (WBC), platelet count, and red blood cell indices (MCV, MCH, MCHC).

Clinical chemistry parameters[2], including blood urea nitrogen (BUN), glutamic-pyruvic transaminase activity (SGPT), alkaline phosphatase activity (AP), glucose (Glu), total protein (T.P.), albumin (Alb),

[1]Ortho ELT-8, Ortho Instruments, Boston, MA. (WBC, RBC, PCV, Hgb, Plat, Indices); Honeywell ACF-1000, Honeywell, Inc., Denver, CO (Diff WBC).

[2]Centrifichem System 400, Methods File, Union Carbide Corp., Rye, NY.

globulins (glob) and total bilirubin (T.Bili) were evaluated on serum samples from each surviving animal after 13-weeks of exposure.

Urinalyses[3] were performed for rats only after 12-week of exposure. Parameters which were evaluated included bilirubin, glucose, ketones, blood, pH, protein, urobilinogen and specific gravity.

Each animal was given a complete gross pathologic examination (including those which died spontaneously or were killed moribund). Ra··· (but not rabbits) were fasted overnight prior to sacrifice. At necropsy, each animal was anesthetized, weighed and sacrificed by decapitation after clamping the trachea to prevent aspiration of blood. Rabbits were anesthetized with CO_2, and rats with methoxyflurane. Weights of liver, kidneys, brain, spleen, thymus, and testes were recorded. Lungs were distended to approximately normal inspiratory volume by tracheal infusion of neutral phosphate-buffered 10% formalin. Nasal cavities were flushed with 10-15 ml of formalin via the pharyngeal duct to insure rapid fixation of nasal mucosa. Tissues listed in Appendix I were retained and preserved in neutral phosphate-buffered 10% formalin, with the exception of testes which were preserved in Bouin's fixative.

Bone marrow smears were prepared from 5 rats of each sex from each exposure group and stained with Wright's stain. Samples of testes from 3 male rats and 3 male rabbits from each exposure level were retained and preserved in the appropriate fixative for possible electron microscopic examination.

Representative sections of the tissues listed in Appendix 1 (except for the sternum, and rabbit nasal turbinates) for all rats in the control and high exposure groups and all rabbits of each of the exposure groups were processed in the standard manner, embedded in paraffin, sectioned at 5-6 µm, stained with hematoxylin and eosin, and examined microscopically by a veterinary pathologist. Histologic examination of tissues from rats of the two intermediate exposure groups was limited to the spleen, thymus, testes, mesenteric lymph nodes, and thoracic vertebral column with spinal cord and bone marrow.

Statistics

Body weights, organ weights, hematology data, urine specific gravity and clinical chemistry data were analyzed according to a statistical routine

[3] T. S. Meter, Amer. Opt. Co., Buffalo, NY (specific gravity); Bililabstix, Ames Co., Elkhart, IN (glu, ketones, blood, pH, protein, urobilinogen, bilirubin).

including Bartlett's test ($p < 0.01$), ANOVA ($p < 0.10$) and either Wilcoxon's or Dunnett's test ($p < 0.05$) depending on whether or not the data was non-homogeneous or homogeneous, respectively, as described by Park and Morden (1980).

RESULTS

Chamber Conditions

The mean daily time-weighted average (TWA) analytical concentrations were within ±2% of the intended target concentration for each exposure chamber (Appendix II). Moreover, there was very close agreement between the mean daily TWA analytical concentrations and mean daily nominal concentrations for each chamber, indicating that test material losses were minimal in the vapor generator and exposure systems.

Observations

One female rabbit in the 100 ppm group was sacrificed moribund after only 9 days on study, as a result of a severe inner-ear infection unrelated to exposure. An additional female rabbit in the 100 ppm group died spontaneously of undetermined causes after 21 days on study.

Four rabbits (2 male and 2 female) in the 300 ppm group died spontaneously or were sacrificed moribund during the course of the study. Broncopneumonia was the immediate cause of death for a male rabbit which was found dead after 18 days on study. No specific cause of death could be identified for the other male rabbit in 300 ppm group; this animal was found dead on the last day of the study. One of the female rabbits in the 300 ppm group was sacrificed moribund due to inanition after 20 days on study, and the other died spontaneously near the end of the study as a result of acute hemorrhagic enteritis complicated by inanition. Of the 6 rabbits which died or were sacrificed moribund, 4 occurred during the first month of the study and 2 occurred very late in the study. The specific cause of death or moribund condition for some of these animals could not be determined, and the relationship of the deaths to EGME exposure is uncertain (see Histopathology section). There were no mortalities of rats prior to scheduled sacrifice.

Other than those rabbits which died or were sacrificed moribund, all other rats and rabbits appeared normal during the course of the study.

Body Weight

The body weights of male and female rats in the 300 ppm group were significantly lower than for controls as a result of treatment (Tables 1 & 2). For female rats exposed to 300 ppm, the reduction in body weight first became statistically significant after 3 weeks, while for male rats the reduction of mean body weight of animals in the 300 ppm group first became statsitically significant after 5 weeks. A less pronounced, but statistically significant, reduction in the mean body weight of female rats in the 100 ppm group occurred after 7 weeks of exposure, as well as on several other occasions thereafter. Body weights of male rats were apparently not altered by exposure to 100 ppm, and neither male nor female rat body weights were appreciably altered by exposure to 30 ppm.

Although the mean body weight values of rabbits were generally not statistically significantly altered at any exposure concentration, there was a general trend toward lower body weights for both male and female rabbits in the 300 ppm group as well as for females in the 100 ppm group (Tables 3 & 4).

Organ Weights

The mean absolute and relative organ weights of thymus glands and testes of male rats and male rabbits in the 300 ppm group were significantly lower than for controls as a result of exposure to EGME (Tables 5 & 6). The mean weights of thymus glands of female rats and female rabbits in the 300 ppm group were also significantly lower than for controls (Tables 5 & 6). All other statistically significant changes in organ weights of rats and rabbits in Tables 5 & 6 were considered to be either reflections of reduced body weight or sporadic occurrences unrelated to exposure.

Although there were no statistically significant changes in organ weights of rats or rabbits in the 100 or 30 ppm groups which were considered to be direct treatment-related effects, the absolute and relative testes weights of rabbits in the 100 ppm group tended on the average to be lower than controls, probably as a result of treatment.

The absolute mean testes weight of rats in the 30 ppm group was significantly lower than for controls; this was considered a sporadic occurrence unrelated to exposure in view of the absence of an effect on testes weights of rats in the intermediate (100 ppm) exposure group,

as well as the absence of gross or histopathologic changes in test rats in either the 30 ppm or 100 ppm groups (see Histopathology section).

Hematology

Hematologic analyses for male rats after 4 weeks of exposure (Table 7), revealed significant reductions in hemoglobin (Hgb) concentration, packed cell volume (PCV), platelet counts (Plat), white blood cell count (WBC), and the various red blood cell indices for animals in the 300 ppm group. In female rats exposed to 300 ppm, red blood cell counts (RBC) were significantly depressed, as well as the aforementioned parameters. Hematologic parameters of rats in the 100 and 30 ppm groups were not appreciably altered by the exposures.

The mean values for RBC, Hgb, PCV, Plat, and WBC as well as the various red blood cell indices for male and female rabbits in the 300 ppm group were also substantially lower than for controls after 4 weeks as a result of treatment (Table 8). Most of these hematologic changes in rabbits were not statistically significantly different from controls, due at least in part to the small group sizes. There were no appreciable changes in hematologic parameters of either male or female rabbits in the 100 or 30 ppm groups after 4 weeks.

Additional hematologic analyses after 12-weeks of exposure revealed the same types of abnormalities in rats and rabbits in the 300 ppm group as were found after 4 weeks (Tables 9 & 10) for the various hematologic parameters. The severity of the effects on WBC counts in rats apparently did not increase during the 8 weeks of treatment between hematologic analyses. Consistent with the results after 4 weeks, exposure to 100 and 30 ppm had no appreciable effect on hematologic parameters of either rats or rabbits.

The abnormal depressions of the cellular elements of the blood (pancytopenia) resulting from exposure to 300 ppm EGME were qualitatively similar in rats and rabbits of both sexes, indicating no species or sex differences in sensitivity. However, the RBC counts in rabbits did appear to be slightly more depressed than in rats exposed to 300 ppm, both at the 4-week interval and at the 12-week interval.

Clinical Chemistry

The mean values for total protein (TP), albumin (Alb) and globulins (Glob) in male and female rats in the 300 ppm group were significantly

lower than for controls (Table 11). the majority of the decrease in total serum protein was apparently due to decreases in globulins. All other statistically significant differences for clinical chemistry parameters in rats were considered sporadic occurrences which were not diagnostic of treatment-related adverse effects.

In rabbits, there were no alterations of TP, Alb or Glob values as occurred in rats and, indeed, no statistically significant changes in clinical chemistry parameters at all (Table 12).

Urinalyses

The mean urine specific gravity values of male and female rats in the 300 ppm group were significantly lower than for controls (Tables 13 & 14), possibly reflective of the decreased serum total protein; however there was no indication of a treatment-related toxic effect on the kidneys. All other urine parameters in treatment groups of male and female rats were apparently unaltered by the exposures.

Gross Pathology

Rats. A tabular summary of the gross pathologic observations for male and female rats is presented in Table 15. Gross pathologic observations attributed to exposure to EGME were limited to rats in the high exposure group (300 ppm) and included: decreased size of the thymus in both sexes; small, flaccid testes in the males; and decreased abdominal adipose tissue in some of the females.

Rabbits. A tabular summary of the gross pathologic observations for male and female rabbits is presented in Table 16.

Gross changes attributed to inhalation of EGME were observed in male rabbits at all three exposure concentrations and in female rabbits at the 300 and 100 ppm levels. The observations in both sexes at 300 ppm included decreased abdominal fat, decreased amounts of mediastinal tissue including fat and thymic tissue, and decreased amounts of lymphoid tissue in the cecal appendix and sacculus rotundus. In addition, the testes of all male rabbits in the 300 ppm exposure group were very small and flaccid. A slight to moderate decrease in the size of the testes relative to the control rabbits was the only grossly observable effect noted in male rabbits at the two lower exposure levels with 4 of 5 showing changes in the 100 ppm group and 2 of 5 appearing slightly smaller at the 30 ppm exposure concentration. At the 100 ppm level, the observation of decreased lymphoid tissue in the

cecal appendix and sacculus rotundus in one of the three female rabbits was also considered an effect of exposure to the test material.

Histopathology

Rats. The histopathologic findings, along with complete listings of all tissues examined microscopically, are presented in Tables 17 & 18 for male and female rats, respectively. Histopathologic effects resulting from inhalation exposure to the test material were also confined only to rats at the highest exposure concentration. The decreased size and flaccid gross appearance of the testes was the result of bilateral, diffuse, moderate to severe degeneration of the germinal epithelium in the seminiferous tubules. In the most severe cases, virtually all of the tubules were affected and were lined almost entirely by Sertoli cells and a few spermatogonia. In a few cases, there was a small percentage of the tubules in which the germinal epithelium was relatively intact but producing little sperm. Reduced numbers of spermatozoa as well as degenerating forms were noted in the epididymides of all affected male rats, and there was an apparent slight reduction in the amount of prostatic secretory material. Reproductive organs of female rats were apparently not altered by exposure to EGME.

Thymic lymphoid atrophy, manifested primarily as a decrease in cortical lymphocytes, was noted in most of the male and female rats in the high (300 ppm) exposure group, accounting for the grossly observed decrease in size. In spite of the alterations in the hematologic parameters, no histopathologic changes were observed in the thoracic vertebral bone marrow sections examined. Wright's stained smears of femoral bone marrow were also examined from 5 rats/sex of the control and 300 ppm groups, and these also were unremarkable.

All other lesions noted histologically were considered spontaneous or incidental. Of particular interest are the suppurative inflammatory and squamous metaplastic lesions of the nasal cavity in males which occurred in a few controls but appeared to be more frequent in the animals of the high exposure group. These changes are believed to be sequelae of orbital eye bleeding trauma because in every instance they were unilateral on the right side (the same side used to obtain the blood sample), and occurred only in the anterior part of the nasal cavity near the opening of the nasolacrimal duct. Many animals also had chronic inflammatory lesions in the right lacrimal gland (Harderian) as a result of blood

elements were commonly observed. Secondary changes in accessory sex glands were not seen. Female reproductive organs were apparently not altered by the exposures.

The remainder of the histopathologic findings were considered spontaneous in nature and common for the strain and species used. The chronic inflammatory lesions involving the brain, renal interstitium, and hepatic portal areas were attributed to the ubiquitous protozoan, Encephalitozoon sp., and although the top dose males appeared to be more frequently affected than their comparable controls, the incidence was uniformily spread across the dose levels in the females.

Spontaneous Deaths and Killed Moribund. Table 21 is a listing of all gross and histopathologic findings for rabbits which died spontaneous or were sacrificed moribund. The immediate cause of death for one of the male rabbits in the 300 ppm group was bronchopneumonia, but no specific cause was determined for the other. Both had the same spectrum of exposure-related effects as the terminal kill male rabbits, including testicular degeneration, even though one of them was only on test for 26 days.

Of the 2 female rabbits in the 100 ppm exposure group which did not survive until termination, one was killed moribund after only 9 days on study as a result of severe otitis media, and the other died spontaneously of undetermined causes at 21 days. In the 300 ppm group, one female rabbit was killed moribund due to inanition after 20 days on study, and the other died spontaneously near the end of the study as a result of acute hemorrhagic enteritis complicated by inanition.

In all of the animals dying spontaneously or killed moribund, decreased liver glycogen and some degree of lymphoid atrophy of the thymus and gut-associated lymphoid organs was present. As with the terminal kill animals, the decreased glycogen content of the liver merely reflects the nutritional status at the time of death. However, the lymphoid atrophy may either be a direct effect of the test compound or reflect non-specific stress in those which did not survive.

sampling trauma, and in one instance purulent exudate was observed extending from a suppurative eye lesion through the nasolacrimal duct to an area of inflammation and squamous metaplasia in the nose.

Rabbits. The histopathologic findings, along with complete listings of all tissues examined microscopically, are presented in Tables 19 & 20 for male and female rabbits, respectively.

As with the gross observations, histopathologic findings attributed to EGME exposure were present in males at all three exposure concentrations and in female rabbits at the 300 and 100 ppm levels. In both males and females at the 300 ppm level, exposure-related effects included slight-to-occasionally-severe lymphoid atrophy of the thymus and gut-associated lymphoid organs (particularly the cecal appendix where changes are more readily detectable by microscopy), and a decrease in the amount of liver glycogen characterized by small hepatocytes with less microvesiculation. The lymphoid atrophy of the thymus and cecal appendix was also observed in a few males and females of the 100 ppm exposure groups.

The most significant and persistent effect of exposure, however, was observed in the testes of male rabbits. A dose-related increase in both the incidence and severity of testicular degenerative changes was present at each of the 3 exposure concentrations. In all 3 surviving rabbits at 300 ppm, the degeneration was diffuse and severe with virtually every tubule affected. Sertoli cells and an occasional spermatogonia were all that lined tubules, most of which were shrunken giving the appearance of a relative increase in interstitial cells. In the 3 affected rabbits of the 100 ppm group, more of a spectrum of effects was noted in that, within the same testis, some tubules were relatively normal in appearance while others contained no germinal elements at all. The testes of two rabbits in this group were indistinguishable microscopically from controls even though one of these had testes grossly observed to be smaller. Microscopic degenerative changes were apparent in only one of the two rabbits in the 30 ppm group which had noticeably smaller testes. The effect in this animal was evident as an excess of tubules in which the germinal epithelium was thinner than normal, with a complete complement of germinal stages, but very few spermatozoa.

The epididymal sperm content generally reflected the degree of testicular damage with noticeable decreases present in those cases which were moderately to severely affected. Degenerating spermatic

Body Weights

The mean body weights of male and female rats in the 300 ppm group were significantly lower than for controls as a result of treatment (Tables 1 & 2). For female rats exposed to 300 ppm, the reduction in body weight first became statistically significant after 3 weeks, while for male rats the reduction of mean body weight of animals in the 300 ppm group first became statsitically significant after 5 weeks. A less pronounced, but statistically significant, reduction in the mean body weight of female rats in the 100 ppm group occurred after 7 weeks of exposure, as well as on several other occasions thereafter. Body weights of male rats were apparently not altered by exposure to 100 ppm, and neither male nor female rat body weights were appreciably altered by exposure to 30 ppm.

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Organ Weights

The mean absolute and relative organ weights of thymus glands and testes of male rats and male rabbits in the 300 ppm group were significantly lower than for controls as a result of exposure to EGME (Tables 5 & 6). The mean weights of thymus glands of female rats and female rabbits in the 300 ppm group were also significantly lower than for controls (Tables 5 & 6). All other statistically significant changes in organ weights of rats and rabbits in Tables 5 & 6 were considered to be either reflections of reduced body weight or sporadic occurrences unrelated to exposure.

Although there were no statistically significant changes in organ weights of rats or rabbits in the 100 or 30 ppm groups which were considered to be direct treatment-related effects, the absolute and relative testes weights of rabbits in the 100 ppm group tended on the average to be lower than controls, probably as a result of treatment.

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as well as the absence of gross or histopathologic changes in testes of rats in either the 30 ppm or 100 ppm groups (see Histopathology section).

Hematology

Hematologic analyses for male rats after 4 weeks of exposure (Table 7) revealed significant reductions in hemoglobin (Hgb) concentration, packed cell volume (PCV), platelet counts (Plat), white blood cell count (WBC), and the various red blood cell indices for animals in the 300 ppm group. In female rats exposed to 300 ppm, red blood cell counts (RBC) were significantly depressed, as well as the aforementioned parameters. Hematologic parameters of rats in the 100 and 30 ppm groups were not appreciably altered by the exposures.

The mean values for RBC, Hgb, PCV, Plat, and WBC as well as the various red blood cell indices for male and female rabbits in the 300 ppm group were also substantially lower than for controls after 4 weeks as a result of treatment (Table 8). Most of these hematologic changes in rabbits were not statistically significantly different from controls, due at least in part to the small group sizes. There were no appreciable changes in hematologic parameters of either male or female rabbits in the 100 or 30 ppm groups after 4 weeks.

Additional hematologic analyses after 12-weeks of exposure revealed the same types of abnormalities in rats and rabbits in the 300 ppm group as were found after 4 weeks (Tables 9 & 10) for the various hematologic parameters. The severity of the effects on WBC counts in rats apparently did not increase during the 8 weeks of treatment between hematologic analyses. Consistent with the results after 4 weeks, exposure to 100 and 30 ppm had no appreciable effect on hematologic parameters of either rats or rabbits.

The abnormal depressions of the cellular elements of the blood (pancytopenia) resulting from exposure to 300 ppm EGME were qualitatively similar in rats and rabbits of both sexes, indicating no species or sex differences in sensitivity. However, the RBC counts in rabbits did appear to be slightly more depressed than in rats exposed to 300 ppm, both at the 4-week interval and at the 12-week interval.

Clinical Chemistry

The mean values for total protein (TP), albumin (Alb) and globulins (Glob) in male and female rats in the 300 ppm group were significantly

SUMMARY

Sprague-Dawley rats and New Zealand White rabbits responded in a qualitatively similar manner when exposed to EGME vapors 6 hours per day, 5 days per week, for 13 weeks. The spectrum of toxicity in both rats and rabbits exposed to 300 ppm included: reductions in body weight as well as in weights of thymus glands and testes, depressions in cellular elements of the blood, lymphoid tissue atrophy, and degeneration of testicular germinal epithelium. Rabbits were apparently more sensitive than rats to EGME vapors based on the fact that: (1) some rabbits (but no rats) died during the course of the exposures, and (2) microscopic treatment-related changes in the testes persisted in 3 of 5 rabbits in the 100 ppm group and 1 of 5 rabbits in the 30 ppm group, while no treatment-related changes occurred in rats in either the 100 or 30 ppm groups.

The treatment-related depressions of cellular elements in the blood (pancytopenia) were apparently no more severe after 12-weeks than after 4-weeks of exposure to 300 ppm, with the possible exception that the red blood cell counts of rabbits seemed to be slightly more depressed at the later time interval. Presumably the observed depressions in cellular elements in the blood reflect a primary effect of the test material on bone marrow, although no microscopic abnormalities were observed in bone marrow of animals in this study. However, the peripheral blood counts are consistent with those observed in a previous shorter-term study (Miller et al., 1980) in which marked reductions in bone marrow cellularity were apparent in animals exposed to 1000 ppm.

Since hematologic changes were not apparent in either rats or rabbits in the two lower exposure groups while some microscopic testicular changes did persist in at least some rabbits, the testicular effects may be a more sensitive index of exposure to EGME in some species than hematologic changes. Testicular changes, however, did not persist in rats at concentrations below those which resulted in hematologic changes.

The only effects attributed to exposure to 30 ppm EGME in this study were slight microscopic changes in testes of 1 of 5 male rabbits. A follow-up study is currently being conducted with larger group sizes to determine if these observations in testes are reproducible in male rabbits exposed to low concentrations of EGME.

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TITLE OF STUDY: ETHYLENE GLYCOL MONOMETHYL ETHER: 13-WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

HET-K-2573-(8)

In compliance with Good Laboratory Practice Regulations, the study phases were inspected by the Quality Assurance Unit and the results of these inspections reported to Management and the Study Director on the dates listed below. The report accurately reflects the data generated in accordance with the regulations and standard operating procedures of the laboratory. All data and the reports are located at the submitting laboratory.

Study Started:	22 July 1980	Report Issued Date:	29 December 1981
Dates of Inspection:	17 July 1980	Date of Report:	17 July 1980
	17 September 1980		25 September 1980
	28 December 1981		29 December 1981

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TABLE 1

ETHYLENE GLYCOL MONOMETHYL ETHER: 13-WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Male Rat Body Weights[a]

Days on Test	ppm			
	0	30	100	300
0	295± 9	293±16	289±10	293±12
7	331±22	337±18	332±11	329±16
14	373±18	367±32	370±14	354±14
21	405±21	391±41	399±16	379±19
28	426±27	412±47	428±15	397±21
32	422±29	403±53	426±14	387±23
35	439±28	414±55	442±13	395±22*
42	461±38	439±56	464±16	422±26
49	481±36	449±64	482±16	433±30*
56	494±37	461±72	499±21	448±32
63	498±37	473±70	511±21	452±29
70	512±41	487±63	522±22	461±32*
77	529±46	500±60	534±26	471±32*
84	542±45	505±60	541±34	474±37*
91	532±55	504±52	540±33	465±42*

*Statistically significant deviation from control group mean using Dunnett's test, $p < 0.05$.

[a]Numbers are Mean ± SD values (g) for n = 10 animals.

TABLE 2

ETHYLENE GLYCOL MONOMETHYL ETHER: 13-WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Female Rat Body Weights[a]

Days on Test	ppm			
	0	30	100	300
0	195±12	193±12	190± 9	196±12
7	217±12	213±15	208±12	215± 9
14	235±16	229±17	225±14	226±13
21	249±19	240±19	232±14	228±14*
28	261±21	254±24	244±18	237±17*
32	257±21	253±23	242±15	227±15*
35	268±21	261±25	251±18	241±14*
42	279±21	267±22	258±17*	251±15*
49	285±22	273±26	264±18	248±14*
56	291±25	277±23	265±17*	250±21*
63	294±25	281±25	272±20	250±21*
70	299±26	287±30	274±22	250±21*
77	304±30	293±30	279±22	258±20*
84	308±29	295±30	275±24*	254±22*
91	310±27	293±30	274±23*	254±22*

*Statistically significant deviation from control group mean using Dunnett's test, $p < 0.05$.

[a]Numbers are Mean ± SD values (g) for n = 10 animals.

TABLE 3

ETHYLENE GLYCOL MONOMETHYL ETHER: 13-WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Male Rabbit Body Weights[a]

Days on Test	0	30	100	300
0	3920 ± 375	3880 ± 169	4013 ± 446	3795 ± 278
7	3909 ± 401	3866 ± 168	3926 ± 355	3752 ± 312
14	3918 ± 411	3861 ± 137	3933 ± 379	3696 ± 251
21	3970 ± 402	3956 ± 188	3976 ± 379	3668 ± 255
28	3909 ± 422	3983 ± 187	3996 ± 419	3668 ± 273[b]
35	3984 ± 422	3976 ± 154	4015 ± 451	3741 ± 376[b]
42	4030 ± 440	4029 ± 167	3933 ± 427	3393 ± 310[b*]
49	4034 ± 430	4088 ± 179	3904 ± 431	3719 ± 351[b]
56	4013 ± 425	4111 ± 210	3956 ± 420	3805 ± 384[b]
63	4051 ± 438	4172 ± 221	3995 ± 554	3790 ± 377[b]
70	4100 ± 469	4176 ± 249	4034 ± 504	3779 ± 368[b]
77	4098 ± 482	4202 ± 244	4055 ± 561	3790 ± 361[b]
84	4109 ± 502	4211 ± 291	4001 ± 511	3748 ± 300[b]
91	4103 ± 528	4255 ± 288	4036 ± 569	3759 ± 303[b]

*Statistically significant deviations from control group mean using Dunnett's test, $p < 0.05$.

[a]Numbers are Mean ± SD values (g) for n = 5 animals except where noted.

[b]Mean ± SD values (g) for n = 4 animals.

TABLE 4

ETHYLENE GLYCOL MONOMETHYL ETHER: 13-WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Female Rabbit Body Weights[a]

Days on Test	0	30	100	300
0	4078 ± 468	4134 ± 360	3973 ± 393	4225 ± 367
7	4030 ± 464	4133 ± 368	3846 ± 371	3843 ± 383
14	4091 ± 491	4193 ± 374	3905 ± 408[b]	3733 ± 567
21	4125 ± 526	4279 ± 379	3681 ± 139[c]	3814 ± 463[b]
28	4194 ± 531	4341 ± 371	3719 ± 170[c]	3831 ± 456[b]
35	4243 ± 534	4399 ± 418	3779 ± 193[c]	3955 ± 395[b]
42	4294 ± 563	4492 ± 377	3790 ± 196[c]	3945 ± 432[b]
49	4310 ± 578	4486 ± 372	3729 ± 226[c]	3874 ± 472[b]
56	4360 ± 594	4566 ± 365	3813 ± 246[c]	3875 ± 474[b]
63	4429 ± 644	4636 ± 383	3857 ± 241[c]	3838 ± 498[b]
70	4456 ± 634	4700 ± 367	3942 ± 229[c]	3859 ± 473[b]
77	4456 ± 636	4693 ± 372	3874 ± 254[c]	3832 ± 477[b]
84	4466 ± 650	4708 ± 421	3857 ± 327[c]	3771 ± 478[b]
91	4511 ± 676	4768 ± 435	3810 ± 410[c]	3945 ± 218[c]

No statistically significant differences from control group mean using Dunnett's test, $p < 0.05$.

[a]Numbers are Mean ± SD values (g) for n = 5 animals except where noted.

[b]Mean ± SD values (g) for n = 4 animals.

[c]Mean ± SD values (g) for n = 3 animals.

TABLE 6

ETHYLENE GLYCOL MONOMETHYL ETHER: 13-WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Terminal Body Weights and Absolute and Relative Organ Weights of Rats[a]

Exposure Conc. (ppm)	N	Sex	Body Wt.	Liver g	Liver g/100	Kidney g	Kidney g/100	Brain g	Brain g/100	Spleen g	Spleen g/100	Thymus g	Thymus g/100	Testes g	Testes g/100
0	10	Male	406.56 53.33	12.07 2.11	2.47 0.23	3.25 0.44	0.67 0.05	2.09 0.05	0.43 0.06	0.75 0.09	0.15 0.01	0.33 0.08	0.07 0.01	3.41 0.53	0.71 0.13
30	10		464.85 52.53	11.54 1.64	2.48 0.13	3.10 0.45	0.67 0.05	2.03 0.08	0.44 0.05	0.69 0.08	0.15 0.02	0.37 0.08	0.08 0.02	2.86* 0.68	0.62 0.17
100	10		500.84 29.91	11.86 1.41	2.36 0.17	3.29 0.41	0.65 0.06	2.00 0.23	0.40 0.05	0.74 0.08	0.15 0.02	0.36 0.07	0.07 0.01	3.54 0.31	0.71 0.05
300	10		432.07* 40.57	10.01* 1.09	2.31 0.08	2.81 0.27	0.65 0.05	1.90* 0.26	0.44 0.06	0.67 0.07	0.16 0.02	0.19* 0.07	0.04* 0.01	1.40* 0.33	0.33* 0.08
0	10	Female	277.13 23.34	7.23 0.75	2.61 0.10	2.00 0.19	0.72 0.05	1.88 0.05	0.68 0.06	0.49 0.09	0.17 0.03	0.38 0.07	0.14 0.03		
30	10		264.22 27.84	7.07 0.79	2.68 0.11	1.98 0.28	0.75 0.07	1.92 0.12	0.73 0.07	0.52 0.08	0.20 0.02	0.35 0.07	0.13 0.02		
100	10		246.58* 21.08	6.48 0.73	2.62 0.17	1.80 0.13	0.73 0.06	1.83 0.08	0.75* 0.07	0.47 0.06	0.19 0.02	0.31 0.07	0.13 0.03		
300	10		229.06* 19.75	6.14* 0.76	2.68 0.23	1.59* 0.13	0.70 0.05	1.75* 0.09	0.77* 0.04	0.43 0.07	0.19 0.03	0.13* 0.04	0.06 0.01		

*Statistically significant deviation from control group mean using Dunnett's test, $p < 0.05$.

[a]Numbers are Mean ± SD for indicated numbers of animals; body weights taken immediately prior to sacrifice following overnight fast.

TABLE 6

ETHYLENE GLYCOL MONOMETHYL ETHER: 13-WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Terminal Body Weights and Absolute and Relative Organ Weights of Rabbits[a]

Exposure Conc. (ppm)	N	Sex	Body Wt.	Liver		Kidney		Brain		Spleen		Thymus		Testes	
				g	g/100	g	g/100	g	g/100	g	g/100	g	g/100	g	g/100
0	5	Male	4102.80	97.62	2.38	17.75	0.41	9.95	0.25	1.11	0.03	6.72	0.16	5.49	0.14
			528.21	16.31	0.30	1.89	0.04	0.20	0.03	0.36	0.01	1.76	0.03	0.54	0.03
30	5		4255.40	104.67	2.44	17.87	0.42	10.46	0.25	1.44	0.03	6.72	0.16	5.47	0.13
			288.16	26.67	0.47	2.59	0.05	0.75	0.01	0.57	0.01	0.70	0.02	1.69	0.04
100	5		4036.00	90.52	2.25	17.30	0.43	9.79	0.25	1.29	0.03	5.78	0.14	4.01	0.10
			568.80	17.40	0.35	1.62	0.06	0.56	0.04	0.36	0.01	1.60	0.02	1.38	0.03
300	3		3745.00	97.08	2.57	21.67	0.50*	9.31	0.25	1.44	0.04	3.26*	0.09*	1.49*	0.04*
			368.97	20.27	0.30	3.95	0.06	0.38	0.02	0.15	0.01	1.26	0.03	0.35	0.01
0	5	Female	4511.40	105.65	2.32	16.98	0.38	9.99	0.23	1.58	0.04	8.11	0.18		
			675.86	24.59	0.33	2.83	0.04	0.36	0.04	0.49	0.01	3.45	0.06		
30	5		4767.80	122.38	2.57	16.96	0.36	9.43	0.20	1.58	0.03	8.14	0.17		
			435.08	10.55	0.15	2.32	0.04	0.35	0.02	0.32	0.01	1.81	0.04		
100	3		3810.33	82.54	2.20	18.29	0.49	9.44	0.25	1.43	0.04	6.08	0.16		
			410.06	14.28	0.58	7.24	0.24	0.79	0.04	0.51	0.01	0.95	0.01		
300	3		3944.67	95.64	2.45	18.10	0.46	10.00	0.25	1.33	0.03	3.61*	0.09*		
			217.89	25.32	0.77	3.79	0.12	0.29	0.01	0.21	0.00	0.43	0.01		

*Statistically significant deviation from control group mean using Dunnett's test, $p < 0.05$.

[a]Numbers are Mean ± SD for indicated numbers of animals; body weights taken immediately prior to sacrifice.

TABLE 7

ETHYLENE GLYCOL MONOMETHYL ETHER: 13-WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Hematology Data for Male Rats After 4 Weeks of Exposure[a]

ppm	RBC x10⁶/cu mm	HGB gm/dl	PCV (HCT) %	MCV μ³	MCH μμg	MCHC %	PLAT x 10³/cu mm	WBC x 10³ cu mm	Differential Count % Neutrophils Seg	Band	Juv	Lym	Mon	Eos	Bas	NucT RBC/100 WBC
0	8.00 0.47	16.7 0.6	49.3 2.0	62 2.0	21.0 0.8	34.0 0.8	1243 142	12.3 2.8	13	0	0	82	4	1	0	0
30	8.10 0.55	16.3 0.8	48.4 2.7	60* 1.3	20.2* 0.5	33.7 0.5	1205 147	12.8 5.7	13	0	0	83	3	1	0	0
100	8.17 0.24	16.4 0.4	48.9 1.0	60* 1.6	20.1* 0.6	33.6 0.6	1210 153	12.3 5.0	11	0	0	84	4	1	0	0
300	7.92 0.50	15.5* 0.9	46.0* 2.4	58* 1.1	19.7* 0.6	33.8 0.5	924* 104	7.5* 2.3	12	0	0	85	3	0	0	0
Hematology Data for Female Rats After 4 Weeks of Exposure[a]																
0	7.72 0.38	15.9 0.7	48.3 2.6	63 1.8	20.7 0.7	33.0 0.6	2664 174	10.2 3.3	13	0	0	85	1	1	0	0
30	7.82 0.53	15.8 0.6	47.9 2.0	61 2.5	20.2 1.0	33.0 0.7	2781 253	10.8 2.6	13	0	0	85	1	1	0	0
100	7.80 0.31	15.7 0.4	47.8 1.1	61 1.3	20.1 0.5	32.8 0.4	2610 218	8.4 2.4	10	0	0	89	1	1	0	0
300	7.26* 0.27	14.1* 0.4	43.8* 1.3	60* 1.7	19.5* 0.6	32.3* 0.5	2111* 328	4.4* 1.0	11	0	0	88	1	1	0	0

*Statistically significant deviation from control mean using Dunnett's test, $p < 0.05$.

[a]Values are Mean ± SD values for n = 10 animals.

TABLE 8

ETHYLENE GLYCOL MONOMETHYL ETHER: 13-WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Hematology Data for Male Rabbits After 4 Weeks of Exposure

ppm	n	RBC x10⁶/ cu mm	HGB gm/dl	PCV (HCT) %	MCV µ³	MCH µµg	MCHC %	PLAT x 10³/ cu mm	WBC x 10³ cu mm	Differential Count % Neutrophils Seg	Bnd	Juv	Lym	Mon	Eos	Bas	Nucl RBC/ 100 WBC
0	5	5.85 0.81	13.8 1.8	39.6 5.1	68 2	23.6 0.9	34.8 0.5	1517 307	9.0 2.6	37	0	0	58	3	1	1	0
30	5	5.73 0.46	13.5 1.2	38.8 3.3	67 1	23.5 0.5	34.7 0.8	1226 150	9.6 2.0	36	0	0	58	2	1	3	0
100	5	5.59 0.40	12.9 0.8	37.2 2.2	67 2	23.2 0.9	34.8 0.8	1188 238	8.1 2.0	29	0	0	65	1	2	3	0
300	3	4.79 0.99	10.7 1.9	31.2 6.4	65 1	22.5 0.7	34.5 0.8	829* 227	4.9* 0.5	28	0	0	66	2	2	2	0
Hematology Data for Female Rabbits After 4 Weeks of Exposure																	
0	5	5.72 0.57	13.5 0.6	38.5 2.4	67 3	23.7 1.4	35.1 0.6	1175 102	8.6 2.4	30	0	0	66	1	1	2	0
30	5	6.03 0.45	13.3 0.9	39.1 2.7	65 2	22.2 0.8	34.1 0.4	1445 221	9.1 3.5	43	0	0	49	2	2	4	0
100	3	5.23 0.18	12.5 0.4	35.3 1.0	67 1	23.9 0.2	35.5 0.1	1263 444	6.8 1.8	33	0	0	58	1	1	7	0
300	4	4.74 0.87	10.3* 2.1	30.9* 4.9	66 2	21.8 1.9	33.3 2.6	1239 554	4.6 1.4	36	0	0	59	1	2	2	0

*Statistically significant deviation from control mean using Dunnett's test, $p < 0.05$.

TABLE 9

ETHYLENE GLYCOL MONOMETHYL ETHER: 13-WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Hematology Data for Male Rats After 12 Weeks of Exposure[a]

ppm	RBC $\times 10^6$/cu mm	HGB gm/dl	PCV (HCT) %	MCV μ^3	MCH µµg	MCHC %	PLAT $\times 10^3$/cu mm	WBC $\times 10^3$/cu mm	Differential Count % Neutrophils Seg	Bnd	Juv	Lym	Mon	Eos	Bas	Nucl RBC/100 WBC
0	8.69 0.68	17.3 1.0	52.1 2.8	60.1 2.2	19.9 0.6	33.1 0.5	1381 140	13.7 5.0	13	0	0	85	1	1	0	0
30	8.70 0.52	16.4 0.6	49.4 2.3	57.4* 1.7	19.1* 0.4	33.2 0.7	1316 179	10.5 2.4	11	0	0	88	0	1	0	0
100	8.83 0.20	16.8 0.5	50.9 1.8	57.6* 1.9	19.1* 0.6	33.1 0.8	1336 127	11.8 2.5	9	0	0	89	0	2	0	0
300	8.48 0.52	15.5* 1.2	46.5* 3.6	54.9* 1.7	18.3* 0.5	33.4 0.6	953* 120	8.6* 2.8	11	0	0	88	0	1	0	0

Hematology Data for Female Rats after 12 Weeks of Exposure[a]

0	7.86 0.38	16.1 0.6	48.8 1.9	62.2 1.8	20.6 0.5	33.1 0.4	1317 156	9.6 2.8	10	0	0	89	0	1	0	0
30	8.12 0.50	16.3 0.6	49.9 2.0	61.5 3.0	20.1 0.9	32.7 0.6	1402 132	8.3 1.9	9	0	0	90	0	1	0	0
100	8.14 0.15	16.2 0.4	49.0 1.3	60.3 1.6	19.9 0.5	33.1 0.5	1345 125	9.0 2.4	10	0	0	88	0	2	0	0
300	7.66 0.38	14.7* 0.6	44.6* 1.9	58.2* 2.3	19.2* 0.8	32.9 0.8	1166* 148	4.5* 1.8	9	0	0	90	0	1	0	0

*Statistically significant deviation from control mean using Dunnett's test, $p < 0.05$.

[a]Numbers are Mean ± SD values for n = 10 animals.

TABLE 10

ETHYLENE GLYCOL MONOMETHYL ETHER: 13-WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Hematology Data for Male Rabbits After 12 Weeks of Exposure

ppm	n	RBC x10⁶/ cu mm	HGB gm/dl	PCV (HCT) %	MCV μ³	MCH μμg	MCHC %	PLAT x 10³/ cu mm	WBC x 10³/ cu mm	Differential Count % Neutrophils Seg	Bnd	Juv	Lym	Mon	Eos	Bas	Nucl RBC/ 100 WBC
0	5	5.90 0.37	14.6 0.9	42.8 2.7	71.4 1.5	24.5 0.9	34.2 0.6	759 153	8.5 1.6	51	0	0	45	0	1	3	0
30	5	5.89 0.24	14.3 0.6	41.9 1.5	71.2 0.5	24.2 0.4	34.0 0.5	732 103	9.9 1.3	40	0	0	55	0	1	4	0
100	5	5.48 0.24	13.4 0.5	39.0 1.7	71.0 1.6	24.5 0.5	34.5 0.4	702 88	8.7 1.5	44	0	0	52	0	1	3	0
300	4	4.02* 0.73	9.6* 1.6	28.1* 5.0	70.0 0.8	24.0 0.6	34.4 0.6	469* 187	4.1* 0.9	40	0	0	56	0	1	3	4

Hematology Data for Female Rabbits After 12 Weeks of Exposure

ppm	n	RBC x10⁶/ cu mm	HGB gm/dl	PCV (HCT) %	MCV μ³	MCH μμg	MCHC %	PLAT x 10³/ cu mm	WBC x 10³/ cu mm	Differential Count % Neutrophils Seg	Bnd	Juv	Lym	Mon	Eos	Bas	Nucl RBC/ 100 WBC
0	5	5.39 0.49	12.7 0.6	37.8 2.4	70.4 2.2	23.7 1.4	33.7 1.1	787 103	7.7 2.7	49	0	0	47	0	0	4	0
30	5	5.60 0.25	12.8 0.3	38.5 1.5	68.8 1.3	22.9 0.9	33.3 0.8	883 255	6.8 1.1	55	0	0	37	0	0	8	0
100	2	4.86 0.52	11.5 0.9	34.3 2.9	70.5 2.1	23.6 0.6	33.4 0.1	924 409	8.3 2.6	49	0	0	45	1	0	5	0
300	4	3.54* 0.31	8.5* 0.8	25.0* 2.2	70.8 1.3	23.9 1.3	33.9 1.4	687 236	3.5* 1.2	73	0	0	23	1	1	2	0

*Statistically significant deviation from control mean using Dunnett's test, $p < 0.05$.

TABLE 11

ETHYLENE GLYCOL MONOMETHYL ETHER: 13-WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Clinical Chemistry Data for Male Rats[a]

ppm	BUN mg/dl	SGPT mU/ml	AP mU/ml	Gluc mg/dl	TP g/dl	Alb g/dl	Glob g/dl	TBili mg/dl
0	17 3	18 4	64 28	136 12	5.7 0.3	3.2 0.2	2.4 0.2	0.3 0.1
30	15 2	20 6	65 14	127 19	6.1* 0.4	3.4 0.1	2.5 0.4	0.3 0.1
100	16 2	18 7	45* 8	131 15	5.6 0.6	3.3 0.2	2.2 0.6	0.3 0.1
300	16 4	11* 3	48 13	139 20	5.0* 0.2	3.1* 0.1	1.9* 0.2	0.2 0.0

Clinical Chemistry Data for Female Rats[a]

0	15 3	14 3	32 7	150 18	6.1 0.3	3.8 0.2	2.4 0.2	0.3 0.1
30	14 2	15 3	29 9	134 12	6.2 0.4	3.9 0.3	2.2 0.2	0.3 0.1
100	15 2	21 12	24 7	133* 11	5.9 0.3	3.7 0.2	2.2 0.2	0.4* 0.1
300	17 3	11* 3	26 8	126* 19	5.1* 0.2	3.4* 0.1	1.6* 0.3	0.4 0.1

*Statistically significant deviation from control mean using Duncett's test, $p < 0.05$.

[a]Numbers are Mean ± SD values for n = 10 animals.

TABLE 12

ETHYLENE GLYCOL MONOMETHYL ETHER: 13-WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Clinical Chemistry Data for Male Rabbits[a]

ppm	n	BUN mg/dl	SGPT mU/ml	AP mU/ml	Gluc mg/dl	TP g/dl	Alb g/dl	Glob g/dl	TBili mg/dl
0	5	17± 3	16± 5	21± 6	166±29	5.7±0.4	3.4±0.1	2.3±0.3	0.3±0.1
30	5	17± 2	19± 4	31± 7	176±23	5.3±0.2	3.5±0.1	1.8±0.2	0.4±0.2
100	5	17± 2	16± 4	21± 7	171±28	5.4±0.6	3.5±0.2	2.0±0.4	0.4±0.2
300	5	36±15	20± 4	20±12	147± 2	6.0±0.1	3.4±0.2	2.6±0.2	0.3±0.1

Clinical Chemistry Data for Female Rabbits

0	5	22± 4	21± 7	24± 6	208±90	5.5±0.3	3.4±0.1	2.1±0.3	0.2±0.1
30	5	23± 2	21±12	24±15	183±42	5.9±0.4	3.4±0.1	2.4±0.3	0.2±0.2
100	5	58±62	26±21	16± 9	153±50	5.3±0.6	3.0±0.4	2.3±0.8	0.3±0.1
300	3	17± 4	26±13	12± 3	165±14	5.2±0.1	3.2±0.1	2.0±0.2	0.2±0.2

[a]Numbers are Mean ± SD values for indicated numbers of animals.

No statistically significant deviation from control group mean using Dunnett's test, $p < 0.05$.

TABLE 13

ETHYLENE GLYCOL MONOMETHYL ETHER: 13-WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Urinalysis Data for Male Rats

ppm	Animal Number	Specific Gravity	pH	Protein	Sugar	Ketones	Bilirubin	Blood	Urobilinogen
0	80-A-1613	1.022	7.5	+	-	-	-	-	1
	1614	1.052	7.5	++	-	-	-	-	1
	1615	1.046	7.5	++	-	-	-	-	1
	1616	1.044	6.5	++	-	-	-	-	1
	1617	1.046	8.0	++	-	-	-	-	1
	1618	1.028	7.5	++	-	-	-	-	1
	1619	1.042	6.5	++	-	-	-	-	1
	1620	1.058	7.0	+++	-	-	QNS	QNS	QNS
	1621	1.058	7.0	++	-	-	-	-	1
	1622	1.048	6.5	++	-	-	-	-	1
	Mean	1.044							1
	±S.D.	0.012							
30	80-A-1623	1.046	8.0	++	-	-	-	-	1
	1624	1.018	7.5	++	-	-	-	-	1
	1625	1.060	6.5	++	-	-	-	-	1
	1626	1.042	7.0	++	-	QNS	QNS	QNS	QNS
	1627	1.020	7.5	+	-	-	-	-	1
	1628	1.034	7.0	++	-	-	-	-	1
	1629	1.042	7.0	++	-	-	-	-	1
	1630	1.022	7.5	++	-	-	-	-	1
	1631	1.040	7.0	++	-	-	-	-	1
	1632	1.034	7.0	++	-	-	-	-	1
	Mean	1.036							1
	±S.D.	0.013							
100	80-A-1633	1.060	7.0	++	-	-	-	-	1
	1634	1.045	8.0	++	-	-	-	-	1
	1635	1.052	7.5	++	-	-	-	-	1
	1636	1.054	6.5	++	-	-	-	-	1
	1637	1.014	7.0	+	-	-	-	-	1
	1638	1.022	6.5	++	-	-	-	-	1
	1639	1.026	7.5	+	-	-	-	-	1
	1640	1.062	6.5	++	-	-	-	-	1
	1641	1.040	7.0	++	-	-	-	-	1
	1642	1.056	6.5	++	-	-	-	-	1
	Mean	1.043							1
	±S.D.	0.017							
300	80-A-1643	1.036	7.0	++	-	-	-	-	1
	1644	1.008	6.5	+	-	-	-	+	1
	1645	QNS	QNS	QNS	QNS	QNS	QNS	QNS	QNS
	1646	1.025	QNS	QNS	QNS	QNS	QNS	QNS	QNS
	1647	1.020	7.0	++	-	-	-	+	1
	1648	QNS	QNS	QNS	QNS	QNS	QNS	QNS	QNS
	1649	1.022	6.5	++	-	-	-	-	1
	1650	1.030	7.0	++	-	-	-	-	1
	1651	QNS	QNS	QNS	QNS	QNS	QNS	QNS	QNS
	1652	1.009	7.0	+	-	-	-	-	1
	Mean	1.021*							
	±S.D.	0.010							

*Statistically significant deviation from control mean using Dunnett's test, $p < 0.05$.

QNS = quantity not sufficient

TABLE 14

ETHYLENE GLYCOL MONOMETHYL ETHER: 13-WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Urinalysis Data for Female Rats

ppm	Animal Number	Specific Gravity	pH	Protein	Sugar	Ketones	Bilirubin	Blood	Urobilinogen
0	80-A-1653	1.062	7.0	++	-	-	-	-	1
	1654	QNS	QNS	QNS	QNS	QNS	QNS	QNS	QNS
	1655	1.010	6.5	+	-	-	-	-	1
	1656	1.046	7.0	++	-	-	QNS	QNS	QNS
	1657	1.046	8.0	++	-	-	-	-	1
	1658	1.010	7.5	++	-	-	QNS	QNS	QNS
	1659	1.033	8.0	++	-	-	-	-	1
	1660	1.032	7.0	+	-	-	-	-	1
	1661	1.038	QNS	QNS	QNS	QNS	QNS	QNS	QNS
	1662	QNS	QNS	QNS	QNS	QNS	QNS	QNS	QNS
	Mean	1.035							
	±S.D.	0.018							
30	80-A-1663	1.030	7.0	+	QNS	QNS	QNS	QNS	QNS
	1664	1.036	7.0	++	-	-	-	-	1
	1665	1.036	7.5	++	-	-	-	-	1
	1666	1.046	7.5	++	-	-	-	-	1
	1667	1.038	7.5	++	-	-	-	-	1
	1668	1.006	6.5	+	-	-	-	-	1
	1669	1.012	7.0	+	-	-	-	-	1
	1670	1.022	8.0	++	-	-	-	-	1
	1671	1.066	7.0	++	-	-	-	-	1
	1672	1.050	6.5	++	-	-	-	-	1
	Mean	1.034							
	±S.D.	0.018							
100	80-A-1673	1.026	7.0	++	-	-	QNS	QNS	QNS
	1674	1.050	7.0	++	-	-	-	-	1
	1675	1.012	7.0	+	QNS	QNS	QNS	QNS	QNS
	1676	1.005	6.5	++	-	-	-	-	1
	1677	1.028	8.0	++	-	-	-	-	1
	1678	1.045	7.5	++	-	-	-	-	1
	1679	QNS	QNS	QNS	QNS	QNS	QNS	QNS	QNS
	1680	1.030	7.5	++	-	-	-	-	1
	1681	1.012	7.0	+	-	-	-	-	1
	1682	1.003	6.5	+	-	-	-	-	1
	Mean	1.024							
	±S.D.	0.016							
300	80-A-1683	1.008	6.5	+	-	-	-	-	1
	1684	1.012	6.5	+	-	-	-	-	1
	1685	1.027	QNS	QNS	QNS	QNS	QNS	QNS	QNS
	1686	1.010	7.0	+	-	-	-	-	1
	1687	1.042	6.5	++	-	-	-	-	1
	1688	QNS	QNS	QNS	QNS	QNS	QNS	QNS	QNS
	1689	1.012	7.5	+	-	-	-	-	1
	1690	1.009	6.5	+	-	-	-	-	1
	1691	1.012	QNS	QNS	QNS	QNS	QNS	QNS	QNS
	1692	1.011	6.5	+	-	-	-	-	1
	Mean	1.016*							
	±S.D.	0.011							

*Statistically significant deviation from control mean using Dunnett's test, $p < 0.05$.

QNS = quantity not sufficient

TABLE 15

ETHYLENE GLYCOL MONOMETHYL ETHER: 13-WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Gross Pathologic Observations in Male and Female Rats[a]

Sex	Male				Female			
Exposure Concentration (ppm)	0	30	100	300	0	30	100	300
Number of rats in group	10	10	10	10	10	10	10	10
Number of rats with no observations	8	6	8	0	10	7	7	0
External								
Corneal cloudiness, unilateral	1	1	0	0	0	0	0	0
Pinpoint lenticular foci, bilateral	0	0	1	0	0	0	1	0
Periorbital hemorrhage with or without enlargement (2° to orbital eye bleeding)	0	2	0	1	0	0	1	0
Broken tooth or teeth	1	3	0	1	0	0	0	0
Overgrown incisor teeth	0	2	0	0	0	0	0	0
Liver								
Slightly accentuated lobular pattern	0	0	1	0	0	0	0	0
Thymus								
Decreased size	0	0	0	6	0	0	0	10
Spleen								
Capsule thickened and white	0	0	0	1	0	0	0	0
Large Intestine								
Focal thickening	1	0	0	0	0	0	0	0
Abdomen								
Decreased amount of fat	0	0	0	0	0	0	0	5
Brain								
Moderate hydrocephalus	0	0	0	0	0	0	0	1
Testes								
Decreased in size and flaccid	0	0	0	10	-	-	-	-
Uterus								
Dilated by clear fluid (normal cyclic changes)	-	-	-	-	0	3	1	0

[a]Data presented as the number of animals with the specified observations. - = Not applicable.

TABLE 16

ETHYLENE GLYCOL MONOMETHYL ETHER: 13-WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Gross Pathologic Observations in Male and Female Rabbits[a]

Sex	Male				Female			
Exposure Concentration (ppm)	0	30	100	300	0	30	100	300
Number of rabbits in group	5	5	5	3[b]	5	5	3[b]	3[b]
Number of rabbits with no observations	5	3	1	0	4	5	2	0
External								
Exudate in ear canal(s)	0	0	0	2	0	0	0	0
Exudate in nose and around eyes	0	0	0	0	0	0	1	0
Fecal soiling on perineum and feet	0	0	0	1	0	0	0	0
Abdomen								
Decreased amount of fat	0	0	0	2	0	0	0	2
Lymphoid Tissue								
Decreased mediastinal tissue (thymus and fat)	0	0	0	2	0	0	0	3
Decreased lymphoid tissue in cecal appendix and sacculus rotundus	0	0	0	3	0	0	1	2
Kidneys								
Pitted capsular surface, bilateral	0	0	0	0	1	0	0	0
Diffusely pale, slightly swollen, bilateral	0	0	0	0	0	0	1	0
Mottled appearance	0	0	0	1	0	0	0	0
Adrenals								
Enlarged, bilateral	0	0	0	1	0	0	0	0
Lungs								
Focal consolidation	0	0	0	1	0	0	0	0
Small Intestines								
Focal areas of necrosis and hemorrhage	0	0	0	0	0	0	1	0
Cecum								
Contents dark (2° to hemorrhage)	0	0	0	0	0	0	1	0
Testes								
Decreased size, slight or moderate	0	2	4	0	-	-	-	-
Decreased in size and flaccid, marked	0	0	0	3	-	-	-	-

[a]Data presented as the number of animals with the specified observations. - = Not applicable.

[b]There were two rabbits in each of these groups which died spontaneously or were killed moribund prior to the scheduled 13-week kill and are not included in this tabulation (see Table 7).

TABLE 17

ETHYLENE GLYCOL MONOMETHYL ETHER: 13 WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Histopathologic Findings in Male Rats[a]

SEX	MALES			
EXPOSURE CONCENTRATION IN PPM	0	30	100	300
NUMBER OF RATS EXAMINED	10	10	10	10
LIVER (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	10	0	0	10
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, PORTAL, MULTIFOCAL: - VERY SLIGHT	3	-	-	8
AGGREGATE(S) OF RETICULOENDOTHELIAL CELLS, MULTIFOCAL: - VERY SLIGHT	1	-	-	0
HEART (NO. OF TISSUES EXAMINED)	6	-	-	2
NO LESIONS RECOGNIZED:	10	0	0	10
AGGREGATE(S) OF RETICULOENDOTHELIAL CELLS, SUBENDOCARDIUM, FOCAL: - VERY SLIGHT	8	-	-	9
DEGENERATION WITH OR WITHOUT INFLAMMATION, MYOCARDIUM, FOCAL: - VERY SLIGHT	1	-	-	1
SPLEEN (NO. OF TISSUES EXAMINED)	1	-	-	0
NO LESIONS RECOGNIZED:	10	10	10	10
ADHESIONS - FIBROUS, CAPSULE, DIFFUSE:	10	10	8	9
EXTRAMEDULLARY HEMATOPOIESIS: - SLIGHT	0	0	0	1
THICKENED, CAPSULE, FOCAL: - SLIGHT	0	0	1	0
	0	0	1	0
BRAIN (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	10	0	0	10
	10	-	-	10
PITUITARY (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	10	0	0	10
	10	-	-	10
SPINAL CORD (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	9	10	10	10
	9	10	10	10
PERIPHERAL NERVE (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	10	0	0	10
	10	-	-	10
PANCREAS (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	10	1	1	10
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, INTERSTITIUM, FOCAL: - VERY SLIGHT	9	1	1	8
ATROPHY, ACINI, FOCAL: - SLIGHT	1	0	0	1
	0	0	0	1
BONE (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	10	10	10	10
	10	10	10	10
BONE MARROW (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	10	10	10	10
	10	10	10	10
ADRENAL (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	10	0	0	10
	10	-	-	10

[a]Data presented as the number of animals with the specified observation or for which the specified tissue was examined. - = Not applicable.

TABLE 17 (continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: 13 WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Histopathologic Findings in Male Rats[a]

SEX		MALES			
EXPOSURE CONCENTRATION IN PPM		0	30	100	300
NUMBER OF RATS EXAMINED		10	10	10	10
KIDNEY (NO. OF TISSUES EXAMINED)		10	0	0	10
NO LESIONS RECOGNIZED:		9	-	-	9
CHRONIC PROGRESSIVE GLOMERULONEPHROPATHY, BILATERAL:					
DILATATION, PELVIS:	- VERY SLIGHT	1	-	-	0
	- SLIGHT	0	-	-	1
STOMACH (NO. OF TISSUES EXAMINED)		10	0	0	10
NO LESIONS RECOGNIZED:		10	-	-	10
SMALL INTESTINE (NO. OF TISSUES EXAMINED)		10	0	0	10
NO LESIONS RECOGNIZED:		10	-	-	10
CECUM (NO. OF TISSUES EXAMINED)		10	0	0	10
NO LESIONS RECOGNIZED:		10	-	-	10
LARGE INTESTINE (NO. OF TISSUES EXAMINED)		10	0	0	10
NO LESIONS RECOGNIZED:		9	-	-	8
INFLAMMATION - SUPPURATIVE, SUBMUCOSA, DIFFUSE:	- MODERATE	1	-	-	0
PARASITES - NEMATODE, LUMEN:		0	-	-	2
CERVICAL LYMPH NODE (NO. OF TISSUES EXAMINED)		2	0	0	5
NO LESIONS RECOGNIZED:		2	-	-	5
MEDIASTINAL LYMPH NODE (NO. OF TISSUES EXAMINED)		10	3	2	9
NO LESIONS RECOGNIZED:		10	2	2	9
HEMORRHAGE, SINUSOIDS:	- SLIGHT	0	1	0	0
PIGMENT - GOLDEN BROWN (HEMATOGENOUS), SINUSOIDS:	- SLIGHT	0	1	0	0
MESENTERIC LYMPH NODE (NO. OF TISSUES EXAMINED)		10	10	10	10
NO LESIONS RECOGNIZED:		10	10	10	10
TESTICLE (NO. OF TISSUES EXAMINED)		10	10	10	10
NO LESIONS RECOGNIZED:		10	10	10	0
DEGENERATION, GERMINAL CELLS, BILATERAL, DIFFUSE:	- MODERATE	0	0	0	3
DEGENERATION, GERMINAL CELLS, BILATERAL, DIFFUSE:	- SEVERE	0	0	0	7
EPIDIDYMIS (NO. OF TISSUES EXAMINED)		10	0	0	10
NO LESIONS RECOGNIZED:		10	-	-	0
DECREASED SPERMATIC ELEMENTS:		0	-	-	10
DEGENERATIVE SPERMATIC ELEMENTS, INTRATUBULAR:		0	-	-	10
SEMINAL VESICLE (NO. OF TISSUES EXAMINED)		10	0	0	10
NO LESIONS RECOGNIZED:		10	-	-	10
COAGULATING GLAND (NO. OF TISSUES EXAMINED)		10	0	0	10
NO LESIONS RECOGNIZED:		10	-	-	10

[a]Data presented as the number of animals with the specified observation or for which the specified tissue was examined. - = Not applicable.

TABLE 17 (continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: 13 WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Histopathologic Findings in Male Rats[a]

SEX		MALES			
EXPOSURE CONCENTRATION IN PPM		0	30	100	300
NUMBER OF RATS EXAMINED		10	10	10	10
PROSTATE (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		10	0	0	10
DECREASED SECRETORY MATERIAL:		8	-	-	1
INFLAMMATION - CHRONIC, INTERSTITIUM:	- MODERATE	1	-	-	9
	- SLIGHT	1	-	-	1
URINARY BLADDER (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		9	0	0	10
		9	-	-	10
LUNGS (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		10	0	0	10
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, SUBPLEURAL, MULTIFOCAL:	- VERY SLIGHT	3	-	-	6
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, PERIVASCULAR, MULTIFOCAL:	- VERY SLIGHT	1	-	-	0
ALVEOLAR HISTIOCYTOSIS, MULTIFOCAL:	- VERY SLIGHT	1	-	-	0
ALVEOLAR HISTIOCYTOSIS, MULTIFOCAL:	- SLIGHT	2	-	-	1
EMPHYSEMA, ALVEOLI, FOCAL:	- VERY SLIGHT	3	-	-	3
INFLAMMATION - ACUTE, INTERSTITIUM, FOCAL:	- VERY SLIGHT	1	-	-	0
		1	-	-	0
SKELETAL MUSCLE (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		10	0	0	10
		10	-	-	10
SALIVARY GLAND (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		10	0	0	10
		10	-	-	10
THYMUS (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		10	10	10	10
ATROPHY, LYMPHOID TISSUE:	- SLIGHT	10	10	10	3
		0	0	0	7
MEDIASTINAL TISSUE (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		10	0	0	10
		10	-	-	10
AORTA (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		10	0	0	10
		10	-	-	10
ESOPHAGUS (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		10	0	0	10
		10	-	-	10
THYROID GLAND (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		10	0	0	10
CYST(S) WITH KERATINOUS DEBRIS, FOCAL:		9	-	-	8
CYST(S) WITH KERATINOUS DEBRIS, MULTIFOCAL:		0	-	-	2
		1	-	-	0
PARATHYROID GLAND (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		8	0	0	9
		8	-	-	9
TRACHEA (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		10	0	0	10
		10	-	-	10

[a]Data presented as the number of animals with the specified observation or for which the specified tissue was examined. - = Not applicable.

TABLE 17 (continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: 13 WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Histopathologic Findings in Male Rats[a]

SEX	MALES			
EXPOSURE CONCENTRATION IN PPM	0	30	100	300
NUMBER OF RATS EXAMINED	10	10	10	10
SKIN (NO. OF TISSUES EXAMINED)	10	0	0	10
NO LESIONS RECOGNIZED:	10	-	-	10
MAMMARY GLAND (NO. OF TISSUES EXAMINED)	8	0	0	9
NO LESIONS RECOGNIZED:	8	-	-	9
EYE (NO. OF TISSUES EXAMINED)	10	0	0	10
NO LESIONS RECOGNIZED:	10	-	-	9
INFLAMMATION - SUPPURATIVE, GENERALIZED, UNILATERAL, DIFFUSE: - SEVERE	0	-	-	1
TONGUE (NO. OF TISSUES EXAMINED)	10	0	0	10
NO LESIONS RECOGNIZED:	10	-	-	10
NASAL TURBINATES (NO. OF TISSUES EXAMINED)	10	0	0	10
NO LESIONS RECOGNIZED:	7	-	-	5
INFLAMMATION - SUPPURATIVE, RESPIRATORY EPITHELIUM, UNILATERAL, FOCAL:	0	-	-	3
INFLAMMATION - SUPPURATIVE, NASOLACRIMAL DUCT, UNILATERAL, FOCAL:	0	-	-	1
METAPLASIA - SQUAMOUS, RESPIRATORY EPITHELIUM, UNILATERAL, FOCAL:	2	-	-	4
INFLAMMATORY EXUDATE, LUMEN:	1	-	-	0
INFLAMMATORY EXUDATE, NASOLACRIMAL DUCT:	0	-	-	1
MESENTERIC TISSUE (NO. OF TISSUES EXAMINED)	9	10	10	10
NO LESIONS RECOGNIZED:	8	9	10	10
INFLAMMATION - CHRONIC, ADIPOSE TISSUE, FOCAL: - VERY SLIGHT	1	0	0	0
PERIARTERITIS: - SLIGHT	0	1	0	0
LACRIMAL GLAND (NO. OF TISSUES EXAMINED)	10	0	0	10
NO LESIONS RECOGNIZED:	5	-	-	7
INFLAMMATION - CHRONIC, UNILATERAL, FOCAL (SECONDARY TO EYE BLEEDING):	5	-	-	3
LARYNX (NO. OF TISSUES EXAMINED)	10	0	0	10
NO LESIONS RECOGNIZED:	9	-	-	10
HYPERPLASIA - EPITHELIAL, DIFFUSE: - SLIGHT	1	-	-	0
INFLAMMATION - CHRONIC, MUCOSA, DIFFUSE: - SLIGHT	1	-	-	0

[a]Data presented as the number of animals with the specified observation or for which the specified tissue was examined. - = Not applicable.

TABLE 18

ETHYLENE GLYCOL MONOMETHYL ETHER: 13 WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Histopathologic Findings in Female Rats[a]

SEX	FEMALES			
EXPOSURE CONCENTRATION IN PPM	0	30	100	300
NUMBER OF RATS EXAMINED	10	10	10	10
LIVER (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	10	0	0	10
AGGREGATE(S) OF RETICULOENDOTHELIAL CELLS, MULTIFOCAL:	4	-	-	6
NECROSIS WITH ACCOMPANYING INFLAMMATION, HEPATOCELLULAR, FOCAL: - VERY SLIGHT	6	-	-	3
	0	-	-	1
HEART (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	10	0	0	10
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, MYOCARDIUM, FOCAL: - VERY SLIGHT	9	-	-	10
	1	-	-	0
SPLEEN (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	10	10	10	10
ADHESIONS - FIBROUS, CAPSULE, DIFFUSE:	9	10	7	7
EXTRAMEDULLARY HEMATOPOIESIS:	0	0	0	2
PIGMENT - HEMATOGENOUS - INCREASED: - MODERATE	0	0	2	0
THICKENED, CAPSULE, FOCAL:	1	0	1	0
- SLIGHT	0	0	0	1
BRAIN (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	10	0	0	10
HYDROCEPHALUS, VENTRICLE:	10	-	-	9
- MODERATE	0	-	-	1
PITUITARY (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	10	0	0	10
CYST, ANTERIOR (PARS DISTALIS), FOCAL:	9	-	-	9
FOCUS(I) OF ALTERED CELLS, ANTERIOR (PARS DISTALIS), FOCAL:	1	-	-	0
	0	-	-	1
SPINAL CORD (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	10	10	10	10
	10	10	10	10
PERIPHERAL NERVE (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	10	0	0	10
	10	-	-	10
PANCREAS (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	10	0	0	10
ATROPHY, ACINI, FOCAL: - SLIGHT	10	-	-	9
	0	-	-	1
BONE (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	10	10	10	10
	10	10	10	10
BONE MARROW (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	10	10	10	10
	10	10	10	10
ADRENAL (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	10	0	0	10
	10	-	-	10
KIDNEY (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	10	0	0	10
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, INTERSTITIUM, MULTIFOCAL: - VERY SLIGHT	9	-	-	8
	1	-	-	1

[a]Data presented as the number of animals with the specified observation or for which the specified tissue was examined. - = Not applicable.

TABLE 18 (continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: 13 WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Histopathologic Findings in Female Rats[a]

SEX		FEMALES			
EXPOSURE CONCENTRATION IN PPM		0	30	100	300
NUMBER OF RATS EXAMINED		10	10	10	10
KIDNEY (CONTINUED)					
MINERALIZATION, CORTICOMEDULLARY JUNCTION, MULTIFOCAL:	- VERY SLIGHT	0	-	-	1
STOMACH (NO. OF TISSUES EXAMINED)		10	0	0	10
NO LESIONS RECOGNIZED:		10	-	-	10
SMALL INTESTINE (NO. OF TISSUES EXAMINED)		10	0	0	10
NO LESIONS RECOGNIZED:		10	-	-	10
CECUM (NO. OF TISSUES EXAMINED)		10	0	0	10
NO LESIONS RECOGNIZED:		10	-	-	10
LARGE INTESTINE (NO. OF TISSUES EXAMINED)		10	0	0	10
NO LESIONS RECOGNIZED:		10	-	-	9
PARASITES - NEMATODE, LUMEN:		0	-	-	1
CERVICAL LYMPH NODE (NO. OF TISSUES EXAMINED)		7	0	0	7
NO LESIONS RECOGNIZED:		6	-	-	6
PLASMOCYTOSIS OF MEDULLARY CORDS:	- MODERATE	1	-	-	1
MEDIASTINAL LYMPH NODE (NO. OF TISSUES EXAMINED)		9	3	2	9
NO LESIONS RECOGNIZED:		7	1	1	4
HEMORRHAGE, SINUSOIDS:	- SLIGHT	2	1	1	2
PIGMENT - GOLDEN BROWN (HEMATOGENOUS), SINUSOIDS:	- SLIGHT	1	1	0	5
MESENTERIC LYMPH NODE (NO. OF TISSUES EXAMINED)		10	10	10	10
NO LESIONS RECOGNIZED:		10	10	10	10
URINARY BLADDER (NO. OF TISSUES EXAMINED)		9	0	0	10
NO LESIONS RECOGNIZED:		9	-	-	10
OVARY (NO. OF TISSUES EXAMINED)		9	0	0	10
NO LESIONS RECOGNIZED:		8	-	-	10
CYST, BILATERAL, MULTIFOCAL:		1	-	-	0
OVIDUCT (NO. OF TISSUES EXAMINED)		9	0	0	10
NO LESIONS RECOGNIZED:		9	-	-	10
UTERUS (NO. OF TISSUES EXAMINED)		9	0	0	10
NO LESIONS RECOGNIZED:		9	-	-	10
CERVIX (NO. OF TISSUES EXAMINED)		9	0	0	10
NO LESIONS RECOGNIZED:		9	-	-	10
LUNGS (NO. OF TISSUES EXAMINED)		10	0	0	10
NO LESIONS RECOGNIZED:		5	-	-	6
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, SUBPLEURAL, MULTIFOCAL:	- VERY SLIGHT	1	-	-	1

[a]Data presented as the number of animals with the specified observation or for which the specified tissue was examined. - = Not applicable.

TABLE 18 (continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: 13 WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Histopathologic Findings in Female Rats[a]

SEX		FEMALES			
EXPOSURE CONCENTRATION IN PPM		0	30	100	300
NUMBER OF RATS EXAMINED		10	10	10	10
LUNGS (CONTINUED)					
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, PERIVASCULAR, MULTIFOCAL:	- VERY SLIGHT	0	-	-	1
ALVEOLAR HISTIOCYTOSIS, FOCAL:	- VERY SLIGHT	2	-	-	1
ALVEOLAR HISTIOCYTOSIS, MULTIFOCAL:	- VERY SLIGHT	2	-	-	1
HETEROTOPIC BONE, FOCAL:	- VERY SLIGHT	1	-	-	0
SKELETAL MUSCLE (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		10	0	0	10
		10	-	-	10
SALIVARY GLAND (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		10	0	0	10
		10	-	-	10
THYMUS (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		10	10	10	9
ATROPHY, LYMPHOID TISSUE:		10	10	10	1
	- SLIGHT	0	0	0	8
MEDIASTINAL TISSUE (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		10	0	0	10
HEMORRHAGE:		9	-	-	9
		1	-	-	1
AORTA (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		10	0	0	10
DISSECTING ANEURYSM:		10	-	-	9
		0	-	-	1
ESOPHAGUS (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		10	0	0	10
		10	-	-	10
THYROID GLAND (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		10	0	0	10
CYST(S) WITH KERATINOUS DEBRIS, FOCAL:		8	-	-	6
CYST(S) WITH KERATINOUS DEBRIS, MULTIFOCAL:		2	-	-	3
		0	-	-	1
PARATHYROID GLAND (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		9	0	0	7
		9	-	-	7
TRACHEA (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		10	0	0	10
		10	-	-	10
SKIN (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		10	0	0	10
		10	-	-	10
MAMMARY GLAND (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		10	0	0	10
		10	-	-	10
EYE (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		10	0	0	10
INFLAMMATION - CHRONIC ACTIVE, RETINA, UNILATERAL, DIFFUSE:		9	-	-	10
	- MODERATE	1	-	-	0

[a]Data presented as the number of animals with the specified observation or for which the specified tissue was examined. - = Not applicable.

TABLE 18 (continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: 13 WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Histopathologic Findings in Female Rats[a]

SEX	FEMALES			
EXPOSURE CONCENTRATION IN PPM	0	30	100	300
NUMBER OF RATS EXAMINED	10	10	10	10
TONGUE (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	10	0	0	10
	10	-	-	10
NASAL TURBINATES (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	10	0	0	10
CYSTIC DILATATION, SUBMUCOSAL GLANDS, FOCAL:	8	-	-	9
INFLAMMATION - SUPPURATIVE, RESPIRATORY EPITHELIUM, UNILATERAL, FOCAL:	2	-	-	0
METAPLASIA - SQUAMOUS, RESPIRATORY EPITHELIUM, UNILATERAL, FOCAL:	0	-	-	1
	0	-	-	1
MESENTERIC TISSUE (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	10	10	10	10
ATROPHY, ADIPOSE TISSUE:	10	10	10	8
	0	0	0	2
LACRIMAL GLAND (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	10	0	0	10
DEGENERATION, ACINI, UNILATERAL, FOCAL:	2	-	-	0
INFLAMMATION - CHRONIC, UNILATERAL, FOCAL (SECONDARY TO EYE BLEEDING):	1	-	-	0
INFLAMMATION - CHRONIC ACTIVE, UNILATERAL, FOCAL:	6	-	-	10
	1	-	-	0
LARYNX (NO. OF TISSUES EXAMINED)				
NO LESIONS RECOGNIZED:	10	0	0	10
	10	-	-	10

[a]Data presented as the number of animals with the specified observation or for which the specified tissue was examined. - = Not applicable.

TABLE 19

ETHYLENE GLYCOL MONOMETHYL ETHER: 13 WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Histopathologic Findings in Male Rabbits[a]

SEX		MALES			
EXPOSURE CONCENTRATION IN PPM		0	30	100	300
NUMBER OF RABBITS EXAMINED		5	5	5	3[b]
LIVER (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	5	3
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, PORTAL, MULTIFOCAL:		1	3	2	0
INFLAMMATION - CHRONIC, PORTAL, MULTIFOCAL:	- VERY SLIGHT	2	2	3	0
NECROSIS WITH ACCOMPANYING INFLAMMATION, HEPATOCELLULAR, FOCAL:	- SLIGHT	1	0	0	3
DECREASED GLYCOGEN, HEPATOCELLULAR:	- VERY SLIGHT	1	0	0	0
		1	1	1	3
GALLBLADDER (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	5	3
		5	5	5	3
HEART (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	5	3
DEGENERATION WITH OR WITHOUT INFLAMMATION, MYOCARDIUM, MULTIFOCAL:		4	5	5	0
	- VERY SLIGHT	1	0	0	3
SPLEEN (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	5	3
PIGMENT - HEMATOGENOUS - INCREASED:	- SLIGHT	5	5	5	2
		0	0	0	1
BRAIN (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	5	3
INFLAMMATION - CHRONIC, CEREBRUM, FOCAL:	- VERY SLIGHT	4	5	5	0
INFLAMMATION - CHRONIC, GENERALIZED, MULTIFOCAL (ENCEPHALITOZOONOSIS):		1	0	0	0
	- VERY SLIGHT	0	0	0	3
PITUITARY (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	4	5	3
		5	4	5	3
SPINAL CORD (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	5	3
INFLAMMATION - CHRONIC, GRAY MATTER, FOCAL:	- VERY SLIGHT	4	5	5	1
PERIVASCULAR MONONUCLEAR (LYMPHOID) CELL CUFFING, GRAY MATTER:		0	0	0	1
	- VERY SLIGHT	1	0	0	1
PERIPHERAL NERVE (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	5	3
PERIVASCULAR MONONUCLEAR (LYMPHOID) CELL CUFFING, FOCAL:		5	5	5	2
	- VERY SLIGHT	0	0	0	1
PANCREAS (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	5	3
ATROPHY, ACINI, FOCAL:		5	5	4	3
	- VERY SLIGHT	0	0	1	0
BONE (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	5	3
		5	5	5	3
BONE MARROW (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	5	3
		5	5	5	3

[a]Data presented as the number of animals with the specified observation or for which the specified tissue was examined. - = Not applicable.

[b]Two rabbits in each of these groups died or were killed moribund prior to scheduled sacrifice and are not included in this tabulation (see Table 7).

TABLE 19 (continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: 13 WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Histopathologic Findings in Male Rabbits[a]

SEX		MALES			
EXPOSURE CONCENTRATION IN PPM		0	30	100	300
NUMBER OF RABBITS EXAMINED		5	5	5	3[b]
ADRENAL (NO. OF TISSUES EXAMINED)		5	5	5	3
NO LESIONS RECOGNIZED:		2	3	5	2
AGGREGATE(S) OF RETICULOENDOTHELIAL CELLS, CORTEX, MULTIFOCAL:	- VERY SLIGHT	2	0	0	1
HYPERPLASIA - NODULAR, EXTRACAPSULAR, FOCAL:		2	0	0	0
HYPERPLASIA - NODULAR, EXTRACAPSULAR, MULTIFOCAL:		0	1	0	0
VACUOLIZATION CONSISTENT WITH FATTY CHANGE, CORTEX, DIFFUSE:	- VERY SLIGHT	0	1	0	0
KIDNEY (NO. OF TISSUES EXAMINED)		5	5	5	3
NO LESIONS RECOGNIZED:		0	2	1	0
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, INTERSTITIUM, MULTIFOCAL:	- VERY SLIGHT	1	1	2	0
ATROPHY, TUBULE(S), MULTIFOCAL:	- VERY SLIGHT	1	0	0	0
DILATATION, TUBULE(S), FOCAL:	- VERY SLIGHT	1	0	1	0
INFLAMMATION - CHRONIC, INTERSTITIUM, MULTIFOCAL (ENCEPHALITOZOONOSIS):	- SLIGHT	1	0	0	2
INFLAMMATION - CHRONIC, INTERSTITIUM, MULTIFOCAL (ENCEPHALITOZOONOSIS):	- MODERATE	0	0	0	1
MINERALIZATION, TUBULE(S), MULTIFOCAL:	- VERY SLIGHT	2	2	2	0
STOMACH (NO. OF TISSUES EXAMINED)		5	5	5	3
NO LESIONS RECOGNIZED:		5	4	5	3
INFLAMMATION - CHRONIC ACTIVE, GLANDULAR MUCOSA, FOCAL:	- SLIGHT	0	1	0	0
SMALL INTESTINE (NO. OF TISSUES EXAMINED)		5	5	5	3
NO LESIONS RECOGNIZED:		5	5	5	3
CECUM (NO. OF TISSUES EXAMINED)		5	5	5	3
NO LESIONS RECOGNIZED:		5	5	4	2
PARASITES - NEMATODE, LUMEN:		0	0	1	1
LARGE INTESTINE (NO. OF TISSUES EXAMINED)		5	5	5	3
NO LESIONS RECOGNIZED:		5	5	5	3
MEDIASTINAL LYMPH NODE (NO. OF TISSUES EXAMINED)		4	5	5	3
NO LESIONS RECOGNIZED:		4	5	5	3
MESENTERIC LYMPH NODE (NO. OF TISSUES EXAMINED)		4	5	5	3
NO LESIONS RECOGNIZED:		4	5	5	3
TESTICLE (NO. OF TISSUES EXAMINED)		5	5	5	3
NO LESIONS RECOGNIZED:		3	3	1	0
ATROPHY, TUBULE(S), FOCAL:	- SLIGHT	1	0	0	0
DEGENERATION, GERMINAL CELLS, BILATERAL, DIFFUSE:	- SLIGHT	0	1	0	0
DEGENERATION, GERMINAL CELLS, BILATERAL, DIFFUSE:	- MODERATE	0	0	2	0
DEGENERATION, GERMINAL CELLS, BILATERAL, DIFFUSE:	- SEVERE	0	0	1	3
HYPERPLASIA, SERTOLI CELL(S), FOCAL:	- SLIGHT	0	0	0	1
MULTINUCLEATED SPERMATIDS, MULTIFOCAL:	- VERY SLIGHT	1	1	1	0

[a]Data presented as the number of animals with the specified observation or for which the specified tissue was examined. - = Not applicable.

[b]Two rabbits in each of these groups died or were killed moribund prior to scheduled sacrifice and are not included in this tabulation (see Table 7).

TABLE 19 (continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: 13 WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Histopathologic Findings in Male Rabbits[a]

SEX		MALES			
EXPOSURE CONCENTRATION IN PPM		0	30	100	300
NUMBER OF RABBITS EXAMINED		5	5	5	3[b]
EPIDIDYMIS (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	5	3
CYST, SUBMUCOSA, FOCAL:		3	4	2	0
NO SPERM PRESENT:		0	1	0	0
DECREASED SPERMATIC ELEMENTS:		0	0	0	3
DEGENERATIVE SPERMATIC ELEMENTS, INTRATUBULAR:		0	0	2	0
INFLAMMATION - CHRONIC ACTIVE, CREMASTER MUSCLE, DIFFUSE:		0	0	3	0
	- SLIGHT	2	0	0	0
PROSTATE (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	5	3
		5	5	5	3
URINARY BLADDER (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	5	3
CYST, SUBMUCOSA, MULTIFOCAL:		5	4	5	3
		0	1	0	0
LUNGS (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	5	3
BRONCHOPNEUMONIA-SUBACUTE:		1	2	2	0
BRONCHOPNEUMONIA-SUBACUTE:	- SLIGHT	0	0	1	0
HYPERPLASIA - LYMPHOID, PERIBRONCHIOLAR:	- MODERATE	0	1	0	1
INFLAMMATION - CHRONIC, INTERSTITIUM, MULTIFOCAL:	- SLIGHT	0	0	1	1
PURULENT EXUATE, BRONCHI:	- SLIGHT	4	3	3	3
		0	0	1	0
SKELETAL MUSCLE (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	5	3
		5	5	5	3
SALIVARY GLAND (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		3	0	0	1
		3	-	-	1
THYMUS (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	5	3
ATROPHY, LYMPHOID TISSUE:		5	5	4	0
ATROPHY, LYMPHOID TISSUE:	- SLIGHT	0	0	1	0
ATROPHY, LYMPHOID TISSUE:	- MODERATE	0	0	0	2
	- SEVERE	0	0	0	1
MEDIASTINAL TISSUE (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	5	3
CYST:		5	5	5	2
		0	0	0	1
AORTA (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	5	3
MINERALIZATION, MEDIA, DIFFUSE:		4	5	5	3
		1	0	0	0
ESOPHAGUS (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	5	3
		5	5	5	3
THYROID GLAND (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		4	5	5	3
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, INTERSTITIUM, MULTIFOCAL:		4	4	3	1
	- VERY SLIGHT	0	1	1	0

[a]Data presented as the number of animals with the specified observation or for which the specified tissue was examined. - = Not applicable.

[b]Two rabbits in each of these groups died or were killed moribund prior to scheduled sacrifice and are not included in this tabulation (see Table 7).

TABLE 19 (continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: 13 WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Histopathologic Findings in Male Rabbits[a]

SEX		MALES			
EXPOSURE CONCENTRATION IN PPM		0	30	100	300
NUMBER OF RABBITS EXAMINED		5	5	5	3[b]
THYROID GLAND (CONTINUED)					
CYSTIC DILATATION, FOLLICLE(S), FOCAL:	- VERY SLIGHT	0	0	0	1
CYSTIC DILATATION, FOLLICLE(S), MULTIFOCAL:	- VERY SLIGHT	0	0	1	0
ULTIMOBRANCHIAL CYST:		0	0	0	1
PARATHYROID GLAND (NO. OF TISSUES EXAMINED)		1	2	3	2
NO LESIONS RECOGNIZED:		1	2	3	2
TRACHEA (NO. OF TISSUES EXAMINED)		5	5	5	3
NO LESIONS RECOGNIZED:		4	5	5	2
PURULENT EXUDATE, LUMEN:		1	0	0	1
SKIN (NO. OF TISSUES EXAMINED)		5	5	5	3
NO LESIONS RECOGNIZED:		5	5	5	3
EYE (NO. OF TISSUES EXAMINED)		5	5	5	3
NO LESIONS RECOGNIZED:		5	5	5	3
TONGUE (NO. OF TISSUES EXAMINED)		5	5	5	3
NO LESIONS RECOGNIZED:		5	5	3	2
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, MUSCLE, FOCAL:	- VERY SLIGHT	0	0	0	1
DEGENERATION, MUSCLE, DIFFUSE:	- SLIGHT	0	0	2	0
MESENTERIC TISSUE (NO. OF TISSUES EXAMINED)		5	5	5	3
NO LESIONS RECOGNIZED:		5	5	5	2
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, FOCAL:	- VERY SLIGHT	0	0	0	1
LACRIMAL GLAND (NO. OF TISSUES EXAMINED)		1	2	0	0
NO LESIONS RECOGNIZED:		1	2	-	-
LARYNX (NO. OF TISSUES EXAMINED)		5	5	5	3
NO LESIONS RECOGNIZED:		3	3	4	3
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, SUBMUCOSA, DIFFUSE:	- VERY SLIGHT	0	1	0	0
PURULENT EXUDATE, LUMEN:		2	2	1	0
SACCULUS ROTUNDUS (NO. OF TISSUES EXAMINED)		5	4	5	3
NO LESIONS RECOGNIZED:		2	2	4	0
ATROPHY, LYMPHOID TISSUE:	- MODERATE	0	0	0	3
PIGMENT, SUBMUCOSA, DIFFUSE:	- SLIGHT	3	2	1	0
APPENDIX (NO. OF TISSUES EXAMINED)		5	5	5	3
NO LESIONS RECOGNIZED:		5	5	2	0
ATROPHY, LYMPHOID TISSUE:	- SLIGHT	0	0	2	0
ATROPHY, LYMPHOID TISSUE:	- MODERATE	0	0	0	2
ATROPHY, LYMPHOID TISSUE:	- SEVERE	0	0	0	1
CYSTIC DILATATION, SUBMUCOSAL GLANDS, MULTIFOCAL:	- VERY SLIGHT	0	0	1	0

[a]Data presented as the number of animals with the specified observation or for which the specified tissue was examined. - = Not applicable.

[b]Two rabbits in each of these groups died or were killed moribund prior to scheduled sacrifice and are not included in this tabulation (see Table 7).

TABLE 20

ETHYLENE GLYCOL MONOMETHYL ETHER: 13 WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Histopathologic Findings in Female Rabbits[a]

SEX		FEMALES			
EXPOSURE CONCENTRATION IN PPM		0	30	100	300
NUMBER OF RABBITS EXAMINED		5	5	3[b]	3[b]
LIVER (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	3	3
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, PORTAL, MULTIFOCAL:		1	2	1	0
HYPERPLASIA, BILE DUCTS, FOCAL:	- VERY SLIGHT	2	2	2	2
INFLAMMATION - CHRONIC, PORTAL, MULTIFOCAL:	- SLIGHT	0	1	0	0
NECROSIS, HEPATOCELLULAR, MULTIFOCAL:	- SLIGHT	2	1	0	0
THROMBUS - ACUTE OR RECENT, MULTIFOCAL:	- SLIGHT	0	0	1	0
NECROSIS WITH ACCOMPANYING INFLAMMATION, HEPATOCELLULAR, FOCAL:		0	0	1	0
NECROSIS WITH ACCOMPANYING INFLAMMATION, HEPATOCELLULAR, MULTIFOCAL:	- VERY SLIGHT	0	0	0	1
DECREASED GLYCOGEN, HEPATOCELLULAR:	- VERY SLIGHT	0	0	0	1
		0	0	1	2
GALLBLADDER (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	3	3
		5	5	3	3
HEART (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	3	3
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, INTERSTITIUM, MULTIFOCAL:	- VERY SLIGHT	4	5	3	3
		1	0	0	0
SPLEEN (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	3	3
PIGMENT - HEMATOGENOUS - INCREASED:	- SLIGHT	4	3	1	3
HYALINIZATION, FOLLICLES (WHITE PULP):	- SLIGHT	1	1	2	0
		0	1	0	0
BRAIN (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	3	3
INFLAMMATION - CHRONIC, GENERALIZED, MULTIFOCAL (ENCEPHALITOZOONOSIS):	- VERY SLIGHT	3	4	3	2
PERIVASCULAR MONONUCLEAR (LYMPHOID) CELL CUFFING, CEREBELLUM, FOCAL:	- VERY SLIGHT	1	1	0	1
		1	0	0	0
PITUITARY (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	3	3
		5	5	3	3
SPINAL CORD (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	4	3	3
INFLAMMATION - CHRONIC, GRAY MATTER, FOCAL:	- VERY SLIGHT	5	4	3	2
		0	0	0	1
PERIPHERAL NERVE (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		3	4	3	3
		3	4	3	3
PANCREAS (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	3	3
		5	5	3	3
BONE (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	3	3
		5	5	3	3

[a]Data presented as the number of animals with the specified observation or for which the specified tissue was examined. - = Not applicable.

[b]Two rabbits in each of these groups died or were killed moribund prior to scheduled sacrifice and are not included in this tabulation (see Table 7).

TABLE 20 (continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: 13 WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Histopathologic Findings in Female Rabbits[a]

SEX		FEMALES			
EXPOSURE CONCENTRATION IN PPM		0	30	100	300
NUMBER OF RABBITS EXAMINED		5	5	3[b]	3[b]
BONE MARROW (NO. OF TISSUES EXAMINED)		5	5	3	3
NO LESIONS RECOGNIZED:		5	5	2	3
HYPERPLASIA, MYELOID:	- MODERATE	0	0	1	0
ADRENAL (NO. OF TISSUES EXAMINED)		5	5	3	3
NO LESIONS RECOGNIZED:		5	5	3	3
KIDNEY (NO. OF TISSUES EXAMINED)		5	5	3	3
NO LESIONS RECOGNIZED:		2	1	0	1
DILATATION, TUBULE(S), FOCAL:	- VERY SLIGHT	0	1	1	0
DILATATION, TUBULE(S), MULTIFOCAL:	- VERY SLIGHT	1	1	0	1
DILATATION, TUBULE(S), BILATERAL, DIFFUSE:	- SLIGHT	0	0	1	0
INFLAMMATION - CHRONIC, INTERSTITIUM, MULTIFOCAL (ENCEPHALITOZOONOSIS):	- SLIGHT	2	1	0	1
MINERALIZATION, TUBULE(S), MULTIFOCAL:	- VERY SLIGHT	1	2	1	2
MINERALIZATION, TUBULE(S), MULTIFOCAL:	- SLIGHT	1	1	1	0
STOMACH (NO. OF TISSUES EXAMINED)		5	5	3	3
NO LESIONS RECOGNIZED:		4	5	3	3
INFLAMMATION - SUBACUTE, SUBMUCOSA, FOCAL:	- SLIGHT	1	0	0	0
SMALL INTESTINE (NO. OF TISSUES EXAMINED)		5	5	3	3
NO LESIONS RECOGNIZED:		5	5	2	3
INFLAMMATION - NECROTIZING, TRANSMURAL, DIFFUSE:	- SEVERE	0	0	1	0
CECUM (NO. OF TISSUES EXAMINED)		5	5	3	3
NO LESIONS RECOGNIZED:		5	4	2	3
INFLAMMATION - SUBACUTE, SUBMUCOSA, DIFFUSE:	- SLIGHT	0	1	0	0
PARASITES - NEMATODE, LUMEN:		0	0	1	0
LARGE INTESTINE (NO. OF TISSUES EXAMINED)		5	5	3	3
NO LESIONS RECOGNIZED:		5	5	3	3
MEDIASTINAL LYMPH NODE (NO. OF TISSUES EXAMINED)		5	5	3	3
NO LESIONS RECOGNIZED:		5	4	2	3
INFLAMMATION - SUBACUTE, DIFFUSE:	- MODERATE	0	0	1	0
PIGMENT - GOLDEN BROWN (HEMATOGENOUS), SINUSOIDS:	- SLIGHT	0	1	0	0
MESENTERIC LYMPH NODE (NO. OF TISSUES EXAMINED)		5	5	3	3
NO LESIONS RECOGNIZED:		5	5	3	3
URINARY BLADDER (NO. OF TISSUES EXAMINED)		5	5	3	3
NO LESIONS RECOGNIZED:		5	4	3	3
INFLAMMATION - SUBACUTE, SUBMUCOSA, DIFFUSE:	- MODERATE	0	1	0	0
OVARY (NO. OF TISSUES EXAMINED)		5	5	3	3
NO LESIONS RECOGNIZED:		5	5	2	3
MULTILOCULAR CYST:		0	0	1	0

[a]Data presented as the number of animals with the specified observation or for which the specified tissue was examined. - = Not applicable.

[b]Two rabbits in each of these groups died or were killed moribund prior to scheduled sacrifice and are not included in this tabulation (see Table 7).

TABLE 20 (continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: 13 WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Histopathologic Findings in Female Rabbits[a]

SEX		FEMALES			
EXPOSURE CONCENTRATION IN PPM		0	30	100	300
NUMBER OF RABBITS EXAMINED		5	5	3[b]	3[b]
OVIDUCT (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	3	3
CYST, SEROSA:		4	4	3	3
INFLAMMATION - CHRONIC, SUBMUCOSA, UNILATERAL, FOCAL:		1	0	0	0
	- SLIGHT	0	1	0	0
UTERUS (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	3	3
CYSTIC DILATATION, ENDOMETRIAL GLANDS, FOCAL:	- SLIGHT	4	5	3	3
		1	0	0	0
CERVIX (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	3	3
		5	5	3	3
LUNGS (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	3	3
BRONCHOPNEUMONIA-SUBACUTE:		1	0	0	0
FIBROSIS, INTERSTITIUM, FOCAL:	- SLIGHT	0	0	1	0
HYPERPLASIA - LYMPHOID, PERIBRONCHIOLAR, FOCAL:	- SLIGHT	1	0	0	0
INFLAMMATION - CHRONIC, INTERSTITIUM, MULTIFOCAL:	- SLIGHT	0	1	0	0
	- VERY SLIGHT	4	4	3	3
SKELETAL MUSCLE (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	4	3	3
		5	4	3	3
SALIVARY GLAND (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	2	3
ATROPHY, ACINI, FOCAL:		3	4	1	3
INFLAMMATION - SUPPURATIVE, FOCAL:	- VERY SLIGHT	1	0	1	0
VACUOLIZATION, ACINI, FOCAL:	- SLIGHT	1	0	0	0
	- SLIGHT	0	1	0	0
THYMUS (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	3	3
ATROPHY, LYMPHOID TISSUE:		5	5	2	1
ATROPHY, LYMPHOID TISSUE:	- MODERATE	0	0	0	2
	- SEVERE	0	0	1	0
MEDIASTINAL TISSUE (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	3	3
		5	5	3	3
AORTA (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	3	3
MINERALIZATION, INTIMA, DIFFUSE:	- SLIGHT	4	5	3	3
		1	0	0	0
ESOPHAGUS (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	3	3
		5	5	3	3
THYROID GLAND (NO. OF TISSUES EXAMINED)					
NO LESIONS RECOGNIZED:		5	5	3	3
AGGREGATE(S) OF MONONUCLEAR (PREDOMINATELY LYMPHOID) CELLS, INTERSTITIUM, FOCAL:	- SLIGHT	4	1	2	2
DILATATION, FOLLICLE(S), FOCAL:	- VERY SLIGHT	0	1	0	0
ULTIMOBRANCHIAL CYST:		1	2	0	1
		0	3	1	0

[a]Data presented as the number of animals with the specified observation or for which the specified tissue was examined. - = Not applicable.

[b]Two rabbits in each of these groups died or were killed moribund prior to scheduled sacrifice and are not included in this tabulation (see Table 7).

TABLE 20 (continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: 13 WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Histopathologic Findings in Female Rabbits[a]

SEX		FEMALES			
EXPOSURE CONCENTRATION IN PPM		0	30	100	300
NUMBER OF RABBITS EXAMINED		5	5	3[b]	3[b]
PARATHYROID GLAND (NO. OF TISSUES EXAMINED)		2	4	2	2
NO LESIONS RECOGNIZED:		2	4	2	2
TRACHEA (NO. OF TISSUES EXAMINED)		5	5	3	3
NO LESIONS RECOGNIZED:		5	5	3	3
SKIN (NO. OF TISSUES EXAMINED)		2	5	3	3
NO LESIONS RECOGNIZED:		2	5	3	3
MAMMARY GLAND (NO. OF TISSUES EXAMINED)		2	5	3	2
NO LESIONS RECOGNIZED:		2	5	3	2
EYE (NO. OF TISSUES EXAMINED)		5	5	3	3
NO LESIONS RECOGNIZED:		5	5	3	3
TONGUE (NO. OF TISSUES EXAMINED)		5	5	3	3
NO LESIONS RECOGNIZED:		4	4	2	3
DEGENERATION, MUSCLE, DIFFUSE:	- SLIGHT	1	1	1	0
MESENTERIC TISSUE (NO. OF TISSUES EXAMINED)		5	5	3	3
NO LESIONS RECOGNIZED:		5	5	3	3
LARYNX (NO. OF TISSUES EXAMINED)		4	5	3	3
NO LESIONS RECOGNIZED:		4	5	3	3
SACCULUS ROTUNDUS (NO. OF TISSUES EXAMINED)		5	5	3	3
NO LESIONS RECOGNIZED:		4	5	3	0
ATROPHY, LYMPHOID TISSUE:	- MODERATE	0	0	0	3
PIGMENT, SUBMUCOSA, DIFFUSE:	- SLIGHT	1	0	0	0
APPENDIX (NO. OF TISSUES EXAMINED)		5	5	3	3
NO LESIONS RECOGNIZED:		5	5	0	0
ATROPHY, LYMPHOID TISSUE:	- SLIGHT	0	0	2	0
ATROPHY, LYMPHOID TISSUE:	- MODERATE	0	0	0	3
ATROPHY, LYMPHOID TISSUE:	- SEVERE	0	0	1	0
PARASITES - NEMATODE, CRYPTS:		0	0	1	0

[a]Data presented as the number of animals with the specified observation or for which the specified tissue was examined. - = Not applicable.

[b]Two rabbits in each of these groups died or were killed moribund prior to scheduled sacrifice and are not included in this tabulation (see Table 7).

TABLE 21

ETHYLENE GLYCOL MONOMETHYL ETHER: 13-WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Summary of Gross and Histopathologic Findings in Rabbits Dying Spontaneously or Killed Moribund

Animal Data[a]	Gross Observations	Histopathologic Findings
80A-1835 Male 300 ppm 26 days Died	Stomach devoid of feed; clotted blood in lumen of small intestine; slight serous atrophy of abdominal fat; diffuse pulmonary consolidation.	Liver - Aggregate(s) of mononuclear (predominately lymphoid) cells, portal, multifocal, very slight. Necrosis, hepatocellular, multifocal, very slight. Decreased glycogen, hepatocellular. Spleen - Pigment, hematogenous, increased, slight. Brain - Inflammation, chronic, cerebrum, focal, very slight. Kidney - Mineralization, tubule(s), multifocal, very slight. Small Intestine - Hemorrhage, submucosa, diffuse, severe. Testicle - Degeneration, germinal cells, bilateral, diffuse, moderate. Epididymis - Degenerative spermatic elements, intratubular. Inflammation, chronic, cremaster muscle, diffuse, slight. Lungs - Bronchopneumonia, suppurative, diffuse, severe. Thymus - Atrophy, lymphoid tissue, severe. Appendix - Atrophy, lymphoid tissue, moderate. Cause of death: Bronchopneumonia.
80A-1834 Male 300 ppm 93 days Died	Both testes extremely small; several wart-like lesions on ventral surface of tongue	Liver - Inflammation, chronic, portal, multifocal, slight. Decreased glycogen, hepatocellular. Heart - Aggregate(s) of mononuclear (predominately lymphoid) cells, interstitium, multifocal, very slight. Brain - Inflammation, chronic, generalized, multifocal, very slight. Spinal Cord - Inflammation, chronic, generalized, multifocal, very slight. Kidney - Inflammation, chronic, interstitium, multifocal, slight. Testicle - Degeneration, germinal cells, bilateral, diffuse, severe. Epididymis - No sperm present. Lungs - Inflammation, chronic, interstitium, multifocal, slight. Tongue - Oral papillomatosis, benign, primary, no metastasis. Sacculus Rotundus - Atrophy, lymphoid tissue, moderate. Appendix - Atrophy, lymphoid tissue, moderate.
80A-1901 Female 100 ppm 9 days Killed moribund	Slight exudate around left eye and in left ear canal; tympanic bullae full of purulent exudate.	Liver - Aggregate(s) of mononuclear (predominately lymphoid) cells, portal, multifocal, very slight. Vacuolization consistent with fatty change, slight. Decreased glycogen, hepatocellular. Spleen - Hyalinization, follicles (white pulp), moderate. Kidney - Dilatation, tubule(s), multifocal, very slight. Mineralization, tubule(s), multifocal, slight. Oviduct - Cyst, serosa. Skeletal Muscle - Degeneration with or without inflammation, muscle fibers, multifocal, very slight. Thymus - Atrophy, lymphoid tissue, moderate. Tongue - Degeneration, muscle, diffuse, slight. Sacculus Rotundus - Atrophy, lymphoid tissue, moderate. Parasites, nematode, crypts. Appendix - Atrophy, lymphoid tissue, moderate. Parasites, nematode, crypts.

[a]Animal data includes animal number, sex, exposure concentration, number of days on test before death, and the mode of death.

TABLE 21 (continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: 13-WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Summary of Gross and Histopathologic Findings in Rabbits Dying Spontaneously or Killed Moribund

Animal Data[a]	Gross Observations	Histopathologic Findings
80A-1902 Female 100 ppm 21 days Died	Lungs congested, possibly edematous.	Liver - Congestion, diffuse, moderate. Decreased glycogen, hepatocellular. Pancreas - Ectopic spleen. Kidney - Congestion, corticomedullary junction, diffuse, moderate. Lungs - Congestion, diffuse, moderate. Inflammation, chronic interstitium, multifocal, very slight. Appendix - Atrophy, lymphoid tissue, moderate.
80A-1905 Female 300 ppm 20 days Killed moribund	Mucoid exudate around nares; liver pale; ball of matted hair in stomach; scant GI contents; CBC results: Hct - 37.5, RBC - 5.96 x $10^6/mm^3$, Hb - 13.2 mg%, WBC - 4.2 x $10^3/mm^3$.	Liver - Inflammation, chronic, portal, multifocal, slight. Vacuolization consistent with fatty change, diffuse, slight. Spleen - Atrophy, generalized, slight. Pancreas - Decreased secretory granules, acini. Adrenal - Mineralization, cortex, multifocal, slight. Vacuolization consistent with fatty change, cortex, bilateral, diffuse, slight. Kidney - Altered cytoplasmic homogeneity - decreased cortical tubules, diffuse, slight. Dilatation, tubule(s), diffuse, slight. Inflammation, chronic, portal, multifocal, slight. Mineralization, tubule(s), multifocal, very slight. Stomach - Edema, pyloric mucosa, diffuse, moderate. Ovary - Follicular cyst. Skeletal Muscle - Degeneration, granular, muscle fibers, diffuse, moderate. Thymus - Atrophy, lymphoid tissue, severe. Thyroid Gland - Dilatation, follicle(s), focal, very slight. Tongue - Decreased secretory material, submucosal glands. Sacculus Rotundus - Atrophy, lymphoid tissue, severe. Appendix - Atrophy, lymphoid tissue, severe. Inflammation, catarrhal, diffuse, slight.
80A-1903 Female 300 ppm 87 days Died	Carcass autolysed; kidneys pitted; GI contents fluid; clotted blood in small intestine; liver decreased in size; decreased abdominal fat.	Liver - Aggregate(s) of mononuclear (predominately lymphoid) cells, portal, multifocal, very slight. Heart - Aggregate(s) of mononuclear (predominately lymphoid) cells, interstitium, focal, very slight. Small Intestine - Inflammation, necrotizing, transmural, diffuse, moderate. Lungs - Abscess, multifocal. Edema, alveoli, diffuse. Thymus - Atrophy, lymphoid tissue, moderate. Aorta - Mineralization, media, diffuse, slight. Tongue - Oral papillomatosis, benign, primary, no metastasis. Sacculus Rotundus - Atrophy, lymphoid tissue, severe. Cause of death: Acute necrotizing enteritis, inanition.

[a]Animal data includes animal number, sex, exposure concentration, number of days on test before death, and the mode of death.

APPENDIX 1

ETHYLENE GLYCOL MONOMETHYL ETHER: 13-WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS

Tissue Samples Obtained and Preserved from all Animals at the Time of Necropsy

Adrenal Glands
Accessory Sex Glands
Aorta
Brain
Cecum
Cervix
Epididymides
Esophagus
Eyes
Gallbladder (rabbits only)
Heart
Kidneys
Large Intestine
Larynx
Liver
Lungs (bronchi)
Lymph Nodes
(Thoracic, Mesenteric)
Mammary Tissue
Mediastinal Tissue
Mesenteric Tissue
Nasal Turbinates
Ovaries
Oviducts
Pancreas
Parathyroid
Peripheral Nerve (Sciatic)
Pituitary
Salivary Glands
(Submandibular)
Skeletal Muscle
Skin
Small Intestine
Spinal Cord and Thoracic
Vertebral Column with
Bone Marrow
Spleen
Sternum
Stomach
Testes
Thymus
Thyroid
Tongue
Trachea
Urinary Bladder
Uterus
Any gross lesions or masses

APPENDIX II

ETHYLENE GLYCOL MONOMETHYL ETHER: 13-WEEK VAPOR INHALATIN STUDY WITH RATS AND RABBITS

Exposure Concentrations and Exposure Chamber Conditions

Target Conc.	Analytical Concentration			Nominal Concentrations		Temp.[c] (°F)	Rel. Hum.[d] (%)
	Analytical Conc.[a]	Coeff. of Variation[b]	Range of Measurements	Mean ± S.D.	Range		
0	-	-	-	-	-	70-79	63.9 ±7.7
30 ppm	30.5 ± 0.9	3%	28-33	29.4± 0.9	28-34	70-78	61.1 ±7.3
100 ppm	101.1 ± 2.3	2%	89-110	98.2± 1.9	93-100	70-78	57.2 ±6.5
300 ppm	305.3 ± 8.8	8%	251-319	295 ± 6.3	281-312	70-78	60.8 ±8.8

[a]Numbers are Mean ± SD daily time-weighted average (TWA) values for n = 72 days.

[b]Coefficient of variation is the standard deviation of the daily TWA measurements divided by the mean value (x100).

[c]Range of minimum and maximum value in each chamber during the course of the study.

[d]Mean ± SD of daily measurements taken while exposures in progress.

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ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY PROBE STUDY IN RATS AND RABBITS†

BY:

T. R. Hanley, Jr., B. L. Yano, K. D. Nitschke
and J. A. John

REVIEWED BY:

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January 29, 1982

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†Sponsored by The Chemical Manufacturers Association

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SUMMARY

The objective of this study was to establish the maximum tolerated exposure level of ethylene glycol monomethyl ether (EGME) in pregnant rats and rabbits during the period of major organogenesis. Bred Fischer 344 rats and inseminated New Zealand white rabbits were exposed to EGME via inhalation for 6 hr/day on days 6 through 15 (rats) or 6 through 18 (rabbits) of gestation.

Among rats, maternal toxicity was observed at an exposure level of 400 ppm as evidenced by significantly reduced body weight gain and changes in spleen and thymus weights reflecting primary toxicity. Significant decreases in liver and kidney weights secondary to decreased body weight gain were also observed. Necropsy examination of these animals revealed decreased thymic size and occasional facial staining with porphyrin pigments. Rats exposed to 200 ppm of EGME exhibited similar, though less severe, indications of maternal toxicity. Embryolethality, evidenced by complete resorption of all litters, was observed in both the 200 and 400 ppm exposure groups. No evidence of maternal or embryo-toxicity was observed among rats exposed to 50 ppm of EGME.

Maternal toxicity was observed among inseminated rabbits exposed to 200 or 400 ppm of EGME. Two of seven rabbits exposed to 400 ppm died during the period of exposure. Maternal body weight gain and organ weights were markedly reduced among rabbits exposed to 200 or 400 ppm of EGME. Necropsy examination revealed dose-related increases in distended gall bladder, small pale liver, decreased thymic size, pale bone marrow and decreased abdominal adipose tissue and intestinal ingesta, among rabbits exposed to 200 or 400 ppm of EGME. Complete resorption of all litters was observed among rabbits at 200 and 400 ppm. Exposure of rabbits to 50 ppm resulted in an increased incidence of resorptions.

Based on the results of this probe study, exposure levels of 200 and 400 ppm were considered maternally toxic and embryo-lethal in both rats and rabbits. An exposure level of 50 ppm was well tolerated by pregnant rats. However, exposure to 50 ppm resulted in an increased incidence of resorptions among pregnant rabbits. Therefore, exposure levels of 3, 10 and 50 ppm were selected for the definitive teratology study in both rats and rabbits.

SUMMARY

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ETHYLENE GLYCOL MONOMETHYL ETHER:
INHALATION TERATOLOGY PROBE STUDY
IN RATS AND RABBITS†

BY:

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January 29, 1982

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SUMMARY

The objective of this study was to evaluate the embryotoxic and teratogenic potential of ethylene glycol monomethyl ether (EGME) in mice via inhalation. Bred CF-1 mice were exposed to 0, 10 or 50 ppm of EGME for 6 hr/day on days 6 through 15 of gestation and the fetuses examined on day 18 of gestation for any deleterious effects on embryonal or fetal development.

Among maternal mice, a slight but statistically significantly lower weight gain was observed at 50 ppm during the last 4 days of exposure. There were no other indications of a maternal effect at 10 or 50 ppm. Low incidences of major malformations were observed among control as well as exposed mice. The incidence of major malformations, considered individually or collectively within each exposure group, was not significantly different from the controls. Significant increases in the incidences of unilateral testicular hypoplasia and extra (lumbar) ribs, both considered minor alterations in mice, were observed at 50 ppm indicating a slight fetotoxic effect. There were no treatment-related effects observed among mice at 10 ppm.

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ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION REPRODUCTION AND DOMINANT LETHAL STUDY IN RATS

B-17c

By:

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SUMMARY

Groups of male and female Sprague-Dawley (CD) rats were exposed to 0, 30, 100, or 300 ppm ethylene glycol monomethyl ether (EGME, DOWANOL* EM) vapor 6 hours/day, 5 days/week for 13 weeks. The 0 and 30 ppm groups each contained 30 rats/sex and the 100 and 300 ppm groups each had 20 rats/sex. Following the exposure period, males were bred to unexposed females to evaluate reproductive capability and dominant lethality. Additional mating of 300 ppm exposed males was performed during the post-exposure period in order to evaluate the recovery of fertility prior to sacrifice at 23 weeks post-exposure. Exposed females were bred with unexposed males to assess reproductive parameters. Female rats were sacrificed 15 weeks post-exposure. At sacrifice a complete gross examination and selected tissue histopathologic evaluation was conducted.

Results of the present study indicate a potential for inhaled EGME to completely suppress fertility in male rats at the 300 ppm level. Fertility of these rats was partially reversible at 13 weeks post-exposure. Body weights of animals in the 300 ppm group were reduced as a result of the exposures. No effect on dominant lethality or fertility was observed in male rats exposed to 30 or 100 ppm EGME. Dominant lethality could not be assessed in the 300 ppm group as a result of infertility. Treatment-related pathologic alterations were observed only in male rats at the 300 ppm level and included decreased testicular size and atrophic seminiferous tubules. Female rats tolerated up to 300 ppm EGME without any adverse reproductive effects. Based on these results, it was concluded that the no-adverse effect level of EGME for fertility and reproduction was 100 ppm in rats.

*Trademark of The Dow Chemical Company.

INTRODUCTION

Ethylene glycol monomethyl ether (DOWANOL* EM; 2-methoxy-ethanol; EGME) is a volatile, nearly odorless liquid with the following properties:

Structural formula:	CH_3-O-CH_2-CH_2-OH
Molecular weight:	76.09
Vapor Pressure:	9.5 mmHg @ 25°C
Solubility:	Miscible with water
Flash Point:	107°F

Rowe and Wolf (1981) have provided a comprehensive review of the available toxicological literature pertaining to EGME. In addition, recent short-term two-week vapor inhalation studies, in which rats, mice and rabbits were exposed to 0, 100, 300 or 1000 ppm (0, 0.31, 0.93 or 3.11 mg/l), resulted in adverse effects on body weight gain, peripheral blood counts, bone marrow, testes, and lymphoid tissues in animals exposed to the high concentration (Miller et al. 1980, 1981). Similar but less pronounced changes in some of these parameters also occurred in animals exposed to 300 ppm, while 100 ppm had no appreciable adverse effects during the course of the two-week studies.

*Trademark of The Dow Chemical Company.

McGregor et al. (1981) recently reported results of multiple assays for the genotoxic potential of EGME. Antifertility effects were seen in a dominant lethal assay during weeks 3-8 of treatment. Frequencies of mouse sperm abnormalities were increased after 5 weeks of exposure, but not at other time points. There was no evidence of a clastogenic response in bone marrow cells, or for increases in bacterial mutations in the Ames assay, or for induction of DNA repair synthesis.

A teratology study was recently reported by Nagano et al., (1981). ICR mice were administered EGME by gavage on days 7 through 14 of gestation, at dose levels of 0, 31.25, 62.5, 125, 250, 500 or 1000 mg/kg/day. Maternal toxicity in the form of marked leucopenia was observed at the highest dose level. A significant increase in fetal deaths was observed at dose levels of 250, 500 and 1000 mg/kg/day and teratogenic effects (exencephaly, umbilical hernia, abnormal digits, spina bifida, and skeletal malformations) were observed at dose levels of 62.5 mg/kg and above. The lowest dose level (31.25 mg/kg) resulted in delayed skeletal ossification indicative of fetotoxicity.

In view of the toxic effect of EGME on the testes of rats in short-term studies, the present study was initiated to (1) evaluate the effect of EGME on the reproductive capability of treated animals, (2) determine a level of exposure to EGME that does not have an effect on reproduction, (3) assess whether any observed effects are mediated via the male or female animal, (4) evaluate the potential dominant lethality in treated male rats, and (5) evaluate the reversibility of any observed effects.

MATERIALS AND METHODS

Chemical EGME was obtained from the production facilities of Dow Chemical USA, Michigan Division, Midland, MI. Gas chromatographic analysis of the test material (Lot 54, tank 374) indicated a purity of 99.78-99.93% (Hermann, 1980).

Animals Male and female Sprague-Dawley rats (6-8 weeks of age) were purchased from Charles River Breeding Laboratories, Portage, MI. This strain was considered preferable to the Fischer 344 strain because of the high background incidence of testicular abnormalities which occur in the Fischer 344 rat. The Sprague-Dawley strain was considered suitable because the testicular effects observed in EGME probe studies were reported in this strain. The animals were acclimated to laboratory conditions for at least 10 days prior to initiation of inhalation exposures.

During the acclimation period, the animals were weighed, and those animals found to be outliers on the basis of their body weight (identified by sequential method described by Grubbs, 1969) were removed from the study, and animals from the extremes of the distribution were discarded until only the number required for the study remained. The animals remaining were ranked by body weight and sequentially selected in a random manner for assignment to each dose level.

Each animal was individually identified with a metal ear tag. During the exposure period all animals were housed two per cage in stainless steel cages with wire bottoms in 14.5 m^3 inhalation chambers. At the completion of the inhalation exposures, animals were housed individually in wire bottomed cages in a room designed to control temperature (approximately 70°F), humidity (approximately 45%), and light cycle (12 hours light and dark). A standard laboratory diet (Purina Certified Laboratory Chow, Ralston Purina Co., St. Louis, MO) was available ad libitum except during exposure periods. Water was available via automatic water devices ad libitum. Animals were exposed 6 hours/day, 5 days/week (excluding holidays) for 13 weeks. Rats and rabbits for a concurrent 90-day toxicity study were housed in the same chambers with the animals for this reproduction study (Miller et al. 1981).

Chambers The exposures were conducted in 14.5 m^3 chambers with stainless steel ceilings, and epoxy resin-coated walls and floors. Air supply to the chambers was controlled by a system designed to maintain temperature at approximately 70°F and relative humidity at approximately 50%. Temperature and relative humidity in the exposure chambers were recorded daily. The chambers were operated under dynamic airflow conditions (total chamber airflow of approximately 2500 liters per minute) at a slight negative pressure relative to the surrounding area. Control and exposure groups of animals were housed in identical chambers. Clean, filtered air was supplied to the exposure chambers during periods when exposures were not being conducted.

Vapor Generation and Analysis Animals were exposed to 0, 30, 100 or 300 ppm (0.09, 0.31 or 0.93 mg/l) 6 hours per day, 5 days per week, for a total of 13-weeks. The test atmospheres were generated as described by Miller et al., (1980), with minor modifications. Liquid test material was metered at calculated rates into glass vaporization tubes. Vapors from the tubes were swept into the chamber inlet ducts with compressed air. The compressed air to the vaporization tubes was preheated to the minimal extent necessary (approximately 120°C) to ensure complete vaporization using a compressed air flameless heat torch (Master, Model FHT-4). The nominal concentration (ratio of the

amount of EGME vaporized to the total airflow through the chamber) was calculated for each chamber on a daily basis. The actual concentration of EGME in each exposure chamber was measured 1-2 times per hour by infrared spectroscopy using a Miran I infrared gas analyzer at a wavelength of 8.8 µm. Concentrations in the chambers were interpolated from standard curves derived from standards of known concentration. Standardization of the analytical system was evaluated with at least one standard prior to each day of exposure.

EXPERIMENTAL DESIGN

The experimental design of the study is summarized in Table 1. Groups of 30 male and 30 female rats were exposed to 0 and 30 ppm of EGME vapor. Groups of 20 male and 20 female rats were exposed to 100 and 300 ppm EGME vapor. Exposure continued for 6 hours/day, 5 days/week (Monday through Friday) for 13 consecutive weeks. Exposures were initiated on 28 July 1980 and were continued up to 24 October 1980.

At the end of the 13-week exposure period, animals were held for a minimum of 13 weeks during which time the effects of the exposure on reproduction were assessed. Female rats were sacrificed on February 3rd and 4th, 1981,

approximately 15 weeks after the termination of exposure, while male rats were sacrificed on April 8th and 9th, 1981, approximately 23 weeks after the termination of exposure.

Observations. The body weights of all exposed rats were recorded weekly throughout the exposure period. Upon entering the breeding, reproductive, and recovery phase of the study, exposed male rats continued to be weighed weekly until sacrifice. Exposed females rats were not weighed on a regular weekly schedule because the variability in the onset of their pregnancies would have prevented meaningful comparisons of the body weights between groups. Individual body weights of exposed females who delivered pups were taken at intervals throughout the lactation period, however. The animals were observed daily for overt signs of toxicity or changes in demeanor. Any exposed animals which appeared moribund or died spontaneously during the course of the study were submitted for gross pathologic evaluation.

Breeding Procedure. Breeding of exposed animals with unexposed rats commenced immediately after termination of the 13-week exposure.

Exposed Females. Each exposed female was bred with one unexposed male for 10 consecutive days. During the breeding period, the pans beneath the mating cages were examined for

the presence of vaginal plugs as an indication of mating. Following the mating period, the exposed females were housed singly in nesting cages containing ground corn cob and allowed to deliver a litter.

Exposed Males. Each exposed male was bred for 2 consecutive 7-day periods with separate groups of 2 unexposed virgin females. During the breeding period, the pans beneath the cages were examined for the presence of vaginal plugs. Following the first mating period, one female bred to each male was selected randomly and placed in a nesting cage and allowed to deliver a litter. During the latter half of the gestation period (between days 10 and 20 of gestation) each female selected for the reproduction phase was palpated to detect pregnancy. If the unexposed female selected was judged to be non-pregnant, one unexposed female bred to that same male was selected randomly from the second breeding period and allowed to litter. Those females selected for this phase which failed to deliver a litter were sacrificed a minimum of 21 days following the last day of cohabitation, and the uterus was stained with sodium sulfide for evidence of implantation sites.

Those females from the first and second breeding periods not selected for the reproduction phase were housed in wire-bottomed stainless steel cages, and used in the

dominant lethal evaluation. Additional breeding of control and 300 ppm exposed males with separate unexposed virgin females was performed at 13 and 19 weeks following termination of exposure (weeks 26 and 32 of the study, respectively) in order to evaluate recovery of reproductive function.

REPRODUCTIVE PARAMETERS

Litter Data. All litters were examined as soon as possible after delivery. The following parameters were recorded on each of the litters: the date of parturition, number of days from the first day of cohabitation to parturition, litter size on the day of parturition, the number of live and dead pups on days 1, 4, 7, 14, and 21 after delivery, the weight of the litter and lactating female on days 1, 4, 7, 14 and 21 of lactation, and on day 21 individual body weights for each male and female pup. Any physical or gross behavioral abnormalities in the neonates were also recorded.

Culling and Weaning. On day four postpartum, each litter was culled if necessary. If the number of pups exceeded 8, the litter size was culled to 4 males and 4 females, if possible, using numbers chosen from a table of random numbers. All pups removed from the litter by culling were sacrificed. The remaining pups, after culling, were sacrificed on day 21 post-partum. The following indices were calculated

for each group of rats: fertility index (the proportion of females that were pregnant), gestation survival index (the proportion of newborn pups that were alive) and the 24-hour, 7, 14 and 21-days survival indices (the proportion of live born pups that survived 1, 7, 14 or 21 days, respectively).

Dominant Lethal Evaluation. Unexposed female rats mated to exposed male rats intended for evaluation of dominant lethality were sacrificed by CO_2 anesthesia 12 days after the last day of cohabitation and the number of corpora lutea, implantation sites and resorptions were counted.

For each exposed male, the following indices were calculated as follows:

$$\text{Male Fertility Index (\%)} = \frac{\text{Number of fertile males}}{\text{Number of males housed with females}} \times 100$$

For each litter, the following indices were calculated:

$$\text{Pre-implantation Loss (\%)} = \frac{\text{(Number of corpora lutea minus number of implantation sites)}}{\text{Number of corpora lutea}} \times 100$$

$$\text{Resorption Rate (\%)} = \frac{\text{Number of resorption sites}}{\text{Number of implantation sites}} \times 100$$

Clinical Laboratory Evaluations. As indicated earlier, a 13-week inhalation toxicity study with EGME was conducted concurrently with this reproduction study employing the same inhalation chambers. Rats from the concurrent toxicity

study exhibited apparent treatment-related changes in some clinical laboratory parameters. In order to assess the recovery from those changes following termination of EGME exposure, it was decided to evaluate similar parameters in rats from the reproduction study. The following parameters were evaluated from 10 rats/sex of the control and high exposure level (300 ppm) groups at approximately 11 weeks after the termination of EGME exposure:

[1]Hematology - packed cell volume, hemoglobin, erythrocyte count, white blood cell count, platelet count and red blood cell indices (MCV, MCH, MCHC).

[2]Urinalysis - bilirubin, glucose, ketones, occult blood, pH, protein, urobilinogen, and specific gravity.

The blood for clinical chemistry was collected from severed blood vessels at the time of sacrifice (females - 15 weeks after the termination of exposure, and males - 23 weeks after the termination of exposure) following an overnight fast. The following analyses[3] were performed on 10 rats/sex at all levels: blood urea nitrogen, SGPT activity, alkaline phosphatase activity, glucose, total protein, albumin, globulin, and total bilirubin.

[1]Ortho ELT-8, Ortho Instruments, Boston, MA. (WBC, RBC, PCV, Hgb, Plat, Indices).

[2]T. S. Meter, Amer. Opt. Co., Buffalo, NY (specific gravity); Multilabstix, Ames Co., Elkhart, IN.

[3]Centrifichem System 500, Methods File, Union Carbide Corp., Rye, NY.

Gross Necropsy and Histopathology. At the termination of the post-exposure period (see experimental design), all rats were submitted to necropsy after an overnight fast, and each was weighed, anesthetized with methoxyflurane, and killed by decapitation after the trachea was clamped to prevent aspiration of blood. A complete gross necropsy was performed on all rats. The liver, kidneys, brain, spleen, thymus, and testes were weighed from 10 rats/sex/exposure level (15 control males), and the organ to body weight ratios were calculated. After examination, the lungs were distended to their approximately normal inspiratory volume by tracheal infusion with formalin and the nasal cavities were flushed with formalin via the pharyngeal duct to ensure rapid fixation of nasal mucosa. Tissues listed in Table 18 were retained and preserved in neutral phosphate-buffered 10% formalin, with the exception of testes which were preserved in Bouin's fixative. Samples of testes from 3 male rats from each exposure level were retained and preserved in the appropriate fixative for possible electron microscopic examination.

Representative sections of spleen, thymus, bone marrow (thoracic vertebra), mesenteric lymph nodes, testes, epididymides, ovaries, uterus, and tissues normally processed with these organs from 10 rats/sex in the control and 300 ppm

exposure levels were processed in the standard manner, embedded in paraffin, sectioned at 5-6 µm, stained with hematoxylin and eosin, and examined microscopically by a veterinary pathologist. The testes from all remaining males in the control and 3 exposure groups were also processed and examined microscopically.

Rats which died spontaneously or were killed moribund during the course of the study were necropsied and representative tissues were saved; however, no histopathologic examinations were performed.

Statistical Evaluation. Body weights, organ weights, hematology, urine specific gravity, clinical chemistry, number of implantations, and number of corpora lutea were evaluated by a one-way analysis of variance (ANOVA); differences between experimental and control groups were analyzed using Dunnett's test or Wilcoxon's Rank Sum Test as appropriate (Steel and Torrie, 1960). The fertility index and other incidence data were analyzed by the Fisher Exact Probability Test (Siegel, 1956). Evaluation of the fetal sex ratio was made by a Binomial Distribution Test (Steel and Torrie, 1960). Survival indices, resorption rate, pre-implantation loss, and incidence of anomalies among the neonates were analyzed using the Wilcoxon Test as modified by Haseman and Hoel (1974). The level of significance chosen in all cases was $p<0.05$.

RESULTS

Chamber Conditions. The mean daily time-weighted average (TWA) analytical concentrations were within ±2% of the intended target concentration for each exposure chamber (Table 2). Moreover, there was very close agreement between the mean daily TWA analytical concentrations and mean daily nominal concentrations for each chamber, indicating that test material losses were minimal in the vapor generator and exposure systems.

Mortality, General Health and Demeanor. No treatment-related alterations in demeanor or physical appearance were observed in any of the rats during the study period. However, during the 25th week of the study (12 weeks post-exposure) a syndrome consistent with a diagnosis of sialodacryoadenitis was observed both among control and treated animals. During this period (weeks 25 and 26), the affected animals showed symptoms of swelling of the submandibular gland, watery eyes and photophobia. These clinical symptoms subsided after the 26th week of the study. During the course of the study three female rats were found dead or were killed moribund. Only one animal died during the exposure phase --a female rat in the 300 ppm exposure group was found dead during the 4th week with a broken jaw,

probably the result of trauma. Two female rats in the 100 ppm exposure group were sacrificed moribund in the post-exposure phase as a result of complications due to retained placental tissues. None of these deaths were interpreted as being associated with exposure to EGME.

Body Weights. The mean body weights of male rats in the 300 ppm group were significantly lower than controls as a result of treatment throughout the study (Table 3). For female rats exposed to 300 ppm, a reduction in body weight first became statistically significant during the 7th week of exposure and continued to be depressed during the rest of the exposure period (Table 4). Body weights of male and female rats exposed to 30 or 100 ppm EGME were comparable with the control animals at each of the weighing intervals.

FERTILITY INDEX

Female Rats. The fertility indices of exposed females, calculated using the female as the experimental unit are presented in Table 5. The fertility indices of EGME-exposed females at the 30 and 100 ppm levels were comparable with concurrent controls. At the 300 ppm level, a slight decrease (not statistically significant) in fertility was observed, however, historically, a mean fertility index of

70% for control rats was observed in similar studies conducted in this laboratory. Hence, the 68% fertility in the exposed females at the 300 ppm level was not considered to be due to treatment.

Male Rats. The fertility indices of exposed male rats were calculated based on their ability to impregnate an unexposed female rat from either the reproduction phase of the study or from the dominant lethal portion of the study as well as overall basis. The fertility indices of males exposed to 30 and 100 ppm EGME were comparable with controls in all cases (Table 5). However, the fertility indices of males exposed to 300 ppm were significantly decreased. In fact, only 4 of 20 females at the 300 ppm level were pregnant when mated to exposed males. All four confirmed matings resulted in complete resorption and the pregnancy was detected by staining the uterus with sodium sulfide. Due to this infertility in the exposed males at 300 ppm level, no litters were obtained in the reproduction phase of the study at this level.

It is significant to note that essentially all exposed males including those infertile males at the 300 ppm level were able to mate with unexposed females. This is borne out by the presence of vaginal plugs (indication of mating) beneath the cage during breeding. These data are summarized as follows:

EXPOSED MALES

	EGME LEVEL PPM	CAGES WITH PLUG(S) / TOTAL NO. OF CAGES	% CAGES WITH PLUGS
Week 1 post-exposure mating			
	0	27/30	90
	30	27/30	90
	100	18/20	90
	300	18/20	90
Week 2 post-exposure mating			
	0	29/30	97
	30	29/30	97
	100	20/20	100
	300	20/20	100

In order to assess the reversibility of the decreased fertility observed in the high exposure level males, two additional breedings of control and 300 ppm males were conducted at 13 and 19 weeks after termination of exposure. At each of these intervals, each control and 300 ppm male was bred for one week with one unexposed female. These matings resulted in a continued significant decrease in fertility at the 300 ppm level (Table 5). However, it is

noteworthy that 50% of the 300 ppm exposed males produced litters in which the majority of implantations appeared viable. This is in contrast with the 10% fertility observed in this group immediately following exposure in which all implantations were non-viable. This clearly suggests that the decreased reproductive function observed at the 300 ppm is partially reversible, although some animals apparently did not recover during the post-exposure period.

REPRODUCTIVE PARAMETERS - MALE RATS

The results presented in this section represent the data obtained from unexposed bred females mated with each of the exposed males immediately following the 13 weeks of exposure and allowed to deliver in order to evaluate neonatal survival and growth.

Maternal Body Weights During Lactation of Unexposed Females Bred to Exposed Males. The maternal body weights of unexposed females mated to males exposed to 30 and 100 ppm EGME were comparable with the controls throughout lactation (Table 6). At the higher exposure level (300 ppm) none of the females delivered a litter, hence no body weights were recorded.

Gestation, Neonatal Survival and Growth and Sex Ratio.

The number of days from cohabitation to parturition was unaffected at 30 and 100 ppm level (Table 7). Neonatal survival indices and sex ratios of pups delivered from these unexposed females were comparable with concurrent controls (Table 7). Pup weights at the 30 and 100 ppm levels were comparable with controls through lactation day 21 (Table 8).

REPRODUCTIVE PARAMETERS - FEMALE RATS

Female rats exposed to EGME for 13 weeks were bred with unexposed male rats for 10 consecutive days. These bred exposed female rats were allowed to deliver at term. Data from these bred exposed female rats are presented in this section.

Maternal Body Weights During Lactation of Exposed Females Bred to Unexposed Males. The maternal body weights of all EGME exposed female rats were comparable with the controls throughout lactation (Table 9).

Gestation, Neonatal Survival and Growth and Sex Ratio.

Days from cohabitation to parturition was unaffected at all levels (Table 10). Neonatal survival and sex ratio of pups delivered from exposed females mated to unexposed males were comparable at all levels with the controls (Table 10). Pup weights at all levels were comparable with controls through lactation day 21 (Table 11).

DOMINANT LETHAL EVALUATION - MALE RATS

Male rats exposed to EGME for 13 weeks were bred with different groups of unexposed female rats for two consecutive weeks. At 30 or 100 ppm, EGME did not induce dominant lethality in male rats following exposure for 13 weeks in either of the two one-week mating periods (Table 12). A significant increase in resorption rate (10%) was observed at the 30 ppm level during the first week post-exposure. This effect was not observed at 100 ppm in the first week post-exposure nor at either 30 or 100 ppm levels in the second week post-exposure breeding. Due to the absence of a dose-response this was not considered treatment-related. Because of essentially complete infertility of male rats at the high exposure (300 ppm) level it was not possible to assess dominant lethality immediately following termination of EGME exposure. As a result the 300 ppm exposed and control males were bred again with unexposed virgin females at weeks 26 and 32 of the study. As previously discussed, the fertility of the 300 ppm exposed males had recovered to 55% (Table 5) at these mating intervals. Under these conditions of reasonable fertility, there was no indication of an increased incidence of resorptions (Table 13) at the 300 ppm level.

CLINICAL LABORATORY FINDINGS

Hematology. The mean values for the various hematologic parameters evaluated (11 weeks post-treatment) in the 300 ppm level males and females did not reveal any treatment-related changes (Table 14). Significant changes in mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) observed at 300 ppm level females were not considered toxicologically significant.

Clinical Chemistry. No treatment-related alterations in any of the clinical chemistry parameters evaluated were apparent (Table 15). However, statistically significant decreases in serum total protein and albumin levels in the 300 ppm females were observed. The significance of this observation is uncertain at this time.

Urinalysis. No treatment-related alterations in any urinalysis parameters evaluated were apparent (Table 16).

ORGAN WEIGHTS

The mean organ weights and organ/body weight ratios for exposed male and female rats are presented in Table 17. No significant changes in organ weights or organ/body weight ratios were observed in exposed females. A significant

decrease in the absolute and relative testes weight was observed in the 300 ppm level males. This was attributed to exposure to EGME. A significant decrease in absolute brain weight was observed in the 300 ppm males; however, this was considered unrelated to EGME exposure. There were no effects observed in absolute and relative organ weights among males exposed to 30 or 100 ppm EGME.

GROSS AND HISTOPATHOLOGIC EVALUATION OF EXPOSED MALE AND FEMALE RATS

A tabular summary of the gross pathologic observations for male and female rats is presented in Table 19. The histopathologic findings, along with complete listings of all tissues examined microscopically, are presented in Tables 20 and 21 for males and females, respectively.

Gross pathologic changes interpreted to be residual effects of exposure to EGME were observed only in rats exposed to 300 ppm and included decreased size of the testes, generally with a flaccid consistency. This effect was noted in 13 of the 20 male rats of the group. The only other grossly-observed change with an incidence suggestive of an association with exposure to EGME was the mesenteric adhesions of the splenic capsule observed in both males and females.

Histopathologic findings which were interpreted to be residual effects of EGME exposure were limited to the testes and epididymides of male rats in the 300 ppm exposure group. The bilateral testicular changes were characterized by variable numbers of atrophic seminiferous tubules, shrunken and lined only by Sertoli cells, admixed with tubules which were histologically normal and producing spermatozoa. In general, all tubules appeared to be either fully functional or totally atrophic with no intermediate degenerative stages present.

These histopathologic effects were noted in 15 of the 20 male rats in the 300 ppm exposure group and were variable in degree with the more severely affected testes containing greater than 75% atrophic tubules and the slightly affected ones having less than 25% atrophic tubules. The majority of rats at all exposure levels, including controls, had an occasional atrophic tubule, generally in a subcapsular location near the rete testis. Five of the 300 ppm rats had so few atrophic tubules as to be indistinguishable from controls in this respect. In some cases (4/10), no sperm were present in the epididymides. These were generally in rats with the highest percentage of atrophic tubules.

One male rat in the 30 ppm exposure group had small testes which were characterized microscopically by slight tubular atrophy, however, this change was not considered exposure-

related since it was accompanied by bilateral hypospermatogenesis suggesting a slowly progressive, active process rather than the apparently static condition observed in the highest exposure group. Diffuse degeneration of germinal epithelium was observed in one testes of another 30 ppm male, but the unilateral nature of the lesions and lack of a dose response made it improbable that this change was exposure-related.

All other histopathologic findings in both male and female rats, except for the fibrous capsular adhesion of the spleen noted in one 300 ppm male, were considered spontaneous or incidental. There were no changes observed within the splenic parenchyma associated with the capsular adhesions noted grossly or microscopically. Capsular adhesions are occassionally observed in this strain of rat, but the grossly-observed incidence in both 300 ppm males and females is excessive in this instance and considered a residual effect of exposure. The significance of this effect, however, is uncertain. Decreased size of the spleens as a result of lymphoid depletion was an effect of higher exposure concentrations in the repeated short-term studies (Miller et al, 1980). Although the spleens were not decreased in size at the end of 13 weeks of exposure at 300 ppm (Miller et al, 1981), the capsular adhesions may have been associated with a transient decrease in size at the beginning of the exposure period.

DISCUSSION

The results of this study demonstrate the potential of inhaled EGME to adversely affect reproductive function in male rats, apparently due to an interference with spermatogenesis. The results observed in males were partially reversed following termination of exposure. In contrast, exposure to EGME had no effects on reproductive function in females.

Exposure of male rats to 300 ppm of EGME for 13 weeks resulted in decreased body weight and essentially complete suppression of fertility, with no apparent affect on mating behavior. An assessment of reproductive function in these males following 13 and 19 weeks post-exposure indicated that over one-half of the affected males had regained a measure of fertility. Gross pathologic examination of these high exposure level males indicated a decrease in the size of the testes and histologic examination of the testes from these males revealed atrophy of variable number of seminiferous tubules admixed with relatively normal tubules. Due to the infertility of the 300 ppm males immediately following exposure, dominant lethality could not be adequately evaluated at this exposure level. Among those males at 300 ppm in which recovery of reproductive function was observed following the recovery phase, no evidence of an increased incidence of resorptions was observed. No effects on body weights,

fertility and reproductive parameters, and no evidence of a dominant lethal mutagenic effect was observed among males at 30 or 100 ppm.

Exposure of female rats to 300 ppm of EGME resulted in reduced body weights during the second half of the 13 week exposure period. No effects were observed on fertility or reproductive parameters in any group of exposed females.

Miller et al., (1981) reported a significant depression of cellular elements in the blood (pancytopenia) of rats exposed to 300 ppm EGME. In order to assess the recovery of hematologic changes induced by EGME, an evaluation of these parameters was performed in this study at 11 weeks post-exposure. It was apparent that all the hematologic changes had returned to normal in the 300 ppm exposed rats by 11-weeks post-exposure.

In conclusion, exposure of rats to 300 ppm of EGME by inhalation for 13 weeks produced a complete suppression of fertility in male rats. However, over one-half of these rats regained their fertility by 13 weeks post-exposure. Decreases in testicular size and atrophic seminiferous tubules were still present in these rats at 19 weeks post-exposure. Exposure to 30 or 100 ppm EGME did not affect

fertility or dominant lethality in male rats. Female rats tolerated up to 300 ppm EGME without any adverse reproductive effects. Based on these results, it was concluded that the no-adverse effect level of EGME for fertility and reproduction was 100 ppm in rats.

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TITLE OF STUDY: EGME: INHALATION REPRODUCTION AND DOMINANT LETHAL STUDY IN RATS

In compliance with Good Laboratory Practice Regulations, this study was inspected by the Quality Assurance Unit and the results of these inspections reported to Management and the Study Director on the dates listed below. The report accurately reflects the data generated in accordance with the regulations and standard operating procedures of the Laboratory. All data and the reports are located at the submitting laboratory.

Study Started:	28 July 1980	Report Issued Date:	10 February 1982
Dates of Inspection:	18 July 1980	Date of Report:	18 July 1980
	17 Sept 1980		25 Sept 1980
	28 Oct 1980		30 Oct 1980
	27 Jan 1981		2 Feb 1981
	26 Jan 1982		27 Jan 1982

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Table 1

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Experimental Design

Treatment Group	EGME, ppm	Number of Rats	
		Males	Females
Control	0	30	30
Low Exposure	30	30	30
Medium Exposure	100	20	20
High Exposure	300	20	20

After 13 Weeks of Exposure:

1) Each exposed male rat was mated with two unexposed females for 7 days at week 1 and again at week 2 post-exposure. One bred female was allowed to deliver for evaluating reproductive parameters, and the other 3 bred females were killed 12 days after the last day of cohabitation for evaluating dominant lethality.

2) Exposed female rats were mated with unexposed male rats for 10 days; later females were allowed to deliver.

3) All pups were weaned and discarded at 21 days post-parturition.

4) Additional breeding of 300 ppm exposed male rats were performed at 13 and 19 weeks post-exposure to assess recovery.

5) All adult female rats were killed 15 weeks after the termination of inhalation exposure while exposed male rats were killed at 23 weeks post-exposure.

TEXT TABLES

Table 2

EGME: INHALATION REPRODUCTION AND DOMINANT LETHAL STUDY IN RATS

Exposure Concentrations and Exposure Chamber Conditions

Target Conc.	Analytical Concentration			Nominal Concentrations		Temp.[c] (°F)	Rel. Hum.[d] (%)
	Analytical Conc.[a]	Coeff. of Variation[b]	Range of Measurements	Mean±S.D.	Range		
0	--	--	--	--	--	70-79	63.9±7.7
30 ppm	30.5±0.9	3%	28-33	29.4±0.9	28-34	70-78	61.1±7.3
100 ppm	101.1±2.3	2%	89-110	98.2±1.9	93-100	70-78	57.2±6.5
300 ppm	305.3±8.8	3%	251-319	295 ±6.3	281-312	70-78	60.8±8.8

[a] Numbers are mean±S.D. daily time-weighted average (TWA) values for n = 72 days.

[b] Coefficient of variation is the standard deviation of the daily TWA measurements divided by the mean value (x100).

[c] Range of minimum and maximum value in each chamber during the course of the study.

[d] Mean±S.D. of daily measurements taken while exposures in progress.

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Table 3

DDME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Mean Body Weights (grams) of Exposed Males[a]

Days on Study	DDME, ppm			
	0	30	100	300
Pre-Exposure				
-1	318±17[b]	317±23	315±22	308±20
Exposure				
5	384±20	383±33	339±27	329±22*
12	372±20	376±27	371±33	350±33*
19	405±20	403±29	408±34	384±26*
27	424±24	426±30	423±36	400±23*
33	441±29	443±31	439±38	409±35*
40	451±24	459±30	451±43	418±40*
47	467±26	477±32	465±44	428±42*
54	480±28	486±32	481±43	439±40*
62	485±34	499±35	498±43	450±39*
68	493±34	507±35	499±42	458±40*
75	507±32	520±32	502±47	454±37*
82	516±32	527±37	515±48	449±47*
Post-Exposure				
95	519±31	529±37	517±42	467±39*
102	520±30	530±36	520±40	470±38*
109	521±31	530±36	520±41	476±36*
116	537±33	546±40	534±47	491±37*
123	538±35	556±40	534±43	500±41*
130	536±34	563±41	551±43	504±44*
137	564±36	569±45	557±44	504±46*
144	557±37	565±47	550±46	502±47*
151	576±40	585±49	569±44	522±46*
158	581±40	589±49	570±46	527±48*
165	577±41	595±50	570±48	528±46*
172	575±41	592±50	570±47	525±49*
179	578±42	591±48	555±46	526±49*
186	581±41	601±49	575±49	529±48*
193	588±42	604±50	580±50	533±47*
200	601±43	614±51	590±55	545±50*
207	596±42	615±57	587±54	519±59*
214	600±44	609±56	585±55	541±52*
221	605±43	614±55	590±60	546±54*
228	601±42	622±56	596±60	536±55*
235	602±44	620±57	592±59	547±54*
242	608±47	626±59	597±61	552±58*
249	617±49	635±60	607±63	563±63*

[a]Male rats were exposed to 0, 30, 100, or 300 ppm DDME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, animals were maintained in the laboratory for recovery.

[b]Mean±standard deviation.

*Significantly different from the control value by Dunnett's test, $p<0.05$.

See Table A-1 for individual animal data.

Table 4

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Mean Body Weights (grams) of Exposed Females[a]

Days on Study	EGME, ppm			
	0	30	100	300
Pre-Exposure				
-1	211±13[b]	210±13	206±13	208±14
Exposure				
5	221±14	225±15	223±12	223±14
12	237±16	244±18	240±13	239±20
19	251±17	258±21	252±15	247±20
27	261±21	265±20	262±17	259±21
33	270±22	270±23	270±19	261±21
40	277±24	281±22	278±18	266±22
47	283±23	285±23	281±21	265±22*
54	286±24	290±26	290±24	271±23
62	288±25	291±25	291±23	277±28
68	292±28	295±25	295±25	272±25*
75	297±28	300±25	299±27	274±23*
82	303±30	302±25	302±29	272±23*
88	294±29	296±26	297±29	267±22*

[a]Female rats were exposed to 0, 30, 100, or 300 ppm EGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks.
[b]Mean±standard deviation.

*Significantly different from the control value by Dunnett's test, $p<0.05$.
See Table A-2 for individual animal data.

Table 5

SGME: INHALATION REPRODUCTION AND DOMINANT LETHAL STUDY IN RATS

Fertility Indices of Exposed Male and Female Rats[a]

	SGME, ppm			
	0	30	100	300
Exposed Females: Reproduction Phase[b]	87% (26/30)	73% (22/30)	95% (19/20)	68% (13/19)[c]
Exposed Males: Reproduction Phase[d]	90% (27/30)	93% (28/30)	95% (19/20)	10%[e] (2/20)[e]
Dominant Lethal[f]	93% (28/30)	93% (28/30)	95% (19/20)	10%[e] (2/20)[e]
Overall[g]	97% (29/30)	93% (28/30)	95% (19/20)	20%[e] (3/20)
Exposed Males: Recovery Phase:				
Week 26[f] of Study (13 weeks post-exposure)	90% (27/30)	— —	— —	55%[e] (11/20)
Week 32[f] of Study (19 weeks post-exposure)	80% (24/30)	— —	— —	50%[e] (10/20)
Overall[g]	97% (29/30)	— —	— —	55%[e] (11/20)

[a]Male and female rats were exposed to 0, 30, 100, or 300 ppm SGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, the animals were bred with unexposed animals of the opposite sex.

[b]Number of exposed females delivering a litter/number of exposed females placed with unexposed males.

[c]One female from 300 ppm exposure level died prior to breeding.

[d]Number of exposed males siring a litter/number of exposed males placed with unexposed females.

[e]Two females had implantation sites detected at necropsy.

[f]Number of fertile exposed males/number of exposed males housed with unexposed females.

[g]Number of fertile exposed males from dominant lethal or reproduction phase/number of exposed males housed with unexposed females.

*Significantly different from the control by Fisher's test, $p<0.05$.

See Tables 1-4 (exposed males) and 1-7 (exposed females) for individual animal data.

Table 6

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Mean Body Weights During Lactation of Unexposed Females Bred to Exposed Males[a]

Body Weight on Post-Partum Day	EGME, ppm			
	0	30	100	300
1	293±17[b]	293±25	287±21	—[c]
4	309±21	306±23	300±25	—
7	313±18	312±25	305±28	—
14	326±17	332±20	323±23	—
21	311±17	316±20	309±15	—

[a]Male rats were exposed to 0, 30, 100, or 300 ppm EGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, animals were bred with unexposed females.

[b]Body weight in grams, mean±standard deviation.

[c]All females bred to 300 ppm exposed males failed to deliver a litter.

None differed significantly from the control value by Dunnett's test, $p<0.05$.

See Table A-3 for individual animal data.

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Table 7

DDME: INHALATION REPRODUCTION AND DOMINANT LETHAL STUDY IN RATS

Reproduction Indices — Unexposed Female Rats Bred to Exposed Males[a]

	DDME, ppm			
	0	30	100	300
Number of Exposed Males[b]	30	30	20	20
Number of Litters	25[c]	28	19	0
Days from Cohabitation to Parturition[d]	25±2	25±2	25±2	—
Number of Live Pups on Day 1	13±2	14±3	13±3	—
Gestation Survival Index[e]	98.7% (375/380)	100% (391/391)	99.2% (254/256)	—
1-Day Survival Index[f]	99.7% (374/375)	99.7% (390/391)	100% (254/254)	—
4-Day Survival Index[f]	99.7% (374/375)	99.2% (388/391)	98.3% (251/254)	—
7-Day Survival Index[f]	100% (223/223)	99.5% (221/222)	100% (149/149)	—
14-Day Survival Index[f]	100% (223/223)	99.5% (221/222)	100% (149/149)	—
21-Day Survival Index[f]	99.5% (222/223)	99.5% (221/222)	99.3% (148/149)	—
Sex Ratio on Day 1 Male:Female	49:51	47:53	47:53	—

[a]Male rats were exposed to 0, 30, 100, or 300 ppm DDME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, the animals were bred with unexposed females.

[b]Each exposed male was bred to four unexposed females, two at a time, in two separate breedings. One female bred to each male from the first breeding was placed on corn-cob bedding. After 10-15 days of gestation these females were palpitated for evidence of pregnancy. In order to obtain a viable litter from each male, another female from the second week breeding was selected for the reproductive phase, whenever the first female was suspected to be non-pregnant

[c]Mean±standard deviation.

[d]Percentage of newborn pups alive at birth.

[e]Percentage of pups that survived for 1 or 4 days.

[f]Percentage of pups that survived for days 4-7, 4-14, or 4-21. All litters were culled on day 4 to 8 pups, 4 males and 4 females, where possible. Percentage calculated on pups that survived after culling.

[g]Two litters were sired from one male.

None differed significantly from the control values by the appropriate statistical test, $p<0.05$.

See Tables 4-4 for individual animal data.

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Table 8

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Pup Body Weights of Litters of Unexposed Females Mated to Exposed Males[a]

Pup Body Weight on Day	EGME, ppm 0	30	100	300
1	7±1[b]	7±1	7±1	--[c]
4	11±2	11±1	11±1	--
7	18±2	17±2	17±2	--
14	35±3	34±3	35±3	--
21-Male	57±5	55±5	58±6	--
21-Female	55±4	53±4	55±5	--

[a]Male rats were exposed to 0, 30, 100, or 300 ppm EGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, animals were bred with unexposed females.

[b]Mean of the average litter body weight±standard deviation (grams).

[c]All females bred to 300 ppm exposed males failed to deliver a litter.

None differed significantly from the control values by Dunnett's test, $p<0.05$.

See Table A-5 for individual animal data.

Table 9

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Mean Body Weights During Lactation of Exposed Females[a]

Body Weight on Post-Partum Day	EGME, ppm 0	30	100	300
1	315±28[b]	313±18	316±23	294±26
4	331±26	325±28	328±22	303±23
7	340±24	337±26	335±21	311±28
14	353±25	352±28	351±20	327±26
21	334±23	335±19	332±19	316±19

[a]Female rats were exposed to 0, 30, 100, or 300 ppm EGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, animals were bred with unexposed males.
[b]Body weight in grams, mean±standard deviation.

None differed significantly from the control values by Dunnett's test, $p<0.05$.
See Table A-6 for individual animal data.

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Table 10

EGME: INHALATION REPRODUCTION AND DOMINANT LETHAL STUDY IN RATS

Reproduction Indices — Exposed Female Rats Bred to Unexposed Males[a]

	EGME, ppm			
	0	30	100	300
Number of Exposed Females	30	30	20	20
Number of Litters	25	22	18	13
Days from Cohabitation to Parturition[b]	24±1	25±1	25±2	26±2
Number of Live Pups on Day 1[c]	13±3	14±4	13±2	11±4
Gestation Survival Index[d]	97.5% (347/356)	99.3% (299/301)	99.2% (234/236)	94.9% (148/156)
1-Day Survival Index[e]	98.5% (342/347)	98.3% (294/299)	98.3% (230/234)	100% (148/148)
4-Day Survival Index[e]	98.5% (342/347)	96.3% (288/299)	99.1%[g] (219/221)	98.5% (146/148)
7-Day Survival Index[f]	100% (204/204)	99.4% (167/168)	100% (136/136)	100% (96/96)
14-Day Survival Index[f]	100% (204/204)	98.8% (166/168)	100% (136/136)	100% (96/96)
21-Day Survival Index[f]	100% (204/204)	98.8% (166/168)	100% (136/136)	100% (96/96)
Sex Ratio on Day 1 Male:Female	51:49	48:52	48:52	40:60[h]

[a] Female rats were exposed to 0, 30, 100, or 300 ppm EGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, the animals were bred with unexposed males.

[b] Exposed females were bred one to one to unexposed males for 2 five-day breeding periods.

[c] Mean±standard deviation.

[d] Percentage of newborn pups alive at birth.

[e] Percentage of pups that survived for 1 or 4 days.

[f] Percentage of pups that survived for days 4-7, 4-14, or 4-21. All litters were culled to 8 pups, 4 males and 4 females, where possible on day 4 of lactation. Percentage calculated on pups that survived after culling.

[g] One female from the 100 ppm exposure level was found to be moribund on day 2 of lactation. Female was submitted for necropsy and the litter was sacrificed. The litter was excluded from day 4, 7, 14, and 21-day survival indices.

[h] Significantly different from the control values by the appropriate statistical test, $p<0.05$.

See Tables A-7 for individual animal data.

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Table 11

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Pup Body Weights of Litters of Exposed Females Mated to Unexposed Males[a]

Pup Body Weight on Day	EGME, ppm 0	30	100	300
1	7±1	7±1	7±1	7±1
4	11±1	10±1	11±1	11±2
7	17±2	17±2	18±2	17±2
14	36±4	35±3	34±3	34±3
21-Male	58±8	55±5	56±5	57±5
21-Female	55±6	52±5	53±5	54±5

[a]Female rats were exposed to 0, 30, 100, or 300 ppm EGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, animals were bred with unexposed males.

[b]Mean of the average litter body weight±standard deviation (grams).

None differed significantly from the control values by Dunnett's test, $p<0.05$.

See Table A-8 for individual animal data.

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Table 12

EGME: INHALATION REPRODUCTION AND DOMINANT LETHAL STUDY IN RATS

Reproductive Parameters from Dominant-Lethal Phase (Weeks 1 and 2 Post-Exposure)[a]

	EGME, ppm			
	0	30	100	300
Week 14 (First Week Post-Exposure)				
Corpora Lutea/Dam[b]	15±2	15±1	15±2	—
Implantations/Litter[b]	15±1	15±2	15±3	—
Resorptions/Litter[b]	0.4±0.6	1.4±2.1	0.3±1.1	—
% Pre-Implantation Loss[c]	2±4	3±7	6±16	—
% Resorption Rate[d]	3±4	10±16*	7±8	—
Week 15 (Second Week Post-Exposure)				
Corpora Lutea/Dam[b]	15±2	15±2	15±2	—
Implantations/Litter[b]	14±2	15±2	15±2	1±0
Resorptions/Litter[b]	0.9±0.9	0.3±0.9	1.2±2.1	1±0
% Pre-Implanation Loss[c]	7±12	4±5	9±12	--
% Resorption Rate[d]	5±6	7±11	7±14	100.0±0*

[a]Male rats were exposed to 0, 30, 100, or 300 ppm EGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, the animals were bred with two new unexposed females each during weeks 14 and 15 of the study (first and second week post-exposure). One female from week 14 was selected for the dominant lethal evaluation. One or two females as necessary were selected for dominant lethal from the week 15 breeding. Data presented are from bred females sacrificed 12 days following the last day of cohabitation.

[b]Mean±standard deviation.

[c]Pre-Implantation Loss (%) = $\frac{\text{\# Corpora Lutea} - \text{\# Implantations}}{\text{\# Corpora Lutea}} \times 100.$

[d]Resorption Rate (%) = $\frac{\text{\# Resorptions}}{\text{\# Implantations}} \times 100.$

*Significantly different from the control value by a modified Wilcoxon test, $p<0.05$.

See Tables A-9 and A-10 for individual animal data.

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Table 13

SDMF: INHALATION REPRODUCTION AND DOMINANT LETHAL STUDY IN RATS

Reproductive Parameters from Dominant-Lethal Phase
(Weeks 13 and 19 Post-Exposure)[a]

	SDMF, ppm	
	0	300
Week 25 (13 Weeks Post-Exposure)		
Corpora Lutea/Dam[b]	13±2	14±2
Implantations/Litter[b]	13±4	13±2
Resorptions/Litter[b]	0.7±0.8	0.7±0.6
% Pre-Implantation Loss[c]	11±21	7±15
% Resorption Rate[d]	8±18	5±5
Week 32 (19 Weeks Post-Exposure)		
Corpora Lutea/Dam[b]	15±3	15±1
Implantations/Litter[b]	13±5	14±1
Resorptions/Litter[b]	1.5±2.1	0.9±1.2
% Pre-Implantation Loss[c]	13±20	4±6
% Resorption Rate[d]	13±22	7±9

[a]Male rats were exposed to 0 or 300 ppm SDMF by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, each exposed male was bred with one separate unexposed female during weeks 25 and 32 of the study (weeks 13 and 19 post-exposure, respectively). Data presented are from bred females sacrificed 12 days following the last day of cohabitation.

[b]Mean±standard deviation.

[c]Pre-Implantation Loss (%) = $\frac{\#\text{ Corpora Lutea} - \#\text{ Implantations}}{\#\text{ Corpora Lutea}} \times 100.$

[d]Resorption Rate (%) = $\frac{\#\text{ Resorptions}}{\#\text{ Implantations}} \times 100.$

*Significantly different from the control value by a modified Wilcoxon test, $p<0.05$.

See Tables A-11 and A-12 for individual animal data.

Table 14

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Exposed Male and Female F_0 Rats: Hematologic Evaluation[b]- 24th Week of Study (11 Weeks Post-Exposure)[a]

Sex	EGME, ppm	n	WBC x $10^3/mm^3$	RBC x $10^6/mm^3$	HgB g/dl	PCV %	MCV (microns)^3	MCH x 10^{-12}g	MCHC %	PLAT x $10^3/mm^3$
M	0	10	15.0±5.1	8.5±0.4	16.5±0.7	47.2±2.0	55.7±1.9	19.5±0.8	35.0±0.8	1020.4±100.7
M	300	10	14.7±1.4	8.7±0.4	16.4±0.6	47.2±1.3	54.5±2.3	18.9±0.7	34.8±0.8	983.4±122.5
F	0	10	13.4±7.6	7.8±0.3	16.6±0.7	47.9±1.6	61.6±1.7	21.4±0.8	34.8±0.6	964.4±154.3
F	300	10	11.4±3.9	8.0±0.3	16.5±0.6	47.8±1.6	59.8±1.7*	20.7±0.7*	34.6±0.4	989.6±106.0

[a]Male and female rats were exposed to 0 or 300 ppm EGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, animals were maintained in the laboratory for recovery.

[b]Values are mean±standard deviation.

*Significantly different from the control values by Dunnett's test, $p<0.05$.

See Tables A-13 (males) and A-14 (females) for individual animal data.

Table 15

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Exposed Male and Female Rats: Clinical Chemistry Values (Post-Exposure Period)[a]

Sex	EGME, ppm	n	BUN mg/d	SGPT mU/ml	AP mU/ml	Gluc mg/dl	TP g/100 ml	Alb g/dl	Glob g/dl	T. Bill mg/dl
M	0	10	14±2[b]	28±28	45±18	141±13	5.6±0.3	3.2±0.2	2.4±0.3	0.29±0.06
M	30	10	13±3	20±11	48±15	141±20	6.0±0.4	3.4±0.2	2.7±0.4	0.30±0.05
M	100	10	12±1	27±34	38±7	144±15	5.9±0.4	3.3±0.1	2.6±0.4	0.26±0.05
M	300	10	13±2	15±7	43±13	140±23	5.7±0.4	3.3±0.3	2.6±0.4	0.26±0.05
F	0	10	17±1	26±29	21±7	133±7	6.6±0.5	4.1±0.4	2.5±0.2	0.26±0.08
F	30	10	19±6	22±8	22±7	128±15	6.6±0.4	4.1±0.2	2.6±0.3	0.29±0.09
F	100	10	17±1	17±6	25±6	129±10	6.5±0.4	4.0±0.3	2.5±0.2	0.31±0.10
F	300	10	16±3	17±5	30±8*	129±10	5.9±0.2*	3.6±0.2*	2.3±0.2	0.26±0.12

[a]Male and female rats were exposed to 0, 30, 100, or 300 ppm EGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, animals were maintained in the laboratory for recovery. Data are from males 23 weeks post-exposure; and females 15 weeks post-exposure.

[b]Mean±standard deviation.

*Significantly different from the control value by Dunnett's test, $p<0.05$.

See Tables A-15 (males) and A-16 (females) for individual animal data.

Table 16

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Exposed Male and Female Rats: Urinalysis - 24th Week of Study (11 Weeks Post-Exposure)[a]

Sex	EGME, ppm	n	Specific Gravity	pH	Protein	Gluc	Ketones	Bilirubin	Blood	Urobilinogen
M	0	9	1.041±0.017[b]	6.0-7.0	Trace to 4+	Neg	Neg	Neg	Trace (1)[c]	0.1
M	300	10	1.041±0.015	6.0-8.0	Trace to 4+	Neg	Neg	Neg	Neg	0.1
F	0	10	1.035±0.017	6.0-8.0	Neg to 4+	Neg	Neg	Neg	Neg	0.1
F	300	9	1.026±0.012	6.0-7.5	Trace to 1+	Neg	Neg	Neg	Trace to 1+	0.1

[a]Male and female rats were exposed to 0 or 300 ppm EGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, animals were maintained in the laboratory for recovery.

[b]Mean±standard deviation.

[c]( ) indicates number of rats affected.

None differed significantly from the control values by Dunnett's test, $p<0.05$.

See Tables A-17 (males) and A-18 (females) for individual animal data.

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Table 17

EGE: INHALATION REPRODUCTION AND DEMINANT-LETHAL STUDY IN RATS

Mean Body Weights, Organ Weights, and Organ/Body Weight Ratios of the Exposed Rats[a]

	EGE, ppm	n	Body Weight (g)	Organ Weights: Absolute, g -- Relative, g per 100 g Body Weight											
				Liver		Kidneys		Brain		Testes		Thymus		Spleen	
				g	g/100	g	g/100	g	g/100	g	g/100	g	g/100	g	g/100
Males	0	15	569±46[b]	13.56±1.46	2.38±0.16	3.61±0.31	0.64±0.05	2.21±0.09	0.39±0.04	3.67±0.32	0.65±0.07	0.28±0.06	0.05±0.01	0.79±0.08	0.14±0.01
	30	10	611±61	14.15±1.74	2.32±0.17	3.81±0.17	0.63±0.05	2.38±0.52	0.39±0.08	3.64±0.50	0.60±0.11	0.33±0.08	0.05±0.01	0.79±0.09	0.13±0.02
	100	10	567±51	13.35±1.58	2.37±0.13	3.61±0.31	0.64±0.06	2.12±0.11	0.38±0.04	3.51±0.25	0.63±0.04	0.29±0.07	0.05±0.01	0.79±0.10	0.14±0.02
	300	10	534±53	12.75±1.61	2.39±0.11	3.52±0.23	0.66±0.04	2.08±0.09*	0.39±0.04	2.62±0.96*	0.49±0.17*	0.27±0.06	0.05±0.01	0.76±0.07	0.14±0.02
Females	0	10	292±24	8.02±0.74	2.76±0.33	2.07±0.15	0.71±0.03	1.89±0.08	0.65±0.07	—	—	0.29±0.07	0.10±0.02	0.57±0.06	0.20±0.03
	30	10	302±39	8.27±1.17	2.76±0.38	2.18±0.23	0.73±0.10	1.95±0.06	0.65±0.08	—	—	0.30±0.06	0.10±0.02	0.61±0.10	0.20±0.04
	100	10	302±28	7.78±0.97	2.58±0.21	2.00±0.28	0.69±0.06	1.93±0.07	0.64±0.05	—	—	0.33±0.09	0.11±0.02	0.58±0.05	0.19±0.03
	300	10	291±30	7.45±0.74	2.56±0.10	2.04±0.21	0.70±0.06	1.90±0.08	0.66±0.07	—	—	0.28±0.09	0.10±0.03	0.59±0.09	0.20±0.03

[a] Male and female rats were exposed to 0, 30, 100, or 300 ppm EGE by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Females were sacrificed 15 weeks post-exposure and males were sacrificed 23 weeks post-exposure.

[b] Mean±standard deviation (grams).

*Significantly different from the control value by Dunnett's test, $p<0.05$.

See Table A-19 and Table A-20 for individual animal data.

TABLE 18

EGME: INHALATION REPRODUCTION AND DOMINANT LETHAL STUDY IN RATS

Tissue Samples Obtained and Preserved from all Animals at the Time of Necropsy

Adrenal Glands
Accessory Sex Glands
Aorta
Brain
Cecum
Cervix
Epididymides
Esophagus
Eyes
Heart
Kidneys
Large Intestine
Larynx
Liver
Lungs (bronchi)
Lymph Nodes (Thoracic, Mesenteric)
Mammary Tissue
Mediastinal Tissue
Mesenteric Tissue
Nasal Turbinates
Ovaries
Oviducts
Pancreas
Parathyroid
Peripheral Nerve (Sciatic)
Pituitary
Salivary Glands (Submandibular)
Skeletal Muscle
Skin
Small Intestine
Spinal Cord and Thoracic Vertebral Column with Bone Marrow
Spleen
Sternum
Stomach
Testes
Thymus
Thyroid
Tongue
Trachea
Urinary Bladder
Uterus
Any gross lesions or masses

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TABLE 19

EGME: INHALATION REPRODUCTION AND DOMINANT LETHAL STUDY IN RATS

Gross Pathologic Observations[a]

Sex[b]	MALES				FEMALES			
Exposure Concentration (ppm)	0	30	100	300	0	30	100	300
Number of rats examined[c]	30	30	20	20	30	30	18	19
No visible lesions internally or externally	24	26	18	4	24	25	18	11
EXTERNAL								
Scab-like lesion in skin	1	0	0	0	0	0	0	0
Porphyrin pigment staining on face	0	0	0	1	0	0	0	0
Malocclusion of incisors	1	2	1	6	0	0	0	1
Focal alopecia	0	0	0	0	0	1	0	1
Discrete, firm mass, subcutaneous (mammary region)	0	0	0	0	1	0	0	0
Lenticular opacity, unilateral	1	0	0	1	2	0	0	0
Shrunken globe, right eye	0	0	0	0	1	0	0	0
LIVER								
Minute red foci	0	0	1	0	0	0	0	0
Pale, raised focus	0	0	0	2	0	0	0	0
Pale appearance	0	0	0	0	3	1	0	0
Diaphragmatic hernia involving liver	1	0	0	1	0	0	0	0
KIDNEYS								
Dilated renal pelvis, unilateral	2	0	1	1	0	0	0	0
Granular white material in pelvis, unilateral	0	0	1	0	0	0	0	0
LARGE INTESTINES								
Area of mucosal hemorrhage	1	0	0	0	0	0	0	0
ABDOMINAL CAVITY								
Decreased abdominal adipose tissue	0	2	0	2	0	0	0	1
Adhesions of splenic capsule to mesentery	0	0	0	5	0	1	0	4
THYMUS								
Decreased in size	0	0	0	0	3	1	0	3
LUNGS								
Aspirated blood in lungs	0	1	0	0	0	0	0	0
Lobe with pale area and focally discolored, consolidated area	0	0	0	0	0	1	0	0
TESTES								
Decreased in size, generally with flaccid consistency, bilateral	0	1	0	13	-	-	-	-
Darkened appearance, unilateral	0	1	0	0	-	-	-	-
UTERUS								
Horns distended by clear fluid	-	-	-	-	0	1	0	0

[a]Data presented as the number of rats with the specified observation. - indicates not applicable.

[b]Male rats were necropsied at approximately 255 days on test. Female rats were necropsied at approxiamtely 191 days on test.

[c]Animals which died spontaneously or were killed moribund during the course of the study are not included in this tabulation.

TABLE 20

SGME: INHALATION REPRODUCTION AND DOMINANT LETHAL STUDY IN RATS

Histopathologic Findings in Males[a]

Exposure Concentration (ppm)	0	30	100	300
Number of rats examined	30	30	20	20
LIVER (No. of tissues examined)				
Aggregate(s) of reticuloendothelial cells, multifocal, very slight	1	0	0	1
Architecture altered secondary to diaphragmatic hernia	0	-	-	1
Area of altered hepatocytes	1	-	-	0
	1	-	-	1
SPLEEN (No. of tissues examined)				
No lesions recognized	10	0	0	10
Adhesions - fibrous, capsule	9	-	-	9
Pigment - hematogenous - increased, slight	0	-	-	1
	1	-	-	0
SPINAL CORD (No. of tissues examined)				
No lesions recognized	10	0	0	8
	10	-	-	8
BONE (No. of tissues examined)				
No lesions recognized	10	0	0	10
	10	-	-	10
BONE MARROW (No. of tissues examined)				
No lesions recognized	10	0	0	10
	10	-	-	10
LARGE INTESTINE (No. of tissues examined)				
Inflammation - granulomatous, submucosa, focal, slight	1	0	0	0
	1	-	-	-
MEDIASTINAL LYMPH NODE (No. of tissues examined)				
No lesions recognized	4	0	0	7
	4	-	-	7
MESENTERIC LYMPH NODE (No. of tissues examined)				
No lesions recognized	9	0	0	10
	9	-	-	10
TESTICLE (No. of tissues examined)				
No lesions recognized	30	20	20	20
Atrophy, tubule(s), very slight (occasional tubule affected, generally subcapsular)	12	7	9	0
Atrophy, tubules, slight (<25% affected)	18	21	11	5
Atrophy, tubules, moderate (25-75% affected)	0	1	0	2
Atrophy, tubules, severe (>75% affected)	0	0	0	4
Degeneration, germinal cells, unilateral, diffuse, moderate	0	0	0	9
Hyperplasia, interstitial cell(s), focal, slight	0	1	0	0
Hypospermatogenesis, bilateral, diffuse	0	1	0	0
	0	1	0	0
EPIDIDYMIS (No. of tissues examined)				
No lesions recognized	10	0	0	10
Aggregate(s) of mononuclear (predominately lymphoid) cells, interstitium, multifocal, very slight	10	-	-	5
No sperm present	0	0	0	1
	0	-	-	4
SEMINAL VESICLE (No. of tissues examined)				
No lesions recognized	10	0	0	10
	10	-	-	10
COAGULATING GLAND (No. of tissues examined)				
No lesions recognized	10	0	0	10
	10	-	-	10

[a]Data presented as the number of animals with the specified observation or for which the specified tissue was examined. - indicates not applicable.

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TABLE 20 (Continued)

SDWC: INHALATION REPRODUCTION AND DOMINANT LETHAL STUDY IN RATS

Histopathologic Findings in Males[a]

Exposure Concentration (ppm)	0	30	100	300
Number of rats examined	30	30	20	20
PROSTATE (No. of tissues examined)	10	0	0	10
No lesions recognized	2	-	-	1
Mineralization, secretory material	8	-	-	9
Inflammatory exudate, acinar lumen, focal, slight	0	-	-	1
URINARY BLADDER (No. of tissues examined)	10	0	0	10
No lesions recognized	10	-	-	10
THYMUS (No. of tissues examined)	10	0	0	10
No lesions recognized	10	-	-	10
MEDIASTINAL TISSUE (No. of tissues examined)	10	0	0	10
No lesions recognized	10	-	-	10
MESENTERIC TISSUE (No. of tissues examined)	10	0	0	10
No lesions recognized	10	-	-	10

[a]Data presented as the number of animals with the specified observation or for which the specified tissue was examined. - indicates not applicable.

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TABLE 21

NOTE: INHALATION REPRODUCTION AND DOMINANT LETHAL STUDY IN RATS

Histopathologic Findings in Females[a]

Exposure Concentration (ppm)	0	300
Number of rats examined	10	10
SPLEEN (No. of tissues examined)	10	10
No lesions recognized	8	9
Pigment - hematogenous - increased, slight	2	1
SPINAL CORD (No. of tissues examined)	10	10
No lesions recognized	10	10
PANCREAS (No. of tissues examined)	1	0
No lesions recognized	1	0
BONE (No. of tissues examined)	10	10
No lesions recognized	10	10
BONE MARROW (No. of tissues examined)	10	10
No lesions recognized	10	10
MEDIASTINAL LYMPH NODE (No. of tissues examined)	7	5
No lesions recognized	7	5
MESENTERIC LYMPH NODE (No. of tissues examined)	9	10
No lesions recognized	9	10
URINARY BLADDER (No. of tissues examined)	10	10
No lesions recognized	10	10
OVARY (No. of tissues examined)	10	10
No lesions recognized	9	9
Follicular cyst	1	1
OVIDUCT (No. of tissues examined)	10	10
No lesions recognized	10	10
UTERUS (No. of tissues examined)	10	10
No lesions recognized	2	3
Cystic dilatation, endometrial glands, focal	1	0
Normal cyclic changes (dilated lumen)	2	0
Pigment-laden macrophages, subserosal, focal (previous implantation site)	5	7
CERVIX (No. of tissues examined)	10	10
No lesions recognized	10	10
THYMUS (No. of tissues examined)	10	10
No lesions recognized	10	7
Ultimobranchial cyst	0	3
MEDIASTINAL TISSUE (No. of tissues examined)	9	10
No lesions recognized	9	10
MESENTERIC TISSUE (No. of tissues examined)	10	10
No lesions recognized	10	10

[a]Data presented as the number of animals with the specified observation or for which the specified tissue was examined. - indicates not applicable.

APPENDIX TABLES

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Table A-1

EGHC: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RAT:[illegible]

Individual and Mean Body Weights (grams) of Exposed Males

Exposure Level: 0 ppm

Animal Number	Pathology Number	Days on Study -1	5	12	19	27	33	40	47	54	62	68	75
80A-3201	80A-2050	300.2	332.1	367.6	401.4	427.3	463.4	471.8	500.1	515.8	539.3	547.4	557.3
3202	2051	298.1	330.0	358.5	393.0	409.7	428.6	442.1	457.6	469.8	482.7	494.6	503.8
3203	2052	300.8	321.4	350.6	390.8	407.1	424.8	443.3	456.1	468.6	468.8	475.1	489.6
3204	2053	316.5	348.5	387.7	417.6	436.2	453.8	463.4	479.1	482.6	503.9	511.9	522.7
3205	2054	319.3	338.5	364.5	385.0	400.8	405.8	415.7	425.0	440.6	454.3	453.5	457.4
3116	2055	309.8	339.0	359.8	383.1	406.4	424.7	432.4	438.1	448.8	446.2	470.1	477.7
3117	2056	324.6	353.3	394.2	429.0	453.1	464.5	474.4	492.7	501.9	506.3	518.4	525.3
3118	2057	312.3	348.9	381.0	422.3	451.2	478.4	486.3	503.5	527.4	530.5	537.3	552.1
3119	2058	334.0	355.8	387.0	428.2	451.0	464.7	472.7	458.7	504.0	514.6	529.4	534.7
3120	2059	349.2	375.0	393.5	423.1	448.0	451.2	460.6	478.4	489.6	501.9	502.8	516.8
3121	2060	292.3	316.1	348.0	381.5	394.2	408.5	418.3	424.0	434.2	436.0	446.2	448.7
3122	2061	288.1	298.4	335.4	382.0	397.2	424.3	437.7	448.2	445.7	447.7	428.2	473.6
3123	2062	312.0	339.7	376.1	416.4	433.8	454.0	470.5	488.7	501.2	510.3	519.6	529.8
3124	2063	316.1	356.3	371.2	399.1	427.2	448.2	461.3	473.0	486.8	505.0	508.3	521.3
3125	2064	304.6	329.3	355.9	384.8	417.6	429.0	443.5	446.3	454.1	463.3	466.3	480.9
3126	2065	310.7	338.0	357.7	358.7	404.0	420.5	437.3	451.0	466.0	473.4	480.9	493.8
3127	2066	327.2	362.7	397.4	414.7	459.0	480.2	455.2	502.0	520.0	537.1	550.7	570.0
3128	2067	328.9	355.0	390.3	433.2	427.8	451.4	415.0	453.8	470.7	482.0	483.7	505.3
3129	2068	317.6	358.9	384.3	418.2	432.6	456.4	462.9	484.1	493.5	398.6	464.2	488.1
3130	2069	294.3	313.2	340.6	367.1	370.4	396.3	399.8	412.0	424.4	430.5	437.1	444.6
3131	2070	309.3	336.9	363.9	400.2	424.9	397.2	436.8	470.0	477.8	485.1	482.9	499.9
3132	2071	309.8	327.8	358.6	385.4	405.8	372.9	430.2	448.0	463.9	475.8	443.4	486.3
3133	2072	307.7	327.4	355.0	390.6	414.8	437.8	459.4	479.4	490.6	506.2	509.2	533.2
3134	2073	320.3	350.6	373.7	408.3	382.5	420.8	435.4	445.8	452.8	473.5	476.5	491.1
3135	2074	327.8	354.0	387.8	412.8	422.3	440.4	466.1	487.5	491.4	496.2	515.8	526.2
3136	2075	323.3	339.8	362.4	387.3	400.6	416.7	428.8	447.0	454.4	465.2	479.2	482.1
3137	2076	341.7	360.4	398.3	420.9	453.3	482.9	490.1	499.7	514.2	515.9	531.1	531.6
3138	2077	329.6	366.8	343.8	389.4	429.6	458.3	466.2	470.8	473.5	475.0	489.2	500.2
3139	2078	358.3	388.1	417.9	449.3	467.8	488.5	500.0	520.7	533.2	532.2	544.8	553.2
3140	2079	346.7	366.2	398.5	427.1	440.1	467.7	447.4	475.5	494.2	503.4	493.9	521.2
	MEAN	317.7	344.3	372.0	404.5	423.5	440.7	450.8	467.2	479.7	485.4	493.1	507.3
	±S.D.	±17.14	±19.52	±20.41	±20.30	±24.09	±28.68	±23.92	±26.39	±28.29	±33.80	±33.88	±31.83

BEST COPY AVAILABLE

EGWE: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS*

Individual and Mean Body Weights (grams) of Exposed Males

Exposure Level: 0 ppm (Continued)

Animal Number	Pathology Number	Days on Study 82	88	95	102	109	116	124	130	137	144	151	158	165
80A-3201	80A-2050	565.5	562.7	552.6	539.8	548.7	573.7	576.5	587.2	593.1	588.1	600.1	603.9	583.6
3202	2051	508.2	502.6	508.8	516.2	525.2	539.5	553.4	564.6	568.4	563.6	582.4	583.7	573.2
3203	2052	500.7	495.0	505.9	505.4	511.7	526.0	537.4	553.1	550.5	552.2	568.6	575.4	574.5
3204	2053	539.8	535.2	545.5	554.9	552.2	575.1	586.3	597.2	602.2	597.3	618.3	623.1	616.3
3205	2054	468.6	462.6	466.9	482.1	481.4	490.7	501.1	505.9	508.2	503.7	523.8	521.5	511.3
3116	2055	479.6	475.1	479.7	481.1	475.5	476.2	495.9	511.5	499.0	497.0	508.2	511.1	502.2
3117	2056	526.8	519.7	513.0	509.4	503.4	520.9	525.8	535.5	539.6	527.5	542.0	552.6	542.8
3118	2057	565.3	555.8	568.6	578.7	576.1	598.9	613.7	618.9	623.4	623.3	649.1	648.4	642.3
3119	2058	540.3	533.3	527.5	519.8	524.4	542.1	545.4	556.7	565.8	558.6	581.8	583.6	564.9
3120	2059	527.1	514.1	521.7	533.1	536.6	560.6	572.0	570.6	588.9	576.7	603.9	599.5	588.0
3121	2060	459.5	455.7	454.5	459.0	459.9	482.3	489.4	497.5	501.8	500.1	514.6	523.3	527.4
3122	2061	491.8	495.3	496.4	511.9	502.9	511.4	503.6	521.9	527.2	517.1	536.2	527.4	510.9
3123	2062	539.3	525.0	537.3	532.6	526.5	554.1	569.1	580.4	600.1	570.4	606.0	611.6	614.2
3124	2063	534.0	531.3	540.0	534.3	510.5	521.7	535.1	553.7	569.0	568.0	583.7	595.6	584.6
3125	2064	481.9	479.8	489.0	496.8	492.3	506.7	523.3	525.8	540.7	523.3	549.7	556.2	559.0
3126	2065	497.8	494.9	506.9	496.7	501.9	519.8	528.3	531.9	539.9	535.6	546.3	559.9	563.4
3127	2066	574.8	567.2	570.4	573.1	572.5	584.4	592.7	596.2	603.7	594.6	608.8	612.2	612.5
3128	2067	518.2	514.5	510.4	516.2	526.6	554.5	574.5	587.2	600.6	601.1	619.0	625.2	620.4
3129	2068	500.6	504.0	524.1	521.2	528.1	540.4	549.4	560.3	571.1	569.2	587.1	584.5	594.9
3130	2069	452.9	444.6	455.8	460.7	456.1	466.9	474.1	483.8	491.8	477.9	494.6	500.6	496.0
3131	2070	515.2	506.9	526.7	536.2	531.5	545.0	563.0	566.6	578.1	569.2	590.0	605.3	602.4
3132	2071	501.5	489.7	501.0	510.3	506.9	529.0	537.2	547.3	561.0	558.7	575.9	585.2	576.9
3133	2072	537.9	533.8	540.2	539.2	554.0	565.6	580.4	585.3	589.5	588.4	601.1	606.2	605.4
3134	2073	491.9	488.1	496.8	490.9	507.7	515.9	527.4	526.8	530.8	527.6	538.6	540.6	553.2
3135	2074	532.5	529.6	543.5	535.2	535.9	552.0	564.2	565.7	569.2	564.4	583.2	587.3	596.6
3136	2075	489.9	479.9	502.7	495.2	498.1	513.8	510.8	519.6	529.0	514.4	532.7	541.4	537.7
3137	2076	538.8	528.2	556.8	552.1	538.8	556.9	571.6	574.9	583.6	572.3	589.7	588.1	593.6
3138	2077	496.2	502.7	538.5	532.6	542.7	560.9	573.9	587.6	602.0	599.8	637.4	651.4	645.8
3139	2078	565.6	545.2	568.7	568.0	571.1	591.3	593.8	602.7	618.3	608.8	627.8	627.0	624.9
3140	2079	526.1	511.5	528.3	526.1	526.8	545.1	561.7	567.7	575.4	566.3	583.3	594.0	593.1
	MEAN	515.6	509.5	519.3	518.9	520.9	537.4	547.7	556.1	564.1	557.2	576.1	580.9	577.1
	±S.D.	±32.00	±30.46	±31.49	±28.64	±30.57	±33.46	±34.70	±33.92	±36.48	±37.13	±39.63	±39.86	±40.50

BEST COPY AVAILABLE

Table [illegible]

EGME: INHALATION REPRODUCTION AND TERATOGENIC-LETHAL STUDY IN RATS[a]

Individual and Mean Body Weights (grams) of Exposed Males

Exposure Level: 0 ppm (Continued)

Animal Number	Pathology Number	Days on Study 172	179	186	193	200	207	214	221	228	235	242	249
80A-3201	80A-2050	591.7	603.0	611.3	614.6	626.8	629.3	633.6	629.9	627.5	634.3	647.3	659.5
3202	2051	589.5	583.2	581.0	587.0	605.6	585.1	597.6	607.9	603.5	597.8	620.0	626.9
3203	2052	573.9	575.5	568.4	575.7	592.8	604.6	602.5	607.9	608.3	606.8	614.8	622.2
3204	2053	577.1	594.3	605.9	606.0	614.2	604.0	612.6	620.1	613.0	607.6	616.3	615.3
3205	2054	505.2	502.3	506.7	518.8	527.4	525.3	515.9	530.5	532.7	523.9	525.4	523.4
3116	2055	508.3	497.9	500.0	507.6	520.1	517.7	505.9	510.2	510.7	514.5	515.9	531.2
3117	2056	533.5	539.6	545.6	558.2	570.9	549.1	562.3	565.0	557.4	555.6	566.0	571.5
3118	2057	635.3	638.7	636.4	643.5	661.5	651.1	660.2	663.3	666.5	660.0	675.9	683.8
3119	2058	567.1	567.0	573.9	578.2	595.2	595.9	596.1	592.5	602.4	587.6	591.9	603.7
3120	2059	587.7	579.8	582.2	578.9	596.0	597.6	604.2	605.0	598.9	605.7	610.0	624.1
3121	2060	527.2	530.9	529.3	540.0	556.3	556.9	564.2	564.8	564.0	566.6	574.3	585.5
3122	2061	530.7	533.5	550.2	555.9	568.1	562.2	549.1	560.9	561.0	550.3	561.3	563.6
3123	2062	612.0	608.7	611.6	614.4	630.6	630.3	628.2	632.8	629.2	626.2	642.4	645.1
3124	2063	593.4	590.4	610.2	612.7	623.3	612.4	610.7	615.0	612.7	616.2	631.5	636.7
3125	2064	531.0	542.1	538.6	544.6	561.0	560.2	566.2	565.0	564.3	570.3	581.1	586.6
3126	2065	560.8	572.8	574.4	580.9	592.6	592.1	601.8	599.6	594.9	602.6	608.9	612.4
3127	2066	617.0	604.4	602.2	611.0	620.2	612.8	624.5	633.8	623.3	630.0	637.6	642.4
3128	2067	619.6	629.0	631.7	639.8	657.4	661.8	671.3	673.9	667.2	677.3	691.5	706.6
3129	2068	596.2	596.3	593.7	599.2	605.7	609.6	611.0	613.0	607.8	610.1	603.3	608.0
3130	2069	494.6	496.0	498.8	505.8	516.9	512.2	524.9	525.5	522.5	513.3	516.4	527.7
3131	2070	612.3	621.2	612.8	625.0	641.3	642.7	651.3	655.5	640.4	649.8	651.1	667.8
3132	2071	578.6	581.3	582.0	589.3	605.3	604.4	596.3	610.0	600.1	608.3	614.5	619.3
3133	2072	592.6	602.3	605.9	615.8	626.0	628.5	628.5	629.5	624.7	622.9	618.5	624.2
3134	2073	538.3	540.7	545.8	546.7	548.4	541.1	555.0	574.9	566.0	564.2	569.9	577.5
3135	2074	596.2	606.9	597.6	607.6	614.9	617.8	615.5	625.3	620.1	630.1	622.0	644.8
3136	2075	541.3	539.3	548.8	549.6	558.7	563.0	564.0	571.1	560.6	558.6	555.1	566.9
3137	2076	576.1	581.3	585.5	586.2	600.0	592.2	603.1	600.9	595.5	599.5	594.4	607.7
3138	2077	665.7	665.2	670.5	680.9	695.3	675.2	681.4	683.5	688.6	688.4	697.7	718.8
3139	2078	615.9	622.2	625.9	647.4	656.0	643.5	648.9	651.6	639.6	639.0	654.0	663.8
3140	2079	586.2	600.3	600.8	602.5	625.8	612.9	620.1	631.0	619.7	629.9	631.4	645.4
	MEAN	575.2	578.2	581.2	587.5	600.5	596.4	600.2	605.0	600.8	601.6	608.0	617.1
	±S.D.	±41.05	±42.19	±41.34	±42.08	±43.10	±42.23	±44.01	±42.86	±42.02	±44.42	±46.67	±48.59

BEST COPY AVAILABLE

Table A-1 (Continued)

EOME: INHALATION REPRODUCTION AND INHEMANT-LETHAL STUDY IN RATS[a]

Individual and Mean Body Weights (grams) of Exposed Males

Exposure Level: 30 ppm

Animal Number	Pathology Number	Days on Study -1	5	12	19	27	33	40	47	54	62	68	75
80A-3146	80A-2080	284.8	302.1	336.4	375.3	397.6	419.9	431.0	481.6	466.5	475.6	491.0	489.7
3147	2081	310.8	336.8	340.2	407.2	433.9	451.4	462.8	460.1	491.1	504.0	510.5	517.3
3148	2082	315.3	340.9	363.4	379.8	431.0	450.1	473.3	491.4	493.2	513.5	520.9	528.4
3149	2083	259.3	312.4	347.1	392.5	408.7	442.2	460.4	447.8	463.3	482.9	496.8	503.9
3150	2084	309.6	371.3	363.6	378.2	408.9	418.6	432.5	448.7	451.8	469.0	474.4	470.6
3151	2085	331.3	333.2	415.3	406.4	477.2	508.2	527.3	548.3	541.1	579.7	595.4	593.7
3152	2086	331.9	361.8	394.0	433.5	457.8	469.7	481.3	491.2	510.8	522.4	523.5	527.1
3153	2087	336.9	404.5	401.0	426.8	449.6	465.4	478.1	485.2	501.4	525.7	532.9	528.6
3154	2088	327.9	358.3	384.4	410.0	435.6	469.8	448.2	464.3	478.6	486.4	488.6	497.0
3155	2089	339.7	360.9	389.4	426.6	419.3	444.8	487.3	511.2	524.9	536.9	552.6	560.1
3156	2090	283.6	309.3	336.6	359.2	366.5	390.8	399.3	410.7	421.0	422.1	430.6	435.4
3157	2091	302.4	348.1	382.9	412.2	426.7	440.9	458.6	488.0	504.2	519.4	521.9	529.4
3158	2092	294.4	307.2	358.9	385.7	397.4	406.4	417.7	432.5	436.0	445.7	456.6	470.8
3159	2093	290.3	237.6	251.8[a]	332.1	384.0	411.3	437.6	458.6	473.1	493.2	495.1	507.8
3160	2094	320.2	352.6	379.5	421.7	448.2	418.7	470.0	489.9	505.2	471.6	499.7	525.0
3161	2095	316.2	342.5	376.3	408.3	421.0	432.2	462.0	484.0	493.2	515.0	521.8	540.0
3162	2096	325.8	364.5	374.5	411.9	429.3	452.6	467.9	488.8	496.5	513.9	504.8	519.0
3163	2097	333.2	370.7	403.7	417.1	450.1	475.2	494.4	509.6	524.8	490.9	508.8	519.9
3164	2098	354.4	380.0	416.6	448.1	460.0	466.6	475.4	502.5	510.7	530.2	536.7	534.8
3165	2099	343.3	371.1	402.6	435.5	455.2	456.9	464.8	492.1	495.7	520.5	523.2	535.9
3166	2100	284.7	311.0	317.4	351.3	365.3	373.3	392.6	412.0	418.5	431.9	438.9	545.6
3167	2101	301.0	341.2	370.8	391.6	401.3	418.7	428.1	446.4	450.9	465.2	463.4	491.8
3168	2102	297.8	316.3	338.1	370.4	386.4	402.5	421.8	451.0	455.8	460.2	469.7	481.9
3169	2103	298.7	314.8	336.8	373.4	395.8	409.2	426.4	452.7	461.0	467.4	476.6	492.0
3170	2104	323.3	349.3	374.9	406.2	428.3	444.7	470.3	488.4	499.4	508.5	523.0	531.1
3171	2105	320.2	361.0	394.7	428.2	449.2	465.0	477.8	505.4	519.6	528.8	536.1	543.3
3172	2106	332.8	314.8	360.8	403.3	433.6	462.0	474.2	499.1	--[b]	527.5	535.1	532.4
3173	2107	337.5	364.4	391.4	420.3	439.2	465.3	462.1	467.2	--[b]	513.7	522.8	535.8
3174	2108	340.7	371.1	405.3	439.4	462.2	473.5	480.3	530.9	494.8	540.4	510.2	532.1
3175	2109	352.8	386.5	420.6	447.7	469.4	487.5	495.3	467.2	516.5	499.4	554.4	565.1
	MEAN	316.7	343.2	375.8	403.3	426.3	443.1	458.6	476.9	485.8	498.7	507.2	519.5
	±S.D.	±23.11	±33.28	±26.68	±28.92	±29.83	±30.85	±29.93	±31.59	±31.69	±34.80	±35.36	±31.66

Table A-1 (Continued)

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS[a]

Individual and Mean Body Weights (grams) of Exposed Males

Exposure Level: 30 ppm (Continued)

Animal Number	Pathology Number	Days on Study												
		82	88	95	102	109	116	124	130	137	144	151	158	165
80A-3146	80A-2080	501.3	497.6	511.5	510.2	509.7	542.6	549.5	553.9	561.9	547.0	578.1	578.1	576.5
3147	2081	520.3	501.3	513.2	521.0	520.1	539.5	550.2	560.0	569.7	561.2	570.8	575.8	577.9
3148	2082	538.0	535.7	542.0	550.0	540.9	550.8	556.6	569.5	570.7	564.8	578.9	579.3	583.1
3149	2083	510.5	515.4	514.9	525.8	524.5	533.1	536.9	541.4	534.0	536.8	555.0	554.3	560.2
3150	2084	480.0	455.7	485.9	499.9	499.9	506.9	522.9	534.1	537.9	539.9	554.1	566.4	564.7
3151	2085	617.5	577.3	602.4	605.3	619.0	638.5	648.3	650.1	661.3	656.0	682.3	685.6	681.4
3152	2086	535.7	532.2	539.1	533.8	537.2	556.8	574.0	581.1	583.4	574.7	605.8	605.7	602.5
3153	2087	537.2	527.5	546.9	548.1	540.5	560.2	569.6	574.8	590.3	580.2	597.8	603.3	621.1
3154	2088	500.3	484.5	497.6	510.6	501.1	528.3	534.6	542.9	546.7	540.9	558.8	565.7	571.6
3155	2089	568.0	567.4	569.9	563.5	576.5	597.1	593.5	603.6	618.7	615.4	647.8	658.4	664.5
3156	2090	452.9	423.7	442.3	438.6	457.2	452.3	465.1	469.1	468.0	444.8	461.7	466.8	475.5
3157	2091	540.7	519.2	543.2	537.0	545.4	558.9	570.3	581.0	589.2	588.4	607.4	607.6	619.1
3158	2092	479.9	458.2	488.3	481.8	493.0	506.1	525.1	522.8	530.1	522.3	536.8	546.0	549.8
3159	2093	515.7	492.3	519.5	537.9	531.0	519.7	521.3	533.2	531.6	549.4	577.7	584.1	592.3
3160	2094	538.2	527.1	542.5	546.2	537.4	560.7	569.4	576.9	577.0	565.8	589.1	578.2	567.6
3161	2095	551.2	547.8	556.5	551.2	536.1	554.7	561.5	572.9	581.0	582.2	596.0	606.4	622.7
3162	2096	526.1	487.9	516.3	512.7	520.5	545.9	550.3	548.3	549.1	542.8	563.7	569.8	582.1
3163	2097	547.5	537.2	562.3	561.8	562.4	580.7	597.9	601.0	609.9	606.3	629.0	637.8	642.3
3164	2098	564.6	521.8	536.2	532.3	536.4	555.8	578.8	592.1	600.9	603.9	616.3	619.0	615.5
3165	2099	547.5	548.8	556.4	537.2	546.7	565.7	577.9	596.9	614.4	608.5	633.5	635.7	650.9
3166	2100	459.1	451.4	454.9	453.1	453.6	462.6	473.8	481.4	491.3	492.0	510.5	510.5	520.5
3167	2101	471.5	469.1	481.8	496.0	478.7	480.9	485.8	482.1	476.5	471.0	489.0	492.0	502.6
3168	2102	494.4	471.1	484.0	501.2	503.0	515.8	529.5	526.4	526.7	526.8	549.3	556.0	559.9
3169	2103	494.7	488.9	506.5	506.4	519.6	524.1	530.6	539.4	546.8	529.8	546.5	548.3	560.0
3170	2104	547.1	533.2	544.7	545.4	557.7	580.3	587.8	598.1	607.8	605.9	629.2	635.3	642.3
3171	2105	557.4	551.3	562.6	552.6	549.0	557.2	566.4	572.3	576.0	578.4	595.7	590.8	594.1
3172	2106	550.9	542.3	547.9	526.0	510.3	546.2	573.8	579.4	595.8	594.7	618.3	624.6	634.9
3173	2107	550.8	551.8	570.7	571.1	570.9	592.7	615.1	624.3	636.7	641.4	656.5	670.1	685.6
3174	2108	541.4	536.9	547.2	538.4	529.3	551.3	558.3	566.9	571.9	573.3	587.7	591.3	600.5
3175	2109	569.1	571.6	581.6	580.7	591.2	600.2	602.2	600.8	606.4	608.5	629.8	630.4	640.1
	MEAN	527.0	514.3	529.0	529.5	530.0	545.5	555.9	562.6	568.7	565.1	585.1	589.1	595.4
	±S.D.	±36.83	±39.19	±37.41	±35.54	±35.90	±39.76	±39.91	±41.13	±44.89	±46.94	±48.65	±49.39	±49.67

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[illegible]

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS[illegible]

Individual and Mean Body Weights (grams) of Exposed Males

Exposure Level: 30 ppm (Continued)

Animal Number	Pathology Number	Days on Study 172	179	186	193	200	207	214	221	228	235	242	249
80A-3146	80A-2080	574.9	577.3	587.3	584.6	601.9	590.4	583.7	591.5	588.9	587.6	593.1	598.6
3147	2081	573.9	572.6	581.2	590.8	596.7	596.9	587.3	588.5	599.6	590.6	597.0	614.9
3148	2082	587.3	591.0	597.0	606.1	615.2	630.7	612.6	613.8	607.7	606.0	613.6	627.0
3149	2083	544.8	537.8	550.9	553.8	566.7	561.1	566.6	566.0	565.4	565.7	562.3	568.4
3150	2084	569.2	574.6	589.8	683.8	579.6	585.3	585.3	583.6	588.7	585.2	586.3	602.9
3151	2085	662.6	677.4	693.2	695.9	709.9	712.0	711.1	707.1	726.5	725.8	736.5	747.0
3152	2086	600.7	606.1	617.4	625.9	636.2	640.3	626.8	643.6	645.4	648.2	657.0	659.5
3153	2087	606.0	598.5	606.2	614.2	628.0	629.3	631.5	637.7	643.0	636.4	657.6	662.5
3154	2088	572.1	574.5	580.3	580.5	597.4	597.0	594.2	596.7	605.9	602.9	644.0	623.8
3155	2089	643.8	660.1	680.5	691.0	690.5	715.3	711.0	714.0	719.1	725.7	737.3	749.1
3156	2090	473.1	490.4	500.0	503.4	514.8	479.7	505.4	496.4	516.3	516.7	529.6	539.3
3157	2091	613.4	594.5	598.8	604.5	611.7	619.2	618.3	617.2	618.7	604.8	610.0	623.4
3158	2092	545.4	543.9	558.7	562.5	572.9	573.6	562.3	574.1	579.2	575.5	575.6	582.3
3159	2093	583.0	588.2	588.0	587.5	591.2	568.7	526.4	564.1	592.0	597.8	593.4	585.3
3160	2094	555.2	557.9	572.6	576.0	581.4	578.7	564.1	587.8	580.9	566.4	567.3	568.5
3161	2095	613.5	620.5	642.1	642.7	648.3	646.4	654.8	652.6	655.2	650.0	656.7	667.4
3162	2096	581.9	576.1	586.8	572.4	592.7	608.3	596.6	607.4	618.5	607.3	608.8	621.4
3163	2097	646.9	642.8	656.3	652.5	658.5	665.6	661.2	657.9	661.1	655.9	659.3	673.9
3164	2098	628.9	615.1	616.9	620.6	630.7	634.5	634.4	644.8	664.6	658.3	662.2	685.8
3165	2099	647.8	635.1	648.1	660.6	690.1	693.8	685.3	679.9	699.5	694.9	694.7	710.3
3166	2100	514.2	514.9	522.4	526.7	537.4	537.4	537.7	534.4	536.5	546.7	546.0	560.6
3167	2101	498.7	499.4	510.6	515.0	522.4	526.2	518.0	526.0	525.7	530.4	531.7	543.3
3168	2102	560.5	565.7	582.5	580.8	592.9	587.8	583.3	584.7	600.2	601.3	604.7	623.4
3169	2103	552.2	554.6	563.3	565.7	571.1	577.0	570.5	572.7	576.7	566.0	574.0	578.8
3170	2104	648.0	644.5	645.0	645.0	656.9	653.7	644.0	651.1	670.8	667.1	681.4	689.8
3171	2105	589.3	583.1	585.9	589.8	592.9	593.7	591.9	591.0	598.4	598.8	598.3	603.0
3172	2106	645.5	637.7	645.1	650.4	662.7	664.2	640.5	653.8	663.3	668.5	674.8	687.5
3173	2107	678.3	690.1	702.4	700.3	717.6	720.6	722.6	726.9	738.0	741.9	746.3	762.1
3174	2108	604.3	586.6	599.7	593.5	609.5	610.9	605.5	606.2	614.4	610.5	609.8	620.5
3175	2109	642.6	616.8	632.2	642.2	653.3	657.8	650.4	650.5	655.6	657.0	656.6	671.2
	MEAN	591.9	590.9	601.4	604.8	614.4	615.2	609.4	614.1	621.9	619.7	625.5	635.0
	±S.D.	±49.66	±48.41	±49.37	±50.06	±51.26	±56.56	±56.11	±54.60	±56.39	±56.84	±58.71	±60.46

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Table A-1 (Continued)

EGHE: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS[a]

Individual and Mean Body Weights (grams) of Exposed Males

Exposure Level: 100 ppm

Animal Number	Pathology Number	Days on Study -1	5	12	19	27	33	40	47	54	62	68	75
80A-3181	80A-2110	308.4	342.3	375.4	409.8	426.4	418.1	437.3	452.7	479.4	494.0	500.8	507.0
3182	2111	281.3	292.5	315.0	343.9	360.1	375.8	368.0	382.5	404.0	432.5	434.2	440.7
3183	2112	289.4	310.2	332.8	364.0	385.3	398.0	399.7	422.4	438.8	455.8	452.7	459.4
3184	2113	272.0	305.2	333.1	363.2	393.8	410.3	428.5	432.7	443.5	443.9	450.7	414.6
3185	2114	307.1	324.0	353.1	383.3	402.3	421.6	430.5	407.0	427.5	455.1	460.5	462.7
3186	2115	323.5	347.5	386.1	422.0	441.4	457.2	474.4	493.1	505.0	526.4	531.5	545.1
3187	2116	324.9	355.2	392.3	426.0	439.9	464.1	476.9	486.9	505.4	524.4	526.5	541.5
3188	2117	301.5	330.7	365.9	403.2	409.4	434.1	449.4	450.7	469.0	483.8	486.1	493.1
3189	2118	331.6	358.3	397.1	427.8	442.9	455.0	457.5	483.5	485.8	503.6	505.0	520.4
3190	2119	338.1	360.2	358.4	396.3	418.5	428.8	439.6	464.0	472.0	488.9	495.1	475.2
3191	2120	342.8	374.6	410.0	445.1	478.0	497.9	506.1	522.6	479.8	547.2	554.8	531.0
3192	2121	288.4	291.9	326.8	359.8	390.0	409.9	427.4	457.6	541.9	494.2	501.6	516.7
3193	2122	302.4	316.3	351.1	387.4	394.2	422.9	430.9	448.2	462.6	470.9	471.4	483.1
3194	2123	308.0	329.4	352.1	380.1	395.0	406.7	408.1	425.2	438.3	453.7	458.2	465.5
3195	2124	318.0	331.3	373.3	394.0	396.9	389.9	405.8	440.2	463.3	483.9	494.4	512.6
3196	2125	314.4	343.3	362.2	406.6	430.4	446.1	456.2	465.9	479.6	488.0	488.5	495.5
3197	2126	346.3	381.0	430.6	463.6	489.0	507.7	533.6	551.5	573.4	596.1	601.6	610.5
3198	2127	317.6	346.8	388.5	430.5	458.8	484.0	501.6	530.4	535.8	549.3	510.0	478.9
3199	2128	322.8	351.6	380.0	404.3	420.3	440.2	455.1	448.5	463.6	488.8	490.5	495.2
3200	2129	356.0	386.1	435.2	473.6	495.0	501.9	522.5	526.1	544.5	569.0	568.7	589.4
	MEAN	314.7	338.9	370.9	404.2	423.4	438.9	450.5	464.6	480.7	497.5	499.1	501.9
	±S.D.	±22.17	±27.12	±32.68	±34.39	±36.41	±37.68	±42.58	±43.90	±43.21	±43.22	±41.96	±47.15

Table A-1 (Continued)

EGHE: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS[a]

Individual and Mean Body Weights (grams) of Exposed Males

Exposure Level: 100 ppm (Continued)

Animal Number	Pathology Number	Days on Study 82	88	95	102	109	116	124	130	137	144	151	158	165
80A-3181	80A-2110	509.3	506.9	514.6	523.9	516.7	540.8	554.6	559.7	568.6	563.9	582.3	585.4	587.7
3182	2111	437.7	429.8	451.0	452.7	454.8	455.0	470.8	476.1	485.6	479.2	502.7	503.3	494.8
3183	2112	460.9	454.3	468.9	473.3	469.2	467.0	490.9	491.1	491.1	479.3	506.1	500.4	495.3
3184	2113	441.5	451.5	472.1	490.5	486.9	486.7	517.0	528.2	532.6	520.5	541.1	542.4	536.8
3185	2114	471.7	477.7	489.8	493.4	490.8	508.6	515.5	517.8	525.9	516.6	540.6	535.2	538.8
3186	2115	559.5	530.8	537.4	538.4	540.4	--[b]	565.8	568.6	577.5	563.5	581.7	571.9	567.2
3187	2116	548.6	550.8	552.3	556.2	549.1	572.1	578.0	586.2	602.4	600.7	620.8	623.7	624.7
3188	2117	501.8	492.5	507.2	510.3	511.4	534.5	536.0	544.6	561.2	545.7	563.8	556.8	559.4
3189	2118	532.6	520.6	512.6	527.1	522.2	546.4	563.1	576.5	577.5	578.2	598.5	599.5	595.3
3190	2119	501.1	495.0	510.7	513.5	511.9	539.9	550.7	560.3	565.6	558.4	593.1	600.8	602.9
3191	2120	567.8	562.1	565.4	573.9	569.2	583.1	582.1	588.5	591.6	581.0	600.8	608.4	607.4
3192	2121	534.4	534.4	529.3	534.2	538.6	557.8	557.6	560.2	564.7	557.6	574.8	582.4	588.9
3193	2122	489.8	491.2	497.4	488.3	494.4	491.6	498.4	501.6	505.1	496.9	504.6	508.8	500.8
3194	2123	468.5	455.3	462.0	463.8	452.8	466.5	472.4	484.3	485.1	479.9	501.1	503.9	503.7
3195	2124	521.0	518.2	514.5	515.7	521.2	541.1	540.2	555.3	555.4	554.7	567.2	575.1	573.2
3196	2125	502.9	502.5	513.4	521.0	518.3	535.5	540.1	550.9	551.2	551.8	563.3	562.3	564.3
3197	2126	620.0	622.5	617.0	602.3	611.3	625.5	635.6	638.3	642.5	644.9	653.4	657.4	655.4
3198	2127	540.0	537.4	546.3	529.5	542.1	569.7	572.8	577.2	585.5	573.3	601.2	592.2	593.9
3199	2128	491.3	432.0	492.4	502.8	501.8	521.0	526.9	534.1	541.3	535.0	556.7	554.1	554.7
3200	2129	590.8	584.5	584.2	596.1	592.6	607.5	612.1	620.5	628.5	620.9	631.7	640.4	645.3
	MEAN	514.6	507.5	516.9	520.3	519.8	534.2	544.0	551.8	556.9	550.1	569.3	570.2	569.5
	±S.D.	±48.18	±50.50	±41.78	±40.00	±41.41	±47.09	±42.91	±42.96	±44.00	±45.55	±43.85	±45.64	±47.70

BEST COPY AVAILABLE

Table 8.1 (Continued)

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS*

Individual and Mean Body Weights (grams) of Exposed Males

Exposure Level: 100 ppm (Continued)

Animal Number	Pathology Number	Days on Study 172	179	186	193	200	207	214	221	228	235	242	249
80A-3181	80A-2110	576.5	578.2	582.6	586.9	594.0	585.3	578.1	584.7	588.9	586.0	593.4	603.6
3182	2111	495.2	499.0	506.1	503.0	517.0	517.5	508.4	516.3	519.5	515.1	518.7	529.6
3183	2112	502.9	499.1	509.3	505.6	510.9	506.6	503.7	496.3	504.6	497.7	497.9	516.6
3184	2113	537.7	541.5	546.7	552.8	557.5	549.0	555.1	549.9	559.6	562.2	562.1	568.3
3185	2114	533.0	535.4	551.8	558.5	565.7	570.2	562.4	568.1	574.5	569.5	581.8	586.3
3186	2115	564.6	564.9	574.8	582.9	591.4	590.6	593.5	595.0	601.4	600.2	601.1	605.1
3187	2116	623.0	618.6	631.7	642.1	656.6	654.4	647.1	651.4	669.9	664.7	676.4	696.2
3188	2117	559.7	546.9	545.3	553.3	562.1	548.4	557.4	561.3	574.9	567.5	577.1	586.4
3189	2118	598.4	599.1	603.7	612.9	620.6	616.2	618.7	621.1	624.5	620.3	629.0	646.0
3190	2119	589.7	587.1	608.2	611.5	623.5	628.4	609.6	628.8	635.1	630.3	628.4	641.0
3191	2120	612.9	578.1	599.3	605.7	625.9	627.5	621.1	629.3	635.1	631.7	642.5	648.9
3192	2121	598.1	577.9	597.1	594.6	611.4	613.0	608.3	618.7	628.3	620.7	621.5	630.7
3193	2122	506.4	500.7	501.9	503.0	503.1	494.3	495.3	494.6	492.8	492.2	492.5	494.5
3194	2123	500.9	483.3	496.6	505.3	509.8	514.1	511.6	509.0	515.3	509.7	513.9	520.8
3195	2124	583.7	577.8	584.1	581.4	591.1	587.4	590.2	591.6	599.4	599.1	599.3	606.5
3196	2125	565.4	567.8	581.8	585.6	590.0	597.6	594.2	599.1	599.3	590.2	594.6	601.5
3197	2126	652.8	636.1	658.2	656.9	681.7	676.2	695.0	701.9	703.9	692.8	697.2	704.8
3198	2127	595.0	605.4	615.5	619.8	639.1	616.0	601.2	621.4	633.2	632.2	644.2	660.9
3199	2128	552.6	554.9	553.0	565.3	566.4	571.3	559.7	556.9	569.8	567.0	570.8	576.1
3200	2129	644.0	643.9	659.6	668.8	686.8	683.2	683.1	698.7	697.0	697.1	706.1	716.5
	MEAN	569.6	564.8	575.4	579.8	590.2	587.4	584.7	589.7	596.3	592.3	597.4	607.0
	±S.D.	±46.80	±45.60	±48.88	±49.95	±54.70	±54.43	±55.44	±59.81	±59.83	±59.43	±61.35	±62.84

BEST COPY AVAILABLE

Table A-1 (Continued)

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS*

Individual and Mean Body Weights (grams) of Exposed Males

Exposure Level: 300 ppm

Animal Number	Pathology Number	Days on Study -1	5	12	19	27	33	40	47	54	62	68	75
80A-3206	80A-2130	299.0	320.5	349.3	373.6	392.5	403.0	370.2	393.9	403.5	417.3	415.9	429.7
3207	2131	299.3	331.9	357.0	389.7	407.7	402.8	419.1	439.1	458.1	475.8	472.1	479.4
3208	2132	308.7	333.4	357.6	390.5	415.7	423.2	449.9	453.3	469.8	481.0	479.8	494.9
3209	2133	301.3	318.5	341.9	375.1	398.5	439.7	439.6	439.6	462.9	459.4	456.0	455.0
3210	2134	296.2	309.5	345.0	374.0	389.3	407.5	418.2	426.5	434.4	448.5	442.8	451.7
3211	2135	317.0	328.1	355.4	386.5	400.6	409.0	363.2	389.5	406.1	406.3	410.1	427.4
3212	2136	318.6	334.0	357.0	380.9	398.1	407.8	413.8	410.7	426.6	438.9	433.5	436.2
3213	2137	334.9	358.7	397.4	427.4	449.9	475.4	485.0	499.7	511.4	531.3	533.5	543.4
3214	2138	302.4	345.6	324.4	371.9	399.3	419.9	413.7	424.6	444.5	455.6	451.8	458.8
3215	2139	340.0	346.9	326.5	376.6	396.9	412.4	414.5	431.4	445.8	453.5	452.1	459.2
3216	2140	284.9	313.0	329.5	363.1	373.2	379.6	391.6	406.5	417.3	441.3	439.6	449.2
3217	2141	293.6	309.3	336.7	357.7	363.4	380.6	381.7	387.7	380.7	397.1	395.5	396.0
3218	2142	293.8	297.6	319.1	332.3	355.4	357.4	371.4	377.5	390.0	408.7	407.2	414.2
3219	2143	280.7	293.6	260.9	272.6#	293.0#	314.4	313.8	302.8	345.3	383.8	390.3	411.9
3220	2144	301.4	313.8	337.3	367.2	387.5	399.5	415.3	433.4	438.2	401.3	392.3	421.5
3221	2145	293.2	325.7	360.8	385.5	403.9	421.2	429.2	443.1	455.2	467.5	453.6	469.1
3222	2146	326.7	357.2	386.3	423.6	421.9	438.2	450.2	466.6	482.5	497.4	494.4	508.4
3223	2147	279.0	312.0	349.5	375.3	392.6	407.4	420.4	426.5	433.8	442.2	431.6	427.9
3224	2148	350.1	375.6	412.9	438.1	407.5	426.2	444.5	454.5	469.0	491.9	493.4	494.2
3225	2149	331.4	354.1	394.4	415.0	439.6	458.6	464.6	474.2	495.1	498.6	503.6	444.2
	MEAN	307.6	328.9	349.9	384.4	399.7	409.2	413.5	424.1	438.5	449.9	447.5	453.6
	±S.D.	±20.23	±21.90	±33.05	±25.90	±22.80	±34.72	±39.74	±42.05	±40.40	±39.44	±39.89	±36.54

BEST COPY AVAILABLE

BEST COPY AVAILABLE

Table A-1 (Continued)

EGDE: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS[a]

Individual and Mean Body Weights (grams) of Exposed Males

Exposure Level: 300 ppm (Continued)

Animal Number	Pathology Number	Days on Study												
		82	88	95	102	109	116	124	130	137	144	151	158	165
80A-3206	80A-2130	433.7	430.5	451.9	450.2	449.0	460.9	473.4	477.1	487.0	474.6	494.3	498.8	488.5
3207	2131	481.4	479.2	502.8	502.0	512.6	536.1	555.2	572.7	573.1	583.4	593.2	602.0	575.8
3208	2132	492.6	494.0	487.1	469.3	478.2	504.9	520.1	530.1	539.0	538.4	554.5	557.7	550.2
3209	2133	434.6	448.8	474.1	466.4	466.3	470.9	471.3	472.9	475.9	477.1	493.7	504.4	499.9
3210	2134	454.9	449.3	467.5	466.9	469.4	483.7	491.3	500.0	512.5	506.7	530.9	525.4	523.7
3211	2135	434.9	424.8	437.0	440.3	449.3	462.5	466.5	472.2	464.9	462.8	480.5	484.7	475.7
3212	2136	410.6	419.3	447.2	463.1	467.4	476.8	497.5	508.5	514.2	509.2	522.4	526.7	536.9
3213	2137	536.2	537.0	541.0	526.1	542.5	550.8	559.3	555.0	557.1	552.2	570.0	585.3	565.7
3214	2138	463.6	459.8	479.6	482.9	501.1	519.4	529.0	532.5	520.2	523.6	539.5	551.9	540.1
3215	2139	461.1	450.9	485.1	479.0	477.5	488.6	489.5	479.2	471.3	468.4	506.4	509.2	490.5
3216	2140	451.0	450.5	472.0	474.1	492.0	507.2	520.3	534.9	540.4	543.3	563.7	576.5	586.9
3217	2141	356.5	363.5	395.6	404.9	415.6	435.0	450.3	459.7	452.7	448.1	463.7	478.4	482.9
3218	2142	415.6	404.3	425.9	434.2	440.7	457.2	460.8	468.9	476.4	470.1	487.7	490.2	495.0
3219	2143	410.1	413.4	416.9	415.1	416.5	430.7	427.5	418.7	409.4	425.4	447.3	448.9	457.1
3220	2144	352.7	373.8	407.0	433.2	439.7	453.5	461.6	448.2	442.6	430.3	455.2	455.3	462.8
3221	2145	455.8	462.3	469.4	475.6	465.5	476.8	476.7	473.2	483.3	468.2	478.9	474.1	471.6
3222	2146	502.6	495.6	506.0	507.6	515.3	522.1	533.9	535.3	527.1	523.7	551.9	545.4	545.2
3223	2147	430.9	423.0	443.8	461.8	468.6	490.4	489.1	500.0	496.1	506.4	534.0	538.0	534.3
3224	2148	506.1	501.1	516.6	508.5	520.2	543.6	555.8	562.7	574.4	564.6	585.0	596.8	594.2
3225	2149	484.6	485.0	514.9	528.8	533.6	554.1	567.1	572.2	565.9	568.5	587.9	597.0	605.3
	MEAN	448.5	448.3	467.1	469.5	476.0	491.3	499.8	503.7	504.2	502.2	522.0	527.3	524.1
	±S.D.	±46.63	±43.46	±39.05	±34.13	±36.31	±37.35	±40.56	±43.98	±46.00	±46.83	±45.84	±48.37	±46.11

BEST COPY AVAILABLE

Table A-1 (Continued)

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS[a]

Individual and Mean Body Weights (grams) of Exposed Males

Exposure Level: 300 ppm (Continued)

Animal Number	Pathology Number	Days on Study 172	179	186	193	200	207	214	221	228	235	242	249
804-3206	804-2130	482.2	480.3	488.0	492.6	500.8	500.2	503.5	505.9	506.7	506.6	504.4	512.6
3207	2131	597.5	601.8	599.9	604.1	613.0	613.6	599.7	604.6	600.5	603.0	614.9	625.0
3208	2132	550.8	563.1	565.8	540.0	558.9	554.9	549.0	562.4	567.6	567.3	583.1	606.0
3209	2133	519.0	529.3	534.1	535.8	542.8	550.4	548.3	550.0	555.2	549.7	560.7	564.6
3210	2134	519.0	523.3	528.7	523.6	543.6	535.8	530.8	535.6	547.5	546.1	552.7	563.2
3211	2135	474.0	479.5	483.5	491.0	499.0	494.4	495.3	492.5	492.2	492.2	492.1	497.0
3212	2136	542.3	542.0	548.0	555.3	561.6	562.6	552.2	562.5	560.9	566.1	579.7	595.6
3213	2137	575.3	578.8	584.5	585.9	601.4	605.4	607.0	612.7	621.0	616.8	629.6	647.8
3214	2138	542.6	551.8	553.0	563.7	582.0	529.9	579.1	598.0	586.0	586.4	571.4	592.7
3215	2139	481.4	478.1	475.6	486.5	498.9	448.1	482.9	489.8	490.5	493.1	497.2	497.9
3216	2140	589.3	592.4	588.6	596.8	616.0	582.6	626.3	634.7	631.2	632.6	638.4	655.0
3217	2141	483.8	486.6	490.9	493.9	501.8	459.9	497.0	503.6	494.2	506.5	499.0	517.1
3218	2142	498.7	497.3	491.5	493.3	503.2	468.2	507.8	513.9	510.3	516.2	521.7	529.0
3219	2143	443.9	447.4	454.4	469.3	475.2	420.8	460.8	460.3	447.7	449.6	442.4	441.9
3220	2144	462.1	463.6	474.1	481.6	493.9	450.2	496.8	501.4	495.3	496.6	508.3	513.4
3221	2145	473.5	465.7	470.0	466.6	474.3	434.9	469.9	469.9	477.0	473.9	479.0	483.6
3222	2146	558.6	539.5	543.5	545.2	566.4	520.5	551.3	553.1	545.1	554.4	560.2	574.1
3223	2147	535.6	538.1	544.8	559.7	563.9	513.5	553.9	560.5	561.6	551.1	559.7	568.2
3224	2148	573.5	545.6	551.5	555.8	571.1	533.6	559.9	568.6	575.6	580.3	581.3	603.2
3225	2149	610.0	614.7	618.4	622.7	634.8	604.6	643.9	645.3	649.1	644.2	659.9	672.4
	MEAN	525.7	525.9	529.4	533.2	545.1	519.2	540.7	546.3	545.8	546.6	551.8	563.0
	±S.D.	±49.21	±49.47	±48.37	±47.42	±49.50	±59.00	±52.06	±53.98	±55.47	±54.20	±58.08	±62.78

[a]Male rats were exposed to 0, 30, 100, or 300 ppm EGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, the animals were maintained in the laboratory for recovery.

[b]No data.

#Statistical outlier identified by sequential outlier test, alpha=0.01; value not included in calculations.

BEST COPY AVAILABLE

Table A-2

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual and Mean Body Weights (grams) of Exposed Females*

Exposure Level: 0 ppm

Animal Number	Pathology Number	Days on Study -1	5	12	19	27	33	40	47	54	62	68	75	82	88
80A-3000	80A-2150	190.9	199.6	213.0	227.3	235.1	241.2	244.9	278.5	255.7	260.0	260.7	261.7	267.9	259.3
3001	2151	195.9	211.0	219.6	244.0	256.3	267.5	271.8	256.0	281.4	287.5	299.9	302.7	311.0	303.3
3002	2152	192.1	203.6	218.3	225.3	235.8	244.8	245.4	253.7	253.5	246.3	254.6	257.5	254.2	258.7
3003	2153	196.8	208.9	222.9	235.3	238.5	253.5	252.5	257.0	261.9	263.9	271.1	272.7	280.7	272.0
3004	2154	200.4	217.3	232.4	239.7	245.5	264.2	267.7	270.8	280.4	276.8	281.1	277.4	286.6	275.6
3005	2155	215.0	223.4	241.8	254.1	268.9	272.2	285.4	288.7	296.3	294.9	299.7	305.9	308.2	300.2
3006	2156	223.5	229.0	249.2	262.2	278.4	290.2	299.9	304.4	311.6	309.9	312.9	312.7	315.7	319.5
3007	2157	226.7	225.1	239.6	259.2	268.5	277.9	287.5	301.3	308.0	301.6	304.6	314.5	304.6	305.6
3008	2158	228.3	241.3	251.7	276.0	282.8	296.4	295.5	307.8	280.7	290.4	307.6	316.0	328.2	321.0
3009	2159	228.1	245.8	257.5	266.9	276.2	288.1	295.6	292.5	303.6	302.1	306.6	305.6	318.8	304.7
3010	2160	188.3	210.3	207.9	227.7	233.6	236.3	248.7	243.3	251.8	265.1	258.6	271.2	288.3	266.7
3011	2161	193.6	200.8	204.4	220.8	224.7	230.6	228.7	256.0	250.6	248.5	247.6	252.8	261.6	250.3
3012	2162	205.4	219.1	233.1	248.0	258.5	267.5	272.8	271.2	272.1	267.7	277.5	267.9	284.2	280.8
3013	2163	199.9	215.2	235.0	246.9	260.0	264.8	274.0	279.1	282.9	278.2	290.3	290.9	296.2	295.2
3014	2164	207.1	221.2	236.0	245.3	247.1	266.8	272.5	275.7	275.0	276.9	267.9	278.5	283.6	276.6
3015	2165	205.8	209.3	221.1	233.3	248.0	240.4	257.7	258.2	256.4	264.0	254.1	265.6	269.7	268.2
3016	2166	214.4	213.5	248.5	267.1	275.1	278.5	299.8	303.8	316.7	315.3	320.6	325.0	325.8	324.3
3017	2167	211.7	218.4	240.0	258.7	274.2	272.9	287.4	287.7	289.2	298.1	298.3	306.1	308.5	294.8
3018	2168	225.2	237.7	255.8	271.1	281.8	294.9	307.2	306.6	311.8	318.6	329.4	334.8	348.9	341.7
3019	2169	238.6	255.2	282.0	299.0	323.2	333.4	346.0	345.1	348.3	353.2	373.6	374.0	383.9	370.0
3020	2170	202.4	202.4	232.8	243.5	249.0	254.5	270.3	277.6	281.4	283.2	283.3	290.2	288.4	277.8
3021	2171	214.8	223.8	244.1	262.0	270.5	285.7	285.7	293.1	295.6	305.7	306.9	314.8	325.8	306.6
3022	2172	203.3	206.3	224.5	238.9	243.7	253.0	252.7	259.1	273.1	270.0	271.6	278.2	282.2	266.4
3023	2173	204.7	215.8	232.7	239.8	252.1	253.9	264.7	274.4	277.9	275.0	282.8	292.8	290.6	275.7
3024	2174	211.3	220.2	233.5	244.0	249.5	260.7	261.9	267.4	272.0	268.3	276.4	274.5	273.4	271.4
3025	2175	215.3	221.7	239.8	257.0	268.8	268.0	280.5	286.9	288.4	291.8	296.8	295.1	304.9	295.1
3026	2176	213.1	214.8	234.8	252.3	260.8	265.3	279.6	290.6	294.9	302.6	304.1	311.3	319.2	305.2
3027	2177	224.4	227.5	240.6	259.8	281.1	282.7	284.1	294.7	307.6	308.6	307.4	317.6	328.5	312.2
3028	2178	220.3	228.3	241.9	249.7	253.5	265.2	271.0	273.0	279.5	280.2	284.9	285.0	292.6	279.7
3029	2179	230.7	248.4	261.7	274.5	286.9	309.6	319.2	321.9	334.3	338.0	340.5	348.1	365.5	350.2
	MEAN	210.9	220.5	236.5	251.0	260.9	269.6	277.0	282.5	286.4	288.1	292.4	296.7	303.3	294.3
	±S.D.	±13.36	±14.17	±16.48	±17.37	±20.56	±22.05	±24.19	±22.59	±24.06	±24.85	±27.67	±27.90	±29.75	±20.56

BEST COPY AVAILABLE

Table A-2 (Continued)

EGMS: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual and Mean Body Weights (grams) of Exposed Females[a]

Exposure Level: 30 ppm

Animal Number	Pathology Number	Days on Study -1	5	12	19	27	33	40	47	54	62	68	75	82	88
80A-3036	80A-2180	118.1	203.6	219.6	231.8	237.3	242.1	251.7	253.3	247.8	249.1	261.2	270.6	264.5	266.6
3037	2181	186.5	195.0	209.0	224.7	232.6	238.0	244.2	251.1	249.5	251.3	255.9	266.3	259.4	257.6
3038	2182	197.6	211.2	226.9	229.9	237.5	248.4	256.2	249.9	259.6	260.6	260.9	265.0	268.7	266.9
3039	2183	216.0	243.1	262.8	275.5	284.3	293.1	307.0	313.2	315.5	325.4	324.3	327.8	330.3	330.2
3040	2184	211.1	218.7	234.6	245.5	256.4	247.3	273.5	280.4	—[b]	267.3	280.8	290.4	291.6	296.9
3041	2185	197.1	217.9	231.2	245.6	255.1	247.0	264.0	266.2	265.3	267.7	276.2	282.0	277.0	271.5
3042	2186	213.5	233.2	254.2	264.7	274.2	285.8	292.9	304.1	309.7	318.5	322.8	330.4	332.5	334.3
3043	2187	225.3	249.3	262.3	288.0	283.8	301.6	314.2	306.3	330.9	321.4	331.6	343.8	336.3	335.6
3044	2188	223.8	240.8	267.0	276.9	271.6	297.5	308.3	310.3	314.4	275.9	309.2	318.8	323.9	320.1
3045	2189	225.3	233.7	266.1	290.6	281.1	305.5	312.5	315.0	316.1	284.1	312.2	321.7	319.6	321.1
3046	2190	189.0	203.8	226.9	243.9	250.8	249.7	268.6	278.2	281.2	281.3	283.0	294.3	295.2	286.6
3047	2191	202.7	211.4	232.3	235.1	256.6	252.9	252.9	263.9	256.8	270.7	269.4	282.2	285.5	276.9
3048	2192	205.5	221.5	233.4	247.6	257.7	256.1	272.9	274.0	270.3	279.1	277.6	286.2	291.5	281.1
3049	2193	210.0	220.8	245.3	249.8	255.4	251.3	258.4	264.2	264.0	288.0	282.9	271.2	284.3	268.6
3050	2194	210.6	223.7	243.0	259.1	275.0	281.3	295.7	296.3	296.2	303.3	311.8	313.2	313.5	308.7
3051	2195	220.8	234.0	261.8	279.4	290.0	281.3	297.3	304.0	308.0	313.1	306.1	309.3	307.7	303.5
3052	2196	217.0	227.4	244.3	261.5	262.7	272.5	277.8	269.4	275.2	281.0	285.8	273.8	271.6	267.2
3053	2197	215.2	232.8	250.0	263.1	268.3	287.8	295.1	296.4	311.2	312.6	312.7	318.3	318.6	316.4
3054	2198	232.3	246.5	282.3	305.8	315.3	324.7	329.2	339.7	343.9	343.4	356.3	358.9	351.3	347.4
3055	2199	224.7	244.5	258.4	267.6	274.4	288.3	282.1	293.3	305.0	304.1	300.6	311.5	319.0	303.4
3056	2200	192.8	207.7	220.5	236.4	243.1	245.6	264.0	261.5	269.8	271.9	271.2	283.0	274.8	271.0
3057	2201	189.8	200.4	212.5	221.5	233.7	249.1	254.7	258.0	263.5	268.9	269.2	271.8	278.8	252.7
3058	2202	192.8	206.7	225.8	240.5	240.1	246.6	257.8	263.7	266.9	272.5	273.0	277.7	286.5	278.6
3059	2203	211.3	228.3	247.3	265.8	278.2	287.7	298.3	303.8	308.6	316.3	326.8	314.1	326.5	314.9
3060	2204	201.0	222.0	234.6	239.9	246.7	263.7	265.0	262.3	274.2	273.7	271.4	266.6	278.7	273.6
3061	2205	214.7	232.8	249.9	260.7	271.7	279.2	291.2	289.9	301.4	303.7	303.8	316.8	314.0	307.1
3062	2206	222.7	232.5	243.8	265.8	277.4	257.4	274.7	281.5	292.1	296.7	288.8	302.2	309.5	298.0
3063	2207	218.6	232.4	246.8	271.9	285.4	259.7	278.9	291.1	300.9	307.1	301.6	312.7	320.1	303.3
3064	2208	226.2	236.6	256.4	270.3	264.2	274.3	286.0	288.8	289.0	291.0	295.3	297.0	298.6	292.7
3065	2209	222.3	242.2	258.1	279.8	284.0	292.9	297.6	316.8	326.9	332.8	329.6	329.8	343.3	323.6
	MEAN	210.1	225.1	243.6	258.0	264.8	270.3	280.8	284.9	290.1	291.1	295.1	300.2	302.4	295.9
	±S.D.	±13.44	±14.94	±17.73	±20.95	±19.66	±22.81	±21.89	±23.19	±26.19	±24.65	±25.16	±25.32	±25.25	±25.87

Table A-2 (Continued)

EGHR: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual and Mean Body Weights (grams) of Exposed Females[a]

Exposure Level: 100 ppm

Animal Number	Pathology Number	Days on Study -1	5	12	19	27	33	40	47	54	62	68	75	82	88
80A-3071	80A-2210	198.9	212.5	232.7	252.1	257.4	260.8	265.1	267.0	271.0	278.4	272.5	282.5	279.3	269.4
3072	2211	195.7	220.0	235.6	244.4	247.7	253.0	258.8	259.3	267.0	260.0	264.6	269.1	274.3	268.6
3073	2212	198.6	213.2	229.4	238.2	249.5	253.3	260.3	264.4	257.0	260.8	259.7	271.9	270.7	265.8
3074	2213	205.9	220.5	237.7	244.5	263.7	273.9	278.7	286.7	295.7	299.7	304.0	304.5	311.3	311.7
3075	2214	217.7	228.7	257.7	262.9	284.9	289.8	292.8	297.5	318.7	316.0	310.4	328.6	327.5	332.8
3076	2215	206.6	227.4	246.3	254.7	276.8	291.8	294.8	291.8	312.2	315.3	322.3	330.9	324.5	317.4
3077	2216	212.2	219.6	236.7	254.5	251.4	269.6	281.0	282.1	288.7	290.3	303.4	307.1	307.6	310.8
3078	2217	203.9	211.9	230.8	246.4	243.0	251.5	265.1	263.6	278.1	278.2	286.2	276.5	285.3	279.2
3079	2218	214.6	230.9	256.2	263.1	271.2	270.1	272.7	298.3	286.6	296.6	295.1	301.6	301.7	292.1
3080	2219	221.9	233.2	255.1	271.7	279.6	282.3	293.4	282.3	303.0	303.6	281.0	317.0	323.4	320.8
3081	2220	185.2	208.4	224.0	237.9	249.4	258.8	259.7	263.3	271.8	267.9	281.9	289.6	292.1	282.3
3082	2221	196.9	216.9	237.9	248.1	258.2	255.6	271.2	276.0	285.9	284.8	321.2	289.4	294.8	285.6
3083	2222	184.3	202.4	215.2	221.9	236.4	238.6	257.0	245.0	256.2	259.9	255.6	250.6	258.2	255.0
3084	2223	194.6	229.0	255.0	262.7	283.2	289.9	297.8	300.6	314.4	312.7	321.8	322.5	331.9	327.5
3085	2224	205.8	220.2	234.0	241.3	251.3	266.8	269.2	270.8	275.3	280.2	286.7	279.6	284.0	284.7
3086	2225	200.7	206.3	223.1	222.0	242.6	246.2	253.1	261.7	265.9	277.5	280.2	282.3	272.4	268.0
3087	2226	209.8	224.0	233.4	250.9	251.6	264.5	268.1	271.6	272.4	268.5	275.1	277.1	275.6	275.5
3088	2227	221.3	239.0	250.7	272.4	275.3	287.0	290.9	296.5	304.5	307.3	310.5	310.0	309.4	301.8
3089	2228	229.9	242.9	249.4	270.7	294.5	310.9	320.2	332.4	345.9	341.5	351.5	359.9	371.7	361.1
3090	2229	224.3	244.6	257.2	270.3	278.5	292.7	302.8	307.4	323.6	321.1	325.0	336.3	342.4	333.5
	MEAN	206.4	222.6	239.9	251.5	262.3	270.4	277.6	280.9	289.7	291.0	295.4	299.3	301.9	297.2
	±S.D.	±12.60	±11.90	±12.76	±15.09	±16.83	±18.96	±18.30	±20.69	±24.40	±23.19	±25.37	±27.30	±28.73	±28.57

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Table A-2 (Continued)

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual and Mean Body Weights (grams) of Exposed Females[a]

Exposure Level: 300 ppm

Animal Number	Pathology Number	Days on Study -1	5	12	19	27	33	40	47	54	62	68	75	82	88
80A-3096	80A-2230	191.4	200.3	232.8	249.0	243.9	258.0	260.2	267.4	266.7	278.3	280.4	279.2	273.8	273.9
3097	2231	185.2	212.2	213.4	215.2	220.1	222.5	227.4	227.7	237.5	226.0	222.2	230.2	227.9	222.8
3090	2232	198.5	212.6	238.7	244.9	251.0	253.9	266.4	264.9	270.6	275.3	268.7	272.0	274.6	265.1
3099	2233	201.6	213.2	229.0	237.8	256.8	273.4	253.8	250.8	261.0	260.6	251.6	251.9	254.0	253.5
3100	2234	209.3	223.8	236.7	245.8	262.0	259.4	268.3	269.3	279.9	281.7	281.4	284.1	280.7	282.4
3101	2235	204.2	219.5	238.1	245.4	260.8	254.7	268.1	270.9	268.7	280.3	279.0	277.3	276.4	266.9
3102	2236	218.9	232.8	243.2	255.4	254.3	260.4	265.5	265.9	274.3	271.4	271.6	275.9	280.7	271.1
3103	2237	209.5	216.6	236.5	252.4	253.9	256.3	267.0	260.2	272.5	277.6	284.2	273.2	269.0	266.7
3104	2238	216.6	237.1	261.3	259.5	269.8	273.9	278.5	271.8	283.9	293.6	281.5	289.5	282.0	277.6
3105	2239	229.8	248.1	274.5	290.7	306.6	307.8	314.0	314.7	327.1	344.8	323.2	323.3	315.4	309.6
3106	2240	181.2	199.5	209.7	220.3	225.5	228.8	225.8	226.2	230.7	232.3	222.4	233.5	231.4	227.7
3107	2241	195.5	223.1	236.0	243.6	248.1	248.1	250.1	247.7	253.2	257.6	259.8	260.0	255.1	246.1
3108	2242	196.5	203.9	224.6	240.2	242.9	243.8	251.3	251.6	264.0	257.4	256.5	262.5	261.5	256.7
3109	2243	205.2	210.4	234.4	228.7	242.4	246.7	244.7	252.7	244.9	248.2	242.9	247.3	248.3	239.8
3110	2244	211.0	238.5	259.0	263.2	279.3	266.2	278.0	288.7	283.1	293.6	295.7	279.4	275.2	278.8
3111	2245	214.6	231.9	192.2	206.0	148.9#	DEAD	--	--	--	--	--	--	--	--
3112	2246	214.5	228.8	258.8	256.8	268.8	278.8	294.8	273.5	285.7	302.0	292.3	299.0	300.2	293.6
3113	2247	223.1	241.5	257.3	268.0	292.1	282.9	286.0	285.5	289.8	315.3	285.4	285.4	290.4	282.9
3114	2248	238.3	239.1	262.6	265.7	277.3	298.7	287.1	291.5	301.2	291.2	298.7	304.6	309.6	295.1
3115	2249	206.3	225.9	237.2	253.2	255.8	248.7	264.0	248.2	257.5	273.5	269.8	281.3	266.5	263.0
	MEAN	207.6	222.9	238.8	247.1	258.5	261.2	265.8	264.7	271.2	276.9	272.0	274.2	272.2	267.0
	±S.D.	±14.27	±14.25	±19.94	±19.53	±21.05	±21.37	±21.74	±21.56	±22.53	±27.87	±25.33	±23.20	±23.14	±22.49

[a]Female rats were exposed to 0, 30, 100, or 300 ppm EGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, animals were maintained in the laboratory for recovery.

[b]No data.

#Statistical outlier identified by sequential outlier test, Alpha=0.01; value not included in calculations.

Table A-3

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual Body Weights During Lactation of Unexposed Females Bred to Exposed Males[a]

Exposure Level: 0 ppm

Animal Number	Post-Partum Day 1	4	7	14	21
80A-3304	242[b]	255	268	298	294
3306	302	311	317	321	316
3310	269	292	309	323	286
3311	297	317	301	320	316
3313	290	303	328	343	311
3318	308	313	299	325	304
3320	282	290	323	332	307
3323	293	302	294	309	286
3325	309	313	312	321	300
3328	317	332	341	329	350
3330	290	308	304	315	294
3331	299	334	318	341	322
3334	314	342	330	341	317
3336	278	304	290	311	287
3338	285	296	313	335	295
3339	278	288	290	304	304
3342	322	357	342	354	325
3346	319	345	333	350	339
3347	277	287	303	311	311
3349	292	295	301	331	309
3352	277	298	292	305	283
3354	294	302	--[c]	361	343
3356	290	312	325	327	319
3357	304	324	330	290[e]	325
3360	289	308	319	348	318
3816	302	308	321	326	315
3819	306	322	--[d]	--[d]	318
3843	283	295	322	326	309
MEAN ±S.D.	293 ±17	309 ±21	313 ±18	326 ±17	311 ±17

Table A-3 (Continued)

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual Body Weights During Lactation of Unexposed Females Bred to Exposed Males[d]

Exposure Level: 30 ppm

Animal Number	Post-Partum Day 1	4	7	14	21
80A-3661	302	304	339	361	344
3663	278	303	300	319	331
3666	268	282	282	312	282
3667	311	317	326	353	319
3672	331	347	331	353	331
3674	306	324	321	326	301
3676	294	302	305	329	312
3677	274	289	296	313	280
3683	283	304	298	329	305
3686	310	321	316	367	351
3690	283	310	309	325	318
3692	328	310	312	345	322
3694	257	289	280	316	305
3695	—[c]	302	323	311	313
3698	344	361	357	359	355
3704	305	305	306	329	294
3705	299	316	332	352	310
3707	270	283	295	325	303
3710	267	289	305	330	310
3712	297	311	315	336	331
3713	303	306	320	330	329
3717	253	263	264	297	294
3720	255	287	278	310	305
3869	266	273	291	305	303
3880	270	278	291	316	303
3900	325	329	356	351	329
3902	293	310	340	325	299
3915	326	350	360	377	356
MEAN	293	306	312	332	316
±S.D.	±25	±23	±25	±20	±20

Table A-3 (Continued)

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual Body Weights During Lactation of Unexposed Females Bred to Exposed Males[a]

Exposure Level: 100 ppm

Animal Number	Post-Partum Day 1	4	7	14	21
80A-3722	263	278	280	304	292
3723	311	250	291	334	308
3726	296	303	320	335	314
3728	298	324	325	300	312
3731	288	303	294	306	289
3735	298	307	302	329	301
3737	--[c]	349	338	354	332
3739	284	308	314	324	334
3742	276	282	296	309	313
3745	273	284	272	290	294
3748	243	276	339	305	282
3750	329	340	338	366	323
3751	286	295	294	327	308
3754	255	268	271	311	297
3756	265	292	301	294	323
3757	305	335	340	354	323
3929	294	294	301	304	300
3934	305	308	332	345	311
3944	295	302	338	347	320
MEAN ±S.D.	287 ±21	300 ±25	305 ±28	323 ±23	309 ±15

[a]Male rats were exposed to 0, 30, 100, or 300 ppm EGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, animals were bred with unexposed females.

[b]Body weight in grams.

[c]Incorrect weight was recorded.

[d]Weights were inadvertantly not recorded on the correct days; data were excluded from the calculations of mean±S.D.

[e]Animal was out of food.

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Table A-4

SCOPE: INHALATION REPRODUCTION AND CONTINUANT-LETHAL STUDY IN RATS

Individual and Mean Litter Sizes of Unexposed Females Mated to Exposed Males[a]

Exposure Level: 0 ppm

Maternal Animal Number	Date of Delivery	Cohabitation to Parturition (Days)[b]	Born Dead	Number of Live Pups on Post-Partum Day 0	1	4[c]	7	14	21	Total Number of Dead Found Day 1-21
30A-3301[d]	—	—	—	—	—	—	—	—	—	—
3304	11/16/80	23	0[e]	12	12	12	8	8	8	0
3306	11/17/80	24	0	13	13	13	8	8	8	0
3308[d]	—	—	—	—	—	—	—	—	—	—
3310	11/16/80	23	0	14	13	13	8	8	8	1
3311	11/19/80	26	0	14	14	14	8	8	8	0
3313	11/15/80	23	0	15	15	15	8	8	8	0
3316[d]	—	—	—	—	—	—	—	—	—	—
3318	11/18/80	25	0	13	13	13	8	8	8	0
3320	11/23/80	30	0	11	11	11	8	8	8	0
3322[d]	—	—	—	—	—	—	—	—	—	—
3323	11/18/80	25	0	13	13	13	8	8	8	0
3325	11/21/80	28	1	13	13	13	8	8	8	0
3328	11/17/80	24	0	14	14	14	8	8	8	0
3330	11/17/80	24	0	14	14	14	8	8	7	1
3331	11/19/80	26	0	16	16	16	8	8	8	0
3334	11/19/80	26	0	13	13	13	8	8	8	0
3336	11/19/80	26	0	12	12	12	8	8	8	0
3338	11/16/80	23	0	13	13	13	8	8	8	0
3339	11/18/80	25	0	12	12	12	8	8	8	0
3342	11/18/80	25	0	20	20	20	8	8	8	0
3343[d]	—	—	—	—	—	—	—	—	—	—
3346	11/19/80	26	0	13	14	14	8	8	8	0
3347	11/17/80	24	2	10	10	10	8	8	8	0
3349[f]	11/21/80	28	0	3	13	13	8	8	8	0
3352	11/19/80	26	0	15	15	15	8	8	8	0
3354[f]	11/15/80	22	0	4	14	14	8	8	8	0
3356	11/17/80	24	1	13	13	13	8	8	8	0
3357	11/17/80	24	0	15	15	15	8	8	8	0
3360	11/16/80	23	0	15	15	15	8	8	8	0
3801[d]	—	—	—	—	—	—	—	—	—	—
3808[d]	—	—	—	—	—	—	—	—	—	—
3815	11/28/80	28	0	7	7	7	7	7	7	0
3819	11/28/80	28	1	14	13	14	8	8	8	0
3821[d]	—	—	—	—	—	—	—	—	—	—
3843[f]	11/23/80	23	0	10	13	13	8	8	8	0
	MEAN±S.D.	25±2	0.18±0.48	13±3	13±2	13±2	8±0.2	8±0.2	8±0.3	0.07±0.25

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Table A-4 (Continued)

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual and Mean Litter Sizes of Unexposed Females Mated to Exposed Males[a]

Exposure Level: 30 ppm

Maternal Animal Number	Date of Delivery	Cohabitation to Parturition (Days)[b]	Born Dead	Number of Live Pups on Post-Partum Day 0	1	4[c]	7	14	21	Total Number of Dead Found Day 1-21
30A-3561[f]	11/16/80	23	0	8	16	16	8	8	8	0
3563	11/19/80	26	0	14	14	14	8	8	8	0
3666[f]	11/17/80	24	0	7	16	16	7[g]	7	7	0
3667	11/21/80	28	0	15	15	15	8	8	8	0
3669[d]	—	—	—	—	—	—	—	—	—	—
3672[f]	11/18/80	25	0	7	15	15	8	8	8	0
3674[f]	11/18/80	25	0	5	14	14	8	8	8	0
3675	11/17/80	24	0	17	17	17	8	8	8	0
3677[f]	11/18/80	25	0	13	14	14	8	8	8	0
3680[d]	—	—	—	—	—	—	—	—	—	—
3682[d]	—	—	—	—	—	—	—	—	—	—
3683	11/19/80	25	0	9	9	9	8	8	8	0
3686[f]	11/15/80	23	0	18	19	19	8	8	8	0
3688[d]	—	—	—	—	—	—	—	—	—	—
3690	11/18/80	25	0	14	14	14	8	8	8	0
3692	11/21/80	28	0	15	15	15	8	8	8	0
3694	11/18/80	25	0	18	17	16	8	8	8	1
3695	11/16/80	23	0	14	14	14	8	8	8	0
3698[f]	11/19/80	25	0	11	12	12	8	8	8	0
3700[d]	—	—	—	—	—	—	—	—	—	—
3701[d]	—	—	—	—	—	—	—	—	—	—
3704	11/17/80	24	0	13	13	13	8	8	8	0
3705	11/16/80	23	0	15	15	15	8	8	8	0
3707	11/17/80	24	0	10	10	10	8	8	8	0
3710[f]	11/21/80	28	0	13	15	15	8	8	8	0
3712	11/17/80	24	0	15	15	15	8	8	8	0
3713	11/15/80	23	0	7	7	6	6	6	6	0
3716[d]	—	—	—	—	—	—	—	—	—	—
3717	11/15/80	22	0	12	12	12	8	8	8	0
3720[f]	11/17/80	24	0	12	17	17	8	8	8	0
3869[f]	11/24/80	24	0	5	13	13	8	8	8	0
3880	11/24/80	24	0	12	12	12	8	8	8	0
3881[d]	—	—	—	—	—	—	—	—	—	—
3887[d]	—	—	—	—	—	—	—	—	—	—
3900	11/24/80	24	0	12	12	12	8	8	8	0
3902	11/23/80	23	0	11	11	11	8	8	8	0
3915	11/25/80	25	0	17	17	16	8	8	8	0
	MEAN±S.D.	25±2	0±0	12±4	14±3	14±3	8±0.4	8±0.4	8±0.4	0.04±0.19

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Table A-3 (Continued)

ZONE: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual and Mean Litter Sizes of Unexposed Females Mated to Exposed Males[a]

Exposure Level: 100 ppm

Maternal Animal Number	Date of Delivery	Cohabitation to Parturition (Days)[b]	Born Dead	Number of Live Pups on Post-Partum Day 0	1	4[c]	7	14	21	Total Number of Dead Found Day 1-21
30A-3722	11/17/80	24	0	13	13	13	8	8	8	0
3723	11/19/80	26	0	10	10	10	8	8	8	0
3725	11/16/80	23	0	13	13	13	8	8	8	0
3728	11/17/80	24	0	18	18	18	8	8	8	0
3730[d]	—	—	—	—	—	—	—	—	—	—
3731[e]	11/19/80	26	0	12	14	14	8	8	8	0
3733[d]	—	—	—	—	—	—	—	—	—	—
3735	11/21/80	28	0	14	14	14	8	8	8	0
3737	11/18/80	25	0	14	15	15	8	8	8	0
3739[e]	11/18/80	25	0	4	8	8	8	8	8	0
3742	11/17/80	24	0	5	5	5	5	5	5	0
3744[d]	—	—	—	—	—	—	—	—	—	—
3745[e]	11/18/80	25	0	13	14	13	8	8	8	0
3748	11/18/80	25	1	14	14	14	8	8	8	0
3750	11/21/80	28	0	15	15	15	8	8	8	0
3751	11/21/80	28	0	14	14	14	8	8	8	0
3754	11/19/80	26	0	14	14	14	8	8	8	0
3756	11/17/80	24	1	13	13	13	8	8	8	0
3757	11/19/80	26	0	14	13	13	8	8	8	0
3760[d]	—	—	—	—	—	—	—	—	—	—
3929	11/24/80	24	0	16	16	15	8	8	7	0
3934	11/23/80	23	0	14	14	14	8	8	8	0
3944[e]	11/23/80	23	0	14	15	16	8	8	8	0
3959[d]	—	—	—	—	—	—	—	—	—	—
	MEAN±S.D.	25±2	0.11±0.32	13±3	13±3	13±3	8±0.7	8±0.7	8±0.7	0±0

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Table A-4 (Continued)

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual and Mean Litter Sizes of Unexposed Females Mated to Exposed Males[a]

Exposure Level: 300 ppm

Maternal Animal Number	Date of Delivery	Cohabitation to Parturition (Days)[b]	Born Dead	Number of Live Pups on Post-Partum Day 0	1	4	7	14	21	Total Number of Dead Found Day 1-21
801-3761[d]	—	—	—	—	—	—	—	—	—	—
3763[d]	—	—	—	—	—	—	—	—	—	—
3766[d]	—	—	—	—	—	—	—	—	—	—
3767[d]	—	—	—	—	—	—	—	—	—	—
3770[d]	—	—	—	—	—	—	—	—	—	—
3771[d]	—	—	—	—	—	—	—	—	—	—
3773[d]	—	—	—	—	—	—	—	—	—	—
3775[d]	—	—	—	—	—	—	—	—	—	—
3778[d]	—	—	—	—	—	—	—	—	—	—
3780[d]	—	—	—	—	—	—	—	—	—	—
3782[d]	—	—	—	—	—	—	—	—	—	—
3784[d]	—	—	—	—	—	—	—	—	—	—
3785[d]	—	—	—	—	—	—	—	—	—	—
3788[d]	—	—	—	—	—	—	—	—	—	—
3790[d]	—	—	—	—	—	—	—	—	—	—
3791[d]	—	—	—	—	—	—	—	—	—	—
3794[d]	—	—	—	—	—	—	—	—	—	—
3796[d]	—	—	—	—	—	—	—	—	—	—
3798[d]	—	—	—	—	—	—	—	—	—	—
3800[d]	—	—	—	—	—	—	—	—	—	—
3961[d]	—	—	—	—	—	—	—	—	—	—
3964[d]	—	—	—	—	—	—	—	—	—	—
3965[n]	—	—	—	—	—	—	—	—	—	—
3968[d]	—	—	—	—	—	—	—	—	—	—
3969[d]	—	—	—	—	—	—	—	—	—	—
3972[d]	—	—	—	—	—	—	—	—	—	—
3973[d]	—	—	—	—	—	—	—	—	—	—
3975[d]	—	—	—	—	—	—	—	—	—	—
3977[d]	—	—	—	—	—	—	—	—	—	—
3979[d]	—	—	—	—	—	—	—	—	—	—
3981[d]	—	—	—	—	—	—	—	—	—	—
3983[d]	—	—	—	—	—	—	—	—	—	—
3986[d]	—	—	—	—	—	—	—	—	—	—
3987[d]	—	—	—	—	—	—	—	—	—	—
3989[d]	—	—	—	—	—	—	—	—	—	—
3992[n]	—	—	—	—	—	—	—	—	—	—
3994[d]	—	—	—	—	—	—	—	—	—	—
3995[d]	—	—	—	—	—	—	—	—	—	—
3997[d]	—	—	—	—	—	—	—	—	—	—
3999[d]	—	—	—	—	—	—	—	—	—	—
MEAN±S.D.		—	—	—	—	—	—	—	—	—

were exposed to 0, 30, 100, or 300 ppm EGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. termination of the exposure period, animals were bred with unexposed females.

calculated from the first day of cohabitation to the date of delivery.

of lactation, all litters were culled to 8 pups, 4 males and 4 females, where possible. Data indicate number of live pups prior to culling.

did not deliver a litter.

pups.

of observation, female was still delivering pups.

died after culling.

was pregnant at time of necropsy, implantations present only after sodium sulfide stain.

Table A-5

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Average Pup Body Weights for Individual Litters of Unexposed Females Mated to Exposed Males[a]

Exposure Level: 0 ppm

Maternal Animal Number	Post-Partum Day 1	4[b]	7	14	21 Male	21 Female
80A-3304	6.3[c]	8.3	13.9	26.9	46.8	41.7
3306	7.2	11.3	19.3	36.0	59.5	53.3
3310	6.8	10.9	15.8	31.5	49.0	48.0
3311	7.2	10.3	16.6	30.6	47.5	50.3
3313	7.7	12.8	17.9	36.0	60.5	60.0
3318	8.2	10.8	17.8	34.0	58.5	58.8
3320	8.4	10.6	16.5	31.4	53.0	52.8
3323	7.4	11.1	17.0	32.4	56.5	52.5
3325	7.2	11.5	19.9	37.4	59.3	57.5
3328	7.5	11.9	19.4	39.6	66.8	59.8
3330	7.4	10.9	17.9	35.6	62.3	58.3
3331	7.6	10.5	17.1	34.5	52.5	52.8
3334	7.8	11.5	18.9	36.3	60.8	56.0
3336	7.8	11.3	18.8	34.0	55.0	52.3
3338	7.2	11.1	16.4	31.5	48.3	48.8
3339	8.3	11.8	18.9	37.3	60.3	60.3
3342	7.0	9.5	16.9	36.8	58.5	60.0
3346	8.0[e]	10.6	17.6	34.5	57.0	54.8
3347	7.6	11.8	17.6	34.4	57.3	53.3
3349	6.5	10.1	17.4	33.1	55.0	50.0
3352	7.0	9.8	17.5	36.8	57.3	53.0
3354	5.8	10.4	16.3	35.1	57.5	54.5
3356	7.3	11.3	19.1	40.0	63.0	57.8
3357	7.2	11.1	18.1	37.0	62.5	57.5
3360	7.5	10.4	18.4	38.8	63.3	58.5
3816	9.3	15.0	23.0	40.7	66.0	59.3
3819	7.4	10.8	—[d]	—[d]	58.0	55.3
3843	6.9	10.1	15.5	30.9	53.6	53.3
MEAN ±S.D.	7.39 ±0.69	10.98 ±1.61	17.76 ±1.71	34.93 ±3.23	57.34 ±5.28	54.66 ±4.40

Table A-5 (Continued)

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Average Pup Body Weight for Individual Litters of Unexposed Females Mated to Exposed Males[a]

Exposure Level: 30 ppm

Maternal Animal Number	Post-Partum Day 1	4b	7	14	21 Male	21 Female
80A-3661	6.9	9.8	14.4	29.6	50.3	48.5
3663	7.2	9.8	17.5	35.0	56.3	56.8
3666	5.9	8.1	13.7	30.3	43.0	44.8
3667	7.1	10.8	18.5	38.1	58.8	54.5
3672	6.2	9.0	15.8	33.8	51.0	53.0
3674	6.6	9.5	16.3	34.9	56.5	55.0
3676	7.0	10.6	17.6	37.9	58.5	54.0
3677	7.2	10.0	17.5	33.1	55.3	54.5
3683	8.4	12.8	18.9	36.5	59.3	55.5
3686	6.2	9.4	13.1	27.0	48.5	43.5
3690	7.4	10.9	19.0	37.9	62.0	57.3
3692	7.7	11.8	19.0	36.3	62.0	59.0
3694	6.1	8.1	14.4	31.3	54.0	51.0
3695	6.4	10.3	16.4	32.1	50.8	48.8
3698	7.8	10.3	18.6	35.5	58.8	56.3
3704	7.3	11.8	17.9	37.4	55.0	52.0
3705	6.5	10.1	15.5	31.5	51.8	48.3
3707	7.8	11.6	17.4	34.4	55.3	50.8
3710	6.7	9.5	16.0	33.1	55.8	52.3
3712	7.3	10.8	16.5	35.6	55.8	56.0
3713	7.9	13.7	18.5	31.0	52.3	48.3
3717	6.0	10.8	15.9	32.1	51.0	48.3
3720	6.8	9.4	14.9	32.0	53.3	52.0
3869	6.5	9.0	15.1	31.0	52.5	47.0
3880	8.3	12.5	20.0	38.0	63.8	58.3
3900	8.2	12.9	21.1	40.0	63.0	61.5
3902	7.2	11.3	18.8	37.3	55.3	56.0
3915	7.1	9.8	16.6	37.0	56.0	56.8
MEAN	7.06	10.51	16.96	34.28	55.21	52.86
±S.D.	±0.71	±1.41	±1.97	±3.18	±4.67	±4.46

Table A-5 (Continued)

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Average Pup Body Weight for Individual Litters of Unexposed Females Mated to Exposed Males[a]

Exposure Level: 100 ppm

Maternal Animal Number	Post-Partum Day 1	4[b]	7	14	21 Male	21 Female
80A-3722	7.5	11.5	17.6	34.4	56.3	54.0
3723	8.4	10.8	14.9	33.8	60.0	54.0
3726	7.7	12.6	19.9	38.4	61.0	58.8
3728	6.3	9.9	16.5	35.0	57.5	55.8
3731	7.1	10.3	16.8	32.3	52.5	52.3
3735	6.3	10.0	16.6	32.5	47.8	51.0
3737	6.5	8.9	15.3	33.1	54.5	53.0
3739	8.3	11.8	17.5	34.4	58.3	53.0
3742	8.8	14.0	21.0	40.2	66.0	63.3
3745	6.9	10.4	17.1	33.3	56.0	51.7
3748	7.6	10.4	17.4	34.9	61.5	57.3
3750	7.3	11.0	18.0	36.3	62.8	60.3
3751	7.4	10.1	17.1	32.8	56.5	53.3
3754	7.4	9.9	16.8	34.3	59.0	53.3
3756	7.1	10.5	17.5	36.4	59.8	57.8
3757	8.2	12.6	21.4	42.8	70.8	63.5
3929	5.6	7.6	13.0	26.6	43.0	40.5
3934	6.6	10.3	17.0	36.1	57.0	54.8
3944	6.6	10.1	16.1	33.3	58.5	52.8
MEAN ±S.D.	7.24 ±0.83	10.67 ±1.41	17.24 ±1.96	34.78 ±3.37	57.83 ±6.06	54.76 ±5.06

[a]Male rats were exposed to 0, 30, 100, or 300 ppm EGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, animals were bred with unexposed females.

[b]On day 4 of lactation, all litters were culled to 8 pups, 4 males and 4 females, where possible. Data presented indicate average body weight of live pups after culling.

[c]Average body weight of litter in grams.

[d]Weights were inadvertently not recorded on the correct days; data were excluded from the calculations of mean±S.D.

[e]Pups were miscounted on Day 1; value was excluded from calculation.

Table A-6

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual Body Weights During Lactation of Exposed Females[a]

Exposure Level: 0 ppm

Animal Number	Post-Partum Day 1	4	7	14	21
80A-3000	296[b]	311	304	320	304
3001	310	331	329	350	332
3002	295	302	324	320	304
3003	288	309	308	332	309
3004	299	315	317	336	315
3005	309	323	343	342	330
3006	316	349	365	368	339
3009	328	324	352	381	346
3010	263	298	316	336	327
3011	291	322	324	317	304
3012	310	318	329	350	325
3013	318	316	334	334	335
3014	319	334	322	348	328
3015	293	307	315	323	310
3016	—[e]	341	352	361	347
3017	337	349	363	372	362
3019	385	399	395	396	388
3020	335	337	357	368	331
3021	353	378	—[c]	396	356
3023	289	311	354	346	344
3024	292	299	316	336	303
3025	325	339	335	342	314
3026	330	342	362	363	351
3027	301	318	349	384	355
3028	328	346	350	369	351
3029	377	388	386	398	373
MEAN ±S.D.	315 ±28	331 ±26	340 ±24	353 ±25	334 ±23

Table A-6 (Continued)

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual Body Weights During Lactation of Exposed Females[a]

Exposure Level: 30 ppm

Animal Number	Post-Partum Day 1	4	7	14	21
80A-3036	287	296	321	320	305
3037	279	286	294	303	300
3038	306	314	322	347	316
3041	313	322	339	365	337
3043	345	368	371	389	374
3044	337	345	361	369	354
3045	320	320	344	355	345
3047	293	265	284	313	322
3049	285	300	312	328	313
3050	310	311	321	332	320
3051	312	317	346	368	335
3052	320	341	338	363	330
3053	338	355	356	370	352
3057	304	322	321	338	330
3058	309	326	318	324	333
3059	325	351	347	380	362
3060	310	315	344	311	322
3061	305	333	354	373	353
3062	317	305	—[d]	—[d]	—[d]
3063	344	372	376	400	345
3064	304	315	330	366	333
3065	—[e]	376	384	378	345
MEAN ±S.D.	313 ±18	325 ±28	337 ±26	352 ±28	335 ±19

INTRODUCTION

Ethylene glycol monomethyl ether (2-methoxyethanol, EGME) is a volatile, nearly odorless liquid with the following properties:

Structural Formula:	$H_3C-O-CH_2CH_2-OH$
Molecular Weight:	76.09
Boiling Point:	124.6°C @ 760 mmHg
Vapor Pressure:	9.5 mmHg @ 25°C
Solubility:	Miscible with water
Flash Point:	107°F

EGME has been used extensively for many years as an industrial solvent for resins, lacquers, paints, dyes, and inks, and as a detergent.

The toxicologic information concerning EGME has recently been reviewed (Rowe and Wolf, 1982). The oral toxicity of EGME is low, with an LD_{50} of 3.5 g/kg in rats, 0.89 g/kg in rabbits and 0.95 g/kg in guinea pigs. EGME is absorbed in toxic amounts through the skin; the rabbit dermal LD_{50} is 2.0 g/kg. Moderate pain and conjunctivitis result after direct application to the eyes of rabbits, but these effects are reversible within 24 hours of application.

Inhalation exposure for 7 hours/day, 5 days/week for 5 weeks of rats to 310 ppm and dogs to 750 ppm for 12 weeks resulted in several erythrocytic changes including hypochromia, reduced hemoglobin concentration and decreased packed cell volume.

Short term inhalation studies were recently completed, by Miller, et al. (1980 a&b) in the Dow Toxicology Research Laboratory in which rats, mice and rabbits were exposed to 0, 100, 300 or 1000 ppm for 9 days during an 11-day interval. The highest level was lethal to rabbits. Histopathologic changes in rats, mice and rabbits exposed to 1000 ppm included moderately reduced bone marrow cellularity which was supported by hematologic abnormalities and degeneration of the testicular germinal epithelium. Similar but less pronounced changes were noted in some animals in the 300 ppm group. No adverse effects were attributed to exposure to 100 ppm.

Following completion of the probe studies, subchronic toxicity studies in rats and rabbits, and reproduction and dominant lethal mutagenicity studies in rats were initiated. Animals in these studies were exposed to 0, 30, 100 or 300 ppm for 6 hours/day, 5 days/week, for 13 weeks.

Interim results from these studies suggest that exposure of rats and rabbits to 300 ppm for 13 weeks results in hematologic abnormalities, decreased testicular and thymus weights, and histopathologic changes in testes. At 100 ppm, histopathologic changes of the testes were found in some rabbits. Slight effects were detected histopathologically in the testes of 1 of 5 rabbits in the 30 ppm group. Infertility was seen in male rats at the 300 ppm level but not at 100 or 30 ppm. No adverse reproductive effect was seen among any of the groups of exposed females. There was no evidence of a dominant lethal mutagenic effect at 30 or 100 ppm; however, the absence of litters at 300 ppm precluded evaluation for dominant lethality at that level.

A teratology study was recently reported by Nagano et al. (1981). ICR mice were administered EGME by gavage on days 7 through 14 of gestation, at dose levels of 0, 31.25, 62.5, 125, 250, 500 or 1000 mg/kg. Maternal toxicity, reflected in marked leucopenia, was observed at the highest dose level. A significant increase in fetal deaths was observed at dose levels of 250 mg/kg and above, and teratogenic effects were observed at dose levels of 62.5 mg/kg and above. The lowest dose level (31.25 mg/kg) resulted in delayed skeletal ossification, indicative of fetotoxicity.

Prior to the publication of data by Nagano et al., (1981), studies to assess the embryotoxic and teratogenic potential of EGME in rats and rabbits via inhalation (the most probable route of human exposure) were proposed. The purpose of this study was to determine the maximum tolerated exposure level for a definitive inhalation teratology study in pregnant rats and rabbits, sponsored by the Chemical Manufacturer's Association.

MATERIALS AND METHODS

Test Material: Ethylene glycol monomethyl ether for use in this study was obtained from The Dow Chemical Company, Michigan Division, Midland, MI and was identified as Lot No. NM 810624. Analysis prior to initiation of the study indicated 99.96% purity.[1]

Test Animals: Stock supplies of male and female Fischer 344 rats (Charles River Breeding Laboratories, Inc., Portage, Michigan) and New Zealand white rabbits (Langshaw Rabbitry, Augusta, Michigan) were obtained. Animals were housed individually in wire-bottomed cages in rooms designed to control temperature at approximately 22°C, relative humidity at approximately 50% and a photocycle of 12 hours light and dark. Animals were acclimated to the laboratory for at

[1]Analysis performed by P. Kastl, Toxicology Research Laboratory, The Dow Chemical Company, Midland, Michigan 15 July 1981.

least two weeks (rats) or three weeks (rabbits) prior to breeding. Adult virgin female Fischer 344 rats (approximately 175-220 g at breeding) were bred to adult males (one female to one male) from the same strain. The day sperm were found in vaginal smears was considered day 0 of gestation. Rabbits (approximately 3.5 - 4.5 kg) were artificially inseminated (Gibson, et al., 1966) with this day considered day zero of gestation.

Randomization of test animals, grouped according to their day zero of gestation, was performed using computer-generated tables of random numbers. All animals were uniquely identified by metal ear tags. Food (Certified Laboratory Animal Chow, Ralston Purina Company, St. Louis, Missouri) and municipal tap water were available ad libitum except during actual inhalation exposure periods.

Experimental Design: Groups of 10 bred female rats and 7 inseminated female rabbits were exposed for 6 hours per day via inhalation to vapor concentrations of 0, 50, 200 or 400 ppm of EGME. Rats were exposed on days 6 through 15 of gestation; rabbits were exposed on days 6 through 18 of gestation. Exposures began on July 16, 1981 and terminated on July 30, 1981. All animals were observed daily for signs of toxicity. Body weights of rats were recorded on days 6,

8, 10 and 16 of gestation; body weights of rabbits were recorded on days 6, 9, 12, 15 and 19 of gestation. Food and water consumptions for rats were recorded at 3-day intervals beginning on day 6 of gestation. Animals were sacrificed by decapitation following methoxyflurane anesthesia (rats on day 16 of gestation) or CO_2 anesthesia (rabbits on day 19 of gestation) and examined for gross pathologic changes by a veterinary pathologist. Maternal body weights, liver, kidney, spleen and thymus weights, as well as the number of corpora lutea, and the number of live and resorbed fetuses were recorded at the time of necropsy. The uteri of apparently non-pregnant animals were stained with a 10% solution of sodium sulfide (Kopf, et al., 1964) and examined for evidence of early resorption sites. Sections of liver, kidney, spleen, thymus, mesenteric lymph nodes and bone (including marrow) were preserved in neutral phosphate buffered 10% formalin for possible histologic examination. All animals found dead during the course of exposure were also subjected to a complete gross necropsy and sections of previously identified tissues were preserved.

Exposure Conditions: Exposures were conducted in 4.1 m^3 inhalation chambers. Temperature and relative humidity in the chambers were controlled by a system designed to maintain temperature at approximately 21°C and relative humidity

at approximately 50%. Temperature and relative humidity in the exposure chambers were recorded during each exposure day.

Vapors were generated by metering the liquid test substance at calculated rates into glass vaporization tubes (Miller, et al., 1980c). Vapors from the tubes were swept into the chamber inlet ducts with compressed air where there was further mixing and dilution with incoming air by turbulence. The compressed air was preheated to the minimum extent required for complete vaporization using a compressed air flameless heat torch (Master, Model FHT-4). Total chamber airflow was maintained at approximately 800 liters per minute. The nominal concentration (ratio of the amount of EGME vaporized to the total amount of air through the chamber) was calculated for each chamber on a daily basis. The actual concentration of EGME in each exposure chamber was measured 1-2 times per hour by infrared spectroscopy using a Miran 1A infrared gas analyzer at a wavelength of 8.8 μ.

Standards were prepared by injecting calculated amounts of EGME into 100 liter SARAN* bags filled with a measured volume of filtered compressed air. These standards were passed through the IR to produce a series of responses at various concentrations, i.e. a standard curve. The

*Trademark of The Dow Chemical Company.

concentration of EGME in the exposure chambers were determined by interpolation from the standard curve. Standard curves were run prior to the first exposure and at least weekly thereafter. A standard was run prior to each exposure as a calibration check of the analytical system.

Statistical Evaluation: Statistical evaluation of the frequency of resorptions among litters and the fetal population was made by the Wilcoxon test as modified by Haseman and Hoel (1974). Analysis of the percentage of pregnancy and other incidence data was made by the Fisher exact probability test (Siegel, 1956). Analysis of other data was done by parametric or non-parametric analysis of variance followed by either Dunnett's test (Steel and Torrie, 1960) or distribution free multiple comparisons (Hollander and Wolfe, 1973) as appropriate. The reported level of statistical significance is $p \leq 0.05$. For food and water consumption data, statistical outliers were identified by a sequential outlier test $p \leq 0.02$ (Grubbs, 1969), and excluded from consideration.

RESULTS

Exposure Conditions: A summary of chamber conditions and vapor concentrations are presented in TABLE 1. Mean daily analytical time weighted averages (TWA) for exposures were within 2.0% of intended target concentrations, and were in good agreement with calculated daily nominal concentrations. Relative humidity values within the chambers were somewhat higher than normally encountered, due to warm, moist atmospheric conditions. However, daily relative humidity values were similar in each exposure chamber.

Rats: Pregnant rats exposed to 400 ppm of EGME gained significantly less weight on days 6 through 7 and 10 through 15 of gestation when compared to controls (TABLE 2). Rats exposed to 200 ppm gained significantly less weight than controls on days 6 through 7 of gestation. The overall body weight gain during gestation (days 6 through 15) of maternal animals was significantly reduced among rats exposed to 200 and 400 ppm of EGME. At necropsy on day 16 of gestation, significant decreases in the absolute weights of the liver, kidneys, spleen and thymus, and the organ-to-body weight ratios for liver, spleen and thymus were observed among rats exposed to 400 ppm of EGME (TABLE 2). Changes in liver and kidney weights were considered a reflection of the decrease

in body weight gain rather than a direct toxic effect of the material. Among rats exposed to 200 ppm, the relative spleen weight was statistically significantly lower than the control value. Food consumption of rats exposed to 400 ppm was significantly decreased throughout the period of exposure compared to control rats (TABLE 3). Among rats exposed to 200 ppm, food consumption was significantly lower than among controls on day 6 through 8 of gestation. Exposure to EGME had no effect on water consumption when compared to controls.

The results of gross necropsy examination of rats are presented in TABLE 4. Rats exposed to 400 ppm of EGME exhibited decreased thymic size and occassional facial soiling with porphyrin pigment. Among rats exposed to 50 and 200 ppm, one animal at each level exhibited decreased thymic size. Changes observed at necropsy among rats exposed to 50 ppm were not conclusive of treatment-related effects. Histologic examination of tissues was not considered necessary.

A summary of the reproductive parameters observed among rats at necropsy are presented in TABLE 5. The pregnancy rate of rats exposed to 200 ppm was significantly lower than the control value, however, this difference is attributable to random variation and is not considered treatment-related.

Examination of the uterine contents revealed total resorption of all litters among rats exposed to 200 or 400 ppm, indicating a high degree of embryolethality. There were no effects on reproductive parameters observed among rats exposed to 50 ppm of EGME.

Rabbits: Maternal toxicity was observed among rabbits exposed to 200 or 400 ppm of EGME on days 6 through 18 of gestation. During the period of exposure, 2 of 7 animals exposed to 400 ppm of EGME exhibited blood beneath their cages suggestive of abortion which was confirmed at necropsy. In addition, one rabbit exposed to 200 ppm exhibited blood beneath its cage. Maternal body weight gain was statistically significantly decreased on days 6 through 14, measured at 3-day intervals, among rabbits exposed to 400 ppm of EGME, and on days 6 through 8 and 12 through 14 among rabbits exposed to 200 ppm (TABLE 6). Overall maternal body weight gain (days 6 through 18 of gestation) was significantly reduced among rabbits exposed to 400 ppm, and there was a trend toward lower overall weight gain among rabbits exposed to 200 ppm when compared to controls. Marked decreases in the absolute and relative weights of the liver, kidneys and thymus were observed among rabbits exposed to 200 or 400 ppm (TABLE 6). However, due to the small group sizes, statistically significant decreases were

observed only in absolute and relative spleen weights (at 400 ppm) and thymus weights (at 200 ppm). Changes in the weights of the liver and kidneys were considered secondary to the decreases in body weight that were observed.

The results of gross necropsy examination of sacrificed rabbits are presented in TABLE 7. Rabbits exposed to 400 ppm of EGME exhibited decreased abdominal adipose tissue and ingesta, distended gall bladders, small-pale livers, decreased thymic size, dark urine and pale bone marrow. Similar changes were observed at a lower frequency among rabbits exposed to 200 ppm of EGME. No conclusive treatment-related gross changes were observed among rabbits exposed to 50 ppm. There were three deaths recorded among rabbits during the course of exposure. Gross necropsy observations for these animals are presented in TABLE 8. The single death which occurred among rabbits exposed to 50 ppm was attributed to an acute bronchopneumonia. Two deaths occurred among rabbits exposed to 400 ppm. The exact cause of death was not determined in either case but changes observed at necropsy in these animals were similar to those observed in sacrificed rabbits exposed to 400 ppm, suggesting that EGME may be reponsible for the deaths, or at least contributory. Histologic examination of tissue section was not considered necessary.

A summary of the reproductive parameters observed among rabbits at necropsy is presented in TABLE 9. As was observed in rats, exposure to 200 or 400 ppm resulted in complete resorption of all litters among pregnant rabbits, indicating embryolethality. Among pregnant rabbits exposed to 50 ppm, there was a marked decrease in the mean litter size. Marked increases in the number of resorptions per litter and the number of resorptions among litters with resorptions were also observed, however, these indices were not statistically evaluated. An increase in the percent of implantations resorbed was observed at 50 ppm, but the percent of litters with resoptions was not affected. The differences observed in the repoductive parameters among rabbits exposed to 50 ppm were considered suggestive of an embryolethal effect.

CONCLUSION

Based on the results of this probe study, exposure levels of 200 and 400 ppm of EGME for 6 hours per day during the period of major organogenesis were considered maternally toxic and embryolethal (complete resorption of all litters) in both rats and rabbits. An exposure level of 50 ppm was tolerated by pregnant rats; however, exposure of pregnant

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rabbits to 50 ppm of EGME resulted in an increase in the number of resorbed fetuses. Taking into account the apparent increased sensitivity of pregnant rabbits to EGME when compared to pregnant rats, exposure levels of 0, 3, 10 and 50 ppm were selected for the definitive teratology study in rats and rabbits.

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*Trademark of The Dow Chemical Company.

TITLE OF STUDY: ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY PROBE STUDY IN RATS AND RABBITS

In compliance with Good Laboratory Practice Regulations, this study was inspected by the Quality Assurance Unit and the results of these inspections reported to Management and the Study Director on the dates listed below. The report accurately reflects the data generated in accordance with the regulations and standard operating procedures of the Laboratory. All data and the reports are located at the submitting laboratory.

Study Started:	16 July 1981	Report Issued Date:	29 Jan 1982
Dates of Inspection:	16 July 1981	Date of Report:	16 July 1981
	21 July 1981		21 July 1981
	27 Jan 1982		28 Jan 1982

W. E. Hoover 29 January 1982

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TABLE 1

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY PROBE STUDY IN RATS AND RABBITS

Chamber Concentration, Temperature and Relative Humidity

Desired Conc. (ppm)	0	50	200	400
Number of Exposure Days	15	15	15	15
Analytical Concentration[a], ppm	-	50±0	200±2	401±3
Analytical Coefficient of Variation[b]	-	0.0	1.0	0.7
Range of Daily Analytical Concentration[c], ppm	-	50-51	196-203	394-405
Nominal Concentration, ppm	-	50±1	193±4	378±5
Nominal/Analytical Conc.	-	1.00	0.97	0.94
Daily Temperature, °C				
Minimum $\bar{X}$±S.D.[d]	23±1	22±1	22±1	23±1
Maximum $\bar{X}$±S.D.[d]	23±1	24±1	23±1	24±1
Daily Relative Humidity, % $\bar{X}$±S.D.[d]	62±4	59±8	63±8	64±8

[a]Data represents Mean ± Standard Deviation of daily time weighted average (TWA).

[b]Analytical $\frac{\text{Standard Deviation}}{\text{Mean}} \times 100$

[c]Data represents range of daily analytical TWA

[d]$\bar{X}$±S.D. = Mean ± Standard Deviation

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TABLE 3

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY PROBE STUDY IN RATS AND RABBITS

Food and Water Consumption of Pregnant Rats[a]

		Ethylene Glycol Monomethyl Ether, PPM			
Exposure Level		0	50	200	400
Number of Dams		10	10	6	8
Food Consumption on Gestation Days[b]	6-8	15±1	15±1	13±1*	10±1*
	9-11	15±1	15±1	14±0.3	12±1*
	12-14	15±1	16±1	16±2	13±2*
Water Consumption on Gestation Days[b]	6-8	22±4	21±8	20±3	16±3
	9-11	26±6	24±20	25±3	22±9
	12-14	30±9	25±5	30±8	32±6

[a]Bred Fischer 344 rats were exposed to 0, 50, 200 or 400 ppm of EGME for 6 hr/day on days 6 through 15 of gestation and necropsied on day 16 of gestation.

[b]Grams/rat/day, mean±S.D.

*Significantly different from the control value, $p<0.05$ by Dunnett's test.

TABLE 2

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY PROBE STUDY IN RATS AND RABBITS

Body and Organ Weights of Pregnant Rats[a]

Exposure level		Ethylene Glycol Monomethyl Ether, PPM 0	50	200	400
Number of dams		10	10	6	8
Maternal Body Weight(g) on Gestation Day[b]	6	206±4	206±10	215±6	212±7
	8	209±4	207±9	213±8	206±7
	10	215±4	213±8	218±8	209±8
	16	235±6	229±8	230±12	216±10*
Maternal Body Weight Gain(g) on Gestation Days[b]	6-7	2±2	1±1	-2±3*	-7±4*
	8-9	6±3	5±2	5±2	3±4
	10-15	21±3	17±10	13±6	7±7*
Total	6-15	29±5	23±11	15±8*	4±8*
Maternal Organ Weights on Gestation Day 16					
Liver - Absolute[b]		8.90±0.50	8.27±0.82	8.32±0.77	7.48±0.63*
- Relative[c]		3.78±0.16	3.60±0.28	3.61±0.17	3.46±0.17*
Kidney - Absolute		1.56±0.06	1.55±0.07	1.54±0.09	1.42±0.05*
- Relative		0.66±0.03	0.68±0.04	0.67±0.01	0.66±0.04
Spleen - Absolute		0.63±0.04	0.63±0.06	0.54±0.08	0.50±0.11*
Relative		0.27±0.02	0.27±0.03	0.23±0.02*	0.23±0.06*
Thymus - Absolute		0.23±0.06	0.19±0.04	0.22±0.05	0.15±0.02*
Relative		0.10±0.03	0.08±0.02	0.09±0.02	0.07±0.01*

[a]Bred Fischer 344 rats were exposed to 0, 50, 200 or 400 ppm of EGME for 6 hr/day on days 6 through 15 of gestation and necropsied on day 16 of gestation.

[b]Mean ±S.D., grams.

[c]Grams organ weight/100 grams body weight, mean ±S.D.

*Significantly different from the control value, $p \leq 0.05$, by Dunnett's test.

TABLE 5

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY PROBE STUDY IN RATS AND RABBITS

Observations Made at Necropsy on Day 16 of Gestation of Rats[a]

	Ethylene Glycol Monomethyl Ether, PPM			
Exposure Level	0	50	200	400
Number of Bred Females	10	10	10	10
Number of Maternal Deaths	0	0	0	0
Percent Pregnant[b]	100(10/10)	100(10/10)	60(6/10)*	80(8/10)
Pregnancies Detected by Sodium Sulfide Stain[c]	-	-	0/4	0/2
Number of Litters	10	10	6	8
Corpora Lutea/Dam[d]	11±1	11±1	-[e]	-[e]
Implantation Sites/Dam[d]	11±1	9±3	10±3	10±3
% Pre-implantation loss[f]	8±6	16±13	-[e]	-[e]
Fetuses/Litter[d]	9±2	8±4	0±0*	0±0*
Resorptions/Litter[d]	1.20±0.79	0.80±1.14	10.00±2.68	10.13±3.04
% Implantations Resorbed	11(12/106)	9(8/87)	100(60/60)*	100(81/81)*
% Litters with Resorptions	80(8/10)	40(4/10)	100(6/6)*	100(8/8)*
Litters totally resorbed	0	1	6	8
Resorptions/Litters with Resorptions	1.5(12/8)	2.0(8/4)	10.0(60/6)	10.1(81/8)

[a]Bred Fischer 344 rats were exposed to 0, 50, 200 or 400 ppm of EGME for 6 hr/day on days 6 through 15 of gestation and necropsied on day 16 of gestation.

[b]Number of females with visible implantation sites at the time of necropsy/total number of bred females.

[c]Number of females with implantation sites detected only after staining the uterus with sodium sulfide/total number stained.

[d]Mean ± S.D.

[e]Corpora lutea not recorded on litters totally resorbed. All litters at this level were totally resorbed.

[f]Percent per litter, mean ± S.D.

*Significantly different from the control value, $p \leq 0.05$, by the appropriate statistical test.

TABLE 4

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY PROBE STUDY IN RATS AND RABBITS

GROSS PATHOLOGIC OBSERVATIONS - RATS[a]

SEX		FEMALES			
EXPOSURE CONCENTRATION IN PPM		0	50	200	400
NUMBER OF RATS EXAMINED		10	10	10	10
LIVER					
NO LESIONS RECOGNIZED.		10	10	9	9
HIATAL HERNIA:		0	0	1	1
OVARY					
NO LESIONS RECOGNIZED.		9	10	9	9
CYST - CLEAR, UNILATERAL:		1	0	1	1
UTERUS					
NO LESIONS RECOGNIZED.		0	0	0	0
DISTENDED - WITH CLEAR FLUID:		0	0	1	0
NONPREGNANT:		0	0	4	2
PREGNANT-ALL FETUS(ES) APPEAR NORMAL:		2	6	0	0
PREGNANT-NORMAL APPEARING FETUS(ES) WITH RESORPTIONS AND/OR DEAD FETUS(ES):		8	3	0	0
PREGNANT-ALL FETUS(ES) APPARENTLY RESORBED:		0	1	6	8
LUNGS					
NO LESIONS RECOGNIZED.		6	7	5	7
FOCUS - DARK, LEFT LOBE:		1	0	0	0
FOCUS - DARK, RIGHT CARDIAC LOBE:		1	0	0	0
FOCUS - DARK, RIGHT DIAPHRAGMATIC LOBE:		0	1	0	0
FOCUS-GRAY, MULTIFOCAL:	- SLIGHT	1	1	1	3
FOCUS-GRAY, MULTIFOCAL:	- MODERATE	0	0	1	0
FOCUS-GRAY, MULTIFOCAL:	- SEVERE	2	0	0	0
HEMORRHAGE - TERMINAL:		0	1	3	0
THYMUS					
NO LESIONS RECOGNIZED.		10	9	9	0
DECREASED SIZE:		0	1	1	10
MAMMARY GLAND					
NO LESIONS RECOGNIZED.		0	1	4	4
INCREASED SIZE:		10	9	6	6
ABDOMINAL CAVITY					
NO LESIONS RECOGNIZED.		10	10	9	10
FAT - STRANGULATED PORTION:		0	0	1	0
EXTERNAL AND SKIN					
NO LESIONS RECOGNIZED.		10	10	10	8
FACIAL SOILING - PORPHYRIN:		0	0	0	2

[a]Bred Fischer 344 rats were exposed to 0, 50, 200 or 400 ppm of EGME for 6 hr/day on days 6 through 15 of gestation and necropsied on day 16 of gestation.

Data listed as the number of animals with the specific observation.
Only positive entries are presented.

TABLE 7

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY PROBE STUDY IN RATS AND RABBITS

GROSS PATHOLOGIC OBSERVATIONS - SACRIFICED RABBITS

SEX		FEMALES			
EXPOSURE CONCENTRATION IN PPM		0	50	200	400
NUMBER OF RABBITS EXAMINED		7	6	7	5
LIVER					
NO LESIONS RECOGNIZED.		2	4	2	0
DECREASED SIZE:		0	0	0	2
INCREASED SIZE:		0	1	0	0
MOTTLED:		4	0	0	1
PALE:	- SLIGHT TO MODERATE	5	1	4	3
PALE:	- SEVERE	0	0	1	2
GALLBLADDER					
NO LESIONS RECOGNIZED.		7	6	5	2
DISTENDED:		0	0	2	3
SPLEEN					
NO LESIONS RECOGNIZED.		6	6	7	5
FAT - STRANGULATED PORTION, CAPSULE:		1	0	0	0
BONE					
NO LESIONS RECOGNIZED.		7	6	6	3
PALE, BONE MARROW:		0	0	1	2
KIDNEY					
NO LESIONS RECOGNIZED.		3	3	7	4
CALCULUS(I), PELVIS, UNILATERAL:		1	0	0	0
MINERALIZATION, CORTEX, MULTIFOCAL:	- SLIGHT	0	1	0	0
MINERALIZATION, CORTEX, LEFT, MULTIFOCAL:	- MODERATE	1	0	0	0
CYST - CLEAR, CORTEX, BILATERAL, MULTIFOCAL:		0	0	0	1
CYST - DARK, CORTEX, BILATERAL, MULTIFOCAL:		0	0	0	1
CALCULUS(I) SAND-LIKE, PELVIS:		0	1	0	0
ROUGHENED SURFACE:		0	1	0	0
MOTTLED - SECONDARY TO ANESTHESIA:		3	1	0	0
STOMACH					
NO LESIONS RECOGNIZED.		7	6	6	5
HAIRBALL:		0	0	1	0
SMALL INTESTINE					
NO LESIONS RECOGNIZED.		7	6	5	3
DECREASED INGESTA:		0	0	2	2
CECUM					
NO LESIONS RECOGNIZED.		7	6	5	4
WATERY INGESTA:		0	0	2	1
URINARY BLADDER					
NO LESIONS RECOGNIZED.		7	6	7	3
DISTENDED:		0	0	0	1
URINE - BLOODY:		0	0	0	1
URINE - DARK:		0	0	0	1
OVARY					
NO LESIONS RECOGNIZED.		7	5	7	5
CYST - CLEAR, UNILATERAL, MULTIFOCAL:		0	1	0	0

TABLE 6

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY PROBE STUDY IN RATS AND RABBITS

Body and Organ Weights of Pregnant Rabbits[a]

		Ethylene Glycol Monomethyl Ether, PPM			
Exposure Level		0	50	200	400
Number of dams		5	5	5	3
Maternal Body Weight(g) on Gestation Day[b]	6	3998±237	3960±199	3784±243	3987±77
	9	3977±194	3863±334	3582±292	3692±201
	12	3986±254	4146±360	3482±259*	3471±179
	15	4048±299	3868±379	3411±232*	3264±179*
	19	3857±234	3855±419	3391±223	3138±153*
Maternal Body Weight Gain(g) on Gestation Days[b]	6-8	-21±57	-98±142	-202±63*	-294±124*
	9-11	8±94	283±40*	-100±71	-222±23*
	12-14	63±71	-277±65*	-71±90*	-207±19*
	15-18	-191±94	-14±72*	-20±144	-126±88
Total	6-18	-141±104	-105±235	-393±277	-849±97*
Maternal Organ Weights on Gestation Day 19					
Liver -	Absolute[b]	88.52±17.18	116.15±30.07	68.79±18.54	60.96±6.91
	Relative[c]	2.29±0.33	3.00±0.58	2.02±0.49	1.94±0.13
Kidney -	Absolute	18.52±3.95	16.71±1.71	13.02±2.99	13.32±5.22
-	Relative	0.48±0.08	0.44±0.04	0.39±0.10	0.42±0.15
Spleen -	Absolute	1.32±0.27	1.54±0.34	1.06±0.35	0.65±0.06*
	Relative	0.03±0.01	0.04±0.01	0.03±0.01	0.02±0.00*
Thymus -	Absolute	4.05±1.00	3.39±0.75	1.85±0.71*	2.44±1.18
-	Relative	0.11±0.03	0.09±0.01	0.05±0.02*	0.08±0.04

[a]Inseminated New Zealand white rabbits were exposed to 0, 50, 200 or 400 ppm of EGME for 6 hr/day on days 6 through 18 of gestation and necropsied on day 19 of gestation.

[b]Mean ± S.D., grams.

[c]Grams organ weight/grams body weight, mean ±S.D.

*Significantly different from the control value, $p \leq 0.05$, by Dunnett's test.

TABLE 8

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY PROBE STUDY IN RATS AND RABBITS

GROSS PATHOLOGIC OBSERVATIONS - SPONTANEOUSLY DEAD RABBITS

SEX		FEMALES			
EXPOSURE CONCENTRATION IN PPM		0	50	200	400
NUMBER OF RABBITS EXAMINED		0	1	0	2
LIVER					
NO LESIONS RECOGNIZED.		0	0	0	1
MOTTLED:		0	1	0	1
PALE:		0	1	0	1
BONE					
NO LESIONS RECOGNIZED.		0	1	0	1
COLOR -RED, BONE MARROW:		0	0	0	1
STOMACH					
NO LESIONS RECOGNIZED.		0	1	0	1
BLOOD, GLANDULAR MUCOSA, MULTIFOCAL:	- SLIGHT	0	0	0	1
URINARY BLADDER					
NO LESIONS RECOGNIZED.		0	1	0	1
CALCULUS(I):		0	0	0	1
AREA - DEPRESSED, MUCOSA:		0	0	0	1
UTERUS					
NO LESIONS RECOGNIZED.		0	1	0	1
PREGNANT-ALL FETUS(ES) APPARENTLY RESORBED:		0	0	0	1
LUNGS					
NO LESIONS RECOGNIZED.		0	0	0	0
EDEMA:		0	0	0	1
AREA - DARK, LEFT APICAL LOBE, FOCAL:		0	1	0	0
AREA - DARK, RIGHT APICAL LOBE, FOCAL:		0	1	0	0
AREA - DARK, RIGHT CARDIAC LOBE:		0	0	0	1
AREA - DARK, RIGHT CARDIAC LOBE, DIFFUSE:		0	1	0	0
DARK:		0	0	0	1
FIRM, LEFT APICAL LOBE, FOCAL:		0	1	0	0
FIRM, RIGHT APICAL LOBE, FOCAL:		0	1	0	0
FIRM, RIGHT CARDIAC LOBE, DIFFUSE:		0	1	0	0
THYMUS					
NO LESIONS RECOGNIZED.		0	1	0	1
DECREASED SIZE:		0	0	0	1
ABDOMINAL CAVITY					
NO LESIONS RECOGNIZED.		0	1	0	1
FAT - DECREASED AMOUNT:		0	0	0	1
EXTERNAL AND SKIN					
NO LESIONS RECOGNIZED.		0	1	0	0
ABSCESS, SUBCUTANEOUS:		0	0	0	1
PERINEAL SOILING:		0	0	0	2
THORACIC CAVITY					
NO LESIONS RECOGNIZED.		0	1	0	1
HYDROTHORAX - SEROSANGUINEOUS:	- SLIGHT	0	0	0	1

TABLE 7 (CONTINUED)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY PROBE STUDY IN RATS AND RABBITS

GROSS PATHOLOGIC OBSERVATIONS - SACRIFICED RABBITS[a]

SEX		FEMALES			
EXPOSURE CONCENTRATION IN PPM		0	50	200	400
NUMBER OF RABBITS EXAMINED		7	6	7	5
UTERUS					
NO LESIONS RECOGNIZED.		0	0	0	0
NONPREGNANT:		2	1	2	2
PREGNANT-ALL FETUS(ES) APPEAR NORMAL:		1	2	0	0
PREGNANT-NORMAL APPEARING FETUS(ES) WITH RESORPTIONS AND/OR DEAD FETUS(ES):		3	3	0	0
PREGNANT-ALL FETUS(ES) APPARENTLY RESORBED:		1	0	5	3
LUNGS					
NO LESIONS RECOGNIZED.		0	1	1	1
ABSCESS, LEFT DIAPHRAGMATIC LOBE, MULTIFOCAL:	- MODERATE	0	1	0	0
HEMORRHAGE - TERMINAL:		7	5	6	4
THYMUS					
NO LESIONS RECOGNIZED.		7	5	3	3
DECREASED SIZE:		0	1	4	2
AORTA					
NO LESIONS RECOGNIZED.		7	4	7	5
MINERALIZATION:		0	2	0	0
TONGUE					
NO LESIONS RECOGNIZED.		4	6	6	3
ULCER, MUCOSA:		0	0	0	1
AREA - ELEVATED:		2	0	1	1
AREA - ELEVATED, MULTIFOCAL:		1	0	0	1
ABDOMINAL CAVITY					
NO LESIONS RECOGNIZED.		7	5	2	1
FAT - DECREASED AMOUNT:		0	0	5	4
ACCESSORY SPLEEN:		0	1	0	0
EXTERNAL AND SKIN					
NO LESIONS RECOGNIZED.		7	5	7	5
PERINEAL SOILING:		0	1	0	0
THORACIC CAVITY					
NO LESIONS RECOGNIZED.		7	5	7	5
ADHESIONS - FIBROUS:	- MODERATE	0	1	0	0

[a]Inseminated New Zealand White rabbits were exposed to 0, 50, 200 or 400 ppm of EGME for 6 hr/day on days 6 through 18 of gestation and necropsied on day 19 of gestation.
Data listed as the number of animals with the specific observation.
Only positive entries are presented.

TABLE 9

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY PROBE STUDY IN RATS AND RABBITS

Observations Made at Necropsy on Day 19 of Gestation of Rabbits[a]

	Ethylene Glycol Monomethyl Ether, PPM			
Exposure Level	0	50	200	400
Number of Females Bred	7	7	7	7
Number of Maternal Deaths	0	1	0	2
Percent Pregnant[b]	71(5/7)	86(6/7)	71(5/7)	71(5/7)
Pregnancies Detected by Sodium Sulfide Stain[c]	0/2	0/1	0/2	0/2
Number of Litters	5	5	5	3
Corpora Lutea/Dam[d]	13±7	10±2	-[e]	-[e]
Implantation Sites/Dam[d]	9±5	8±3	8±3	8±4
% Pre-implantation Loss[f]	12±16	28±17	-[e]	-[e]
Fetuses/Litter[d]	7±5	5±2	0±0	0±0
Resorptions/Litter[d]	1.40±1.14	2.80±3.11	7.80±2.59	8.00±3.61
% Implantations Resorbed	16(7/43)	37(14/38)	100(39/39)*	100(24/24)*
% Litters with Resorptions	80(4/5)	60(3/5)	100(5/5)*	100(3/3)*
Litters Totally Resorbed	1	0	5	3
Resorptions/Litters with Resorptions	1.8(7/4)	4.7(14/3)	7.8(39/5)	8.0(24/3)

[a]Inseminated New Zealand white rabbits were exposed to 0, 50, 200 or 400 ppm of EGME for 6 hr/day on days 6 through 18 of gestation and necropsied on day 19 of gestation.

[b]Number of females with visible implantation sites at the time of necropsy/total number of bred females.

[c]Number of females with implantation sites detected only after staining the uterus with sodium sulfide/total number stained.

[d]Mean ± S.D.

[e]Corpora lutea not recorded on litters totally resorbed. All litters at this level were totally resorbed.

[f]Percent per litter, mean ± S.D.

*Significantly different from the control value, $p \leq 0.05$, by the appropriate statistical test.

Contains NO CBI

B-17d

#4

Ethylene Glycol Monomethyl Ether: Inhalation Teratology Study in Rats and Rabbits†

By:

T. R. Hanley, Jr., B. L. Yano, K. D. Nitschke and J. A. John

Reviewed by:

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September 20, 1982

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SUMMARY

The objective of this study was to determine the embryotoxic and teratogenic potential of inhaled ethylene glycol monomethyl ether (EGME) in rats and rabbits. Bred Fischer 344 rats and inseminated New Zealand white rabbits were exposed to 0, 3, 10 or 50 ppm of EGME via inhalation for 6 hours/day on days 6 through 15 (rats) or 6 through 18 (rabbits) of gestation, and the fetuses were evaluated near term.

Exposure of pregnant rabbits to 50 ppm of EGME produced conclusive evidence of teratogenicity and fetotoxicity. Significant increases in the incidences of major malformations involving the cardiovascular, urogenital and skeletal systems were observed in fetal rabbits at 50 ppm. A total of 63% of the fetuses from 91% of the litters exposed to 50 ppm exhibited at least one major malformation, with numerous fetuses exhibiting multiple alterations. By comparison, only 4% of the control fetuses from a total of 26% of the control litters exhibited major malformations. Maternal effects observed at 50 ppm were limited to a transient decrease in maternal weight gain. In addition, a significant increase in the resorption rate, and a decrease in fetal body weight were observed at 50 ppm. The resorption rate among rabbits exposed to 10 ppm was significantly higher than the concurrent control rate; however, comparison with historical data indicated this apparent increase was the result of an unusually low concurrent control value and this was not considered treatment related. No other significant differences were observed among rabbits exposed to 10 or 3 ppm.

Among rats exposed to 50 ppm, a transient decrease in maternal weight gain during the initial period of exposure was observed. The incidences of major malformations among fetal rats, considered either individually or collectively at each exposure level, were not significantly increased in any exposure group when compared to controls. Isolated statistical increases in the incidences of two minor skeletal variations were observed at 50 ppm, but these increases were considered indications of only a slight fetotoxic effect. The lack of any other effects on fetal parameters among rats exposed to 50 ppm indicate these differences were of questionable toxicologic significance. There was no evidence of maternal or fetal effects among rats exposed to 3 or 10 ppm of EGME.

In conclusion, EGME was teratogenic in the rabbit by the inhalation route at 50 ppm but not at 10 or 3 ppm, and was not teratogenic in the rat at concentrations of up to 50 ppm of EGME.

INTRODUCTION

Ethylene glycol monomethyl ether (EGME, 2-methoxyethanol) is a volatile, nearly odorless liquid with the following properties:

Structural Formula:	$H_3C-O-CH_2CH_2-OH$
Molecular Weight:	76.09
Boiling Point:	124.6°C @ 760 mmHg
Vapor Pressure:	9.5 mmHg @ 25°C
Solubility:	Miscible with water
Flash Point:	107°F

EGME has been used extensively for many years as a solvent for resins, lacquers, paints, dyes, and inks, and as a surfactant.

The toxicologic information concerning EGME has recently been reviewed (Rowe and Wolf, 1982). The oral toxicity of EGME is low, with an LD_{50} of 3.5 g/kg in rats, 0.89 g/kg in rabbits and 0.95 g/kg in guinea pigs. EGME is absorbed in toxic amounts through the skin; the rabbit dermal LD_{50} is 2.0 g/kg. Moderate pain and conjunctivitis result after direct application to the eyes of rabbits, but these effects are reversible within 24 hours of application. Subchronic inhalation exposure of rats (310 ppm for 5 weeks) and dogs (750 ppm for 12 weeks) for 7 hours/day, 5 days/week resulted in hypochromasia, reduced hemoglobin concentration and decreased packed red cell volume.

Miller, et al. (1981) reported the results of short term inhalation studies in which rats and mice were exposed to 0, 100, 300 or 1000 ppm for 9 days during an 11-day interval. Histopathologic changes in rats and mice exposed to 1000 ppm included moderately reduced bone marrow cellularity, hematologic abnormalities and testicular degeneration. Similar but less pronounced changes were noted in some animals in the 300 ppm group. No adverse effects were attributed to exposure to 100 ppm.

Subchronic exposure of rats and rabbits to 0, 30, 100 or 300 ppm of EGME for 6 hr/day, 5 days/week for 13 weeks resulted in hematologic abnormalities, decreased testicular and thymic weights, and histopathologic changes of the testes and thymus in rats and rabbits at 300 ppm (Miller, et al, 1982a). Similar histopathologic changes were found in the testes of three of five rabbits at 100 ppm, and slight changes were seen in one of five rabbits at 30 ppm. In a subsequent study (Miller, et al, 1982b), no effects were found in the testes of ten rabbits exposed to 30 ppm. A fertility study (Rao, et al, 1982) was conducted concurrently with the subchronic study. Infertility was seen in male rats at 300 ppm but not at 100 or 30 ppm. No adverse reproductive effect was observed among any of the groups of exposed females. There was no evidence of a dominant lethal mutagenic effect at 30 or 100 ppm among males, however, the absence of litters at 300 ppm precluded evaluation for dominant lethality at that level.

Teratology studies of EGME in mice and rats have recently been published. Nagano, et al, (1981) reported that oral administration of EGME to pregnant ICR mice on days 7 through 14 of gestation produced fetotoxicity starting at 31.25 mg/kg/day (the lowest dose level), teratogenicity at 62.5 mg/kg/day and above and maternal toxicity at 1000 mg/kg/day (the top dose level). Nelson, et al., (1982) reported that inhalation exposure for 7 hr/day to 50 or 100 ppm of EGME produced skeletal and cardiovascular defects in Sprague-Dawley rats.

Prior to the published reports by Nagano, et al, (1981) and Nelson, et al, (1982), studies to assess the embryotoxic and teratogenic potential of EGME in rats and rabbits via inhalation (the most probable route of human exposure) were undertaken. In a preliminary study (Hanley, et al., 1982), exposure levels of 200 or 400 ppm of EGME for 6 hr/day produced maternal toxicity and resulted in complete resorption of all litters in both rats and rabbits. An increased incidence of resorptions was observed among rabbits at 50 ppm, though no evidence of embryotoxicity was observed among rats at 50 ppm.

The purpose of this study was to evaluate the teratogenic potential of EGME in the Fischer 344 rat and New Zealand white rabbit. The Fischer 344 rat was selected on the basis of its extensive use in toxicology testing within this laboratory and its positive response within this laboratory to a known teratogenic agent (Vitamin A; Hayes et al., 1981). The New Zealand white rabbit was selected as a second

(non-rodent) test species on the basis of extensive historical use within this laboratory. Pregnant rats were exposed on days 6 through 15 of gestation and pregnant rabbits on days 6 through 18 of gestation to EGME via inhalation and the fetuses were examined for deleterious effects on embryonal or fetal development. This study was sponsored by the U.S. ethylene glycol ethers producers under the auspices of the Chemical Manufacturers Association[1].

MATERIALS AND METHODS

Test Material: Ethylene glycol monomethyl ether for use in this study was obtained from The Dow Chemical Company, Michigan Division, Midland, Michigan and was identified as Lot No. MM 810624. Analysis prior to initiation of the study indicated 99.96% purity[2].

Test Animals: Stock supplies of male and female Fischer 344 rats (Charles River Breeding Laboratories, Inc., Portage, Michigan) and New Zealand white rabbits (Langshaw Farms, Augusta, Michigan) were obtained. Animals were housed in wire-bottomed cages in rooms designed to control temperature at approximately 22°C, relative humidity at approximately 50% and a photocycle of 12 hours light and dark. Animals were acclimated to the laboratory for at least two weeks prior to

[1]Texaco, ICI America, PPG, Olin Chemicals, Union Carbide Corporation and Dow Chemical U.S.A.

[2]Analysis performed by P. Kastl, Toxicology Research Laboratory, The Dow Chemical Company, Midland, Michigan 15 July 1981.

breeding. Adult virgin female Fischer 344 rats (approximately 175-220 g at breeding) were bred to adult males (one female to one male) from the same strain. The day sperm were found in vaginal smears was considered day 0 of gestation. Rabbits (approximately 3.5-4.5 kg) were artificially inseminated (Gibson, et al, 1966) with this day considered day 0 of gestation.

Randomization of test animals, grouped according to their day 0 of gestation, was performed using computer-generated tables of random numbers. All animals were uniquely identified by metal ear tags. Food (Certified Laboratory Animal Chow, Ralston Purina Company, St. Louis, Missouri) and municipal tap water were available ad libitum, except during actual inhalation exposure periods. Analysis of Purina Certified Chow was performed by the Ralston Purina Company to confirm that the diets provide adequate nutrition, and to quantify the levels of selected contaminants associated with the formulation process. Analysis of tap water (municipal water supply) was performed according to the Standard Operating Procedures of the Toxicology Research Laboratory.

Experimental Design: Groups of 30-31 bred rats and 29-30 inseminated rabbits were exposed by inhalation to EGME. Rats and rabbits were exposed to levels of 0, 3, 10 or 50 ppm for 6 hours/day -- rats on days 6 through 15 of gestation and rabbits on days 6 through 18 of gestation. Control groups of 30 rats and 30 rabbits were exposed to filtered air in an exposure chamber in a manner similar to the treated groups.

Chambers: Exposures were conducted in 4.3 m^3 inhalation chambers. Temperature and relative humidity in the chambers were controlled by a system designed to maintain temperature at approximately 21°C and relative humidity at approximately 50%. Temperature and relative humidity in the exposure chambers were recorded during each exposure day.

Vapor Generation and Analysis: Vapors were generated by metering the liquid test substance at calculated rates into glass vaporization tubes (Miller, et al., 1980c). Vapors from the tubes were swept into the chamber inlet ducts with compressed air where there was further mixing and dilution with incoming air by turbulence. The compressed air was preheated to the minimum extent required for complete vaporization using a compressed air flameless heat torch (Master, Model FHT-4). Total chamber airflow was maintained at approximately 800 liters per minute. The nominal concentration (ratio of the amount of EGME vaporized to the total amount of air through the chamber) was calculated for each chamber on a daily basis. The actual concentration of EGME in each exposure chamber was measured at least 2 times per hour by infrared spectroscopy using a Miran 1A infrared gas analyzer at a wavelength of 8.8μm.

Standards were prepared by injecting calculated amounts of EGME into 100 liter SARAN bags filled with a measured volume of filtered compressed air. These standards were passed through the IR to produce

a series of responses at various concentrations, i.e. a standard curve. The concentrations of EGME in the exposure chambers were determined by interpolation from the standard curve. Standard curves were generated prior to the first exposure and at least weekly thereafter. A standard was analyzed prior to each exposure as a calibration check of the analytical system.

Maternal Observations: Animals were observed daily throughout the experimental period for indications of toxicity and adverse effects of treatment were recorded. Animals found dead or moribund were submitted for gross pathologic examination. Body weights for rats were recorded on gestation days 6, 9, 12, 16 and 21; food and water consumption were recorded for each at 3-day intervals starting on day 6 of gestation. Body weights for rabbits were recorded on gestation days 6, 9, 12, 15, 19 and 29. Maternal liver, thymus and spleen weights of rats and rabbits were recorded at the time of cesarean section, and sections of maternal spleen, thymus, mesenteric lymph nodes and bone (including marrow) from rats (vertebrae) and rabbits (proximal femur) were preserved in 10% formalin but were not examined histologically. At cesarean section, blood was collected from 10 pregnant rats and rabbits/dose level for hematologic evaluation[3] (excluding differential white cell counts on blood smears).

[3]Red blood cell (RBC) count, hemoglobin concentration (HGB), packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), platlet count, and white blood cell (WBC) count. ELT-8, Ortho Instruments, Westwood, MA.

Fetal Observations: Test animals were sacrificed by carbon dioxide inhalation on day 21 of gestation for rats, day 29 for rabbits. The uterine horns were exteriorized through a mid-line incision in the abdominal wall and the following data were recorded: 1) number and position of fetuses *in utero*, 2) number of live and dead fetuses, 3) number and position of resorption sites, 4) the number of corpora lutea, 5) the sex, body weight and crown-rump length of each fetus, and 6) any gross external alteration. The uteri of apparently non-pregnant animals were stained with a 10% solution of sodium sulfide (Kopf, *et al*, 1964) and examined for evidence of implantation sites. This procedure was conducted solely to determine the incidence of pregnancy; implantations detected only by staining the uterus were not included in the calculation of the resorption rate. One-half of each litter, selected using a table of random numbers, was examined immediately by dissection under a low power microscope for evidence of soft tissue alterations (Staples, 1974). The heads of rat fetuses examined by dissection were removed, placed in Bouin's fixative and examined by the serial sectioning technique of Wilson (1965). All fetuses were then preserved in alcohol, eviscerated and subsequently cleared and stained with alizarin red-S (Dawson, 1926) and examined for skeletal alterations.

Statistical Evaluation: Statistical evaluation of the frequency of alterations and of resorptions among litters and the fetal population was performed using the Wilcoxon test as modified by Haseman and Hoel

(1974). Analysis of the percentage of pregnancy and other incidence data was made by the Fisher exact probability test (Siegel, 1956). The fetal sex ratio was analyzed by a binomial distribution test (Steel and Torrie, 1960). Analysis of other data was performed using parametric or nonparametric analysis of variance followed by either Dunnett's test (Steel and Torrie, 1960) or the Wilcoxon rank sum test with Bonferroni's correction (Miller, 1966) as appropriate. The nominal alpha level used for statistical analysis was $\alpha=0.05$. For food and water consumption data, statistical outliers were identified by a sequential outlier test $\alpha=0.02$ (Grubbs, 1969) and deleted from the calculation of mean values.

RESULTS

Exposure Condition: A summary of the exposure conditions is presented in Table 1. For each chamber, the daily time weighted average (TWA) analytical concentration was very close to the intended target concentration. Moreover, there was close agreement between the mean daily TWA analytical concentrations and mean daily nominal concentrations, indicating that test material losses were minimized in the vapor generation and exposure systems.

Rats: No overt signs of toxicity were observed among pregnant rats exposed to EGME at levels up to 50 ppm. Maternal body weight gain among rats exposed to 50 ppm was identified statistically as being lower than controls on days 6 through 8 of gestation (Table 2). There

were no statistical differences in body weight gain among exposed animals at any other time period. Table 3 presents a summary of food and water consumption data. Food consumption among rats exposed to 50 ppm was identified statistically as being increased over the control value on days 12 through 14 of gestation; however, this difference was not considered treatment-related. Water consumption among EGME exposed rats was comparable to control values. Rats exposed to 50 ppm had statistically higher absolute liver weights (Table 4); however, the relative liver weights were not significantly different from the controls. Thus this difference was not considered treatment-related. There were no statistical differences in liver weights observed at 3 or 10 ppm, or in spleen and thymus weights at any exposure level.

A summary of the hematologic parameters measured on day 21 of gestation is presented in Table 4. Statistically significant differences were observed in mean hemoglobin concentration (HGB) and in packed red cell volume (PCV) at all exposure levels when compared to controls. A statistically significant decrease in the red blood cell counts (RBC) was observed among pregnant rats exposed to 50 ppm, with small, though not statistically significant, decreases observed in RBC's at 10 and 3 ppm. The decreases in these parameters (RBC, HGB, & PCV) were slight (2.6-6.3%), but appeared to be dose-related.

Table 5 presents a summary of the reproductive parameters measured in rats at the time of cesarean section. There were no statistical

differences in pregnancy rates, pre-implantation loss, litter size, resorption rates or fetal body weight and lengths in the exposure groups when compared to controls. A single animal exposed to 3 ppm delivered a litter prior to scheduled cesarean section.

The incidence of external, soft-tissue, and skeletal alterations among litters of rats exposed to EGME are presented in Table 6. The incidence of major malformations observed externally, internally or by skeletal examination, whether considered individually or collectively in each exposure group, was not statistically significantly different from the control incidence. There were no major malformations observed among the controls. Among rats exposed to 3 ppm, a single fetus exhibited situs inversus (a complete transposition of all of the visceral organs). A single fetus from the 10 ppm exposure group exhibited a misalignment of the first phalanx of the right hindfoot. Among rats exposed to 50 ppm, there were three fetuses from different litters which exhibited major malformations. A single fetus exhibited bilateral anophthalmia, dilated lateral ventricles of the brain, a hemivertebra and was missing half of one cervical vertebra resulting in a misalignment of the ribs on one side of the thoracic cavity. Two other fetuses from different litters exhibited a cervical (extra) rib.

A number of minor alterations or instances of delayed skeletal ossification were observed among controls as well as exposed animals. A single

fetus from the 10 ppm exposure group exhibited facial edema. Statistically significant increases in the incidence of delayed ossification of the cervical centra and in the incidence of lumbar spurs, both considered minor skeletal variations, were observed at 50 ppm. A statistically significant decrease in delayed sternebral ossification was observed at 50 ppm; however, this was considered a reflection of normal variation. There were no significant differences in the incidence of minor alterations among rats exposed to 3 or 10 ppm of EGME when compared to controls.

Rabbits: No treatment-related changes were observed in the general appearance or demeanor of pregnant rabbits exposed to levels of up to 50 ppm of EGME. Three spontaneous deaths occurred during this study. The deaths of two control animals were attributed to pneumonia based upon a gross necropsy examination. The cause of death of a single rabbit exposed to 10 ppm of EGME was not determined.

The mean body weight gain among rabbits exposed to 50 ppm was statistically lower than among controls on days 6 through 8 and 12 through 14 of gestation (Table 7). Rabbits exposed to 50 ppm also exhibited statistically significantly increased absolute liver weight (Table 8), accompanied by a slight (nonsignificant) increase in the relative liver weight. While this increase in liver weight may reflect maternal toxicity, previous studies (Miller, et al., 1981, 1982 a&b) have not identified the liver as a target organ. There were no significant changes in body weight gain or absolute or relative liver weights among rabbits

exposed to 10 or 3 ppm, nor any significant differences in spleen or thymus weights (consider primary target organs) at 50 ppm or below. Table 8 also presents a summary of the hematologic parameters measured among pregnant rabbits exposed to EGME. There were no statistical differences identified in any of the parameters measured, nor were there any changes suggesting treatment associated differences as were observed among pregnant rats.

The pregnancy rate of rabbits was not affected by exposure to EGME (Table 9). Upon staining with sodium sulfide, the uteri of two apparently non-pregnant rabbits from the 3 ppm exposure group, and from a single female from the 50 ppm exposure group showed evidence of early resorption sites. In addition, four females, two from the 3 ppm exposure group and two from the 50 ppm group, delivered litters prior to the time of scheduled cesarean section. No effects on the mean number of corpora lutea, pre-implantation loss, or mean litter size were observed among rabbits at 50 ppm of EGME or below (Table 9). However, exposure to 50 ppm resulted in a significant increase in the resorption rate among rabbits when compared to control, which was considered treatment related. A statistically identified increase in the resorption rate was also observed among rabbits exposed to 10 ppm; however, the resorption rate observed at 10 ppm was comparable to the historical incidence of resorptions among fetuses (mean 11%, range 7-15%) and litters (mean 55%, range 38-74%) observed in similar studies conducted in this laboratory. The statistical difference observed at 10 ppm was considered a consequence of the unusually low control

incidence. A significant decrease in mean fetal body weight was observed among rabbits exposed to 50 ppm as well. There were no other effects on the reproductive parameters at any exposure level which suggested a treatment-related effect.

Examination of fetal rabbits for external, soft tissue and skeletal alterations revealed a significant increase in the incidence of major malformations among rabbits exposed to 50 ppm of EGME. Sixty-three percent of the fetuses exposed to 50 ppm exhibited at least one major alteration, and 91% of the litters had at least one fetus with a major malformation. A summary of the incidence of malformations observed among fetal rabbits is presented in Table 10.

Among rabbits exposed to 50 ppm, statistically significantly increased incidences of major malformations were observed in essentially all organ systems. (The incidences of fetal alterations are presented in parenthesis as the total number of fetuses affected/litters affected.) The most predominant major external alterations observed at 50 ppm involved the extremities and included arthrogryposis (abnormal flexure of the forelimbs-54/15), anonychia (10/6), brachydactyly (6/4) and ectrodactyly (6/4). Also observed were kinky tail (4/4) and ventral body wall defects classified as either omphalocele (5/2) or thinning of the abdominal wall (6/3) apparently resulting from a shortening or lack of a portion of the abdominal musculature. Visceral examination of fetal rabbits at 50 ppm revealed high incidences of ventricular septal

defects (34/15) and coarctation (segmental constriction) of the aortic arch (13/6). In approximately half of the fetuses exhibiting a coarctation, the constriction was so severe that the segment could not be visualized under a dissecting microscope (30x magnification). Visceral examination also revealed a grossly observed splenic hypoplasia (26/14), with the spleen in some cases so small as to be barely distinguishable from adjacent mesenteric connective tissue, and dilated renal pelvis (28/14). Skeletal examination revealed significant fetal incidences of missing phalanges (7/4), and metatarsals (9/4) which were consistent with the alterations observed externally.

Other major malformations which were observed at 50 ppm included microphthalmia (3/3), medial rotation of the digits (4/3), hypoplastic tail (2/2) which was confirmed skeletally, unilateral renal agenesis (2/2) with one fetus exhibiting what appeared to be a persistent unilateral mesonephric structure, shortened nasals, maxillae and mandibles (6/1), missing metacarpals (4/2), shortened ribs (4/2), cervical (extra) ribs (2/2) and single instances of polyonychia, syndactyly, inward rotation of the hindfeet, agenesis of the right subclavian artery, diaphragmatic hernia, aplastic spleen, shortened long bones, fused ribs, forked ribs, fused vertebrae, misaligned vertebrae, and double sternum. Though the individual incidences of these malformations were not statistically identified as being different from control, they were considered further evidence of the teratogenic potential of EGME at 50 ppm in rabbits.

In addition to the major malformations observed, numerous minor variations and indicators of delayed development including patent ductus arteriosis (5/4) which in a fetus examined approximately 24 hours prior to full term was considered delayed development, pale spleen (30/16), dilated ureter (5/4), convoluted ureter (12/8), paraovarian cyst (9/8), and delayed ossification of the hyoid (14/8), tarsals (17/8) and sternebrae (127/22), as well as an increase in the incidence of lumbar (extra) ribs (13/7) were statistically identified at 50 ppm as being different from the control incidences. One additional minor alteration detected at external examination was an irregularity in the pattern of the palatine rugae (27/11), the transverse ridges of the palatine shelf. A similar change in rugal pattern has been reported in rats following phenytoin (Lorente, et al, 1981) and cacodylic acid (Rogers, et al, 1981). These differences were considered evidence of fetotoxicity among rabbits at 50 ppm.

In contrast to the teratogenic effects observed at 50 ppm, the incidences of major malformations among rabbits exposed to 10 or 3 ppm, when considered individually or collectively in each exposure group, were not significantly different from controls. At 10 ppm, the major malformations observed consisted of single instances of arthrogryposis, dilated renal pelvis and fused ribs, all occurring in separate litters. Of the minor variations observed in rabbits at 10 ppm, the incidence of delayed ossification of the sternebrae was statistically identified as being higher than the concurrent control incidence. Comparison of the

incidence of delayed sternebral ossification with historical control data indicated the incidence among fetuses (66%) and litters (100%) were only slightly above the control means and were within the range of control values for fetuses (mean 57%, range 16-89%) and litters (mean 88%, range 44-100%). In addition, the incidence of delayed ossification of the thoracic centra was statistically identified as being lower than the control incidence.

Among fetuses exposed to 3 ppm of EGME, single fetuses from different litters had arthrogryposis, fused ribs, dilated renal pelvis and a misshapen kidney. Dissection of the misshapen kidney revealed a unilateral double kidney with the second, smaller kidney fused to a normal sized kidney at the renal hilus with a duplication of the proximal portion of the ureter. The contralateral kidney in this fetus appeared normal. Scattered incidences of minor variations were observed among rabbits at 3 ppm, but in no instance was the incidence statistically identified as being different from controls.

Among controls, six separate fetuses from a total of six litters had major malformations. One fetus exhibited a hypoplastic tail upon external examination, which was confirmed at skeletal examination. Other major malformations observed among controls included single fetuses with fused ribs, forked ribs or calloused ribs, one fetus with fused ribs and a missing atlas, and one fetus missing one half of a lumbar vertebra.

DISCUSSION

Exposure of pregnant rabbits to 50 ppm of EGME for 6 hr/day during the period of major organogenesis produced conclusive evidence of teratogenicity, embryo- and fetotoxicity. Fetal rabbits exposed to 50 ppm exhibited major malformations involving the cardiovascular, urogenital and/or skeletal systems, as well as decreased fetal body weight and an increased resorption rate. Statistically significant increases in the incidences of minor variations in skeletal ossification were also observed at 50 ppm. Maternal effects observed at 50 ppm were minimal. There were no effects which were considered treatment related at 10 or 3 ppm, and these levels were not considered fetotoxic or teratogenic.

In contrast to the effects observed in rabbits, exposure of pregnant Fischer 344 rats produced no evidence of a teratogenic effect at exposure levels up to 50 ppm. Among fetal rats exposed to 50 ppm, two fetuses had a cervical rib which was considered a major malformation. Though no control fetuses from this study exhibited this alteration, cervical ribs have been observed among control fetuses from similar studies at an incidence of up to 1%. Thus, the presence of cervical ribs among fetuses at 50 ppm was considered a spontaneous malformation. At 50 ppm, increases in the incidences of two minor skeletal variants (the presence of rib spurs and delayed ossification of the cervical centra) were considered an indication of only slight fetotoxicity. The

lack of any effects on fetal body weight or any other fetal parameters among rats at 50 ppm indicated that these changes were of minimal toxicologic significance. Maternal effects from exposure to levels up to 50 ppm were minimal. There were no indications of a fetotoxic or teratogenic potential among rats exposed to 3 or 10 ppm.

Hematologic evaluation of maternal rats revealed apparent dose-related decreases in erythrocytic parameters, with the magnitude of the changes observed ranging from a 6.3% decrease in hemoglobin concentration at 50 ppm, to a 4.0% decrease at 3 ppm. Despite the apparent changes in the hematologic values, no significant maternal or fetal effects were observed at 3 and 10 ppm, and indications of only minimal maternal and fetal toxicity were observed at 50 ppm. In contrast, there were no apparent hematologic alterations in rabbits, which proved to be more sensitive than rats to the teratogenic and fetotoxic potential of EGME. The lack of any other maternal effects in rats combined with the lack of any detrimental effects on fetal rat development suggested that these hematologic changes were of no apparent clinical significance and minimal toxicologic significance.

The teratogenic effects observed in rabbits in the present study are consistent with reports published recently for mice (Nagano, et al, 1981) and rats (Nelson, et al, 1982). Nagano administered EGME orally to pregnant ICR mice at dose levels of 0, 31.25, 62.5, 125, 250, 500

and 1000 mg/kg/day on days 7 through 14 of gestation. Marked leucopenia observed at 1000 mg/kg/day was the only indication of maternal toxicity. Embryolethality was observed at 250 mg/kg/day and above, teratogenic effects were seen at 62.5 mg/kg/day and above, and fetotoxicity was evident down to 31.25 mg/kg/day. Nelson, et al, (1982) reported that inhalation exposure of pregnant Sprague-Dawley rats to EGME for 7 hr/day on days 7 through 15 of gestation produced skeletal and cardiovascular defects at 50 and 100 ppm. Exposure to 200 ppm resulted in complete resorption of all litters. Thus, there appears to be a consistent pattern of teratogenic effects across species.

Interspecies comparisons are possible if one assumes that the percentage of the dose absorbed is the same irrespective of the route of administration. Assuming comparable absorption, a respiratory minute volume of 24 ml/min for mice (Guyton, 1947), and an average body weight of 35g for mice, the teratogenic dose of 62.5 mg/kg in mice would correspond to a six hour exposure concentration of approximately 81 ppm. The 50 ppm exposure concentration over a seven hour exposure period (Nelson, et al, 1982) would correspond to a six hour exposure concentration of approximately 58 ppm. The differences observed at 50 ppm in rats between the Nelson study and the present study may be a reflection of the difference in the duration of the exposure periods. Though strain differences may also contribute to the observed

differences, preliminary studies in this laboratory (Hanley, et al, 1982) in which pregnant Fischer 344 rats were exposed to 200 ppm of EGME for 6 hr/day also produced complete resorption of all litters, similar to the effect in Sprague-Dawley rats reported by Nelson, et al, (1982). Based upon the substantial teratogenic effects in rabbits observed in the present study, as well as data reported by Miller, et al., (1982a), the rabbit appeared to be the species most sensitive to the toxicologic potential of EGME.

One important aspect of the present study is the establishment of a no effect level in both rats and rabbits. Previous teratologic studies (Nagano, et al, 1981; Nelson, et al, 1982) conducted at high dose levels produced adverse effects even at the lowest levels tested. The present study, conducted at lower levels, indicated that an exposure level of 10 ppm produced no evidence of teratogenicity or fetotoxicity in either species. The establishment of 10 ppm as a no effect level also points out the steep dose-response relationship which exists for EGME, since a five-fold increase in concentration over the no effect level of 10 ppm produced substantial teratogenic effects in rabbits and slight fetotoxicity in rats. A further four-fold increase in exposure concentration over the teratogenic level resulted in complete

embryolethality in both species. Hence, there was a substantial spectrum of effects over a rather narrow range of exposure concentrations.

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TITLE OF STUDY: ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

In compliance with Good Laboratory Practice Regulations, the study phases were inspected by the Quality Assurance Unit and the results of these inspections reported to Management and the Study Director on the dates listed below. The report accurately reflects the data generated in accordance with the regulations and standard operating procedures of the laboratory. All data and the reports are located at the submitting laboratory.

Study Started:	8 Sept. 1981	Report Issued Date:	20 Sept. 1982
Dates of Inspection:	4 Sept. 1981	Date of Report:	4 Sept. 1981
	12 Oct. 1981		12 Oct. 1981
	3 Nov. 1981		3 Nov. 1981
	20 July 1982		21 July 1982

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Table 1

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Chamber Concentration, And Atmospheric Conditions

Desired Concentration, ppm	0	3	10	50
Number of Exposures[a]	47	47	47	47
Analytical Concentration[b], ppm.	--	3.0±0.2	10.0±0.4	50.5±0.8
Analytical Coefficient of Variation[c]	--	6.7	4.0	1.6
Range of Daily Analytical Concentration[d], ppm	--	2.6-3.3	8.5-10.8	49.1-53.4
Nominal Concentration, ppm	--	2.8±0.1	10.6±0.4	48.2±1.7
Nominal/Analytical Conc.	--	0.93	1.06	0.95
Daily Temperature, °C				
Minimum $\overline{X}$ ± S.D.[e]	22±1	22±1	22±1	22±1
Maximum $\overline{X}$ ± S.D.	24±1	24±1	24±1	24±1
Daily Relative Humidity, %				
$\overline{X}$ ± S.D.	52±7	53±2	52±3	54±3

[a]Number of days of chamber operations.

[b]Data represent Mean ± Standard Deviation of daily time weighted average (TWA).

[c]Analytical $\frac{\text{Standard Deviation}}{\text{Mean}} \times 100$

[d]Data represents range of daily analytical TWA.

[e]$\overline{X}$ ± S.D. = Mean ± Standard Deviation

Table 2

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Body Weights of Pregnant Rats[a]

Exposure Level		Ethylene Glycol Monomethyl Ether, ppm 0	3	10	50
Number of Dams		29	28	28	30
Maternal Body Weight (g) on Gestation day	6	191±7[b]	192±6	192±6	194±5*
	9	196±7	195±6	195±6	196±7
	12	205±7	204±6	204±7	207±7
	16	220±7	219±8	220±7	222±7
	21	260±15	259±13	261±9	264±10
Maternal Body Weight Gain (g) on Gestation Days	6-8	5±5[b]	3±3	3±3	2±6*
	9-11	9±5	10±3	10±3	10±3
	12-15	15±4	15±3	16±5	15±4
	16-20	40±10	40±8	41±7	41±7
Overall	6-20	69±14	67±10	69±8	69±9

[a]Bred Fischer 344 rats were exposed to 0, 3, 10 or 50 ppm of EGME by inhalation for 6 hr/day on days 6 through 15 of gestation.

[b]Mean ± S.D.

*Significantly different from the control value by Dunnett's test.

See Table A-1 for individual animal data.

Table 3

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Food and Water Consumption of Pregnant Rats[a]

		Ethylene Glycol Monomethyl Ether, PPM			
Exposure Level		0	3	10	50
Number of Dams		29	28	28	30
Maternal Food Consumption on Gestation Days	6-8	13.6±0.8[b]	13.9±1.0	13.8±0.9	13.6±1.0
	9-11	14.6±0.9	15.1±1.3	15.1±1.2	15.2±1.2
	12-14	15.3±0.9	15.5±1.0	15.5±0.9	15.9±1.3*
	15-17	16.9±0.9	16.8±1.2	16.7±1.4	16.8±1.4
	18-20	17.1±1.0	16.6±0.5	16.6±1.2	16.8±1.4
Maternal Water Consumption on Gestation Days	6-8	18.4±2.8[b]	19.5±2.0	19.0±2.5	19.0±2.7
	9-11	22.1±3.1	23.1±3.0	24.0±3.3	23.4±2.6
	12-14	26.4±3.9	26.5±2.7	27.0±2.9	27.5±4.1
	15-17	29.8±4.1	29.8±3.3	30.0±4.4	30.5±4.2
	18-20	28.7±2.7	28.3±2.5	29.0±3.2	29.3±3.7

[a]Bred Fischer 344 rats were exposed to 0, 3, 10 or 50 ppm of EGME by inhalation for 6 hr/day on days 6 through 15 of gestation.

[b]Grams/rat/day, Mean±S.D.

*Significantly different from the control value by Dunnett's test.

See Tables A-2 and A-3 for individual animal data.

Table 4

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Organ Weights and Hematologic Parameters in Pregnant Rats[a]

Exposure Level	Ethylene Glycol Monomethyl Ether, PPM			
	0	3	10	50
Number of Dams	29	28	28	30
Maternal Organ Weight on Gestation Day 21				
Liver - Absolute[b]	9.59±0.47	9.51±0.49	9.62±0.64	9.96±0.58*
Relative[c]	3.70±0.26	3.68±0.16	3.69±0.21	3.78±0.23
Spleen - Absolute	0.47±0.04	0.48±0.04	0.48±0.05	0.51±0.08
Relative	0.18±0.02	0.19±0.02	0.19±0.02	0.19±0.04
Thymus - Absolute	0.21±0.06	0.18±0.04	0.18±0.03	0.18±0.05
Relative	0.08±0.02	0.07±0.02	0.07±0.01	0.07±0.02
Hematologic Parameters Measured on Gestation Day 21				
RBC $X10^6/mm^3$	6.49±0.16[d]	6.32±0.21	6.29±0.13	6.18±0.23*
HGB (g/dl)	12.6±0.3	12.1±0.4*	12.0±0.2*	11.8±0.4*
PCV (%)	35.5±0.9	34.0±1.4*	33.7±0.6*	33.4±0.9*
MCV (μ^3)	54.8±0.4	53.9±0.6	53.5±0.7	54.1±1.5
MCH (μμg)	19.4±0.3	19.2±0.3	19.1±0.4	19.1±0.4
MCHC (%)	35.5±0.4	35.7±0.7	35.7±0.8	35.4±0.8
Platlets $X10^3/mm^3$	1133±78	1150±88	1132±80	1113±96
WBC $X10^3/mm^3$	3.5±2.1	3.0±1.7	2.1±1.5	5.0±2.3
N=	9[e]	10	10	10

[a]Bred Fischer 344 rats were exposed to 0, 3, 10 or 50 ppm of EGME by inhalation for 6 hr/day on days 6 through 15 of gestation.

[b]Grams, Mean±S.D.

[c]Grams organ weight/100 grams body weight, Mean±S.D.

[d]Mean±S.D.

[e]Excludes one outlier with litter size of one.

*Significantly different from the control value by Dunnett's test.

See Table A-4 and A-5 for individual animal data.

Table 5

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Observations Made at the Time of Cesarean Section of Rats[a]

Exposure Level	Ethylene Glycol Monomethyl Ether, PPM			
	0	3	10	50
Number of Bred Females	30	31	31	30
Percent Pregnant[b]	97(29/30)	94(29/31)	90(28/31)	100(30/30)
Pregnancies Detected by Stain[c]	0/1	0/2	0/3	--
Number of Litters	29	28	28	30
Corpora Lutea/Dam[d]	11±1	11±1	12±1	12±2
Implantation Sites/Dam[d]	11±3	11±2	11±2	11±1
Pre-implantation Loss[e]	8±21	8±15	5±12	6±11
Fetuses/Litter[d]	10±3	10±2	10±2	10±2
Resorptions/Litter[d]	0.6±0.8	0.4±0.7	0.4±0.6	0.7±1.2
% Implantations Resorbed	6(18/305)	4(11/294)	4(12/305)	6(20/327)
% Litters with Resorptions	45(13/29)	29(8/28)	39(11/28)	40(12/30)
Litters Totally Resorbed	0	0	0	0
Resorptions/Litters with Resorptions	1.4(18/13)	1.4(11/8)	1.1(12/11)	1.7(20/12)
% Dead Fetuses	0	0	0	0
Sex Ratio, M:F	53:47	51:49	46:54	51:49
Fetal Body Weight, (g)[f]	4.33±0.20	4.33±0.23	4.39±0.15	4.34±0.13
Fetal Crown-Rump Length, mm[f]	42.7±2.1	42.7±1.7	43.0±1.7	43.0±1.4

[a]Bred Fischer 344 rats were exposed to 0, 3, 10 or 50 ppm of EGME by inhalation for 6 hr/day on days 6 through 15 of gestation.
[b]Number of females with visible implantations at the time of cesarean section/total number bred. Includes one female at 3 ppm which delivered a litter prior to cesarean section on day 21 of gestation.
[c]Number of females with implantation sites detected only after staining the uterus with sodium sulfide/total stained.
[d]Mean±S.D.
[e]Percent per litter, Mean±S.D.
[f]Mean of litter means±S.D.
See Table A-6 for individual animal data.

Table 6

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION
TERATOLOGY STUDY IN RATS AND RABBITS

Incidence of Fetal Alterations Among Litters of Rats[a]

Exposure Level		Ethylene Glycol Monomethyl Ether, ppm 0	3	10	50
		Number of Fetuses (Number of Litters)			
EXTERNAL EXAMINATION		287(29)	283(28)	293(28)	307(30)
SOFT TISSUE EXAMINATION		149(29)	149(28)	155(28)	160(30)
SKELETAL EXAMINATION		287(29)	283(28)	293(28)	307(30)
BONES OF THE SKULL[b]		138(27)	134(27)	139(28)	147(29)
		% Affected (Number Affected)			
Total Major Malformations	F[c]	0	0.4(1)	0.3(1)	1(3)
	L	0	4(1)	4(1)	10(3)
External Alterations					
Anophthalmia[†]	F	0	0	0	0.3(1)[d]
	L	0	0	0	3(1)[d]
Facial Edema	F	0	0	0.3(1)	0
	L	0	0	4(1)	0
Soft Tissue Alterations					
Situs Inversus[†]	F	0	0.7(1)	0	0
	L	0	4(1)	0	0
Dilated Lateral Ventricles[†]	F	0	0	0	0.6(1)[d]
	L	0	0	0	3(1)[d]
Skeletal Alterations					
Skull					
-Delayed Ossification	F	0	0	0	0.7(1)
	L	0	0	0	3(1)
-Foramen	F	0	0.7(1)	1(2)	0.7(1)
	L	0	4(1)	7(2)	3(1)
Vertebrae					
-Delayed Ossification					
-Cervical Arches	F	0	0	0	0.3(1)[d]
	L	0	0	0	3(1)[d]
-Centra	F	1(4)	1(3)	2(6)	6(19)*
	L	14(4)	11(3)	18(5)	43(13)*
-Vertebrae	F	0.3(1)	0	0.3(1)	0
	L	3(1)	0	4(1)	0
-Hemivertebra[†]	F	0	0	0	0.3(1)[d]
	L	0	0	0	3(1)[d]
-Missing Half of Cervical Vertebra[†]	F	0	0	0	0.3(1)[d]
	L	0	0	0	3(1)[d]
Ribs					
-Extra Ribs - Cervical[†]	F	0	0	0	0.7(2)
	L	0	0	0	7(2)
-Spurs	F	6(18)	5(13)	7(20)	19(57)*
	L	41(12)	36(10)	46(13)	87(26)*

Table 6 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Incidence of Fetal Alterations Among Litters of Rats[a]

Exposure Level		Ethylene Glycol Monomethyl Ether, ppm 0	3	10	50
Sternebrae					
-Delayed Ossification	F	44(125)	50(142)	45(131)	32(97)*
	L	97(28)	96(27)	96(27)	93(28)*
-Fused	F	0	0.4(1)	0	0
	L	0	4(1)	0	0
-Extra Site of Ossification	F	0	0	0.3(1)	0
	L	0	0	4(1)	0
Cartilage					
-Misaligned	F	0	0	0.3(1)	0
	L	0	0	4(1)	0
-Asymmetric	F	0.3(1)	0	0	0.3(1)[d]
	L	3(1)	0	0	3(1)[d]
-Fused	F	0	0	0	0.3(1)[d]
	L	0	0	0	3(1)[d]
Other					
-Misaligned Phalange[f]	F	0	0	0.3(1)	0
	L	0	0	4(1)	0

[a]Bred Fischer 344 rats were exposed to 0, 3, 10 or 50 ppm of EGME by inhalation for 6 hr/day on days 6 through 15 of gestation.

[b]All fetuses from litters with three fetuses or less were examined for soft tissue alterations and the heads were removed. In addition, one fetus at 10 ppm was examined for soft tissue alterations but the head was not removed.

[c]F = fetuses, L = litters.

[d]Alterations occurred in the same fetus.

[f]Considered a major malformation.

*Significantly different from the control value.

See Table A-7 for individual litter data.

Table 7

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Body Weights of Pregnant Rabbits[a]

		Ethylene Glycol Monomethyl Ether, PPM			
Exposure Level		0	3	10	50
Number of Dams		23	24	24	24
Maternal Body Weight (g) on Gestation Day	6	3985±332[b]	4032±352	4054±293	4211±260*
	9	3984±314	3987±350	4027±319	4085±412
	12	4002±307	4030±341	4080±309	4144±279
	15	4071±326	4083±337	4130±331	4127±294
	19	4128±301	4125±337	4170±320	4184±309
	29	4251±321	4179±392	4276±347	4377±304
Maternal Body Weight Gain (g) on Gestation Days	6-8	-1±61[b]	-45±64	-26±87	-125±258*
	9-11	18±62	43±52	52±54	59±217
	12-14	69±73	53±63	50±59	-17±109*
	15-18	57±89	42±60	40±49	58±125
	19-28	122±82	54±204	106±134	193±198
Overall	6-28	272±142	147±200	222±183	166±225

[a]Inseminated New Zealand white rabbits were exposed to 0, 3, 10 or 50 ppm of EGME by inhalation for 6 hr/day on days 6 through 18 of gestation.

[b]Mean±S.D.

*Significantly different from the control value by Dunnett's test.

See Table A-8 for individual animal data.

Table 8

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION
TERATOLOGY STUDY IN RATS AND RABBITS

Organ Weights and Hematologic Parameters in Pregnant Rabbits[a]

Exposure Level	Ethylene Glycol Monomethyl Ether, PPM			
	0	3	10	50
Number of Dams	23	24	24	24
Maternal Organ Weight on Gestation Day 29				
Liver - Absolute[b]	107.44±15.70	107.20±21.96	103.22±20.02	123.01±23.88*
Relative[c]	2.58±0.39	2.56±0.44	2.41±0.37	2.81±0.51
Spleen - Absolute	1.33±0.34	1.61±0.52	1.95±2.41	1.59±0.82
Relative	0.03±0.01	0.04±0.01	0.05±0.06	0.04±0.02
Thymus - Absolute	4.20±1.66	4.00±1.60	4.44±1.09	5.05±1.49
Relative	0.10±0.04	0.10±0.04	0.10±0.03	0.12±0.04
Hematologic Parameters Measured on Gestation Day 29				
RBC $X10^6/mm^3$	5.62±0.61[d]	5.24±0.59	5.36±0.31	5.37±0.50
HGB (g/dl)	12.8±1.3	12.0±1.2	12.1±0.8	12.1±0.9
PCV (%)	41.1±4.3	38.5±4.1	38.9±2.1	38.7±3.1
MCV (μ^3)	73.1±1.5	73.5±2.1	72.8±2.4	72.1±1.7
MCH (µug)	22.8±0.9	22.9±0.9	22.6±1.0	22.6±1.1
MCHC (%)	31.2±0.9	31.2±0.9	31.1±0.8	31.3±0.9
Platlets $X10^3/mm^3$	480±121	504±139	414±147	456±149
WBC $X10^3/mm^3$	4.3±2.2	5.0±3.3	3.9±2.7	4.4±2.4
N=	10	10	10	10

[a]Inseminated New Zealand white rabbits were exposed to 0, 3, 10 or 50 ppm of EGME by inhalation for 6 hr/day on days 6 through 18 of gestation.

[b]Grams, Mean±S.D.

[c]Grams organ weight/100 grams body weight, Mean±S.D.

[d]Mean±S.D.

*Significantly different from the control value by Dunnett's test.

See Table A-9 and A-10 for individual animal data.

Table 9

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Observations Made at the Time of Cesarean Section of Rabbits[a]

Exposure Level	Ethylene Glycol Monomethyl Ether, PPM			
	0	3	10	50
Number of Dams	30	30	29	30
Number of Maternal Deaths	2	0	1	0
Percent Pregnant[b]	80(24/30)	87(26/30)	86(25/29)	87(26/30)
Pregnancies Detected by Stain[c]	0/6	2/4	0/4	1/4
Percent Pregnant, Total[d]	80(24/30)	93(28/30)	86(25/29)	90(27/30)
Number of Litters	23	24	24	24
Corpora Lutea/Dam[e]	9±2	10±3	11±2	10±2
Implantation Sites/Dam[e]	8±2	8±3	9±3	8±2
Pre-implantation Loss[f]	16±20	17±22	18±23	15±19
Fetuses/Litter[e]	8±2	7±3	8±3	6±3
Resorptions/Litter[e,g]	0.3±0.7	0.6±0.8	1.0±1.1	1.9±2.0
% Implantations Resorbed[g]	4(7/180)	8(14/186)	11(23/210)*	24(46/191)*
% Litters with Resorptions[g]	22(5/23)	42(10/24)	58(14/24)*	67(16/24)*
Litters Totally Resorbed[g]	0	1	0	2
Resorptions/Litters with Resorptions[g]	1.4(7/5)	1.4(14/10)	1.6(23/14)	2.9(46/16)
% Dead Fetuses	0	0	0	0
Sex Ratio, M:F	50:50	49:51	48:52	50:50
Fetal Body Weight, (g)[h]	39.57±5.48	39.13±6.24	38.83±4.54	35.88±3.79*
Fetal Crown-Rump Length, mm[h]	96.2±5.7	95.1±5.3	94.8±5.9	95.0±3.3

[a]Inseminated New Zealand white rabbits were exposed to 0, 3, 10 or 50 ppm of EGME by inhalation for 6 hr/day on days 6 through 18 of gestation.
[b]Number of females with visible implantations at the time of cesarean section of necropsy/total number bred. Two animals each at the 3 and 50 ppm levels which delivered litters prior to cesarean section are included.
[c]Number of females with implantation sites detected only after staining the uterus with sodium sulfide/total number stained.
[d]Number of females pregnant at visual inspection of the uterus or after staining/total number bred.
[e]Mean±S.D.
[f]Percent per litter, mean±S.D.
[g]Resorptions detected only by staining the uterus were not included in these calculations.
[h]Mean of litter mean±S.D.
*Significantly different from the control value, by the appropriate statistical test.

See Table A-11 for individual animal data.

Table 10

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Incidence of Fetal Observations Among Litters of Rabbits[a]

Exposure Level		Ethylene Glycol Monomethyl Ether, ppm 0	3	10	50
		Number of Fetuses (Number of Litters)			
EXTERNAL EXAMINATION		173(23)	172(23)	187(24)	145(22)
SOFT TISSUE EXAMINATION		95(23)	93(23)	101(24)	80(22)
SKELETAL EXAMINATION		173(23)	172(23)	187(24)	145(22)
		% Affected (Number Affected)			
TOTAL MAJOR MALFORMATIONS[b]	F	4(6)	2(4)	2(3)	63(91)*
	L	26(6)	17(4)	13(3)	91(20)*
EXTERNAL ALTERATIONS					
Arthrogryposis†	F	0	0.6(1)	0	37(54)*
	L	0	4(1)	0	68(15)*
Anonychia†	F	0	0	0	10(14)*
	L	0	0	0	27(6)*
Polyonychia†	F	0	0	0	0.7(1)
	L	0	0	0	5(1)
Brachydactyly†	F	0	0	0	4(6)*
	L	0	0	0	18(4)*
Ectrodactyly†	F	0	0	0	4(6)*
	L	0	0	0	18(4)*
Syndactyly†	F	0	0	0	0.7(1)
	L	0	0	0	5(1)
Microphthalmia†	F	0	0	0	2(3)
	L	0	0	0	14(3)
Misalignment of Palatine Rugae	F	0	0	0	19(27)*
	L	0	0	0	50(11)*
Medial Rotation of Digits†	F	0	0	0	3(4)
	L	0	0	0	14(3)
Inward Rotation of Hind Feet†	F	0	0	0.5(1)	0.7(1)
	L	0	0	4(1)	5(1)
Omphalocele†	F	0	0	0	3(5)
	L	0	0	0	9(2)
Thinning of Abdominal Wall†	F	0	0	0	4(6)
	L	0	0	0	14(3)
Hypoplastic Tail†	F	0.6(1)[c]	0	0	1(2)
	L	4(1)	0	0	9(2)
Kinky Tail†	F	0	0	0	3(4)*
	L	0	0	0	18(4)*
Narrowed Tip of Tail	F	0	0	0	4(6)*
	L	0	0	0	27(6)*

Table 10 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Incidence of Fetal Observations Among Litters of Rabbits[a]

Exposure Level		Ethylene Glycol Monomethyl Ether, ppm 0	3	10	50
SOFT TISSUE ALTERATIONS					
Coarctation of the Aortic Arch†	F	0	0	0	16(13)*
	L	0	0	0	23(6)*
Ventricular Septal Defect†	F	0	0	0	43(34)*
	L	0	0	0	68(15)*
Agenesis of Subclavian Artery†	F	0	0	0	1(1)
	L	0	0	0	5(1)
Extra Vessel Off Aortic Arch	F	1(1)	3(3)	2(2)	1(1)
	L	4(1)	13(3)	8(2)	5(1)
Patent Ductus Arteriosis	F	0	1(1)	0	6(5)*
	L	0	4(1)	0	18(4)*
Hydropericardium	F	1(1)	1(1)	0	1(1)
	L	4(1)	4(1)	0	5(1)
Valvular Hematoma-Tricuspid	F	0	0	0	1(1)
	L	0	0	0	5(1)
Retroesophageal Subclavian	F	0	0	0	1(1)
	L	0	0	0	5(1)
Edema of the Pulmonary Artery	F	0	0	0	1(1)
	L	0	0	0	5(1)
Diaphragmatic Hernia†	F	0	0	0	1(1)
	L	0	0	0	5(1)
Hepatic Cysts-Multifocal	F	0	0	0	4(3)
	L	0	0	0	9(2)
Hepatic Necrosis-Focal	F	0	1(1)	0	1(1)
	L	0	4(1)	0	5(1)
Gall Bladder - Aplastic†	F	0	0	0	1(1)
	L	0	0	0	5(1)
- Hypoplastic	F	0	0	0	5(4)*
	L	0	0	0	18(4)*
- Bilobed	F	2(2)	0	0	0
	L	9(2)	0	0	0

Table 10 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Incidence of Fetal Observations Among Litters of Rabbits[a]

Exposure Level		Ethylene Glycol Monomethyl Ether, ppm 0	3	10	30
SOFT TISSUE ALTERATIONS -- Continued					
Spleen - Aplastic[†]	F	0	0	0	1(1)
	L	0	0	0	5(1)
- Hypoplastic[†]	F	0	0	0	31(25)*
	L	0	0	0	59(13)*
- Pale	F	4(4)	2(2)	1(1)	38(30)*
	L	4(1)	4(1)	4(1)	73(16)*
-Accessory	F	0	0	0	4(3)
	L	0	0	0	14(3)
-Bilobed	F	0	0	0	1(1)
	L	0	0	0	5(1)
Adrenal-Accessory	F	0	0	1(1)	3(2)
	L	0	0	4(1)	5(1)
Kidney - Agenesis-Unilateral[†]	F	0	0	0	3(2)
	L	0	0	0	9(2)
- Misshapen[†]	F	0	1(1)	0	0
	L	0	4(1)	0	0
- Dilated Renal Pelvis[†]	F	0	1(1)	1(1)	35(28)*
	L	0	4(1)	4(1)	64(14)*
-Mineral-Like Renal Deposits	F	0	1(1)	1(1)	1(1)
	L	0	4(1)	4(1)	5(1)
Ureter - Dilated	F	0	0	0	9(7)*
	L	0	0	0	27(6)*
- Convoluted	F	3(3)	2(2)	0	15(12)*
	L	9(2)	9(2)	0	36(8)*
- Retrocaval	F	0	0	0	3(2)
	L	0	0	0	9(2)
Ovarian Agenesis[†]	F	0	0	0	1(1)
	L	0	0	0	5(1)
Hyperplastic Ovary[†]	F	0	0	0	1(1)
	L	0	0	0	5(1)
Paraovarian Cyst	F	0	1(1)	1(1)	11(9)*
	L	0	5(1)	4(1)	36(8)*
Testicular Cyst	F	0	0	0	6(5)
	L	0	0	0	14(3)

Table 10 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Incidence of Fetal Observations Among Litters of Rabbits[a]

Exposure Level		Ethylene Glycol Monomethyl Ether, ppm 0	3	10	50
SKELETAL ALTERATIONS					
Skull					
- Enlarged Interparietals	F	0	0	0	3(5)
	L	0	0	0	5(1)
- Shortened Nasals, Maxillae and Mandibles†	F	0	0	0	4(6)
	L	0	0	0	5(1)
- Foramen-Frontal	F	0	0	0.5(1)	0
	L	0	0	4(1)	0
- Crooked Hyoid	F	4(6)	1(2)	1(2)	7(10)
	L	13(3)	9(2)	8(2)	32(7)
-Delayed Ossification - Hyoid	F	0.6(1)	1(2)	1(2)	10(14)*
	L	4(1)	9(2)	8(2)	36(8)*
- Frontals, Parietals, and Interparietals	F	0	0	0.5(1)	0
	L	0	0	4(1)	0
Extremities					
- Missing Phalange(s)†	F	0	0	0	5(7)*
	L	0	0	0	18(4)*
- Missing Metacarpal(s)†	F	0	0	0	3(4)
	L	0	0	0	9(2)
- Missing Metatarsal(s)†	F	0	0	0	6(9)*
	L	0	0	0	18(4)*
- Delayed Ossification Tarsal(s)	F	0	2(3)	0.5(1)	12(17)*
	L	0	13(3)	4(1)	36(8)*
-Shortened Long Bones†	F	0	0	0	0.7(1)
	L	0	0	0	5(1)
Ribs					
- Extra - Cervical†	F	0	0	0	1(2)
	L	0	0	0	9(2)
- Lumbar	F	0	0	0	9(13)*
	L	0	0	0	32(7)*
- Shortened†	F	0	0	0	3(4)
	L	0	0	0	9(2)
- Fused†	F	1(2)	0.6(1)	0.5(1)	0.7(1)
	L	9(2)	4(1)	4(1)	5(1)
- Forked†	F	0.6(1)	0	0	0.7(1)
	L	4(1)	0	0	5(1)

Table 10 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Incidence of Fetal Observations Among Litters of Rabbits[a]

Exposure Level		Ethylene Glycol Monomethyl Ether, ppm 0	3	10	30
SKELETAL ALTERATIONS — Continued					
- Thickened	F	0.6(1)	0.6(1)	0	0
	L	4(1)	4(1)	0	0
- Calloused†	F	0.6(1)	0	0	0
	L	4(1)	0	0	0
- Irregular Pattern of Ossification	F	0	0	0	1(2)
	L	0	0	0	9(2)
- Asymmetrical Cartilage	F	0	0	0	0.7(1)
	L	0	0	0	5(1)
- Extra Site of Ossification	F	0	0	0	0.7(1)
	L	0	0	0	5(1)
Vertebrae					
- Fused†	F	1(2)[d]	0	0	0.7(1)
	L	9(2)	0	0	5(1)
- Missing					
- Caudal†	F	0.6(1)[c]	0	0	1(2)
	L	4(1)	0	0	9(2)
- Sacral†	F	0.6(1)[c]	0	0	0.7(1)
	L	4(1)	0	0	5(1)
- Partial†	F	0.6(1)	0	0	0
	L	4(1)	0	0	0
- Atlas†	F	0.6(1)[d]	0	0	0
	L	4(1)	0	0	0
- Extra Site of Ossification	F	0.6(1)	0.6(1)	0	0.7(1)
	L	4(1)	4(1)	0	5(1)
- Delayed Ossification	F	0	0.6(1)	0	1(2)
	L	0	4(1)	0	9(2)
- Misaligned†	F	0	0	0	0.7(1)
	L	0	0	0	5(1)
Centra					
- Misaligned	F	0.6(1)	0	0	0
	L	4(1)	0	0	0
- Delayed Ossification	F	2(4)	1(2)	0*	8(11)
	L	17(4)	9(2)	0*	36(8)
- Fused	F	0.6(1)	0	0	0
	L	4(1)	0	0	0
- Extra Site of Ossification	F	0	0	0	0.7(1)
	L	0	0	0	5(1)
- Fused to Vertebra	F	0	0	0	1(2)
	L	0	0	0	9(2)

Table 10 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Incidence of Fetal Observations Among Litters of Rabbits[a]

Exposure Level		Ethylene Glycol Monomethyl Ether, ppm 0	3	10	50
SKELETAL ALTERATIONS -- Continued					
Sternebrae					
- Fused	F	2(3)	1(2)	0	8(11)
	L	13(3)	9(2)	0	36(8)
- Delayed Ossification	F	47(82)	54(93)	66(123)*	88(127)*
	L	100(23)	100(23)	100(24)*	100(22)*
- Asymmetric Cartilage	F	0.6(1)	0.6(1)	1(2)	2(3)
	L	4(1)	4(1)	9(2)	14(3)
- Extra Site of Ossification	F	0	0	0	3(4)
	L	0	0	0	14(3)
Other					
- Double Sternum†	F	0	0	0	0.7(1)
	L	0	0	0	5(1)
- Irregular Pattern of Ossification - Scapula	F	0	0	0	1(2)
	L	0	0	0	9(2)

[a]Inseminated New Zealand white rabbits were exposed to 0, 3, 10 or 50 ppm of EGME by inhalation for 6 hr/day on days 6 through 18 of gestation.
[b]Numbers reflect the number of fetuses and litters which exhibited at least one major malformation. Numerous fetuses at 50 ppm exhibited multiple alterations. F=Fetuses, L=Litters.
[c]Alterations occurred in the same fetus.
[d]Alterations occurred in the same fetus.
†Considered a major malformation.
*Significantly different from the control value.

See Tables A-12 and A-13 for individual litter data.

TABLE A-1

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Body Weights and Body Weight Gains of Pregnant Rats[a]

Exposure Level: Control (0 ppm)

ANIMAL NUMBER	MATERNAL BODY WEIGHT (G) DAYS OF GESTATION 6	9	12	16	21	MATERNAL BODY WEIGHT GAIN (G) 6-9	9-12	12-16	16-21
8109699	189.9	194.7	204.2	214.4	245.6	4.8	9.5	10.2	31.2
8109700	186.2	190.0	196.2	211.2	246.7	3.8	6.2	15.0	35.5
8109701	199.9	201.4	208.2	222.6	258.6	1.5	6.8	14.4	36.0
8109702	193.5	192.9	201.0	204.3	216.0	-0.6	8.1	3.3	11.7
8109703	202.0	205.3	221.1	238.1	284.0	3.3	15.8	17.0	45.9
8109719	184.4	191.0	196.5	212.5	250.0	6.6	5.5	16.0	37.5
8109720	190.7	196.9	205.3	222.9	262.1	6.2	8.4	17.6	39.2
8109721	193.2	200.6	214.1	229.5	279.5	7.4	13.5	15.4	50.0
8109722	192.5	196.0	205.3	226.8	279.1	3.5	9.3	21.5	52.3
8109723	191.4	194.4	206.1	219.5	267.6	3.0	11.7	13.4	48.1
8109739	191.3	197.6	207.3	224.4	267.3	6.3	9.7	17.1	42.9
8109740	197.2	202.6	209.5	226.2	271.2	5.4	6.9	16.7	45.0
8109746	191.1	193.8	204.4	219.8	260.3	2.7	10.6	15.4	40.5
8109747	184.8	189.1	197.7	209.7	223.4	4.3	8.6	12.0	13.7
8109748	187.0	193.8	207.2	220.6	267.0	6.8	13.4	13.4	46.4
8109750	187.5	193.0	207.6	221.4	251.5	5.5	14.6	13.8	30.1
8109751	185.6	192.9	200.8	217.4	253.4	7.3	7.9	16.6	36.0
8109768	189.2	192.8	203.5	216.8	256.6	3.6	10.7	13.3	39.8
8109769	197.8	205.1	211.3	230.3	273.1	7.3	6.2	19.0	42.8
8109770	179.7	182.9	192.4	207.9	251.9	3.2	9.5	15.5	44.0
8109771	192.2	199.0	205.7	221.3	251.5	6.8	6.7	15.6	30.2
8109786	191.2	199.9	206.5	219.1	261.8	8.7	6.6	12.6	42.7
8109787	186.9	195.2	200.4	215.4	264.0	8.3	5.2	15.0	48.6
8109788	192.0	214.5	204.5	220.4	258.0	22.5	-10.0	15.9	37.6
8109789	205.6	198.4	217.7	227.0	281.6	-7.2	19.3	9.3	54.6
8109803	195.8	200.3	212.0	224.9	265.5	4.5	11.7	12.9	40.6
8109804	193.6	197.9	207.9	225.1	272.5	4.3	10.0	17.2	47.4
8109813	183.2	191.1	197.3	216.8	262.1	7.9	6.2	19.5	45.3
8109814	174.0	175.2	191.2	212.8	252.3	1.2	16.0	21.6	39.5
MEAN	190.7	195.8	204.9	220.0	259.8	5.1	9.1	15.0	39.8
S.D.	6.55	7.20	6.87	7.35	15.29	4.62	5.10	3.64	9.74

TABLE A-1 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Body Weights and Body Weight Gains of Pregnant Rats[a]

Exposure Level: 3 ppm

ANIMAL NUMBER	MATERNAL BODY WEIGHT (G) DAYS OF GESTATION 6	9	12	16	21	MATERNAL BODY WEIGHT GAIN (G) 6-9	9-12	12-16	16-21
8109705	189.0	188.8	199.9	210.6	247.8	-0.2	11.1	10.7	37.2
8109707	189.3	194.3	200.2	219.3	265.6	5.0	5.9	19.1	46.3
8109708	190.0	193.2	200.6	214.5	256.8	3.2	7.4	13.9	42.3
8109724	191.6	195.5	205.6	225.0	274.0	3.9	10.1	19.4	49.0
8109725	215.0	218.0	226.5	249.1	298.6	3.0	8.5	22.6	49.5
8109726	193.5	198.2	206.8	223.0	269.3	4.7	8.6	16.2	46.3
8109727	196.2	194.6	207.2	226.1	268.8	-1.6	12.6	18.9	42.7
8109728	190.3	197.4	206.7	219.2	260.9	7.1	9.3	12.5	41.7
8109741	194.3	197.1	203.7	212.1	230.4	2.8	6.6	8.4	18.3
8109742	195.1	195.4	208.8	226.6	264.9	0.3	13.4	17.8	38.3
8109752	189.2	197.0	207.2	222.9	263.8	7.8	10.2	15.7	40.9
8109753	193.9	199.3	210.5	222.2	258.1	5.4	11.2	11.7	35.9
8109754	191.6	191.8	201.4	216.9	261.1	0.2	9.6	15.5	44.2
8109755	195.6	196.9	209.0	221.0	250.9	1.3	12.1	12.0	29.9
8109756	193.2	193.6	208.6	222.6	265.1	0.4	15.0	14.0	42.5
8109772	184.6	194.0	199.4	218.8	251.6	9.4	5.4	19.4	32.8
8109774	193.6	198.3	202.6	220.2	244.6	4.7	4.3	17.6	24.4
8109775	189.2	195.9	203.5	220.7	259.9	6.7	7.6	17.2	39.2
8109776	188.4	189.9	197.4	209.7	250.2	1.5	7.5	12.3	40.5
8109790	192.7	190.1	202.6	213.1	250.8	-2.6	12.5	10.5	37.7
8109791	197.3	195.4	208.7	221.6	273.9	-1.9	13.3	12.9	52.3
8109792	187.7	190.8	200.7	214.1	252.8	3.1	9.9	13.4	38.7
8109793	185.2	185.9	196.6	210.0	253.0	0.7	10.7	13.4	43.0
8109805	191.3	194.2	201.0	221.9	258.3	2.9	6.8	20.9	36.4
8109806	196.4	193.5	205.2	218.8	261.7	-2.9	11.7	13.6	42.9
8109807	188.2	194.0	202.6	220.5	269.4	5.8	8.6	17.9	48.9
8109815	183.9	185.5	195.2	207.9	245.5	1.6	9.7	12.7	37.6
8109816	185.9	192.2	197.3	210.9	241.7	6.3	5.1	13.6	30.8
MEAN	191.9	194.7	204.1	219.3	258.9	2.8	9.5	15.1	39.6
S.D.	5.84	5.75	6.08	7.90	12.85	3.25	2.75	3.49	7.56

TABLE A-1 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Body Weights and Body Weight Gains of Pregnant Rats[a]

Exposure Level: 10 ppm

ANIMAL NUMBER	MATERNAL BODY WEIGHT (G) DAY(S) OF GESTATION 6	9	12	16	21	MATERNAL BODY WEIGHT GAIN (G) 6-9	9-12	12-16	16-21
8109709	166.2	189.8	197.2	213.8	258.0	3.6	7.4	16.6	44.2
8109710	190.1	197.9	204.6	223.1	264.7	-0.2	6.7	18.5	41.6
8109713	191.9	190.4	200.8	216.1	259.9	-1.5	10.4	15.3	43.8
8109729	187.7	192.3	202.8	217.3	262.5	4.6	10.5	14.5	45.2
8109730	198.4	201.2	212.0	229.3	277.0	2.8	10.8	17.3	47.7
8109731	195.8	198.0	206.9	223.6	259.3	2.2	8.9	16.7	35.7
8109732	193.9	198.6	210.5	229.2	277.2	4.7	11.9	18.7	48.0
8109733	192.4	196.6	205.8	221.5	252.5	4.2	9.2	15.7	31.0
8109743	196.4	201.6	212.5	225.4	271.2	3.2	10.9	12.9	45.8
8109757	187.8	184.9	198.7	211.9	254.0	-2.9	13.8	13.2	42.1
8109758	183.3	186.2	195.9	219.0	245.2	2.9	9.7	23.1	26.2
8109759	186.4	189.6	203.7	209.5	264.7	3.2	14.1	5.8	55.2
8109760	187.9	186.7	193.4	220.1	263.3	-1.2	6.7	26.7	43.2
8109762	206.4	211.1	221.2	234.9	274.0	4.7	10.1	13.7	39.1
8109777	185.9	187.9	197.0	219.1	260.8	2.0	9.1	22.1	41.7
8109778	185.9	189.3	196.6	218.8	253.0	3.4	7.3	22.2	34.2
8109779	191.5	193.1	201.8	219.4	254.9	1.6	8.7	17.6	35.5
8109780	193.4	196.8	203.4	219.0	257.0	3.4	6.6	15.6	38.0
8109794	185.7	193.3	198.6	211.8	257.7	7.6	5.3	13.2	45.9
8109795	190.5	193.4	204.4	220.0	263.2	2.9	11.0	15.6	43.2
8109796	188.9	194.1	203.2	212.4	255.1	5.2	9.1	9.2	42.7
8109797	203.9	202.0	215.9	219.5	241.8	-1.9	13.9	3.6	22.3
8109798	193.7	195.9	211.5	223.8	270.4	2.2	15.6	12.3	46.6
8109808	190.5	195.8	200.3	219.5	258.4	5.3	4.5	19.2	38.9
8109809	194.5	198.0	204.3	213.5	260.4	3.5	6.3	9.2	46.9
8109810	184.6	189.8	198.0	213.0	258.5	5.2	8.2	15.0	45.5
8109817	205.4	207.3	216.5	235.3	282.6	1.9	9.2	18.8	47.3
8109818	185.8	194.6	203.8	214.9	252.1	8.8	9.2	11.1	37.2
MEAN	192.0	194.9	204.3	219.8	261.0	2.9	9.5	15.5	41.2
S.D.	6.36	6.21	6.91	6.61	9.42	2.67	2.72	5.06	7.00

TABLE A-1 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Body Weights and Body Weight Gains of Pregnant Rats[a]

Exposure Level: 50 ppm

ANIMAL NUMBER	MATERNAL BODY WEIGHT (G) DAYS OF GESTATION 6	9	12	16	21	MATERNAL BODY WEIGHT GAIN (G) 6-9	9-12	12-16	16-21
8109714	193.6	191.0	203.5	215.9	255.9	-2.6	12.5	12.4	40.0
8109715	196.1	198.3	207.2	228.1	267.1	2.2	8.9	20.9	39.0
8109716	191.5	194.2	207.9	216.1	233.0	2.7	13.7	8.2	16.9
8109717	193.3	193.4	201.4	216.9	259.7	0.1	8.0	15.5	42.8
8109718	196.2	193.9	202.5	219.0	263.0	-2.3	8.6	16.5	44.0
8109734	197.2	202.1	208.8	231.6	279.4	4.9	6.7	22.8	47.8
8109735	197.7	202.5	216.1	236.4	279.9	4.8	13.6	20.3	43.5
8109736	195.9	203.0	209.5	228.6	275.2	7.1	6.5	19.1	46.6
8109737	191.0	192.9	201.7	219.1	260.5	1.9	8.8	17.4	41.4
8109738	201.6	206.0	211.2	214.0	265.1	4.4	5.2	2.8	51.1
8109744	192.6	197.7	208.8	223.6	266.2	5.1	11.1	14.8	42.6
8109745	193.3	196.5	205.2	220.1	262.1	3.2	8.7	14.9	42.0
8109763	204.3	202.1	212.4	225.5	260.7	-2.2	10.3	13.1	35.2
8109764	198.3	202.3	216.2	233.0	271.8	4.0	13.9	16.8	38.8
8109765	202.6	211.3	223.1	237.1	279.3	8.7	11.8	14.0	42.2
8109766	192.2	195.8	203.6	222.8	266.1	3.6	7.8	19.2	43.3
8109767	186.9	192.9	205.9	217.5	255.6	6.0	13.0	11.6	38.1
8109781	190.2	186.4	200.3	217.4	253.5	-3.8	13.9	17.1	36.1
8109782	192.2	192.7	205.5	220.6	256.4	0.5	12.8	15.1	35.8
8109783	192.0	196.4	205.0	221.0	257.9	4.4	8.6	16.0	36.9
8109784	190.7	194.0	204.3	221.5	270.1	3.3	10.3	17.2	48.6
8109785	188.1	194.5	205.4	223.9	263.5	6.4	10.9	18.5	39.6
8109799	194.3	196.4	208.1	223.4	270.5	2.1	11.7	15.3	47.1
8109800	192.4	192.4	205.8	218.4	269.6	0.0	13.4	12.6	51.2
8109801	189.3	191.4	203.0	215.7	251.0	2.1	11.6	12.7	35.3
8109802	194.1	200.8	212.4	221.0	259.9	6.7	11.6	8.6	38.9
8109811	200.8	173.5	186.7	210.4	259.6	-27.3	13.2	23.7	49.2
8109812	202.6	206.3	212.7	228.0	272.6	3.7	6.4	15.3	44.6
8100386	184.3	188.7	199.1	212.1	248.4	4.4	10.4	13.0	36.3
8100367	196.8	203.7	213.3	226.6	271.6	6.9	9.6	13.3	45.0
MEAN	194.4	196.4	206.9	222.2	263.5	2.0	10.4	15.3	41.3
S.D.	4.82	7.17	6.57	6.75	10.11	6.35	2.53	4.33	6.60
	*					*			

[a]Bred Fischer 344 rats were exposed to 0, 3, 10 or 50 ppm of EGME for 6 hr/day on days 6 through 15 of gestation.

*Significantly different from control value.

BEST COPY AVAILABLE

TABLE A-2

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Food Consumption of Pregnant Rats [a]

Exposure Level: Control (0 ppm)

ANIMAL NUMBER	MATERNAL FOOD CONSUMPTION (G/DAY) DAYS OF GESTATION 0-9	9-12	12-15	15-18	18-21
8109699	12.7	13.9	15.2	15.7	17.0
8109700	13.3	13.8	15.2	15.8	17.5
8109701	12.6	13.5	14.3	14.5	14.2
8109702	12.9	13.4	14.2	15.3	16.1
8109703	13.7	15.9	17.6	17.9	18.1
8109719	14.5	14.2	13.5	16.2	16.2
8109720	13.5	14.9	15.3	17.3	17.4
8109721	13.8	16.3	15.0	16.9	17.7
8109722	15.9	15.1	16.4	18.3	19.9
8109723	14.4	15.6	15.0	17.3	16.9
8109739	14.3	14.5	15.1	18.7	17.5
8109740	15.0	14.6	16.1	17.5	17.5
8109746	13.4	14.7	15.9	16.9	16.8
8109747	12.6	14.3	16.0	16.7	17.8
8109748	12.8	14.7	14.6	15.9	16.6
8109750	13.5	15.8	16.4	16.7	16.9
8109751	12.9	14.5	16.1	16.8	15.9
8109768	12.9	15.2	15.7	16.3	17.2
8109769	15.1	15.9	16.2	18.1	16.5
8109770	12.9	14.1	13.5	16.1	15.2
8109771	12.9	14.2	14.3	17.4	16.8
8109786	13.3	15.1	13.8	16.6	16.5
8109787	12.7	13.6	14.9	17.2	17.1
8109788	15.7	16.7	15.4	17.7	18.0
8109789	14.6	14.5	16.1	17.3	18.6
8109805	14.0	14.6	15.5	16.5	16.8
8109804	13.6	14.1	15.5	17.4	17.4
8109813	13.1	13.3	14.6	16.9	17.0
8109814	6.08	12.9	16.0	17.7	17.4
MEAN	13.6	14.6	15.3	16.9	17.1
S.D.	0.83	0.94	0.94	0.93	1.03

BEST COPY AVAILABLE

TABLE A-2 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Food Consumption of Pregnant Rats [a]

Exposure Level: 3 ppm

ANIMAL NUMBER	DAILY FOOD CONSUMPTION (G/DAY) DAYS OF GESTATION 6-9	9-12	12-15	15-18	18-21
8109704	15.6	16.6	17.3	18.4	16.7
8109705	12.2	14.0	14.0	14.5	13.8
8109707	12.8	14.1	15.7	15.2	17.2
8109706	12.3	14.5	15.6	15.8	16.0
8109724	13.6	15.6	16.4	18.6	16.8
8109725	14.8	16.5	17.2	20.1	19.3
8109726	14.9	16.5	15.4	18.6	17.7
8109727	13.9	15.6	15.7	18.1	17.0
8109728	14.9	16.3	15.0	17.0	16.8
8109741	15.1	14.3	15.7	16.6	16.6
8109742	13.3	14.9	15.7	17.9	16.3
8109752	14.6	17.4	17.0	16.2	16.9
8109753	15.2	17.5	16.5	16.7	16.6
8109754	13.7	14.9	15.3	16.5	16.8
8109755	15.2	17.4	16.5	15.6	16.4
8109756	14.4	16.2	16.9	16.5	16.8
8109772	13.2	15.3	15.4	16.8	15.7
8109774	13.6	14.4	28.0	16.4	20.5
8109775	14.3	15.4	15.7	16.8	16.5
8109776	13.5	15.3	15.3	16.1	16.2
8109790	13.6	15.5	15.7	17.3	16.7
8109791	15.2	16.1	16.1	17.9	17.4
8109792	12.8	13.6	15.1	17.8	17.3
8109793	12.2	14.5	14.0	16.4	16.5
8109605	13.4	12.5	15.3	16.2	16.2
8109606	13.9	13.9	15.4	16.7	16.0
8109607	13.9	13.5	14.6	15.9	15.9
8109615	12.8	12.9	13.7	15.3	15.5
8109616	13.3	13.9	13.4	15.9	16.3
MEAN	13.9	15.1	15.5	16.8	16.6
S.D.	0.98	1.34	1.00	1.22	0.52

BEST COPY AVAILABLE

TABLE A-2 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Food Consumption of Pregnant Rats [a]

Exposure Level: 10 ppm

ANIMAL NUMBER	MATERNAL FOOD CONSUMPTION (G/DAY) DAYS OF GESTATION 6-9	9-12	12-15	15-18	18-21
8109709	13.2	13.6	14.5	14.7	15.5
8109710	12.2	14.2	15.3	16.3	17.9
8109713	12.8	14.4	15.0	15.2	17.1
8109729	13.6	14.8	14.6	16.9	16.4
8109730	15.0	16.2	15.9	17.4	17.5
8109731	13.3	15.6	16.1	17.6	16.9
8109732	14.8	16.5	17.0	18.8	18.0
8109733	14.5	15.5	15.7	17.0	16.0
8109743	15.6	15.7	16.1	18.4	16.9
8109757	12.6	14.5	15.1	14.6	15.9
8109758	13.3	14.3	15.5	16.5	17.5
8109759	13.7	15.9	16.0	15.2	14.6
8109760	11.7	14.8	15.2	17.3	17.1
8109762	14.8	18.5	17.6	15.7	18.0
8109777	13.4	15.7	15.9	17.0	15.9
8109778	14.5	15.7	17.0	16.1	14.7
8109779	14.3	15.6	15.6	16.9	17.1
8109780	13.7	14.5	14.9	16.0	14.4
8109794	14.4	14.1	15.0	17.4	17.3
8109795	13.5	15.4	16.2	18.7	17.3
8109796	13.2	15.3	13.6	15.4	15.5
8109797	14.3	15.4	15.6	18.8	18.0
8109798	13.5	16.0	15.0	17.5	18.0
8109808	14.3	13.6	16.0	16.8	15.3
8109809	14.2	13.4	14.8	14.0	15.8
8109810	13.6	12.5	14.7	16.7	17.9
8109817	14.5	15.7	16.8	18.5	18.0
8109818	15.3	14.8	14.5	14.7	15.5
MEAN	13.8	15.1	15.5	16.7	16.6
S.D.	0.92	1.16	0.90	1.36	1.16

Table A-6 (Continued)

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual Body Weights During Lactation of Exposed Females[a]

Exposure Level: 100 ppm

Animal Number	Post-Partum Day 1	4	7	14	21
80A-3072	278	289	302	311	297
3073	290	302	317	331	323
3074	337	354	345	366	335
3075	353	361	364	385	337
3076	313	316	329	—[e]	340
3077	312	327	329	339	332
3078	299	314	311	340	310
3079	318	327	349	353	340
3080	337	345	341	336	329
3082	309	311	328	360	325
3083	283	306	299	332	313
3084	332	366	374	368	366
3085	304	326	320	331	324
3086	312	330	348	369	342
3087	299	311	337	356	330
3088	314	346	340	369	325
3089	348	—[f]	—[f]	—[f]	—[f]
3090	356	350	363	370	380
MEAN	316	328	335	351	332
±S.D.	±23	±22	±21	±20	±19

Table A-6 (Continued)

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual Body Weights During Lactation of Exposed Females[a]

Exposure Level: 300 ppm

Animal Number	Post-Partum Day 1	4	7	14	21
80A-3096	294	308	323	336	329
3098	300	306	308	337	303
3099	283	276	284	310	293
3100	320	321	339	341	341
3101	295	306	318	295	317
3105	345	352	368	373	346
3106	247	264	264	277	285
3107	272	314	326	343	322
3108	289	291	301	307	300
3109	258	277	276	313	297
3112	308	314	322	351	324
3113	313	319	320	339	333
3115	292	287	298	331	318
MEAN ±S.D.	294 ±26	303 ±23	311 ±28	327 ±26	316 ±19

[a]Female rats were exposed to 0, 30, 100, or 300 ppm EGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, animals were bred with unexposed males.

[b]Body weight in grams.

[c]No weight taken.

[d]No pups were found alive on day 4 of lactation. No additional body weights were taken after day 4.

[e]Incorrect weight was recorded: value was not included in calculation of mean±S.D.

[f]Female was found moribund on day 2 of lactation and was submitted for a pathological examination.

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Table A-7

SIME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual and Mean Litter Sizes of Exposed Females Mated to Unexposed Males[a]

Exposure Level: 0 ppm

Maternal Animal Number	Date of Delivery	Cohabitation to Parturition (Days)[b]	Born Dead	Number of Live Pups on Post-Partum Day 0	1	4[c]	7	14	21	Total Number of Dead Found Day 1-21
301A-3000	11/19/80	25	1[d]	10	10	10	8	8	8	0
3001	11/17/80	24	0	15	15	15	8	8	8	0
3002	11/17/80	24	0	12	12	12	8	8	8	0
3003	11/18/80	25	0	13	13	13	8	8	8	0
3004	11/19/80	25	0	13	14	14	8	8	8	0
3005	11/16/80	23	0	13	13	13	8	8	8	0
3006	11/19/80	25	0	16	16	16	8	8	8	0
3007[e]	—	—	—	—	—	—	—	—	—	—
3008[e]	—	—	—	—	—	—	—	—	—	—
3009[f]	11/16/80	23	0	9	12	12	8	8	8	0
3010[f]	11/15/80	23	0	8	16	15	8	8	8	0
3011	11/19/80	26	0	12	12	12	8	8	8	0
3012	11/17/80	24	1	10	10	10	8	8	8	0
3013[f]	11/16/80	23	0	1	14	14	8	8	8	0
3014	11/18/80	25	0	14	14	14	8	8	8	0
3015	11/15/80	23	0	13	13	13	8	8	8	0
3016	11/19/80	26	0	4	4	4	4	4	4	0
3017	11/16/80	23	2	13	13	13	8	8	8	0
3018[e]	—	—	—	—	—	—	—	—	—	—
3019	11/17/80	24	0	16	16	15	8	8	8	0
3020	11/16/80	23	0	16	16	16	8	8	8	0
3021	11/20/80	27	0	15	15	15	8	8	8	0
3022[e]	—	—	—	—	—	—	—	—	—	—
3023[f]	11/15/80	22	0	3	15	14	8	8	8	0
3024	11/19/80	26	0	17	16	15	8	8	8	0
3025	11/19/80	26	0	15	15	15	8	8	8	0
3026	11/16/80	23	2	13	13	13	8	8	8	0
3027[f]	11/15/80	23	0	0	12	12	8	8	8	2
3028	11/19/80	25	0	12	12	12	8	8	8	0
3029	11/18/80	25	3	11	11	11	8	8	8	0
	MEAN±S.D.	23±5	0.35±0.80	11±5	13±3	13±2	8±0.3	8±0.3	8±0.3	0.08±0.39

BEST COPY AVAILABLE

Table A-7 Continued)

SUBJ: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual and Mean Litter Sizes of Exposed Females Mated to Unexposed Males[a]

Exposure Level: 30 ppm

Maternal Animal Number	Date of Delivery	Cohabitation to Parturition (Days)[b]	Born Dead	Number of Live Pups on Post-Partum Day 0	1	14	7	14	21	Total Number of Dead Found Day 1-21
301-3036	11/17/80	24	0	14	14	14	5	8	8	0
3037	11/18/80	25	0	9	9	9	8	8	8	0
3038	11/18/80	25	0	12	12	12	8	8	8	0
3039[e]	—	—	—	—	—	—	—	—	—	—
3040[e]	—	—	—	—	—	—	—	—	—	—
3041	11/17/80	24	0	15	15	15	8	8	8	0
3042[e]	—	—	—	—	—	—	—	—	—	—
3043[f]	11/18/80	25	0	2	17	17	8	8	8	0
3044	11/17/80	24	1	16	16	16	8	8	8	0
3045	11/17/80	24	0	19	19	18	8	8	8	0
3046[e]	—	—	—	—	—	—	—	—	—	—
3047	11/17/80	24	0	12	12	12	7[g]	6	6	1
3048[e]	—	—	—	—	—	—	—	—	—	—
3049[f]	11/17/80	24	0	3	16	15	8	8	8	1
3050	11/17/80	24	0	14	14	14	8	8	8	0
3051	11/16/80	23	0	12	12	12	8	8	8	0
3052	11/19/80	25	0	17	17	17	8	8	8	0
3053	11/19/80	25	0	17	16	16	8	8	8	0
3054[e]	—	—	—	—	—	—	—	—	—	—
3055[e]	—	—	—	—	—	—	—	—	—	—
3056[e]	—	—	—	—	—	—	—	—	—	—
3057[f]	11/19/80	25	0	8	10	9	8	8	8	0
3058[f]	11/18/80	25	0	7	14	13	8	8	8	0
3059	11/18/80	25	0	14	14	14	8	8	8	0
3060	11/17/80	24	0	10	10	10	8	8	8	0
3061	11/16/80	23	0	14	13	13	8	8	8	1
3062[f]	11/18/80	25	0	1	2	0	0	0	0	0
3063	11/19/80	25	0	17	16	16	8	8	8	0
3064	11/17/80	24	1	13	13	13	8	8	8	0
3065	11/19/80	25	0	14	14	14	8	8	8	0
	MEAN±S.D.	25±1	0.09±0.29	12±5	13±4	12±4	8±2	8±2	8±2	0.14±0.35

BEST COPY AVAILABLE

Table A-7 (Continued)

SOME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual and Mean Litter Sizes of Exposed Females Mated to Unexposed Males[a]

Exposure Level: 100 ppm

Maternal Animal Number	Date of Delivery	Cohabitation to Parturition (Days)[b]	Born Dead	Number of Live Pups on Post-Partum Day 0	1	4[d]	7	14	21	Total Number of Dead Found Day 1-21
SCA-3071[e]	—	—	—	—	—	—	—	—	—	—
3072	11/17/80	24	0	11	11	11	8	8	8	0
3073[f]	11/17/80	24	0	12	13	13	8	8	8	0
3074[f]	11/18/80	25	0	11	13	13	8	8	8	0
3075	11/16/80	23	1	13	13	12	8	8	8	0
3076	11/16/80	23	0	12	12	12	8	8	8	0
3077	11/17/80	24	0	12	12	12	8	8	8	0
3078	11/18/80	25	1	12	12	12	8	8	8	0
3079	11/17/80	24	0	9	9	9	8	8	8	0
3080	11/21/80	28	0	15	15	15	8	8	8	0
3081[a]	—	—	—	—	—	—	—	—	—	—
3082	11/16/80	23	0	17	17	17	8	8	8	0
3083[f]	11/18/80	25	0	13	15	15	8	8	8	0
3084	11/19/80	26	0	14	13	13	8	8	8	0
3085	11/18/80	25	0	17	17	17	8	8	8	0
3086	11/16/80	23	0	12	12	12	8	8	8	0
3087	11/16/80	23	0	8	8	8	8	8	8	0
3088	11/19/80	26	0	16	16	16	8	8	8	0
3089	11/22/80	29	0	11	10[i]	—	—	—	—	3
3090	11/17/80	24	0	12	12	12	8	8	8	0
	MEAN±S.D.	25±2	0.11±0.32	13±2	13±3	13±2	8±0	8±0	8±0	0.17±0.71

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Table A-7 (Continued)

DGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual and Mean Litter Sizes of Exposed Females Mated to Unexposed Males[a]

Exposure Level: 300 ppm

Maternal Animal Number	Date of Delivery	Cohabitation to Parturition (Days)[b]	Born Dead	Number of Live Pups on Post-Partum Day 0	1	4[c]	7	14	21	Total Number of Dead Found Day 1-21
3001-3096	11/23/80	30	4	16	16	14	8	8	8	2
3097[e]	—	—	—	—	—	—	—	—	—	—
3098	11/19/80	26	0	10	11	11	8	8	8	0
3099	11/18/80	25	0	9	9	8	8	8	8	0
3100	11/17/80	24	0	12	12	12	8	8	8	0
3101	11/17/80	24	0	10	10	10	8	8	8	0
3102[e]	—	—	—	—	—	—	—	—	—	—
3103[e]	—	—	—	—	—	—	—	—	—	—
3104	—	—	—	—	—	—	—	—	—	—
3105	11/17/80	24	0	7	7	7	7	7	7	0
3106	11/18/80	25	0	13	13	13	8	8	8	0
3107[f]	11/22/80	29	0	17	18	17	8	8	8	1
3108	11/17/80	24	0	4	4	4	4	4	4	0
3109[f]	11/18/80	25	0	14	15	15	8	8	8	0
3110[e]	—	—	—	—	—	—	—	—	—	—
3112	11/19/80	26	0	13	13	13	8	8	8	0
3113	11/18/80	25	4	5	5	5	5	5	5	0
3114[e]	—	—	—	—	—	—	—	—	—	—
3115	11/21/80	28	0	15	15	15	8	8	8	0
	MEAN±S.D.	26±2	0.52±1.50	11±4	11±4	11±4	7±1	7±1	7±1	.23±0.50

[a]Female rats were exposed to 0, 30, 100, or 300 ppm DGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, animals were bred with unexposed males.

[b]Days were calculated from the first day of cohabitation to the date of delivery.

[c]On day 4 of lactation, all litters were culled to 8 pups, 4 males and 4 females, where possible. Data presented indicate number of live pups prior to culling.

[d]Number of pups.

[e]Female did not deliver a litter.

[f]At time of observation, female was still delivering pups.

[g]One pup died after culling.

[h]Female #3081 was found moribund and submitted for pathologic exam: pregnant at necropsy.

[i]Female #3089 was found moribund on day 2 of lactation. Animal was submitted for pathological exam.

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Table A-8

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Average Pup Body Weights for Individual Litters of Exposed Females Mated to Unexposed Males[a]

Exposure Level: 0 ppm

Maternal Animal Number	Post-Partum Day 1	4[b]	7	14	21 Male	21 Female
80A-3000	6.8[c]	10.3	15.6	32.5	51.0	50.0
3001	6.7	9.8	15.8	34.9	55.5	52.0
3002	7.3	11.5	18.5	38.4	60.5	56.5
3003	7.4	9.9	15.0	32.1	53.0	49.5
3004	7.1	9.4	16.4	32.4	52.8	52.8
3005	8.1	10.0	16.9	35.1	56.5	53.3
3006	6.8	10.5	17.0	36.5	59.3	58.5
3009	7.4	10.8	16.6	32.8	58.0	54.5
3010	6.1	8.5	15.1	33.0	56.8	51.8
3011	7.3	10.1	17.4	34.6	54.7	52.0
3012	8.0	12.0	18.6	36.3	59.5	57.3
3013	6.8	9.9	15.6	31.8	54.3	52.8
3014	7.2	9.8	16.8	34.8	57.5	54.8
3015	7.0	10.5	16.8	30.1	50.5	51.0
3016	8.8	15.0	24.8	46.8	83.0	70.7
3017	7.5	11.5	19.0	38.4	63.0	60.3
3019	7.7	11.3	18.3	36.4	57.5	55.0
3020	7.1	10.5	16.0	33.8	61.3	53.6
3021	8.2	12.3	—[d]	41.6	68.8	61.8
3023	6.1	9.0	15.8	28.1	44.0	42.3
3024	6.8	9.3	15.5	34.3	54.5	52.8
3025	6.5	9.9	16.8	36.3	58.8	57.0
3026	7.3	11.8	19.5	39.3	65.8	60.3
3027	6.2	8.9	14.0	30.9	51.0	51.3
3028	8.3	11.1	19.0	39.5	64.5	62.5
3029	8.2	12.6	21.5	43.0	67.8	62.3
MEAN ±S.D.	7.26 ±0.71	10.62 ±1.39	17.29 ±2.30	35.53 ±4.20	58.46 ±7.57	55.26 ±5.57

Table A-8 (Continued)

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Average Pup Body Weight for Individual Litters of Exposed Females Mated to Unexposed Males[a]

Exposure Level: 30 ppm

Maternal Animal Number	Post-Partum Day 1	4[b]	7	14	21 Male	21 Female
80A-3036	7.4	11.3	18.5	36.8	58.3	54.8
3037	8.2	11.8	18.1	35.9	57.0	53.5
3038	7.3	10.8	18.3	37.4	61.8	59.8
3041	7.1	10.6	18.5	37.4	58.0	54.5
3043	6.2	8.3	14.4	33.1	56.8	51.8
3044	6.6	9.6	16.5	34.5	53.5	50.3
3045	5.9	8.3	14.4	30.8	46.8	43.0
3047	7.6	7.3	9.7	24.8	42.0	39.0
3049	5.6	8.5	14.4	30.6	46.5	44.5
3050	6.8	10.1	14.1	30.5	47.5	47.8
3051	7.3	11.8	18.8	36.4	55.0	54.5
3052	6.5	9.9	17.4	36.8	58.5	55.3
3053	7.3	10.3	17.5	36.5	58.8	52.3
3057	7.4	10.9	18.4	37.6	56.0	56.4
3058	6.7	10.3	18.4	37.1	56.3	56.0
3059	7.0	9.8	17.1	35.8	57.3	54.5
3060	6.9	11.5	18.1	33.6	50.0	47.5
3061	6.7	9.9	16.1	33.8	58.2	53.7
3062	6.5	—[e]	—[e]	—[e]	—[e]	—[e]
3063	6.9	10.6	18.3	38.5	60.8	58.5
3064	7.5	11.4	19.4	37.4	57.8	54.5
3065	6.9	11.4	17.4	35.5	56.0	53.5
MEAN	6.92	10.21	16.85	34.80	54.90	52.18
±S.D.	±0.59	±1.25	±2.31	±3.32	±5.26	±5.18

Table A-8 (Continued)

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Average Pup Body Weights for Individual Litters of Exposed Females Mated to Unexposed Males[a]

Exposure Level: 100 ppm

Maternal Animal Number	Post-Partum Day 1	4[b]	7	14	21 Male	21 Female
80A-3072	7.5	10.5	16.4	30.9	51.3	50.5
3073	6.9	10.3	16.1	33.3	56.5	51.3
3074	7.2	10.8	18.8	37.5	60.0	55.0
3075	7.6	11.8	19.0	36.6	60.3	59.5
3076	7.3	11.1	18.1	—[f]	60.3	58.5
3077	7.8	12.3	19.6	37.0	59.0	56.5
3078	6.8	9.6	16.9	33.5	48.3	45.3
3079	9.0	14.4	21.6	39.1	63.5	60.5
3080	6.8	10.0	16.8	33.4	54.8	52.5
3082	6.2	8.8	14.8	30.6	47.5	44.3
3083	6.9	10.4	18.0	37.4	55.0	53.3
3084	7.2	11.0	18.6	35.0	55.3	52.5
3085	6.8	9.5	17.0	34.3	52.5	52.3
3086	7.3	10.9	17.1	33.1	55.3	54.3
3087	8.6	12.5	19.3	36.9	61.4	57.0
3088	7.3	10.0	16.4	34.5	55.8	48.0
3089	6.5	—[g]	—[g]	—[g]	—[g]	—[g]
3090	8.5	12.5	20.1	25.1	48.0	43.9
MEAN ±S.D.	7.34 ±0.74	10.96 ±1.38	17.92 ±1.71	34.26 ±3.43	55.58 ±4.86	52.71 ±5.04

Table A-8 (Continued)

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Average Pup Body Weights for Individual Litters of Exposed Females Mated to Unexposed Males[a]

Exposure Level: 300 ppm

Maternal Animal Number	Post-Partum Day 1	4[b]	7	14	21 Male	21 Female
80A-3096	6.5	9.5	15.3	30.4	55.0	51.0
3098	7.4	10.9	17.4	33.4	52.8	51.3
3099	7.1	11.4	17.0	33.1	60.0	51.7
3100	7.8	12.4	19.6	39.6	63.3	63.3
3101	8.0	12.0	19.3	33.8	61.5	56.7
3105	8.9	13.7	19.9	36.7	66.0	62.2
3106	6.7	8.6	13.9	27.3	48.8	44.0
3107	6.0	8.9	14.9	32.9	54.8	52.3
3108	7.5	11.3	17.5	32.3	55.5	51.0
3109	6.5	8.9	15.0	33.4	57.5	54.3
3112	6.9	10.4	16.8	34.9	57.0	52.8
3113	8.8	13.0	19.2	35.8	57.0	52.0
3115	6.7	10.0	16.6	34.8	56.0	55.5
MEAN ±S.D.	7.29 ±0.89	10.85 ±1.64	17.11 ±1.97	33.72 ±2.97	57.32 ±4.53	53.70 ±5.01

[a]Female rats were exposed to 0, 30, 100, or 300 ppm EGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, animals were bred with unexposed males.

[b]On day 4 of lactation, all litters were culled to 8 pups, 4 males and 4 females, where possible. Data presented indicate average body weight of live pups after culling.

[c]Average body weight of litter in grams.

[d]Litter inadvertently not weighed.

[e]Litter died after day 1.

[f]Incorrect weight recorded; value not included in calculations for mean±S.D.

[g]Maternal animal was found moribund on day 2 of lactation and was submitted for a pathological exam. Pups were sacrificed.

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Table 1-9

SCOPE: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual Observations Made at the Time of Necropsy of Unexposed Females Mated with Exposed Males - 18th Week of Study (First Week of Post-Exposure)[a]

Exposure Level: 0 ppm

Male Animal Number	Female Animal Number	Corpora Lutea	Implantations	Resorptions	$\bar{X}$ Pre-Imp Loss[b]	$\bar{X}$ Resorption Rate[b]
80A-3201	80A-3302	—[c]	—	—	—	—
3202	3303	Non-Pregnant	—	—	—	—
3203	3305	17	16	1	5	5
3204	3307	15	15	0	0	0
3205	3309	16	14	1	13	7
3116	3312	15	15	0	0	0
3117	3314	17	16	1	5	5
3118	3315	Non-Pregnant	—	—	—	—
3119	3317	13	13	0	0	0
3120	3319	16	16	0	0	0
3121	3321	Non-Pregnant	—	—	—	—
3122	3324	13	14	1	0	7
3123	3325	16	16	0	0	0
3124	3327	14	14	0	0	0
3125	3329	12	15	0	0	0
3126	3332	13	14	0	0	0
3127	3333	13	14	1	0	7
3128	3335	13	15	0	0	0
3129	3337	17	16	1	6	6
3130	3340	14	14	0	0	0
3131	3341	14	14	0	0	0
3132	3344	15	16	2	0	13
3133	3345	12	13	0	0	0
3134	3348	Non-Pregnant	—	—	—	—
3135	3350	15	14	0	7	0
3136	3351	16	16	0	0	0
3137	3353	12	13	1	0	7
3138	3355	15	15	1	0	7
3139	3358	14	13	0	7	0
3140	3359	14	17	0	0	0
	MEAN	14.5	14.7	0.3	1.3	2.5
	±S.D.	±1.5	±1.2	±0.5	±3.5	±3.9

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Table A-9 (Continued)

SGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual Observations Made at the Time of Necropsy of Unexposed Females Mated with Exposed Males - 13th Week of Study (First Week of Post-Exposure)[a]

Exposure Level: 30 ppm

Male Animal Number	Female Animal Number	Corpora Lutea	Implantations	Resorptions	$\bar{x}$ Pre-Imp Loss[b]	$\bar{x}$ Resorption Rate[b]
80A-3146	80A-3662	13	141	2	0	14
3147	3664	Non-Pregnant	—	—	—	—
3148	3665	13	14	1	0	7
3149	3668	15	15	0	0	0
3150	3670	14	14	2	0	14
3151	3671	15	15	0	0	0
3152	3673	16	15	1	6	7
3153	3675	16	16	0	0	0
3154	3678	13	13	7	0	54
3155	3679	15	15	0	0	0
3156	3681	Non-Pregnant	—	—	—	—
3157	3684	16	16	1	0	6
3158	3685	16	13	8	19	62
3159	3687	Non-Pregnant	—	—	—	—
3160	3689	14	16	2	0	13
3161	3691	Non-Pregnant	—	—	—	—
3162	3693	12	9	0	25	0
3163	3696	16	15	2	6	13
3164	3697	16	17	0	0	0
3165	3699	Non-Pregnant	—	—	—	—
3166	3702	17	17	0	0	0
3167	3703	Non-Pregnant	—	—	—	—
3168	3705	16	16	1	0	6
3169	3708	Non-Pregnant	—	—	—	—
3170	3709	15	16	1	0	6
3171	3711	18	16	0	11	0
3172	3714	15	15	1	0	7
3173	3715	15	15	0	0	0
3174	3718	15	16	1	0	6
3175	3719	Non-Pregnant	—	—	—	—
	MEAN	15.0	14.9	1.4	3.0	9.3
	±S.D.	±1.4	±1.7	±2.1	±6.3	±15.4

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Table 4-9 (Continued)

DOME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual Observations Made at the Time of Necropsy of Unexposed Females Mated With Exposed Males - 14th Week of Study (First Week of Post-Exposure)[a]

Exposure Level: 100 ppm

Male Animal Number	Female Animal Number	Corpora Lutea	Implantations	Resorptions	$\bar{X}$ Pre-Imp Loss[b]	$\bar{X}$ Resorption Rate[b]
201-3181	201-3721	16	15	3	6	20
3182	3724	17	17	0	0	0
3183	3725	14	9	2	36	22
3184	3727	16	16	1	0	6
3185	3729	14	15	0	0	0
3186	3732	17	17	3	0	18
3187	3733	15	16	2	0	13
3188	3736	17	16	0	6	0
3189	3738	12	9	0	25	0
3190	3740	14	15	2	0	13
3191	3741	Non-Pregnant	—	—	—	—
3192	3743	Non-Pregnant	—	—	—	—
3193	3746	14	15	0	0	0
3194	3747	15	15	1	0	7
3195	3749	18	18	0	0	0
3196	3752	13	15	1	0	7
3197	3753	18	16	0	11	0
3198	3755	16	14	0	13	0
3199	3758	Non-Pregnant	—	—	—	—
3200	3759	Non-Pregnant	—	—	—	—
	MEAN	15.4	14.9	0.9	6.1	6.5
	±S.D.	±1.7	±2.5	±1.1	±10.5	±8.1

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Table A-9 (Continued)

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual Observations Made at the Time of Necropsy of Unexposed Females Mated with Exposed Males - 14th Week of Study (First Week of Post-Exposure)[a]

Exposure Level: 300 ppm

Male Animal Number	Female Animal Number	Corpora Lutea	Implantations	Resorptions	$\bar{X}$ Pre-Imp Loss[b]	$\bar{X}$ Resorption Rate[b]
80A-3206	80A-3762	Non-Pregnant	—	—	—	—
3207	3764	Non-Pregnant	—	—	—	—
3208	3765	Non-Pregnant	—	—	—	—
3209	3768	Non-Pregnant	—	—	—	—
3210	3769	Non-Pregnant	—	—	—	—
3211	3772	Non-Pregnant	—	—	—	—
3212	3773	Non-Pregnant	—	—	—	—
3213	3776	Non-Pregnant	—	—	—	—
3214	3777	Non-Pregnant	—	—	—	—
3215	3779	Non-Pregnant	—	—	—	—
3216	3781	Non-Pregnant	—	—	—	—
3217	3783	Non-Pregnant	—	—	—	—
3218	3786	Non-Pregnant	—	—	—	—
3219	3787	Non-Pregnant	—	—	—	—
3220	3789	Non-Pregnant	—	—	—	—
3221	3792	Non-Pregnant	—	—	—	—
3222	3793	Non-Pregnant	—	—	—	—
3223	3795	Non-Pregnant	—	—	—	—
3224	3797	Non-Pregnant	—	—	—	—
3225	3799	Non-Pregnant	—	—	—	—
	MEAN	—	—	—	—	—
	±S.D.	—	—	—	—	—

[a]Male rats were exposed to 0, 30, 100, or 300 ppm EGME by inhalation for 6 hours/day, 5 days/week for 12 consecutive weeks. Following termination of the exposure period, animals were mated with unexposed females.

[b]Males and females mated one to one.

[c]Animal was found to be a cryptorchid male at necropsy.

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Table A-10

SCME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual Observations Made at the Time of Necropsy of Unexposed Females Mated With Exposed Males - 15th Week of Study (Second Week of Post-Exposure)[a]

Exposure Level: 0 ppm

Male Animal Number	Female Animal Number	Corpora Lutea	Implantations	Resorptions	$\bar{X}$ Pre-Imp Loss[b]	$\bar{X}$ Resorption Rate[b]
SCA-3201	SCA-3802	Non-Pregnant	—	—	—	—
3202	3803	13	7	0	23	4
	3804	15	15	1	—	—
3203	3805	Non-Pregnant	—	—	24	13
	3806	21	16	2	—	—
3204	3807	15	15	1	0	7
3205	3809	16	16	0	0	0
	3810	13	14	0	—	—
3116	3811	15	13	1	10	7
	3812	16	15	1	—	—
3117	3813	18	19	0	0	4
	3814	12	12	1	—	—
3118	3815	Non-Pregnant	—	—	—	—
3119	3817	Non-Pregnant	—	—	6	7
	3818	16	15	1	—	—
3120	3820	Non-Pregnant	—	—	—	—
3121	3822	14	13	1	7	7
3122	3823	15	15	0	0	0
	3824	Non-Pregnant	—	—	—	—
3123	3825	16	16	0	11	0
	3826	Non-Pregnant	—	—	—	—
3124	3827	14	15	3	0	20
	3828	Non-Pregnant	—	—	—	—
3125	3829	14	14	0	6	14
	3830	17	15	4	—	—
3126	3831	13	13	2	0	8
	3832	13	13	0	—	—
3127	3833	15	14	0	4	0
	3834	16	16	0	—	—
3128	3835	18	18	4	0	11
	3836	15	15	0	—	—
3129	3837	15	13	0	7	0
	3838	15	16	0	—	—
3130	3839	14	14	1	0	7
	3840	Non-Pregnant	—	—	—	—
3131	3841	Non-Pregnant	—	—	16	0
	3842	19	16	0	—	—
3132	3844	13	14	0	0	0
3133	3845	14	15	0	0	0
	3846	Non-Pregnant	—	—	—	—
3134	3847	13	13	1	10	4
	3848	16	13	0	—	—
3135	3849	Non-Pregnant	—	—	0	0
	3850	15	15	0	—	—
3136	3851	12	14	0	0	10
	3852	16	16	3	—	—
3137	3853	15	12	0	56	0
	3854	12	1	0	—	—
3138	3855	16	16	2	0	10
	3856	14	14	1	—	—
3139	3857	14	15	2	0	13
	3858	Non-Pregnant	—	—	—	—
3140	3859	15	15	0	4	0
	3860	13	12	0	—	—
	MEAN	15.2	14.4	0.9	6.8	5.4
	±S.D.	±1.3	±1.9	±0.9	±12.0	±5.6

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Table A-10 (Continued)

ZOME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual Observations Made at the Time of Necropsy of Unexposed Females Mated with Exposed Males - 15th Week of Study (Second Week of Post-Exposure)[a]

Exposure Level: 30 ppm

Male Animal Number	Female Animal Number	Corpora Lutea	Implantations	Resorptions	$\bar{X}$ Pre-Imp Loss[b]	$\bar{X}$ Resorption Rate[b]
80A-3146	80A-3861	Non-Pregnant	—	—	0	0
	3862	16	17	0	—	0
3147	3863	16	16	0	0	0
	3864	Non-Pregnant	—	—	—	—
3148	3865	14	12	0	11	3
	3866	13	12	2	—	—
3149	3867	15	15	2	0	7
	3868	14	14	0	—	—
3150	3870	11	10	0	9	0
3151	3871	18	17	0	6	0
	3872	Non-Pregnant	—	—	—	—
3152	3873	15	15	2	0	7
	3874	16	16	0	—	—
3153	3875	14	11	3	11	14
	3876	17	17	0	—	—
3154	3877	15	17	2	0	5
	3878	14	14	0	—	—
3155	3879	Non-Pregnant	—	—	—	—
3156	3882	Non-Pregnant	—	—	—	—
3157	3883	13	14	0	0	0
	3884	Non-Pregnant	—	—	—	—
3158	3885	14	15	0	3	3
	3886	14	13	1	—	—
3159	3888	Non-Pregnant	—	—	—	—
3160	3889	Non-Pregnant	—	—	0	6
	3890	16	16	1	—	—
3161	3891	Non-Pregnant	—	—	0	6
	3892	16	16	1	0	—
3162	3893	15	13	1	13	8
	3894	16	14	0	—	—
3163	3895	15	16	1	3	10
	3896	15	14	2	—	—
3164	3897	18	16	4	11	25
	3898	Non-Pregnant	—	—	—	—
3165	3899	14	15	0	0	0
3166	3901	Non-Pregnant	—	—	—	—
3167	3903	13	15	0	0	0
	3904	Non-Pregnant	—	—	—	—
3168	3905	14	16	1	4	7
	3906	15	14	1	—	—
3169	3907	13	14	0	0	0
	3908	17	17	0	—	—
3170	3909	17	17	0	0	0
	3910	Non-Pregnant	—	—	—	—
3171	3911	13	15	2	0	7
	3912	12	12	0	—	—
3172	3913	17	15	1	12	33
	3914	—[c]	1	1	—	—
3173	3916	15	14	1	7	7
3174	3917	12	12	1	3	10
	3918	18	17	2	—	—
3175	3919	Non-Pregnant	—	—	5	0
	3920	17	16	0	—	—
	MEAN	15.2	14.7	0.8	2.9	7.0
	±S.D.	±1.5	±2.1	±0.9	±4.7	±11.2

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Table A-10 (Continued)

SCOPE: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual Observations Made at the Time of Necropsy of Unexposed Females Mated With Exposed Males - 15th Week of Study (Second Week of Post-Exposure)[a]

Exposure Level: 100 ppm

Male Animal Number	Female Animal Number	Corpora Lutea	Implantations	Resorptions	$\bar{X}$ Pre-Imp Loss[b]	$\bar{X}$ Resorption Rate[b]
80A-3181	80A-3921	16	16	0	0	0
	3922	Non-Pregnant	—	—	—	—
3182	3923	Non-Pregnant	—	—	—	—
	3924	13	13	0	0	0
3183	3925	15	15	1	—	—
	3926	16	14	0	7	4
3184	3927	11	2	0	—	—
	3928	13	14	1	41	4
3185	3930	Non-Pregnant	—	—	—	—
3186	3931	Non-Pregnant	—	—	—	—
	3932	12	13	0	0	0
3187	3933	Non-Pregnant	—	—	—	—
3188	3935	16	15	0	—	—
	3936	Non-Pregnant	—	—	6	0
3189	3937	13	13	2	—	—
	3938	14	14	2	0	15
3190	3939	15	14	1	—	—
	3940	17	17	0	4	4
3191	3941	14	15	9	—	—
	3942	13	14	8	0	59
3192	3943	19	16	0	—	—
3193	3945	Non-Pregnant	—	—	16	0
	3946	20	17	1	15	6
3194	3947	13	13	0	—	—
	3948	15	14	1	7	4
3195	3949	16	15	1	—	—
	3950	11	13	0	3	4
3196	3951	14	13	0	—	—
	3952	12	6	1	29	9
3197	3953	13	14	1	—	—
	3954	14	14	0	0	4
3198	3955	14	14	0	—	—
	3956	17	16	1	3	3
3199	3957	19	16	0	—	—
	3958	Non-Pregnant	—	—	16	0
3200	3960	Non-Pregnant	—	—	—	—
	MEAN	15.2	14.5	1.2	8.6	6.3
	±S.D.	±2.4	±2.0	±2.1	±11.6	±14.0

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Table A-10 (Continued)

DDVP: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual Observations Made at the Time of Necropsy of Unexposed Females Mated with Exposed Males - 15th Week of Study (Second Week of Post-Exposure)[a]

Exposure Level: 300 ppm

Male Animal Number	Female Animal Number	Corpora Lutea	Implantations	Resorptions	$\bar{X}$ Pre-Imp Loss[b]	$\bar{X}$ Resorption Rate[b]
80A-3206	80A-3962	Non-Pregnant	—	—	—	—
3207	3963	Non-Pregnant	—	—	—	—
3208	3966	Non-Pregnant	—	—	—	—
3209	3967	Non-Pregnant	—	—	—	—
3210	3970	—[b]	1[c]	1[d]	—	—
3211	3971	Non-Pregnant	—	—	—	100
3212	3978	Non-Pregnant	—	—	—	—
3213	3976	Non-Pregnant	—	—	—	—
3214	3975	Non-Pregnant	—	—	—	—
3215	3980	—[b]	1[c]	1[d]	—	—
3216	3982	Non-Pregnant	—	—	—	100
3217	3984	Non-Pregnant	—	—	—	—
3218	3985	Non-Pregnant	—	—	—	—
3219	3988	Non-Pregnant	—	—	—	—
3220	3990	Non-Pregnant	—	—	—	—
3221	3991	Non-Pregnant	—	—	—	—
3222	3993	Non-Pregnant	—	—	—	—
3223	3996	Non-Pregnant	—	—	—	—
3224	3998	Non-Pregnant	—	—	—	—
3225	4000	Non-Pregnant	—	—	—	—
	Mean	—	1.0	1.0	—	100.0
	S.D.	—	±0.0	±0.0	—	±0.0

[a]Male rats were exposed to 0, 30, 100, or 300 ppm DDVP by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, animals were mated with untreated females.

[b]No data.

[c]Observed only after staining with sodium sulfide.

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Table 1-11

SCOPE: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual Observations Made at the Time of Necropsy of Unexposed Females Mated With Exposed Males - 26th Week of Study (13 Weeks Post-Exposure)[a]

Exposure Level: 0 ppm

Male Animal Number	Female Animal Number	Corpora Lutea	Implantations	Resorptions	$\bar{\lambda}$ Pre-imp Loss[b]	$\bar{\lambda}$ Resorption Rate[b]
SOA-3201	SOA-4201	14	14	2	0	14
3202	4202	Non-Pregnant	—	—	—	—
3203	4203	13	14	0	0	0
3204	4204	16	9	2	44	22
3205	4205	Non-Pregnant	—	—	—	—
3116	4206	12	6	1	50	16
3117	4207	14	15	0	0	0
3118	4208	14	13	0	3	0
3119	4209	15	15	2	0	13
3120	4210	12	12	0	0	0
3121	4211	Non-Pregnant	—	—	—	—
3122	4212	5[c]	3	2	40	67
3123	4213	14	12	1	14	8
3124	4214	16	17	0	0	0
3125	4215	14	15	1	0	7
3126	4216	13	13	0	0	0
3127	4217	14	13	1	7	8
3128	4218	13	16	2	0	13
3129	4219	14	15	1	0	7
3130	4220	13	3	1	76	33
3131	4221	12	12	0	0	0
3132	4222	15	15	0	0	0
3133	4223	15	15	0	0	0
3134	4224	9	4	0	55	0
3135	4225	14	13	0	7	0
3136	4226	13	14	0	0	0
3137	4227	15	15	1	0	7
3138	4228	13	15	0	0	0
3139	4229	15	15	2	0	13
3140	4230	13	13	0	0	0
	MEAN	13.3	12.5	0.7	11.2	7.9
	±S.D.	±2.2	±4.0	±0.8	±21.2	±13.9

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Table A-11 (Continued)

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual Observations Made at the Time of Necropsy of Unexposed Females Mated with Exposed Males - 26th Week of Study (13 Weeks Post-Exposure)[a]

Exposure Level: 300 ppm

Male Animal Number	Female Animal Number	Corpora Lutea	Implantations	Resorptions	$\bar{X}$ Pre-Imp Loss[b]	$\bar{X}$ Resorption Rate[b]
30A-3206	80A-4281	Non-Pregnant	—	—	—	—
3207	4282	14	14	0	0	0
3208	4283	Non-Pregnant	—	—	—	—
3209	4284	17	10	0	41	0
3210	4285	15	15	1	0	7
3211	4286	12	12	0	0	0
3212	4287	13	16	1	0	6
3213	4288	12	13	1	0	7
3214	4289	Non-Pregnant	—	—	—	—
3215	4290	Non-Pregnant	—	—	—	—
3216	4291	12	8	1	33	13
3217	4292	14	14	0	0	0
3218	4293	Non-Pregnant	—	—	—	—
3219	4294	12	15	1	0	7
3220	4295	12	14	2	0	14
3221	4296	15	15	1	6	7
3222	4297	Non-Pregnant	—	—	—	—
3223	4298	Non-Pregnant	—	—	—	—
3224	4299	Non-Pregnant	—	—	—	—
3225	4300	Non-Pregnant	—	—	—	—
	MEAN	13.5	13.2	0.7	7.3	5.5
	±S.D.	±1.3	±2.4	±0.6	±14.9	±5.1

[a]Male rats were exposed to 0, 30, 100, or 300 ppm EGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, animals were bred 13 weeks post-exposure with untreated females.

[b]Males and females mated one to one.

[c]Corpora lutea for only the left side were counted because of uterine horn aplasia.

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Table A-12

SCOPE: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual Observations Made at the Time of Necropsy of Unexposed Females Mated With Exposed Males - 32nd Week of Study (19 Weeks Post-Exposure)[a]

Exposure Level: 0 ppm

Male Animal Number	Female Animal Number	Corpora Lutea	Implantations	Resorptions	$\bar{X}$ Pre-Imp Loss[b]	$\bar{X}$ Resorption Rate[b]
30A-3201	30A-4231	13	13	0	0	0
3202	4232	16	17	0	0	0
3203	4233	12	13	3	0	23
3204	4234	Non-Pregnant	—	—	—	—
3205	4235	15	3	2	47	25
3116	4236	11	10	0	9	0
3117	4237	Non-Pregnant	—	—	—	—
3118	4238	16	17	0	0	0
3119	4239	14	14	1	0	7
3120	4240	19	15	5	21	33
3121	4241	Non-Pregnant	—	—	—	—
3122	4242	20	18	0	10	0
3123	4243	15	15	1	0	7
3124	4244	13	13	0	0	0
3125	4245	13	14	0	0	0
3126	4246	25	18	3	28	17
3127	4247	19	20	2	0	10
3128	4248	20	19	0	5	0
3129	4249	—	9[c]	9[c]	—	100
3130	4250	15	15	1	0	7
3131	4251	12	12	2	0	17
3132	4252	Non-Pregnant	—	—	—	—
3133	4253	Non-Pregnant	—	—	—	—
3134	4254	16	16	1	0	5
3135	4255	2	1	0	50	0
3136	4256	12	12	4	0	33
3137	4257	14	13	0	7	0
3138	4258	12	5	0	58	0
3139	4259	13	6	1	54	17
3140	4260	Non-Pregnant	—	—	—	—
	MEAN	14.7	13.0	1.5	12.6	12.5
	±S.D.	±4.4	±4.7	±2.1	±20.0	±21.6

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Table A-12 (Continued)

SDMF: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual Observations Made at the Time of Necropsy of Unexposed Females Mated with Exposed Males - 32nd Week of Study (19 Weeks Post-Exposure)[a]

Exposure Level: 300 ppm

Male Animal Number	Female Animal Number	Corpora Lutea	Implantations	Resorptions	$\bar{X}$ Pre-imp Loss[b]	$\bar{X}$ Resorption Rate[b]
80A-3206	80A-4251	Non-Pregnant	—	—	—	—
3207	4252	15	16	0	0	0
3208	4253	Non-Pregnant	—	—	—	—
3209	4254	14	13	1	7	8
3210	4255	13	14	1	0	7
3211	4256	14	15	0	0	0
3212	4257	16	15	1	6	7
3213	4258	12	12	1	0	8
3214	4259	Non-Pregnant	—	—	—	—
3215	4270	Non-Pregnant	—	—	—	—
3216	4271	15	14	4	7	29
3217	4272	17	14	1	17	7
3218	4273	Non-Pregnant	—	—	—	—
3219	4274	14	15	0	0	0
3220	4275	Non-Pregnant	—	—	—	—
3221	4276	15	16	0	0	0
3222	4277	Non-Pregnant	—	—	—	—
3223	4278	Non-Pregnant	—	—	—	—
3224	4279	Non-Pregnant	—	—	—	—
3225	4280	Non-Pregnant	—	—	—	—
	MEAN	14.5	14.3	0.9	3.7	5.5
	±S.D.	±1.4	±1.2	±1.2	±5.5	±8.7

[a]Male rats were exposed to 0, 20, 100, or 300 ppm SDMF by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, animals were held 19 weeks post-exposure with untreated females.

[b]Males and females mated one to one.

[c]Observed only after staining with sodium sulfide.

Table A-13

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Exposed Male Rats: Hematologic Evaluation - 24th Week of Study (11 Weeks Post-Exposure)[a]

EGME, ppm	Pathology Number	WBC x $10^3/mm^3$	RBC x $10^6/mm^3$	Hgb g/dl	PCV %	MCV (microns)^3	MCH x 10^{-12}g	MCHC %	PLAT x $10^3/mm^3$
0	80A-2050	15.40	7.90	15.20	45.00	57.00	19.20	33.80	1126.00
	2051	13.00	8.70	16.60	46.60	54.00	19.10	35.60	1162.00
	2052	13.40	8.44	17.00	47.80	57.00	20.10	35.60	1032.00
	2053	10.20	8.30	16.40	47.80	58.00	19.80	34.30	902.00
	2054	13.60	8.80	17.60	50.40	57.00	20.00	34.90	1050.00
	2055	20.60	8.48	17.00	48.00	57.00	20.00	35.40	906.00
	2056	27.20	8.84	16.00	46.00	52.00	18.10	34.80	1038.00
	2057	12.60	7.82	16.00	43.80	56.00	20.50	36.50	878.00
	2058	11.00	8.60	16.60	47.60	55.00	19.30	34.90	988.00
	2059	13.20	9.14	17.00	49.40	54.00	18.60	34.40	1122.00
	MEAN	15.02	8.50	16.54	47.24	55.70	19.47	35.02	1020.40
	±S.D.	±5.13	±0.41	±0.68	±1.97	±1.89	±0.75	±0.78	±100.71
300	80A-2130	13.40	8.10	16.20	46.00	57.00	20.00	35.20	988.00
	2131	14.20	8.80	16.40	46.60	53.00	18.60	35.20	1016.00
	2132	13.00	8.28	16.80	48.20	58.00	20.30	34.90	862.00
	2133	13.80	8.34	15.80	45.60	55.00	18.90	34.60	710.00
	2134	14.80	8.62	16.00	48.00	56.00	18.60	33.30	998.00
	2135	13.60	8.34	15.80	47.00	56.00	18.90	33.60	972.00
	2136	10.40	9.14	17.60	49.60	54.00	19.30	35.50	1124.00
	2137	13.80	9.36	17.20	48.00	51.00	18.40	35.80	1116.00
	2138	15.80	9.04	16.20	46.60	52.00	17.90	34.80	982.00
	2139	14.00	8.66	16.00	46.00	53.00	18.50	34.80	1066.00
	MEAN	13.68	8.67	16.40	47.16	54.50	18.94	34.77	983.40
	±S.D.	±1.39	±0.41	±0.61	±1.26	±2.27	±0.74	±0.78	±122.51

[a]Male rats were exposed to 0 or 300 ppm EGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, animals were maintained in the laboratory for recovery.

Table A-14

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Exposed Female Rats: Hematologic Evaluation - 24th Week of Study (11 Weeks Post-Exposure)[a]

EGME, ppm	Pathology Number	WBC x 10^3/mm^3	RBC x 10^6/mm^3	Hgb g/dl	PCV %	MCV (microns)^3	MCH x 10^{-12}g	MCHC %	PLAT x 10^3/mm^3
0	80A-2150	16.00	8.02	17.60	49.40	62.00	21.90	35.60	742.00
	2151	8.80	7.54	16.60	47.80	63.00	22.00	34.70	1022.00
	2152	33.20	7.42	15.80	45.40	61.00	21.30	34.80	1304.00
	2153	16.60	8.02	17.60	50.20	63.00	21.90	35.10	1040.00
	2154	9.00	7.74	17.40	49.60	64.00	22.50	35.10	802.00
	2155	11.40	7.52	16.40	46.20	61.00	21.80	35.50	966.00
	2156	7.40	7.62	15.80	46.20	61.00	20.70	34.20	1032.00
	2157	11.20	8.06	16.60	47.80	59.00	20.60	34.70	926.00
	2158	10.40	7.70	16.20	48.20	63.00	21.00	33.60	882.00
	2159	10.00	8.14	16.40	47.80	59.00	20.10	34.30	928.00
	MEAN	13.40	7.78	16.64	47.86	61.60	21.38	34.76	964.40
	±S.D.	±7.56	±0.26	±0.68	±1.58	±1.71	±0.76	±0.61	±154.33
300	80A-2230	8.00	7.94	17.00	48.80	61.00	21.40	34.80	996.00
	2231	17.60	8.50	16.60	48.80	57.00	19.50	34.00	1154.00
	2232	17.20	8.24	17.60	50.40	61.00	21.40	34.90	1058.00
	2233	9.00	8.12	16.00	46.40	57.00	19.70	34.50	924.00
	2234	10.00	7.80	16.20	46.40	59.00	20.80	34.90	1084.00
	2235	15.20	8.00	16.80	49.20	62.00	21.00	34.10	1044.00
	2236	8.40	8.00	16.80	48.40	61.00	21.00	34.70	994.00
	2237	6.80	7.78	16.40	46.60	60.00	21.10	35.20	988.00
	2238	10.80	7.54	15.40	45.00	60.00	20.40	34.20	814.00
	2239	11.20	8.02	16.60	47.80	60.00	20.70	34.70	840.00
	MEAN	11.42	7.99	16.54	47.78	59.80	20.70	34.60	989.60
	±S.D.	±3.89	±0.26	±0.60	±1.64	±1.69	±0.65	±0.39	±106.02

[a]Female rats were exposed to 0 or 300 ppm EGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, animals were maintained in the laboratory for recovery.

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Table A-15

EDME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Exposed Male Rats: Clinical Chemistry Values - 35th Week of Study (23 Weeks Post-Exposure)[a]

EDME, ppm	Pathology Number	BUN mg/dl	SGPT mu/ml	AP mu/ml	Gluc mg/dl	TP g/dl	Alb g/dl	Glob g/dl	T. Bili g/dl
0	80A-2051	17.00	105.00	87.00	152.00	5.10	2.80	2.30	0.40
	2052	11.00	30.00	36.00	122.00	5.50	3.40	2.20	0.30
	2053	12.00	10.00	34.00	122.00	5.30	3.30	2.00	0.30
	2054	14.00	17.00	58.00	136.00	5.70	3.30	2.40	0.30
	2055	15.00	12.00	52.00	139.00	6.20	3.10	3.10	0.20
	2056	14.00	33.00	46.00	135.00	5.30	3.30	2.50	0.30
	2057	14.00	23.00	48.00	153.00	5.50	3.20	2.30	0.30
	2058	17.00	19.00	28.00	146.00	5.80	3.20	2.60	0.30
	2059	15.00	14.00	27.00	163.00	5.50	3.30	2.20	0.30
	2060	13.00	14.00	34.00	140.00	5.30	3.30	2.50	0.20
	MEAN	14.20	27.70	45.00	140.30	5.64	3.23	2.41	0.29
	±S.D.	±1.93	±28.20	±18.04	±13.17	±0.31	±0.18	±0.30	±0.06
30	80A-2080	14.00	25.00	40.00	142.00	5.50	3.00	2.60	0.20
	2081	16.00	10.00	64.00	133.00	6.00	3.40	2.60	0.30
	2082	12.00	35.00	43.00	125.00	6.00	3.20	2.80	0.30
	2083	10.00	41.00	45.00	123.00	6.30	3.10	3.20	0.30
	2084	17.00	14.00	34.00	121.00	5.80	3.40	2.40	0.30
	2085	13.00	12.00	36.00	144.00	5.80	3.30	2.50	0.40
	2086	17.00	17.00	70.00	141.00	6.00	3.40	2.60	0.30
	2087	12.00	17.00	60.00	144.00	7.10	3.70	3.40	0.30
	2088	12.00	12.00	27.00	190.00	5.80	3.40	2.40	0.30
	2089	11.00	16.00	61.00	146.00	6.00	3.60	2.40	0.30
	MEAN	13.40	20.00	48.00	140.90	6.04	3.35	2.69	0.30
	±S.D.	±2.50	±10.54	±14.65	±19.69	±0.42	±0.21	±0.35	±0.05
100	80A-2110	12.00	118.00	37.00	131.00	5.50	3.60	1.90	0.30
	2111	11.00	12.00	33.00	128.00	5.40	3.40	2.00	0.30
	2112	12.00	10.00	39.00	145.00	5.50	3.20	2.30	0.30
	2113	13.00	10.00	27.00	119.00	5.90	3.10	2.80	0.20
	2114	12.00	8.00	40.00	144.00	6.10	3.40	2.70	0.20
	2115	14.00	12.00	40.00	171.00	5.80	3.30	2.50	0.30
	2116	12.00	44.00	46.00	156.00	6.00	3.20	2.80	0.30
	2117	12.00	25.00	45.00	143.00	6.40	3.30	3.10	0.30
	2118	11.00	12.00	29.00	142.00	6.10	3.40	2.70	0.20
	2119	14.00	15.00	43.00	159.00	6.60	3.40	3.20	0.20
	MEAN	12.40	25.70	37.30	143.30	5.93	3.33	2.60	0.25
	±S.D.	±1.07	±33.34	±6.61	±15.47	±0.39	±0.14	±0.43	±0.05
300	80A-2130	15.00	10.00	52.00	123.00	5.70	3.20	2.50	0.30
	2131	14.00	28.00	42.00	129.00	5.10	3.60	2.50	0.30
	2132	10.00	12.00	52.00	179.00	5.60	3.40	2.20	0.20
	2133	10.00	23.00	46.00	113.00	5.70	3.50	2.20	0.30
	2134	12.00	23.00	67.00	119.00	5.90	3.50	2.40	0.30
	2135	13.00	8.00	30.00	133.00	5.60	3.30	2.30	0.30
	2136	15.00	16.00	43.00	142.00	6.20	3.30	2.90	0.30
	2137	15.00	8.00	24.00	157.00	5.90	3.20	2.70	0.20
	2138	13.00	13.00	36.00	174.00	5.20	2.30	3.40	0.20
	2139	15.00	10.00	33.00	131.00	5.30	2.80	2.50	0.20
	MEAN	13.20	15.20	42.50	140.00	5.72	3.26	2.56	0.26
	±S.D.	±1.99	±7.11	±12.58	±22.30	±0.35	±0.28	±0.37	±0.05

[a]Male rats were exposed to 0, 30, 100, or 300 ppm EDME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, animals were maintained in the laboratory for recovery.

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Table A-16

SGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Exposed Female Rats: Clinical Chemistry Values - 28th Week of Study (15 Weeks Post-Exposure)[a]

SGME, ppm	Pathology Number	BUN mg/dl	SGPT mu/ml	AP mu/ml	Gluc mg/dl	TP g/dl	Alb g/dl	Glob g/dl	T. Bili g/dl
0	301-2150	18.00	32.00	33.00	134.00	7.00	4.40	2.60	0.40
	2151	18.00	10.00	24.00	133.00	6.20	3.50	2.70	0.30
	2152	18.00	10.00	19.00	123.00	5.60	3.60	2.00	0.10
	2153	16.00	10.00	22.00	134.00	6.00	3.80	2.20	0.20
	2154	19.00	10.00	18.00	136.00	6.40	4.00	2.40	0.20
	2155	17.00	25.00	21.00	147.00	6.70	4.10	2.60	0.20
	2156	17.00	28.00	15.00	121.00	6.90	4.40	2.50	0.30
	2157	15.00	19.00	12.00	131.00	7.20	4.60	2.60	0.30
	2159	15.00	105.00	31.00	120.00	6.90	4.10	2.30	0.30
	2150	18.00	12.00	16.00	137.00	7.10	4.60	2.50	0.30
	MEAN	17.10	25.10	21.10	132.50	6.50	4.11	2.39	0.26
	±S.D.	±1.37	±28.97	±6.74	±7.29	±0.53	±0.39	±0.24	±0.08
30	301-2180	17.00	14.00	30.00	125.00	6.30	4.10	2.20	0.20
	2181	34.00	26.00	31.00	120.00	6.50	4.20	2.40	0.30
	2182	21.00	17.00	22.00	106.00	6.50	4.00	2.60	0.40
	2183	17.00	14.00	27.00	119.00	6.20	3.50	2.40	0.30
	2184	19.00	12.00	21.00	137.00	6.50	4.00	2.50	0.20
	2185	20.00	28.00	22.00	125.00	5.40	3.70	2.70	0.30
	2186	14.00	33.00	24.00	125.00	6.50	4.20	2.40	0.20
	2187	16.00	17.00	13.00	116.00	7.20	4.20	3.00	0.40
	2188	16.00	25.00	15.00	143.00	6.60	4.20	2.40	0.40
	2190	17.00	35.00	13.00	159.00	7.30	4.30	3.00	0.20
	MEAN	19.10	22.20	21.80	127.50	6.63	4.07	2.56	0.29
	±S.D.	±5.53	±8.40	±6.55	±15.15	±0.36	±0.19	±0.27	±0.09
100	301-2210	18.00	14.00	19.00	113.00	5.70	4.10	2.50	0.20
	2211	18.00	21.00	24.00	129.00	6.90	4.10	2.80	0.30
	2212	16.00	14.00	16.00	133.00	6.10	3.50	2.30	0.20
	2213	17.00	19.00	30.00	144.00	5.60	4.10	2.50	0.30
	2214	15.00	21.00	19.00	121.00	7.20	4.70	2.50	0.30
	2215	15.00	10.00	31.00	132.00	6.30	3.70	2.60	0.30
	2216	19.00	16.00	25.00	133.00	6.50	3.90	2.50	0.20
	2217	17.00	12.00	36.00	132.00	5.30	3.70	2.60	0.50
	2218	16.00	14.00	24.00	115.00	6.30	3.90	2.40	0.40
	2219	17.00	32.00	25.00	138.00	6.00	3.80	2.20	0.30
	MEAN	16.80	17.30	24.30	129.00	6.49	3.96	2.53	0.31
	±S.D.	±1.32	±6.34	±6.12	±9.34	±0.37	±0.32	±0.16	±0.10
300	301-2230	17.00	14.00	39.00	137.00	6.00	3.70	2.30	0.10
	2231	17.00	25.00	46.00	124.00	5.00	3.70	2.30	0.30
	2232	17.00	14.00	21.00	130.00	5.90	3.50	2.40	0.30
	2233	20.00	16.00	24.00	117.00	6.10	3.60	2.50	0.30
	2234	12.00	17.00	24.00	136.00	5.80	3.50	2.30	0.40
	2235	17.00	10.00	33.00	111.00	5.60	3.30	2.30	0.10
	2236	19.00	14.00	28.00	125.00	5.80	3.70	2.10	0.10
	2237	13.00	19.00	22.00	133.00	5.70	3.60	2.10	0.30
	2238	14.00	15.00	27.00	147.00	6.20	3.90	2.30	0.30
	2239	16.00	19.00	31.00	126.00	5.20	3.60	2.60	0.40
	MEAN	16.20	16.70	29.50	128.70	5.93	3.61	2.32	0.26
	±S.D.	±2.53	±3.79	±7.99	±10.35	±0.21	±0.16	±0.15	±0.12

[a] Female rats were exposed to 0, 30, 100, or 300 ppm SGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, animals were maintained in the laboratory for recovery.

Table A-17

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Exposed Male Rats: Urinalysis - 24th Week of Study (11 Weeks Post-Exposure)[a]

EGME, ppm	Pathology Number	Specific Gravity	pH	Protein	Glucose	Ketones	Bilirubin	Blood	Urobilinogen
0	80A-2050	1.058	6.0	4+	neg	neg	neg	neg	.1
	2051	1.020	7.0	1+	neg	neg	neg	neg	.1
	2052	1.011	7.0	Trace	neg	neg	neg	neg	.1
	2053	1.058	6.0	3+	neg	neg	neg	neg	.1
	2054	b	b	b	b	b	b	b	b
	2055	1.048	7.0	2+	neg	neg	neg	neg	.1
	2056	1.052	7.0	1+	neg	neg	neg	neg	.1
	2057	1.044	7.0	2+	neg	neg	neg	neg	.1
	2058	1.046	7.0	2+	neg	neg	neg	Trace	.1
	2059	1.028	7.0	3+	neg	neg	neg	neg	.1
	MEAN	1.041							
	±S.D.	±0.017							
300	80A-2130	1.027	7.0	Trace	neg	neg	neg	neg	.1
	2131	1.030	8.0	1+	neg	neg	neg	neg	.1
	2132	1.027	8.0	1+	neg	neg	neg	neg	.1
	2133	1.040	6.0	1+	neg	neg	neg	neg	.1
	2134	1.036	7.5	1+	neg	neg	neg	neg	.1
	2135	1.056	7.5	2+	neg	neg	neg	neg	.1
	2136	1.068	6.0	4+	neg	neg	neg	neg	.1
	2137	1.050	6.5	2+	neg	neg	neg	neg	.1
	2138	1.052	6.5	2+	neg	neg	neg	neg	.1
	2139	1.026	8.0	1+	neg	neg	neg	neg	.1
	MEAN	1.041							
	±S.D.	±0.015							

[a]Male rats were exposed to 0 or 300 ppm EGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, animals were maintained in the laboratory for recovery.

[b]Quantity not sufficient.

Table A-18

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Exposed Female Rats: Urinalysis - 24th Week of Study (11 Weeks Post-Exposure)[a]

EGME, ppm	Pathology Number	Specific Gravity	pH	Protein	Glucose	Ketones	Bilirubin	Blood	Urobilinogen
0	80A-2150	1.014	6.5	Trace	neg	neg	neg	neg	.1
	2151	1.033	6.5	1+	neg	neg	b	b	b
	2152	1.048	7.0	2+	neg	neg	neg	neg	.1
	2153	1.038	7.0	Trace	neg	neg	neg	neg	.1
	2154	1.028	7.5	Trace	neg	neg	neg	neg	.1
	2155	1.046	7.0	1+	neg	neg	neg	neg	.1
	2156	1.042	7.0	2+	b	b	b	b	b
	2157	1.066	6.0	4+	neg	neg	neg	neg	.1
	2158	1.030	7.5	Trace	neg	neg	neg	neg	.1
	2159	1.008	8.0	neg	neg	b	b	b	b
	MEAN	1.035							
	±S.D.	±0.017							
300	80A-2230	1.019	7.0	Trace	neg	neg	neg	neg	.1
	2231	1.028	6.5	1+	neg	neg	neg	pos	.1
	2232	1.042	7.5	1+	neg	neg	neg	neg	.1
	2233	b	b	b	b	b	b	b	b
	2234	1.016	6.5	Trace	neg	neg	neg	Trace	.1
	2235	1.008	6.0	b	b	b	b	b	b
	2236	1.026	7.5	Trace	neg	neg	neg	neg	.1
	2237	1.018	6.0	Trace	b	b	b	b	b
	2238	1.040	6.5	1+	neg	neg	neg	neg	.1
	2239	1.034	6.5	1+	neg	neg	neg	neg	.1
	MEAN	1.026							
	±S.D.	±0.012							

[a]Female rats were exposed to 0 or 300 ppm EGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Following termination of the exposure period, animals were maintained in the laboratory for recovery.

[b]Quantity not sufficient.

Table A-19

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual and Mean Body Weights, Organ Weights, and Organ/Body Weight Ratios of Exposed Males[a]

Exposure Level: 0 ppm

Pathology Number	Body Weight (g)[b]	Organ Weights											
		Liver		Kidneys		Brain		Testes		Thymus		Spleen	
		g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]
80A-2050	625.1	15.47	2.47	3.87	0.62	2.16	0.35	3.69	0.59	0.42	0.07	0.76	0.12
2051	575.6	14.32	2.49	3.29	0.57	2.23	0.39	3.45	0.60	0.19	0.03	0.81	0.14
2052	599.5	13.68	2.28	3.54	0.59	2.11	0.35	3.78	0.63	0.22	0.04	0.89	0.15
2053	586.4	14.17	2.42	3.98	0.68	2.18	0.37	3.48	0.59	0.20	0.03	0.91	0.16
2054	493.6	10.81	2.19	3.21	0.65	2.37	0.48	3.39	0.69	0.27	0.05	0.72	0.15
2055	496.2	13.16	2.65	3.44	0.69	2.14	0.43	3.55	0.72	0.30	0.06	0.72	0.15
2056	538.0	14.20	2.64	4.02	0.75	2.28	0.42	3.53	0.66	0.28	0.05	0.80	0.15
2057	644.9	15.26	2.37	3.70	0.57	2.21	0.34	3.42	0.53	0.37	0.06	0.87	0.13
2058	564.9	12.38	2.19	3.62	0.64	2.26	0.40	3.79	0.67	0.29	0.05	0.72	0.13
2059	579.2	13.87	2.39	3.65	0.63	2.18	0.38	3.56	0.61	0.24	0.04	0.84	0.15
2060	549.3	12.79	2.33	3.25	0.59	2.18	0.40	3.43	0.62	0.26	0.05	0.67	0.12
2061	514.9	11.14	2.16	3.20	0.62	2.40	0.47	4.09	0.79	0.31	0.06	0.76	0.15
2062	615.5	15.25	2.48	3.61	0.59	2.08	0.34	3.85	0.63	0.27	0.04	0.85	0.14
2063	601.5	14.73	2.45	4.18	0.69	2.29	0.38	4.56	0.76	0.31	0.05	0.79	0.13
2064	547.6	12.10	2.21	3.57	0.65	2.14	0.39	3.42	0.62	0.27	0.05	0.68	0.12
MEAN	568.81	13.56	2.38	3.61	0.64	2.21	0.39	3.67	0.65	0.28	0.05	0.79	0.14
±S.D.	±45.70	±1.46	±0.16	±0.31	±0.05	±0.09	±0.04	±0.32	±0.07	±0.06	±0.01	±0.08	±0.01

Table A-19 (Continued)

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual and Mean Body Weights, Organ Weights, and Organ/Body Weight Ratios of Exposed Males[a]

Exposure Level: 30 ppm

Pathology Number	Body Weight (g)[b]	Organ Weights											
		Liver		Kidneys		Brain		Testes		Thymus		Spleen	
		g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]
80A-2080	561.3	12.38	2.21	3.48	0.62	2.20	0.39	4.00	0.71	0.38	0.07	0.79	0.14
2081	574.1	15.08	2.63	3.65	0.64	2.13	0.37	3.80	0.66	0.24	0.04	0.89	0.16
2082	599.1	13.51	2.26	3.96	0.66	2.16	0.36	3.89	0.65	0.43	0.07	0.66	0.11
2083	539.8	11.21	2.08	3.73	0.69	2.25	0.42	3.63	0.67	0.23	0.04	0.80	0.15
2084	557.0	12.39	2.22	3.79	0.68	2.28	0.41	3.85	0.69	0.35	0.06	0.81	0.15
2085	705.2	16.58	2.35	3.97	0.56	2.23	0.32	3.40	0.48	0.40	0.06	0.94	0.13
2086	642.3	14.43	2.25	3.77	0.59	3.85	0.60	2.28	0.35	0.25	0.04	0.80	0.12
2087	623.2	15.80	2.54	3.75	0.60	2.19	0.35	3.80	0.61	0.25	0.04	0.75	0.12
2088	589.4	14.43	2.45	4.02	0.68	2.29	0.39	3.84	0.65	0.40	0.07	0.65	0.11
2089	713.8	15.70	2.20	3.99	0.56	2.18	0.31	3.86	0.54	0.36	0.05	0.78	0.11
MEAN	610.52	14.15	2.32	3.81	0.63	2.38	0.39	3.64	0.60	0.33	0.05	0.79	0.13
±S.D.	±60.55	±1.74	±0.17	±0.17	±0.05	±0.52	±0.08	±0.50	±0.11	±0.08	±0.01	±0.09	±0.02

Table A-19 (Continued)

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual and Mean Body Weights, Organ Weights, and Organ/Body Weight Ratios of Exposed Males[a]

Exposure Level: 100 ppm

Pathology Number	Body Weight (g)[b]	Organ Weights											
		Liver		Kidneys		Brain		Testes		Thymus		Spleen	
		g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]
80A-2110	565.3	14.52	2.57	3.74	0.66	2.03	0.36	3.70	0.65	0.30	0.05	0.89	0.16
2111	497.5	11.90	2.39	3.88	0.78	2.11	0.42	3.15	0.63	0.22	0.04	0.65	0.13
2112	482.1	11.39	2.36	2.97	0.62	2.31	0.48	3.15	0.65	0.18	0.04	0.74	0.15
2113	536.1	11.69	2.18	3.32	0.62	1.99	0.37	3.52	0.66	0.28	0.05	0.83	0.15
2114	550.9	12.69	2.30	3.49	0.63	2.09	0.38	3.72	0.68	0.26	0.05	0.73	0.13
2115	572.9	14.07	2.46	3.71	0.65	2.25	0.39	3.67	0.64	0.31	0.05	0.84	0.15
2116	653.8	16.49	2.52	3.85	0.59	2.10	0.32	3.78	0.58	0.35	0.05	0.82	0.13
2117	555.6	12.98	2.34	3.58	0.64	2.00	0.36	3.22	0.58	0.25	0.04	0.73	0.13
2118	604.6	14.54	2.40	4.04	0.67	2.23	0.37	3.67	0.61	0.30	0.05	0.99	0.16
2119	601.8	13.23	2.20	3.49	0.58	2.06	0.34	3.56	0.59	0.41	0.07	0.73	0.12
MEAN	562.06	13.35	2.37	3.61	0.64	2.12	0.38	3.51	0.63	0.29	0.05	0.79	0.14
±S.D.	±50.92	±1.58	±0.13	±0.31	±0.06	±0.11	±0.04	±0.25	±0.04	±0.07	±0.01	±0.10	±0.02

Table A-19 (Continued)

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual and Mean Body Weights, Organ Weights, and Organ/Body Weight Ratios of Exposed Males[a]

Exposure Level: 300 ppm

Pathology Number	Body Weight (g)[b]	Organ Weights											
		Liver		Kidneys		Brain		Testes		Thymus		Spleen	
		g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]
80A-2130	483.3	11.98	2.48	3.35	0.69	2.04	0.42	1.30	0.27	0.23	0.05	0.73	0.15
2131	594.4	14.06	2.37	3.82	0.64	2.13	0.36	3.20	0.54	0.27	0.05	0.63	0.11
2132	564.0	14.36	2.55	3.34	0.59	2.02	0.36	1.28	0.23	0.30	0.05	0.73	0.13
2133	540.5	12.39	2.29	3.69	0.68	2.05	0.38	2.88	0.53	0.19	0.04	0.78	0.14
2134	522.6	12.58	2.41	3.43	0.66	2.12	0.41	3.88	0.74	0.28	0.05	0.88	0.17
2135	455.3	9.75	2.14	3.23	0.71	2.11	0.46	3.04	0.67	0.22	0.05	0.75	0.16
2136	558.4	13.70	2.45	3.86	0.69	2.26	0.40	3.29	0.59	0.29	0.05	0.70	0.13
2137	607.6	14.74	2.43	3.74	0.62	2.05	0.34	3.55	0.58	0.40	0.07	0.78	0.13
2138	550.3	13.24	2.41	3.45	0.63	1.92	0.35	2.18	0.40	0.29	0.05	0.84	0.15
2139	459.1	10.72	2.34	3.30	0.72	2.10	0.46	1.59	0.35	0.18	0.04	0.78	0.17
MEAN	533.55	12.75	2.39	3.52	0.66	2.08	0.39	2.62	0.49	0.27	0.05	0.76	0.14
±S.D.	±53.09	±1.61	±0.11	±0.23	±0.04	±0.09	±0.04	±0.96	±0.17	±0.06	±0.01	±0.07	±0.02

[a]Male rats were exposed to 0, 30, 100, or 300 ppm EGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Males were sacrificed 23 weeks post-exposure.

[b]Absolute weight of the organ in grams.

[c]Relative weight of the organ in grams per 100 grams body weight.

Table A-20

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual and Mean Body Weights, Organ Weights, and Organ/Body Weight Ratios of Exposed Females[a]

Exposure Level: 0 ppm

Pathology Number	Body Weight (g)	Organ Weights									
		Liver		Kidneys		Brain		Thymus		Spleen	
		g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]
80A-2150	273.8	7.30	2.67	1.82	0.66	1.81	0.66	0.19	0.07	0.47	0.17
2151	321.6	8.23	2.56	2.20	0.68	1.94	0.60	0.41	0.13	0.63	0.20
2152	269.3	7.24	2.69	1.89	0.70	1.99	0.74	0.24	0.09	0.53	0.20
2153	277.7	7.84	2.82	2.04	0.73	1.89	0.68	0.33	0.12	0.67	0.24
2154	293.5	6.91	2.35	2.06	0.70	1.89	0.64	0.31	0.11	0.59	0.20
2155	297.7	7.64	2.57	2.15	0.72	1.80	0.60	0.24	0.08	0.52	0.17
2156	250.0	9.01	3.60	1.96	0.78	1.91	0.76	0.34	0.14	0.61	0.24
2157	325.4	8.97	2.76	2.31	0.71	1.76	0.54	0.23	0.07	0.53	0.16
2159	313.8	8.46	2.70	2.17	0.69	1.99	0.63	0.35	0.11	0.53	0.17
2160	294.1	8.55	2.91	2.11	0.72	1.88	0.64	0.28	0.10	0.59	0.20
MEAN	291.69	8.02	2.76	2.07	0.71	1.89	0.65	0.29	0.10	0.57	0.20
±S.D.	±24.31	±0.74	±0.33	±0.15	±0.03	±0.08	±0.07	±0.07	±0.02	±0.06	±0.03

Table A-20 (Continued)

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual and Mean Body Weights, Organ Weights, and Organ/Body Weight Ratios of Exposed Females[a]

Exposure Level: 30 ppm

Pathology Number	Body Weight (g)	Organ Weights									
		Liver		Kidneys		Brain		Thymus		Spleen	
		g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]
80A-2180	284.6	7.96	2.80	2.24	0.79	1.97	0.69	0.31	0.11	0.60	0.21
2181	258.9	6.47	2.50	1.83	0.71	1.94	0.75	0.26	0.10	0.57	0.22
2182	272.8	7.37	2.70	1.87	0.69	1.85	0.68	0.24	0.09	0.54	0.20
2183	358.9	8.99	2.50	2.25	0.63	1.92	0.53	0.33	0.09	0.60	0.17
2184	317.7	8.06	2.54	2.08	0.65	2.02	0.64	0.25	0.08	0.54	0.17
2185	297.9	7.24	2.43	1.97	0.66	1.96	0.66	0.24	0.08	0.55	0.18
2186	249.4	9.35	3.75	2.40	0.96	1.93	0.77	0.36	0.14	0.59	0.24
2187	359.8	10.40	2.89	2.54	0.71	1.99	0.55	0.41	0.11	0.75	0.21
2188	330.0	9.03	2.74	2.36	0.72	2.02	0.61	0.32	0.10	0.56	0.17
2190	289.0	7.82	2.71	2.23	0.77	1.85	0.64	0.27	0.09	0.82	0.28
MEAN	301.90	8.27	2.76	2.18	0.73	1.95	0.65	0.30	0.10	0.61	0.20
±S.D.	±38.84	±1.17	±0.38	±0.23	±0.10	±0.06	±0.08	±0.06	±0.02	±0.10	±0.04

Table A-20 (Continued)

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual and Mean Body Weights, Organ Weights, and Organ/Body Weight Ratios of Exposed Females[a]

Exposure Level: 100 ppm

Pathology Number	Body Weight (g)	Organ Weights									
		Liver		Kidneys		Brain		Thymus		Spleen	
		g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]
80A-2210	289.6	6.88	2.38	2.08	0.72	1.94	0.67	0.31	0.11	0.58	0.20
2211	268.3	6.93	2.58	1.93	0.72	1.87	0.70	0.33	0.12	0.60	0.22
2212	260.4	6.44	2.47	1.88	0.72	1.90	0.73	0.25	0.10	0.55	0.21
2213	309.5	8.92	2.88	2.38	0.77	1.90	0.61	0.35	0.11	0.58	0.19
2214	337.7	9.32	2.76	2.57	0.76	2.04	0.60	0.54	0.16	0.56	0.17
2215	301.3	8.73	2.90	2.13	0.71	2.05	0.68	0.25	0.08	0.58	0.19
2216	344.1	7.74	2.25	2.00	0.58	1.99	0.58	0.41	0.12	0.55	0.16
2217	282.6	7.20	2.55	1.94	0.69	1.86	0.66	0.26	0.09	0.71	0.25
2218	296.7	7.50	2.53	1.84	0.62	1.89	0.64	0.30	0.10	0.51	0.17
2219	326.6	8.10	2.48	2.04	0.62	1.88	0.58	0.30	0.09	0.58	0.18
MEAN	301.68	7.78	2.58	2.08	0.69	1.93	0.64	0.33	0.11	0.58	0.19
±S.D.	±28.15	±0.97	±0.21	±0.23	±0.06	±0.07	±0.05	±0.09	±0.02	±0.05	±0.03

Table A-20 (Continued)

EGME: INHALATION REPRODUCTION AND DOMINANT-LETHAL STUDY IN RATS

Individual and Mean Body Weights, Organ Weights, and Organ/Body Weight Ratios of Exposed Females[a]

Exposure Level: 300 ppm

Pathology Number	Body Weight (g)	Organ Weights									
		Liver		Kidneys		Brain		Thymus		Spleen	
		g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]	g[b]	g/100[c]
80A-2230	308.6	8.11	2.63	1.97	0.64	1.77	0.57	0.45	0.15	0.73	0.24
2231	238.8	6.33	2.64	1.69	0.71	1.84	0.77	0.19	0.08	0.54	0.23
2232	301.6	8.12	2.69	2.22	0.74	1.78	0.59	0.28	0.09	0.48	0.16
2233	262.8	6.65	2.53	1.86	0.71	1.89	0.72	0.26	0.10	0.70	0.27
2234	292.3	7.87	2.69	2.16	0.74	1.92	0.66	0.36	0.12	0.60	0.21
2235	283.7	7.17	2.53	1.90	0.67	2.04	0.72	0.31	0.11	0.66	0.23
2236	293.0	7.02	2.40	1.83	0.62	1.92	0.66	0.20	0.07	0.55	0.19
2237	288.0	7.21	2.50	2.15	0.75	1.90	0.66	0.19	0.07	0.49	0.17
2238	290.0	7.31	2.52	2.34	0.81	1.96	0.68	0.20	0.07	0.55	0.19
2239	354.1	8.72	2.46	2.24	0.63	1.96	0.55	0.36	0.10	0.62	0.18
MEAN	291.29	7.45	2.56	2.04	0.70	1.90	0.66	0.28	0.10	0.59	0.20
±S.D.	±29.80	±0.74	±0.10	±0.21	±0.06	±0.08	±0.07	±0.09	±0.03	±0.09	±0.03

[a]Female rats were exposed to 0, 30, 100, or 300 ppm EGME by inhalation for 6 hours/day, 5 days/week for 13 consecutive weeks. Females were sacrificed 15 weeks post-exposure.

[b]Absolute weight of the organ in grams.

[c]Relative weight of the organ in grams per 100 grams body weight.

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TABLE A-2 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Food Consumption of Pregnant Rats [a]

Exposure Level: 50 ppm

ANIMAL NUMBER	MATERNAL FOOD CONSUMPTION (G/DAY) DAYS OF GESTATION 6-9	9-12	12-15	15-18	18-21
8109714	13.0	14.4	14.4	13.3	13.1
8109715	13.1	14.5	16.8	16.9	18.6
8109716	14.7	16.2	17.7	17.2	19.1
8109717	11.7	12.8	13.7	15.4	16.0
8109718	12.5	13.1	14.8	15.6	18.6
8109734	15.1	16.4	16.7	18.5	10.0#
8109735	15.7	17.1	17.6	19.2	17.4
8109736	14.7	15.6	17.0	19.0	18.2
8109737	12.7	15.4	15.0	16.8	16.8
8109738	13.9	15.5	15.8	18.1	17.7
8109744	14.3	14.9	15.4	18.2	16.9
8109745	13.0	14.3	-43.2#	16.7	15.7
8109763	13.4	13.9	15.4	15.9	16.9
8109764	13.3	17.1	16.3	16.6	16.5
8109765	14.9	16.8	18.1	17.5	19.8
8109766	13.2	15.0	16.3	16.2	16.1
8109767	13.9	16.4	15.9	14.6	16.1
8109781	12.1	15.2	15.5	16.0	14.8
8109782	13.8	16.3	16.7	17.2	16.5
8109783	14.8	16.4	16.6	16.7	16.8
8109784	13.7	15.8	15.1	17.3	17.0
8109785	12.3	15.1	17.8	17.2	16.8
8109799	13.9	15.0	15.1	17.3	16.6
8109800	12.8	14.8	14.7	17.7	18.3
8109801	12.1	15.1	15.6	16.0	15.5
8109802	14.2	16.0	15.9	18.2	16.2
8109811	6.9#	9.4#	17.9	13.0	18.0
8109812	14.8	14.9	N.D.	17.4	16.6
8100386	12.8	12.7	13.4	16.2	15.0
8100387	14.3	15.2	15.2	17.4	16.8
MEAN	13.6	15.2	15.9	16.8	16.8
S.D.	1.03	1.18	1.25	1.43	1.38

[a]Bred rats were exposed to 0, 3, 10 or 50 ppm of EGME for 6 hr/day on days 6 through 15 of gestation.

#Statistical outlier identified by sequential outlier test, alpha = 0.02. Value not included in calculations.

*Significantly different from the control value.

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TABLE A-3

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Water Consumption of Pregnant Rats [a]

Exposure Level: Control (0 ppm)

ANIMAL NUMBER	WATER USAGE DAYS OF GESTATION 6-9	9-12	12-15	15-18	18-21
	WATER CONSUMPTION (G/DAY)				
8109699	16.9	21.4	26.0	27.4	28.8
8109700	18.1	20.6	25.0	28.7	27.2
8109701	16.7	21.2	27.2	26.0	25.7
8109702	14.4	17.9	21.6	20.2	24.4
8109703	21.8	27.6	31.9	35.7	31.4
8109719	16.6	19.5	20.8	27.5	26.9
8109720	17.9	20.2	25.1	24.3	30.5
8109721	22.1	24.0	27.9	30.3	30.3
8109722	19.2	24.7	32.2	33.2	32.8
8109723	18.4	21.7	27.0	28.2	29.9
8109739	19.9	20.8	24.1	33.7	29.4
8109740	19.4	19.9	26.0	29.6	33.3
8109746	18.7	18.1	35.5	37.5	34.5
8109747	16.4	9.9#	22.5	25.8	25.4
8109749	16.3	20.2	24.3	29.2	28.6
8109750	16.6	20.8	23.9	26.5	25.6
8109751	15.3	17.2	22.7	27.6	26.1
8109768	17.7	23.4	27.8	30.1	29.9
8109769	23.5	23.0	28.2	36.3	30.9
8109770	19.7	21.6	24.3	30.4	29.1
8109771	18.5	20.7	21.7	27.4	26.3
8109786	17.2	23.4	27.6	32.5	29.0
8109787	15.3	19.3	23.2	29.5	27.6
8109788	23.8	30.3	31.9	36.2	30.0
8109789	22.9	21.6	36.1	36.1	32.6
8109803	17.5	21.0	23.9	26.6	25.0
8109804	19.5	26.9	25.9	29.4	28.2
8109813	20.0	25.9	25.4	32.3	27.0
8109814	10.6	26.6	26.7	27.2	24.7
MEAN	18.4	22.1	26.4	29.8	28.7
S.D.	2.84	3.13	3.91	4.08	2.74

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TABLE A-3 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Water Consumption of Pregnant Rats[a]

Exposure Level: 3 ppm

ANIMAL NUMBER	DAILY WATER CONSUMPTION (G/DAY) DAYS OF GESTATION 6-9	9-12	12-15	15-18	18-21
B109704	21.3	25.2	27.1	32.1	32.7
B109705	15.7	19.7	21.2	24.6	24.8
B109707	19.1	20.9	24.2	26.5	27.6
B109708	16.5	20.9	26.0	25.5	25.7
B109724	19.4	22.7	27.8	33.8	30.1
B109725	21.0	22.7	25.5	33.0	33.9
B109726	20.2	22.5	25.1	29.3	30.4
B109727	19.2	22.0	23.0	28.6	28.3
B109728	20.7	23.8	28.0	31.4	32.4
B109741	20.9	19.5	26.3	27.7	29.1
B109742	19.5	22.9	33.7	34.1	26.6
B109752	21.3	27.0	30.2	30.0	26.5
B109753	21.7	26.3	27.2	29.2	30.2
B109754	21.4	25.1	30.6	52.7#	30.8
B109755	20.7	31.2	27.5	27.7	27.2
B109756	21.0	38.1#	29.5	32.0	28.7
B109772	19.7	N.D.	24.5	28.3	26.9
B109774	18.2	18.3	25.4	28.9	27.8
B109775	19.3	21.7	26.6	26.9	26.2
B109776	17.3	20.3	23.1	25.4	28.5
B109790	17.7	22.4	24.4	27.2	23.2
B109791	20.8	27.3	28.3	33.2	29.6
B109792	16.8	21.1	26.0	30.9	28.2
B109793	15.4	20.1	21.8	27.3	25.0
B109805	18.4	20.5	27.2	28.5	27.4
B109806	19.9	22.5	25.3	35.4	30.5
B109807	19.2	22.4	28.5	29.1	26.8
B109815	24.7	28.4	26.2	38.5	27.2
B109816	17.6	25.0	25.1	28.0	27.1
MEAN	19.5	23.1	26.5	29.8	28.3
S.D.	2.04	3.04	2.71	3.30	2.45

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TABLE A-3 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Water Consumption of Pregnant Rats [a]

Exposure Level: 10 ppm

ANIMAL NUMBER	WATERUAL WATER CONSUMPTION (G/DAY) DAYS OF GESTATION 6-9	9-12	12-15	15-18	18-21
6109709	14.6	18.2	23.1	24.5	26.8
6109710	15.8	20.6	25.8	27.8	28.1
8109713	16.1	19.0	23.0	26.3	25.6
8109729	21.2	21.7	25.3	31.8	28.9
6109730	20.7	23.0	30.7	37.9	29.2
6109731	15.2	21.5	27.0	28.1	28.4
8109732	21.9	27.1	33.6	39.5	32.7
8109733	19.3	22.4	27.1	29.7	26.7
6109743	20.7	22.8	25.9	31.7	31.4
6109757	22.9	25.8	26.6	26.0	25.3
6109758	15.5	32.4	32.3	45.9#	31.2
6109759	18.6	31.9	25.2	26.6	38.0
6109760	16.3	54.6#	30.1	35.9	33.5
8109762	20.6	55.3#	28.6	32.2	32.8
6109777	17.0	25.1	26.7	27.7	27.2
8109778	21.4	24.5	11.7#	29.5	33.5
8109779	16.8	25.2	27.9	32.5	30.2
8109780	18.4	24.0	25.6	28.0	28.9
8109794	20.6	24.7	24.4	32.7	61.4#
8109795	21.0	23.4	29.4	30.2	26.0
6109796	17.6	21.8	22.9	24.6	27.7
6109797	38.9#	22.1	27.5	30.4	26.8
6109798	17.7	24.1	26.6	31.7	27.2
8109808	21.4	25.4	30.9	29.4	25.2
8109809	18.8	21.8	24.2	22.4	26.5
8109810	18.0	22.9	22.9	26.0	25.1
6109817	18.9	24.4	28.7	32.8	30.1
8109818	24.0	28.7	25.9	26.7	30.8
MEAN	19.0	24.0	27.0	30.0	29.0
S.D.	2.49	3.32	2.87	4.37	3.21

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TABLE A-3 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Water Consumption of Pregnant Rats [a]

Exposure Level: 50 ppm

ANIMAL NUMBER	MATERNAL WATER CONSUMPTION (G/DAY) DAYS OF GESTATION 6-9	9-12	12-15	15-18	18-21
6109714	15.6	20.7	20.5	22.3	25.4
6109715	19.8	26.3	38.1	34.9	34.3
6109716	19.8	25.5	28.3	29.0	30.1
6109717	14.5	18.9	23.9	23.4	29.5
6109718	16.5	21.2	24.9	33.5	29.3
6109734	19.0	21.8	26.4	29.2	19.2
6109735	18.2	25.3	26.1	30.9	30.1
6109736	24.9	25.0	26.8	30.1	35.2
6109737	16.2	20.5	28.6	27.0	27.9
6109738	18.7	23.0	26.2	31.1	31.0
6109744	24.1	21.7	27.6	39.7	31.1
6109745	19.3	22.9	24.7	29.1	27.5
6109763	18.1	23.6	28.2	27.8	26.5
6109764	19.1	22.7	26.3	29.6	31.8
6109765	23.0	24.7	30.7	32.4	35.6
6109766	17.2	20.0	25.3	29.2	26.4
6109767	18.1	17.7	26.8	30.0	27.8
6109761	15.2	23.7	26.9	25.3	24.9
6109762	21.7	24.3	35.3	31.8	35.0
6109783	24.2	23.7	27.0	33.2	31.0
6109784	6.3#	23.9	27.5	29.8	28.6
6109785	40.4#	28.6	28.6	33.0	33.8
6109799	19.2	27.4	33.9	36.2	29.3
6109800	18.9	25.3	23.6	31.1	30.8
6109801	16.7	22.9	22.8	25.6	25.0
6109802	18.8	28.2	36.9	37.3	30.2
6109811	1.3#	3.7#	29.9	0.5#	33.1
6109812	18.5	23.6	27.2	28.9	26.7
6100366	17.8	21.9	20.9	24.9	23.8
6100367	20.0	24.6	25.7	30.8	28.0
MEAN	19.0	23.4	27.5	30.5	29.3
S.D.	2.67	2.57	4.13	4.23	3.73

[a]Bred Fischer 344 rats were exposed to 0, 3, 10 or 50 ppm of EGME for 6 hr/day on days 6 through 15 of gestation.

#Statistical outlier identified by sequential outlier test, alpha = 0.02. Value not included in calculations.

There were no statistically significant differences from the control values.

Table A-4

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TEREATOLOGY STUDY IN RATS AND RABBITS

Individual Organ Weights of Pregnant Rats[a]

Exposure Level: Control (0 ppm)

Animal Number	Liver		Spleen		Thymus	
	Absolute[b]	Relative[c]	Absolute	Relative	Absolute	Relative
81A-9699	9.95	4.05	0.49	0.20	0.26	0.11
9700	9.62	3.90	0.47	0.19	0.27	0.11
9701	8.99	3.48	0.47	0.18	0.27	0.10
9702	9.88	4.57	0.53	0.25	0.33	0.15
9703	10.71	3.77	0.51	0.18	0.29	0.10
9719	9.53	3.81	0.44	0.18	0.19	0.08
9720	9.92	3.78	0.49	0.19	0.23	0.09
9721	10.16	3.64	0.50	0.18	0.23	0.08
9722	10.44	3.74	0.50	0.18	0.18	0.06
9723	8.83	3.30	0.46	0.17	0.25	0.09
9739	9.15	3.42	0.42	0.16	0.23	0.09
9740	9.32	3.44	0.39	0.14	0.15	0.06
9746	9.51	3.65	0.46	0.18	0.18	0.07
9747	9.41	4.21	0.49	0.22	0.19	0.09
9748	9.74	3.65	0.42	0.16	0.13	0.05
9750	9.46	3.76	0.45	0.18	0.20	0.08
9751	8.86	3.50	0.43	0.17	0.12	0.05
9768	9.68	3.77	0.45	0.18	0.18	0.07
9769	9.89	3.62	0.45	0.16	0.19	0.07
9770	8.81	3.50	0.40	0.16	0.16	0.06
9771	9.08	3.61	0.44	0.17	0.18	0.07
9786	9.81	3.75	0.52	0.20	0.16	0.06
9787	9.19	3.48	0.51	0.19	0.16	0.06
9788	9.16	3.55	0.49	0.19	0.16	0.06
9789	9.65	3.43	0.52	0.18	0.16	0.06
9803	9.79	3.69	0.48	0.18	0.33	0.12
9804	9.57	3.51	0.53	0.19	0.25	0.09
9813	9.99	3.81	0.54	0.21	0.23	0.09
9814	9.98	3.96	0.50	0.20	0.17	0.07
Mean	9.59	3.70	0.47	0.18	0.21	0.08
±S.D.	0.47	0.26	0.04	0.02	0.06	0.02

Table A-4 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TEREATOLOGY STUDY IN RATS AND RABBITS

Individual Organ Weights of Pregnant Rats[a]

Exposure Level: 3 ppm

Animal Number	Liver		Spleen		Thymus	
	Absolute[b]	Relative[c]	Absolute	Relative	Absolute	Relative
81A-9705	9.48	3.83	0.50	0.20	0.22	0.09
9707	10.15	3.82	0.55	0.21	0.29	0.11
9708	9.29	3.62	0.48	0.19	0.27	0.11
9724	10.24	3.74	0.42	0.15	0.19	0.07
9725	10.67	3.57	0.53	0.18	0.20	0.07
9726	9.79	3.64	0.52	0.19	0.18	0.07
9727	9.46	3.52	0.40	0.15	0.18	0.07
9728	9.44	3.62	0.44	0.17	0.18	0.07
9741	9.85	4.28	0.49	0.21	0.18	0.08
9742	9.69	3.66	0.46	0.17	0.14	0.05
9752	9.71	3.68	0.42	0.16	0.12	0.05
9753	9.84	3.81	0.43	0.17	0.20	0.08
9754	9.65	3.70	0.45	0.17	0.17	0.07
9755	9.43	3.76	0.48	0.19	0.13	0.05
9756	9.87	3.72	0.45	0.17	0.07	0.03
9772	8.66	3.44	0.46	0.18	0.20	0.08
9774	9.56	3.91	0.46	0.19	0.21	0.09
9775	9.42	3.62	0.47	0.18	0.18	0.07
9776	9.04	3.61	0.46	0.18	0.13	0.05
9790	8.94	3.56	0.52	0.21	0.20	0.08
9791	10.11	3.69	0.48	0.18	0.18	0.07
9792	9.06	3.58	0.56	0.22	0.21	0.08
9793	9.11	3.60	0.54	0.21	0.13	0.05
9805	9.62	3.72	0.52	0.20	0.21	0.08
9806	9.21	3.52	0.48	0.18	0.20	0.08
9807	9.57	3.55	0.51	0.19	0.18	0.07
9815	8.52	3.47	0.46	0.19	0.19	0.08
9816	8.83	3.65	0.45	0.19	0.21	0.09
Mean	9.51	3.68	0.48	0.19	0.18	0.07
±S.D.	0.49	0.16	0.04	0.02	0.04	0.02

Table A-4 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TEREATOLOGY STUDY IN RATS AND RABBITS

Individual Organ Weights of Pregnant Rats[a]

Exposure Level: 10 ppm

Animal Number	Liver		Spleen		Thymus	
	Absolute[b]	Relative[c]	Absolute	Relative	Absolute	Relative
81A-9709	9.05	3.51	0.57	0.22	0.24	0.09
9710	10.20	3.85	0.53	0.20	0.25	0.09
9713	9.61	3.70	0.51	0.20	0.19	0.07
9729	9.05	3.45	0.46	0.18	0.17	0.06
9730	9.62	3.47	0.48	0.17	0.14	0.05
9731	9.28	3.58	0.48	0.19	0.15	0.06
9732	9.65	3.48	0.45	0.16	0.18	0.06
9733	8.62	3.41	0.45	0.18	0.19	0.08
9743	10.27	3.79	0.49	0.18	0.12	0.04
9757	9.63	3.79	0.43	0.17	0.18	0.07
9758	9.24	3.77	0.37	0.15	0.15	0.06
9759	10.60	4.00	0.48	0.18	0.20	0.08
9760	10.25	3.89	0.46	0.17	0.22	0.08
9762	10.51	3.84	0.59	0.22	0.16	0.06
9777	11.06	4.24	0.45	0.17	0.19	0.07
9778	8.82	3.49	0.42	0.17	0.16	0.06
9779	9.30	3.65	0.40	0.16	0.16	0.06
9780	9.51	3.70	0.49	0.19	0.20	0.08
9794	9.23	3.58	0.56	0.22	0.16	0.06
9795	9.92	3.77	0.57	0.22	0.13	0.05
9796	8.83	3.46	0.54	0.21	0.13	0.05
9797	9.26	3.83	0.55	0.23	0.17	0.07
9798	9.64	3.57	0.48	0.18	0.22	0.08
9808	8.92	3.45	0.43	0.17	0.20	0.08
9809	9.55	3.67	0.47	0.18	0.20	0.08
9810	8.91	3.45	0.49	0.19	0.18	0.07
9817	10.73	3.80	0.48	0.17	0.21	0.07
9818	10.11	4.01	0.49	0.19	0.16	0.06
Mean	9.62	3.69	0.48	0.19	0.18	0.07
±S.D.	0.64	0.21	0.05	0.02	0.03	0.01

Table A-4 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Organ Weights of Pregnant Rats[a]

Exposure Level: 50 ppm

Animal Number	Liver		Spleen		Thymus	
	Absolute[b]	Relative[c]	Absolute	Relative	Absolute	Relative
81A-9714	9.24	3.61	0.48	0.19	0.24	0.09
9715	10.67	3.99	0.59	0.22	0.31	0.12
9716	10.18	4.37	0.89	0.38	0.37	0.16
9717	10.20	3.93	0.50	0.19	0.20	0.08
9718	10.17	3.87	0.51	0.19	0.20	0.08
9734	9.20	3.29	0.47	0.17	0.15	0.05
9735	9.70	3.47	0.51	0.18	0.16	0.06
9736	9.83	3.57	0.56	0.20	0.18	0.07
9737	9.77	3.75	0.55	0.21	0.18	0.07
9738	10.60	4.00	0.51	0.19	0.25	0.09
9744	10.20	3.83	0.48	0.18	0.14	0.05
9745	9.05	3.45	0.44	0.17	0.13	0.05
9763	10.23	3.92	0.46	0.18	0.12	0.05
9764	10.83	3.98	0.44	0.16	0.14	0.05
9765	11.04	3.95	0.45	0.16	0.21	0.08
9766	10.79	4.05	0.49	0.18	0.19	0.07
9767	10.18	3.98	0.42	0.16	0.17	0.07
9781	9.51	3.75	0.50	0.20	0.17	0.07
9782	9.65	3.76	0.43	0.17	0.21	0.08
9783	9.78	3.79	0.53	0.21	0.19	0.07
9784	10.51	3.89	0.47	0.17	0.16	0.06
9785	9.70	3.68	0.48	0.18	0.17	0.06
9799	10.42	3.85	0.49	0.18	0.18	0.07
9800	10.21	3.79	0.51	0.19	0.11	0.04
9801	8.91	3.55	0.45	0.18	0.12	0.05
9802	9.38	3.61	0.49	0.19	0.12	0.05
9811	9.13	3.52	0.47	0.18	0.18	0.07
9812	9.51	3.49	0.54	0.20	0.19	0.07
81B-0386	9.64	3.88	0.54	0.22	0.18	0.07
0387	10.56	3.89	0.56	0.21	0.20	0.07
Mean	9.96*	3.78	0.51	0.19	0.18	0.07
±S.D.	0.58	0.23	0.08	0.04	0.05	0.02

[a]Bred Fischer 344 rats were exposed to 0, 3, 10 or 50 ppm of EGME for 6 hr/day on days 6 through 15 of gestation.
[b]Grams
[c]Grams/100g body weight.

*Significantly different from the control value.

Table A-5

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Hematology Data for Pregnant Rats[a]

Exposure Level ppm	Animal Number	RBC X $10^6/mm^3$	HGB GM/DL	PCV %	MCV Cubic Microns	MCH Micro Microgm	MCHC %	PLAT X $10^3/mm^3$	WBC X $10^3/mm^3$
Control	81A-9699	6.80	13.0	37.4	55.00	19.10	34.80	1082.	2.2
	9700	6.58	13.0	36.0	55.00	19.80	36.10	1128.	4.8
	9701	6.56	12.4	35.6	54.00	18.90	34.80	1164.	2.4
	9702[b]	7.50	14.8	41.4	55.00	19.70	35.70	988.	7.6
	9703	6.36	12.6	35.2	55.00	19.80	35.80	1194.	6.8
	9719	6.38	12.4	34.8	55.00	19.40	35.60	1134.	3.4
	9720	6.52	12.6	35.8	55.00	19.30	35.20	1038.	2.4
	9721	6.36	12.4	34.8	55.00	19.50	35.60	1214.	2.4
	9722	6.26	12.2	34.4	55.00	19.50	35.50	1230.	1.6
	9723	6.58	12.6	35.6	54.00	19.10	35.40	1162.	1.8
	Mean	6.49	12.6	35.5	54.80	19.41	35.45	1133.	3.5
	±S.D.	0.16	0.3	0.9	0.42	0.31	0.42	78	2.1
3	81A-9705	6.64	12.6	35.6	54.00	19.00	35.40	1186.	4.8
	9707	6.24	12.0	33.6	54.00	19.20	35.70	1238.	6.0
	9708	5.94	11.4	31.4	53.00	19.20	36.30	1034.	1.6
	9724	6.20	11.8	33.6	54.00	19.00	35.10	1304.	2.0
	9725	6.46	12.8	35.2	54.00	19.80	36.40	1162.	2.6
	9726	6.24	11.8	32.8	53.00	18.90	36.00	1146.	2.6
	9727	6.36	12.4	34.2	54.00	19.50	36.30	1202.	1.6
	9728	6.16	11.8	33.2	54.00	19.20	35.50	1100.	1.2
	9752	6.36	12.2	34.4	54.00	19.20	35.50	1026.	5.4
	9753	6.62	12.4	36.2	55.00	18.70	34.30	1102.	2.0
	Mean	6.32	12.1*	34.0*	53.90	19.17	35.65	1150.	3.0
	±S.D.	0.21	0.4	1.4	0.57	0.31	0.65	88.	1.7
10	81A-9709	6.36	12.0	34.2	54.00	18.90	35.10	1242.	0.8
	9710	6.30	11.8	33.8	54.00	18.70	34.90	1116.	0.8
	9713	6.42	12.0	34.0	53.00	18.70	35.30	1210.	3.6
	9729	6.38	12.2	34.0	53.00	19.10	35.90	1216.	1.2
	9730	6.22	11.8	33.6	54.00	19.00	35.10	1068.	3.4
	9731	6.48	12.2	34.6	53.00	18.80	35.30	984.	4.8
	9732	6.06	11.8	32.6	54.00	19.50	36.20	1134.	1.8
	9733	6.34	12.2	33.0	52.00	19.20	37.00	1160.	0.4
	9757	6.22	12.0	33.8	54.00	19.30	35.50	1064.	1.0
	9759	6.16	12.2	33.0	54.00	19.80	37.00	1126.	2.8
	Mean	6.29*	12.0*	33.7*	53.50	19.10	35.73	1132.	2.1
	±S.D.	0.13	0.2	0.6	0.71	0.36	0.77	80.	1.5
50	81A-9714	6.28	12.2	32.8	52.00	19.40	37.20	1260.	4.4
	9715	6.36	12.2	34.2	54.00	19.20	35.70	1120.	7.2
	9716	5.72	11.4	33.0	58.00	19.90	34.50	1296.	9.0
	9717	6.14	11.6	32.8	53.00	18.90	35.40	1036.	2.0
	9718	6.04	11.4	32.4	54.00	18.90	35.20	1116.	3.4
	9734	6.12	11.4	33.0	54.00	18.60	34.50	1088.	4.0
	9735	6.00	11.6	32.4	54.00	19.30	35.80	1074.	2.2
	9736	6.48	12.4	34.8	54.00	19.10	35.60	984.	5.4
	9737	6.22	12.0	33.6	54.00	19.30	35.70	1078.	7.4
	9738	6.46	12.0	34.8	54.00	18.60	34.50	1078.	5.2
	Mean	6.18*	11.8*	33.4*	54.10	19.12	35.41	1113.	5.0
	±S.D.	0.23	0.4	0.9	1.52	0.39	0.82	96.	2.3

[a]Bred Fischer 344 rats were exposed to 0, 3, 10 or 50 ppm of EGME for 6 hr/day on day 6 through 15 of gestation. Terminal (day 21) blood samples were obtained by cardiac puncture from 10 rats/exposure level.
[b]Statistical outlier excluded from consideration due to unusually small litter size.
*Significantly different from the control value using Dunnett's test.

Table A-6

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Litter Summary of Observations Made at Cesarean Section in Rats[a]

Exposure Level: Control (0 ppm)

Animal Number	Corpora Lutea	Implantations	Pre-Implantation Loss	Resorptions	Litter Size	Sex Ratio M/F	Fetal Body Weight (g)	Fetal Crown-Rump Length (mm)
81A-9699	10	8	2	1	7	3/4	4.44	44.14
9700	8	8	0	0	8	5/3	4.65	44.58
9701	11	11	0	0	11	7/4	4.31	44.65
9702	12	2	10	1	1	1/0	4.80	46.80
9703	13	13	0	1	12	6/6	4.34	44.59
9719	11	12	0	2	10	7/3	4.27	42.51
9720	11	11	0	1	10	3/7	4.28	40.37
9721	12	12	0	0	12	7/5	4.45	42.68
9722	13	13	0	0	13	7/6	4.26	42.18
9723	13	12	1	0	12	4/8	4.31	39.54
9739	12	12	0	0	12	3/9	4.24	39.58
9740	13	12	1	0	12	7/5	4.30	41.38
9746	10	10	0	0	10	3/7	4.35	45.14
9747	10	2	8	1	1	0/1	3.56	42.70
9748	11	11	0	0	11	7/4	4.55	45.33
9749	Non-Pregnant							
9750	11	11	0	3	8	5/3	4.38	44.81
9751	10	10	0	0	10	3/7	4.38	44.85
9768	12	12	0	2	10	6/4	4.31	40.04
9769	12	12	0	0	12	8/4	4.18	41.44
9770	11	11	0	0	11	6/5	4.29	41.67
9771	11	10	1	1	9	6/3	4.39	42.39
9786	12	12	0	1	11	5/6	4.22	41.52
9787	11	11	0	1	10	6/4	4.42	42.45
9788	12	11	1	0	11	8/3	4.16	40.55
9789	12	12	0	0	12	7/5	4.36	41.45
9803	10	10	0	0	10	5/5	4.20	39.82
9804	12	12	0	0	12	6/6	4.32	40.26
9813	11	12	0	1	11	6/5	4.27	44.53
9814	11	10	1	2	8	4/4	4.52	44.39
Mean±S.D.	11±1	11±3	8±21[b]*	0.6±0.8	10±3	53/47	4.33±0.20	42.7±2.1

Table A-6 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Litter Summary of Observations Made at Cesarean Section in Rats[a]

Exposure Level: 3 ppm

Animal Number	Corpora Lutea	Implantations	Pre-Implantation Loss	Resorptions	Litter Size	Sex Ratio M/F	Fetal Body Weight (g)	Fetal Crown-Rump Length (mm)
81A-9704	Delivered early on day 21 of gestation.							
9705	11	10	1	0	10	4/6	4.41	45.18
9706	Non-Pregnant							
9707	14	13	1	0	13	6/7	4.20	44.38
9708	10	10	0	0	10	4/6	4.52	46.16
9724	13	13	0	0	13	8/5	4.30	42.47
9725	13	13	0	1	12	8/4	4.47	42.28
9726	13	13	0	1	12	7/5	4.28	43.16
9727	11	12	0	0	12	4/8	4.20	42.61
9728	12	10	2	0	10	8/2	4.43	41.87
9741	11	3	8	0	3	1/2	3.34	39.37
9742	12	10	2	0	10	6/4	4.20	41.38
9752	13	11	2	0	11	6/5	4.26	44.05
9753	12	10	2	0	10	9/1	4.40	45.44
9754	12	11	1	0	11	4/7	4.33	44.60
9755	11	10	1	2	8	5/3	4.37	44.06
9756	11	11	0	0	11	1/10	4.30	44.27
9772	9	10	0	0	10	6/4	4.58	42.62
9773	Non-Pregnant							
9774	10	7	3	1	6	4/2	4.67	40.67
9775	11	11	0	0	11	6/5	4.32	42.04
9776	10	10	0	0	10	4/6	4.43	41.96
9790	10	9	1	0	9	4/5	4.32	40.39
9791	14	13	1	0	13	7/6	4.39	40.25
9792	10	10	0	1	9	6/3	4.36	41.49
9793	10	10	0	0	10	5/5	4.49	41.52
9805	11	11	0	2	9	5/4	4.39	41.64
9806	12	12	0	2	10	6/4	4.47	41.78
9807	12	13	0	0	13	6/7	4.19	41.39
9815	9	9	0	0	9	3/6	4.37	44.57
9816	10	9	1	1	8	2/6	4.38	44.40
Mean±S.D.	11±1	11±2	8±15[b]	0.4±0.7	10±2	51/49	4.33±0.23	42.7±1.7

Table A-6 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Litter Summary of Observations Made at Cesarean Section in Rats[a]

Exposure Level: 10 ppm

Animal Number	Corpora Lutea	Implantations	Pre-Implantation Loss	Resorptions	Litter Size	Sex Ratio M/F	Fetal Body Weight (g)	Fetal Crown-Rump Length (mm)
81A-9709	11	11	0	0	11	4/7	4.42	45.14
9710	13	12	1	2	10	4/6	4.53	45.28
9711	Non-Pregnant							
9712	Non-Pregnant							
9713	13	11	2	0	11	6/5	4.56	45.12
9729	13	13	0	1	12	3/9	4.30	41.06
9730	13	12	1	0	12	8/4	4.35	41.07
9731	10	9	1	0	9	5/4	4.49	40.98
9732	15	13	2	0	13	3/10	4.20	42.49
9733	9	9	0	1	8	4/4	4.74	44.01
9743	13	12	1	1	11	7/4	4.28	41.55
9757	12	11	1	0	11	4/7	4.18	44.47
9758	11	11	0	0	11	4/7	4.18	45.03
9759	12	12	0	1	11	5/6	4.30	44.95
9760	12	12	0	0	12	6/6	4.28	44.93
9761	Non-Pregnant							
9762	10	10	0	1	9	7/2	4.77	45.17
9777	11	11	0	0	11	4/7	4.39	42.45
9778	10	10	0	0	10	6/4	4.39	41.14
9779	11	10	1	0	10	5/5	4.41	42.04
9780	11	11	0	0	11	1/10	4.31	42.26
9794	11	11	0	0	11	6/5	4.32	41.61
9795	11	11	0	1	10	7/3	4.47	41.75
9796	11	11	0	0	11	6/5	4.22	39.39
9797	11	4	7	0	4	1/3	4.64	41.68
9798	12	12	0	1	11	8/3	4.45	45.25
9808	11	11	0	1	10	3/7	4.28	41.44
9809	11	11	0	0	11	7/4	4.38	42.35
9810	11	11	0	1	10	6/4	4.48	42.73
9817	13	12	1	0	12	4/8	4.38	44.33
9813	11	11	0	1	10	2/8	4.25	43.07
Mean±S.D.	12±1	11±2	5±12[b]	0.4±0.6	10±2	46/54	4.39±0.15	43.0±1.7

Table A-5 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Litter Summary of Observations Made at Cesarean Section in Rats[a]

Exposure Level: 50 ppm

Animal Number	Corpora Lutea	Implantations	Pre-Implantation Loss	Resorptions	Litter Size	Sex Ratio M/F	Fetal Body Weight (g)	Fetal Crown-Rump Length (mm)
81A-9714	13	12	1	0	12	6/6	4.19	43.79
9715	10	10	0	0	10	6/4	4.48	44.70
9716	19	8	11	6	2	1/1	3.97	41.25
9717	11	10	1	0	10	6/4	4.20	44.00
9718	12	12	0	0	12	7/5	4.17	44.01
9734	13	12	1	0	12	7/5	4.33	41.57
9735	12	12	0	0	12	4/8	4.41	41.64
9736	12	11	1	0	11	7/4	4.57	42.07
9737	10	11	0	1	10	5/5	4.57	42.36
9738	12	10	2	1	9	6/3	4.57	41.69
9744	11	10	1	0	10	2/8	4.30	40.88
9745	11	11	0	0	11	6/5	4.29	41.72
9763	10	9	1	1	8	4/4	4.36	44.24
9764	11	11	0	0	11	5/6	4.26	43.95
9765	13	12	1	2	10	4/6	4.37	44.11
9766	12	12	0	0	12	6/6	4.28	44.04
9767	12	10	2	0	10	5/5	4.22	43.84
9781	11	11	0	1	10	5/5	4.40	41.90
9782	—c	10	—c	0	10	4/6	4.38	41.12
9783	11	10	1	1	9	7/2	4.49	42.79
9784	13	13	0	1	12	5/7	4.38	41.23
9785	11	11	0	1	10	4/6	4.36	41.47
9799	12	12	0	0	12	9/3	4.29	45.33
9800	10	11	0	0	11	9/2	4.48	45.73
9801	11	10	1	0	10	5/5	4.31	45.32
9802	10	9	1	0	9	0/9	4.37	44.71
9811	11	11	0	1	10	7/3	4.36	42.48
9812	11	11	0	0	11	5/6	4.39	42.23
818-0386	13	13	0	3	10	5/5	4.17	43.05
0387	11	12	0	1	11	5/6	4.25	42.85
Mean±S.D.	12±2	11±1	5±11	0.7±1.2	10±2	51/49	4.34±0.13	43.0±1.4

[a]Bred Fischer 344 rats were exposed to 0, 3, 10 or 50 ppm of EGME for 6 hr/day on days 6 through 15 of gestation.

[b]Expressed as percent per litter, Mean ± S.D.

[c]Data not recorded at cesarean section.

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Table A-7

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Litter Summary of Alterations Among Litters of Rats*

Exposure Level: Control (0 ppm)

Animal Numbers	81A-9699	9700	9701	9702	9703	9719	9720	9721	9722	9723	9739	9740	9746	9747	9748	9750	9751	9768	9769	9770	9771	9786	9787	9788	9789	9803	9804	9813	9814	Total Fetuses	Total Litters
External Examination	7	8	11	1	12	10	12	12	13	12	12	12	10	1	11	8	10	10	12	11	9	11	10	11	12	10	12	11	8	287	29
Soft Tissue Examination	4	4	6	1	6	5	5	6	7	6	6	6	5	1	6	4	5	5	6	6	5	6	5	6	6	5	6	6	4	149	29
Skeletal Examination	7	8	11	1	12	10	10	12	13	12	12	12	10	1	11	8	10	10	12	11	9	11	10	11	12	10	12	11	8	287	29
Bones of the Skull	3	4	5	0	6	5	5	6	6	6	6	6	5	0	5	4	5	5	6	5	4	5	5	5	6	5	6	5	4	138	27
Total Major Malformations	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
External Alterations																															
Anophthalmia†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Facial Edema	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Soft Tissue Alterations																															
Situs Inversus†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Dilated Lateral Ventricles†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Skeletal Alterations																															
Skull																															
- Delayed Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
- Foramen	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Vertebrae																															
- Delayed Ossification																															
- Cervical Arches	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
- Centra	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0	0	0	4	4
- Vertebrae	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
- Hemivertebra†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
- Missing Half of Cervical Vertebra†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Ribs																															
- Extra Ribs-Cervical†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
- Spurs	1	0	0	1	0	0	1	3	2	0	3	0	1	0	0	0	1	1	0	0	0	0	0	1	0	1	0	0	2	18	12
Sternebrae																															
- Delayed Ossification	1	2	2	0	9	4	7	5	7	6	8	7	5	1	2	2	4	5	2	10	3	5	3	4	3	4	6	6	2	125	28
- Fused	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
- Extra Site of Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Cartilage																															
- Misaligned	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
- Asymmetric	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
- Fused	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Other																															
- Misaligned Phalange†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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Table A-7 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Litter Summary of Alterations Among Litters of Rats*

Exposure Level: 3 ppm

Animal Numbers	81A-9705	9707	9708	9724	9725	9726	9727	9728	9741	9742	9752	9753	9754	9755	9756	9772	9774	9775	9776	9790	9791	9792	9793	9805	9806	9807	9815	9816	Total Fetuses	Total Litters
External Examination	10	13	10	13	12	12	12	10	3	10	11	10	11	8	11	10	6	11	10	9	13	9	10	9	10	13	9	8	203	20
Soft Tissue Examination	5	7	5	7	6	6	6	5	3	5	6	5	6	4	6	5	3	6	5	5	7	5	5	5	5	7	5	4	149	20
Skeletal Examination	10	13	10	13	12	12	12	10	3	10	11	10	11	8	11	10	6	11	10	9	13	9	10	9	10	13	9	8	203	20
Bones of the Skull	5	6	5	6	6	6	6	5	0	5	5	5	5	4	5	5	3	5	5	4	6	4	5	4	5	6	4	4	134	27
Total Major Malformations	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	1
External Alterations																														
Anophthalmia†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Facial Edema	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Soft Tissue Alterations																														
Situs Inversus†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	1
Dilated Lateral Ventricles†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Skeletal Alterations																														
Skull																														
- Delayed Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
- Foramen	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	1
Vertebrae																														
- Delayed Ossification																														
- Cervical Arches	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
- Centra	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	3	3
- Vertebrae	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
- Hemivertebra†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
- Missing Half of Cervical Vertebra†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Ribs																														
- Extra Ribs-Cervical†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
- Spurs	0	0	0	0	2	1	0	1	1	2	0	1	0	0	0	1	0	0	0	2	0	0	1	0	0	1	0	0	13	10
Sternebrae																														
- Delayed Ossification	5	0	4	4	4	6	11	6	3	7	0	1	5	3	9	4	3	3	0	6	3	0	6	4	4	0	6	3	142	27
- Fused	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
- Extra Site of Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Cartilage																														
- Misaligned	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
- Asymmetric	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
- Fused	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Other																														
- Misaligned Phalange†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Table A-7 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Litter Summary of Alterations Among Litters of Rats[a]

Exposure Level: 10 ppm

Animal Numbers	BIA-9707	9710	9713	9729	9730	9731	9732	9733	9743	9757	9758	9759	9760	9762	9777	9778	9779	9780	9794	9795	9796	9797	9798	9808	9809	9810	9817	9818	Total Fetuses	Total Litters
External Examination	11	10	11	12	12	9	13	8	11	11	11	11	12	9	11	10	10	11	11	10	11	4	11	10	11	10	12	10	293	28
Soft Tissue Examination	6	5	6	6	6	5	7	4	6	6	6	6	6	5	6	5	5	6	6	5	6	3	6	5	6	5	6	5	155	28
Skeletal Examination	11	10	11	12	12	9	13	8	11	11	11	11	12	9	11	10	10	11	11	10	11	3	11	10	11	10	12	10	293	28
Bones of the Skull	5	5	5	6	6	4	6	4	6[b]	5	5	5	6	4	5	5	5	5	5	5	5	1	5	5	5	5	6	5	139	28
Total Major Malformations	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
External Alterations																														
Anophthalmia[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Facial Edema	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	1
Soft Tissue Alterations																														
Situs Inversus[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Dilated Lateral Ventricles[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Skeletal Alterations																														
Skull																														
- Delayed Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
- Foramen	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	2	2
Vertebrae																														
- Delayed Ossification																														
- Cervical Arches	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
- Centra	0	2	0	1	0	0	0	0	1	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	6	5
- Vertebrae	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
- Hemivertebra[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
- Missing Half of Cervical Vertebra[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Ribs																														
- Extra Ribs-Cervical[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
- Spurs	2	0	0	0	1	2	0	0	0	1	0	3	1	0	0	1	1	2	0	0	2	1	0	0	0	0	1	2	20	13
Sternebrae																														
- Delayed Ossification	4	3	6	5	8	3	10	2	4	8	5	2	9	3	8	2	3	6	5	2	6	0	2	6	4	3	8	4	131	27
- Fused	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
- Extra Site of Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1
Cartilage																														
- Misaligned	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1
- Asymmetric	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
- Fused	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Other																														
- Misaligned Phalange[†]	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1

BEST COPY AVAILABLE

Table 4-F (Continued)

[illegible] STUDY IN RATS AND RABBITS

Individual Litter Summary of Alterations Among Litters of Term[a]

Exposure Level: 50 ppm

Animal Number	9714	9715	9716	9717	9718	9734	9735	9736	9737	9738	9744	9745	9753	9754	9755	9756	9757	9761	9762	9763	9766	9767	9768	9769	9770	9772	9773	9774	9775	9776	9777	9778	Total Females	Total Litters
Extremities																																		
Examination	12	10	2	10	12	12	12	11	10	9	10	11	6	11	10	12	10	10	10	9	12	10	12	11	10	9	10	11	10	11	307	30
Soft Tissue																																		
Examination	6	5	2	5	6	6	6	6	5	5	5	6	4	6	5	6	6	5	5	5	6	5	6	6	5	5	5	6	5	6	168	30
Skeleton																																		
Examination	12	10	2	10	12	12	12	11	10	9	10	11	6	11	10	12	10	10	10	9	12	10	12	11	10	9	10	11	10	11	307	30
Bones of the Head	6	5	0	5	6	6	6	5	5	4	5	5	4	5	5	6	4	5	5	4	6	5	6	5	5	4	5	5	5	5	147	29
Total Major Malformations	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	3	3
Extremities																																		
Alterations																																		
Hemorrhagic[b]	1[c]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Partial Edema	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Soft Tissue																																		
Alterations																																		
Slight Hemorrhage[b]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Bilateral Lumbar Hemorrhage[b]	1[c]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Skeleton Alterations																																		
Skull																																		
- Delayed Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
- Fontanelle	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	1	1
Vertebrae																																		
- Delayed Ossification																																		
- Centrum Anomaly	1[c]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
- Centrum	0	2	0	0	1	2	2	1	0	0	0	0	0	0	0	2	1	1	2	1	0	1	3	2	1	0	0	0	0	0	19	13
- Hemivertebra	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
- Hemivertebra[b]	1[c]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
- Missing Half of Centrum Hemivertebra[b]	1[c]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Ribs																																		
- Extra Rib on Centrum[b]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	0	0	0	0	1	0	0	0	0	0	0	0	0	0	2	2
- Short	2	4	2	1	4	1	1	3	2	3	1	0	3	1	1	2	1	3	3	1	3	3	1	4	0	1	0	0	2	2	37	20
Sternebrae																																		
- Delayed Ossification	4	3	0	4	6	2	3	1	4	2	4	2	2	0	4	2	3	6	3	3	6	1	1	6	2	4	3	3	3	4	97	28
- Fusion	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
- Extra Site of Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Carpiliage																																		
- Misaligned	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
- Abnormality	1[c]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
- Fusion	1[c]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Other																																		
- Misaligned Phalanges[b]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

[a] Dams [illegible] were exposed to 0, 3, 10 or 30 ppm of [illegible] for 6 days/day on days 6 through 15 of gestation.
[b] This mean or sum value considered for soft tissue alterations was not measured.
[c] Alterations observed in this dam female.
[d] Considered a major malformation.

TABLE A-8

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Body Weights and Body Weight Gains of Pregnant Rabbits[a]

Exposure Level: Control (0 ppm)

ANIMAL NUMBER	MATERNAL BODY WEIGHT (G) DAYS OF GESTATION 6	9	12	15	19	29	MATERNAL BODY WEIGHT GAIN (G) 6-9	9-12	12-15	15-19	19-29
8100019	4477.2	4519.4	4507.2	4593.5	4605.1	4798.0	42.2	-12.2	86.3	11.6	192.9
8100020	4043.1	4135.7	4027.6	4085.8	4078.0	4149.8	92.6	-108.1	62.2	-11.8	71.8
8100021	3888.9	3874.1	3990.8	3983.3	4068.4	4093.4	-14.8	116.7	-7.5	85.1	25.0
8100022	3588.5	3623.4	3647.5	3773.5	3837.5	4118.7	34.9	24.1	126.0	64.0	281.2
8100031	4496.3	4369.8	4237.6	4373.6	4318.8	4424.1	-126.5	-132.2	136.0	-54.8	105.3
8100032	3946.1	3965.6	3976.4	4127.8	4212.8	4387.2	19.5	10.8	151.4	85.0	174.4
8100046	3451.3	3464.6	3498.1	3561.8	3626.6	3735.9	13.3	33.5	63.7	64.8	109.3
8100055	3586.2	3686.7	3704.8	3748.5	3796.8	3814.5	100.5	18.1	43.7	48.3	17.7
8100056	3576.8	3570.9	3578.9	3633.8	3691.5	3906.8	-5.9	8.0	54.9	57.7	215.3
8100067	4269.5	4223.3	4186.3	4265.8	4372.0	4538.0	-46.2	-37.0	79.5	106.2	166.0
8100068	4179.0	4059.8	4113.1	4214.4	4251.6	4329.0	-119.2	53.3	101.3	37.2	77.4
8100103	4657.2	4670.3	4697.6	4815.1	4893.8	4882.0	13.1	27.3	121.5	74.7	-11.8
8100105	4036.0	3936.8	3954.6	4087.4	4171.3	4310.0	-99.2	17.8	132.8	83.9	138.7
8100080	3857.1	3936.2	3929.5	4007.5	4095.7	4195.3	79.1	-6.7	78.0	88.2	99.6
8100092	4007.3	3985.0	4015.5	4193.7	4193.7	4187.6	-22.3	30.5	178.2	0.0	-6.1
8100093	4378.4	4357.8	4443.6	4533.7	4587.1	4867.2	-20.6	85.8	90.1	53.4	280.1
8100094	3791.7	3831.3	3886.0	4012.0	4030.8	4220.6	39.6	54.7	126.0	18.8	189.8
8100115	3851.6	3842.0	3921.6	3964.6	4023.1	N.D.	-9.6	79.6	43.0	58.5	N.D.
8100116	4235.0	4226.5	4206.9	4316.2	4203.4	N.D.	-8.5	60.4	29.3	-112.8	N.D.
8100127	4083.9	4008.9	4130.2	3964.4	4113.7	4213.0	-75.0	121.3	-165.8	149.3	99.3
8100128	3637.0	3665.6	3617.8	3567.9	3943.7	4059.0	28.6	-47.8	-49.9	375.8	115.3
8100129	3596.0	3605.0	3655.3	3710.3	3753.1	3840.0	9.0	50.3	55.0	42.8	86.9
8100130	4018.2	4065.0	4030.4	4082.2	4070.0	4208.0	46.8	-34.6	51.8	-12.2	138.0
MEAN	3984.9	3983.6	4001.6	4070.6	4127.8	4251.3	-1.2	18.0	69.0	57.1	122.2
S.D.	332.43	313.52	307.34	326.14	301.27	321.06	61.21	62.16	73.01	89.08	82.38

TABLE A-8 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Body Weights and Body Weight Gains of Pregnant Rabbits[a]

Exposure Level: 3 ppm

ANIMAL NUMBER	MATERNAL BODY WEIGHT (G) DAY(S) OF GESTATION 6	9	12	15	19	29	MATERNAL BODY WEIGHT GAIN (G) 6-9	9-12	12-15	15-19	19-29
8100023	4248.5	4235.5	4209.8	4422.8	4504.3	4663.5	-13.0	-25.7	213.0	81.5	159.2
8100024	4078.7	3916.1	4071.7	4198.6	4208.1	4176.3	-162.6	155.6	126.9	9.5	-31.8
8100033	3507.0	3365.1	3417.6	3418.1	3437.6	3659.2	-141.9	52.5	0.5	19.5	221.6
8100034	4298.6	4222.1	4297.8	4295.9	4275.5	4244.9	-76.5	75.7	2.1	-24.4	-30.6
8100036	3562.6	3544.0	3577.1	3692.4	3711.5	3848.7	-18.6	33.1	115.3	19.1	137.2
8100047	4563.6	4590.7	4597.3	4560.5	4485.2	4963.8	27.1	6.6	-36.8	-75.3	478.6
8100048	3559.2	3589.9	3738.9	3856.2	3878.7	4122.6	30.7	149.0	117.3	22.5	243.9
8100057	4308.0	4232.5	4217.5	4151.0	4082.4	4013.1	-75.5	-15.0	-66.5	-68.6	-69.3
8100058	4178.7	4156.4	4191.8	4300.9	4358.9	4489.5	-22.3	35.4	109.1	58.0	130.6
8100059	4447.9	4434.7	4465.5	4540.8	4537.1	4526.9	-13.2	30.8	75.3	-3.7	-10.2
8100060	4364.2	4265.7	4243.3	4255.9	4299.8	4569.5	-98.5	-22.4	12.6	43.9	269.7
8100069	4028.8	3927.8	3984.2	4039.2	4070.3	4250.0	-101.0	56.4	55.0	31.1	179.7
8100071	4218.7	4223.7	4293.2	4398.8	4439.6	4237.0	5.0	69.5	100.6	45.8	-202.6
8100072	3639.3	3639.4	3663.2	3750.6	3807.0	3963.0	0.1	23.8	87.4	56.4	156.0
8100108	3909.5	3843.2	3867.4	3925.3	3964.8	3987.0	-66.3	24.2	57.9	39.5	22.2
8100082	4017.9	4039.3	4112.6	4059.3	4189.7	4176.8	21.4	73.3	-53.3	130.4	-12.9
8100083	3909.7	3915.0	3912.7	3988.4	4010.0	3721.5	5.3	-2.3	75.7	21.6	-288.5
8100084	3409.2	3505.2	3563.9	3611.7	3760.3	3228.1	96.0	58.7	47.8	148.6	-532.2
8100095	4314.2	4309.8	4412.6	4461.2	4576.0	4614.7	-4.4	102.8	48.6	114.8	38.7
8100096	3868.6	3762.0	3767.0	3617.6	3839.7	4051.2	-126.6	5.0	50.6	22.1	211.5
8100117	3820.1	3699.3	3682.4	3684.8	3820.4	3999.6	-120.8	-16.9	2.4	135.6	179.2
8100119	3585.6	3520.5	3634.3	3688.2	3675.5	3746.1	-65.1	113.8	53.9	-12.7	70.6
8100120	4331.0	4260.9	4234.6	4297.4	4357.4	4379.5	-70.1	-26.3	62.8	60.0	22.1
8100132	4577.7	4490.1	4553.1	4565.0	4708.7	4663.0	-87.6	63.0	15.9	139.7	-45.7
MEAN	4032.0	3987.0	4029.6	4082.6	4124.9	4179.0	-44.9	42.5	53.1	42.3	54.0
S.D.	351.51	350.07	340.56	337.32	337.36	392.35	63.94	52.21	63.05	60.45	204.20

TABLE A-8 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Body Weights and Body Weight Gains of Pregnant Rabbits[a]

Exposure Level: 10 ppm

ANIMAL NUMBER	MATERNAL BODY WEIGHT (G) DAYS OF GESTATION 6	9	12	15	19	29	MATERNAL BODY WEIGHT GAIN (G) 6-9	9-12	12-15	15-19	19-29
8100025	4441.3	4600.5	4595.0	4744.6	4766.2	5041.8	159.2	-5.5	149.6	21.6	275.6
8100026	3952.2	3836.7	3996.0	4115.9	4154.8	4363.2	-115.5	159.3	123.9	34.9	208.4
8100038	3649.0	3611.5	3838.7	3873.7	3843.9	3915.4	-37.5	27.2	35.0	-29.8	71.5
8100039	4491.2	4407.5	4425.8	4444.9	4395.1	4434.7	-83.7	18.3	19.1	-49.8	39.6
8100049	3676.3	3435.8	3405.4	3413.1	3438.5	3552.8	-240.5	-30.4	7.7	25.4	114.3
8100050	3904.5	3835.7	3949.6	3956.6	4009.8	3931.2	-68.8	113.9	7.0	53.2	-78.6
8100061	4231.4	4223.4	4290.9	4382.9	4434.7	4354.6	-8.0	67.5	92.0	51.8	-80.1
8100064	4329.8	4248.4	4194.9	4243.1	4283.9	4504.7	-81.4	-53.5	48.2	40.8	220.8
8100073	4013.6	4021.4	3991.7	4089.8	4165.6	4223.0	7.8	-29.7	98.1	75.8	57.4
8100075	4390.0	4301.6	4362.5	4471.4	4476.1	4552.0	-88.4	60.9	108.9	4.7	75.9
8100076	3937.2	3910.2	3971.5	4051.6	4078.5	4286.0	-27.0	61.3	80.1	26.9	207.5
8100109	4062.9	4087.7	4126.4	4172.0	4249.8	4363.0	24.8	38.7	45.6	77.8	113.2
8100085	4263.8	4244.7	4267.3	4404.9	4413.4	4704.6	-19.1	22.6	137.6	8.5	291.2
8100086	3792.1	3687.7	3807.2	3846.9	3849.9	4089.8	-104.4	119.5	39.7	3.0	239.9
8100087	3756.9	3692.6	3778.2	3648.3	3817.7	3996.7	-64.3	85.6	-129.9	169.4	179.0
8100088	4010.3	3977.9	4011.8	4036.4	4112.6	4233.4	-32.4	33.9	24.6	76.2	120.8
8100097	3482.5	3490.3	3524.5	3630.9	3647.9	3855.0	7.8	34.2	106.4	17.0	207.1
8100098	4309.8	4328.9	4381.9	4394.1	4378.3	4413.9	19.1	53.0	12.2	-15.8	35.6
8100121	3501.4	3667.5	3834.5	3820.4	3897.3	3945.0	166.1	167.0	-14.1	76.9	47.7
8100122	3929.2	3876.6	3947.8	3997.8	4027.9	4131.3	-52.6	71.2	50.0	30.1	103.4
8100123	4211.7	4186.7	4273.6	4327.7	4358.4	4520.1	-25.0	86.9	54.1	30.7	161.7
8100124	4491.0	4598.7	4662.6	4688.0	4729.8	4841.8	107.7	63.9	25.4	41.8	112.0
8100133	3997.9	3931.6	3984.2	4039.0	4189.1	3861.0	-66.3	52.6	54.8	150.1	-328.1
8100134	4259.3	4247.9	4288.0	4318.5	4362.4	4508.0	-11.4	40.1	30.5	43.9	145.6
MEAN	4053.6	4027.1	4079.6	4129.9	4170.1	4276.0	-26.4	52.4	50.3	40.2	105.9
S.D.	292.75	319.02	308.81	330.51	319.70	346.85	86.68	54.32	58.68	49.21	133.50

TABLE A-8 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Body Weights and Body Weight Gains of Pregnant Rabbits[a]

Exposure Level: 50 ppm

ANIMAL NUMBER	MATERNAL BODY WEIGHT (G) DAY(S) OF GESTATION 6	9	12	15	19	29	MATERNAL BODY WEIGHT GAIN (G) 6-9	9-12	12-15	15-19	19-29
8100027	3892.4	2708.3	3574.6	3581.5	3710.2	3807.5	1184.1	866.3	6.9	128.7	97.3
8100028	4170.9	4107.2	4077.6	4091.9	4006.6	4280.8	-63.7	-29.6	14.3	-85.3	274.2
8100029	4502.4	4419.5	4402.8	4476.8	4437.2	4018.0	-82.9	-16.7	74.0	-39.6	-419.2
8100030	4269.3	4219.6	4158.0	4218.1	4234.3	4438.8	-49.7	-61.6	60.1	16.2	204.5
8100041	4289.4	4250.7	4233.7	4276.0	4399.8	4559.8	-38.7	-17.0	42.3	123.8	160.0
8100042	4220.3	4271.5	4169.8	4140.8	4383.8	4366.6	51.2	-101.7	-29.0	243.0	-17.2
8100051	4298.2	4319.4	4372.9	4426.7	4506.7	4770.9	21.2	53.5	53.8	80.0	264.2
8100052	3859.7	3857.2	3794.5	3822.9	3830.8	3948.6	-2.5	-62.7	28.4	7.9	117.8
8100053	4530.0	4306.2	4538.7	4525.0	4544.3	4797.5	-223.8	232.5	-13.7	19.3	253.2
8100054	3879.1	3278.5	3825.6	3873.0	3964.4	4053.1	-600.6	547.1	47.4	91.4	88.7
8100065	4450.9	4394.0	4352.9	4456.6	4486.9	4748.2	-56.9	-41.1	103.7	30.3	261.3
8100077	4286.8	4250.4	4272.3	4237.4	4398.5	4650.0	-36.4	21.9	-34.9	161.1	251.5
8100078	4669.6	4589.1	4579.7	4308.6	4270.6	4802.0	-80.5	-9.4	-271.1	-38.0	531.4
8100111	4711.8	4608.2	4655.3	4671.8	4867.1	4764.0	-103.6	47.1	16.5	195.3	-103.1
8100112	3939.9	3892.3	3882.9	3894.4	3825.6	4055.0	-47.6	-9.4	11.5	-68.8	229.4
8100113	4044.6	4023.8	4029.0	3990.8	4207.9	4361.0	-20.8	5.2	-38.2	217.1	153.1
8100090	4068.0	4034.7	4057.0	3842.4	3602.5	4180.1	-33.3	22.3	-214.6	-239.9	577.6
8100101	3872.5	3883.9	3955.5	4036.4	4175.6	4589.0	11.4	71.6	80.9	139.2	413.4
8100102	4282.3	4172.7	4200.7	4254.1	4063.0	4262.7	-109.6	28.0	53.4	-191.1	199.7
8100125	4181.9	4155.0	4191.0	4251.6	4293.0	4569.8	-26.9	36.0	60.6	41.4	276.8
8100135	4290.9	4148.5	3994.8	3668.7	3889.8	4215.0	-142.4	-153.7	-326.1	221.1	325.2
8100136	3810.5	3746.0	3698.8	3655.3	3834.0	3965.0	-64.5	-47.2	-39.5	174.7	131.0
8100137	4451.1	4437.9	4416.0	4335.8	4411.6	4537.0	-13.2	-21.9	-76.2	71.8	125.4
8100138	4079.5	3969.2	4015.9	3995.0	4076.0	4302.0	-110.3	46.7	-20.9	81.0	226.0
MEAN	4210.5	4085.2	4143.7	4126.6	4184.2	4376.8	-125.3	58.6	-17.1	57.5	192.6
S.D.	259.50	411.69	278.84	294.34	308.87	304.18	257.84	217.16	108.68	125.18	198.35
	*						*		*		

[a]Inseminated New Zealand white rabbits were exposed to 0, 3, 10 or 50 ppm of EGME for 6 hr/day on days 6 through 18 of gestation.

*Significantly different from the control value.

Table A-9

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Organ Weights of Pregnant Rabbits[a]

Exposure Level: Control (0 ppm)

Animal Number	Liver		Spleen		Thymus	
	Absolute[b]	Relative[c]	Absolute	Relative	Absolute	Relative
81B-0019	101.61	2.12	2.00	0.04	5.31	0.111
0020	86.32	2.08	1.28	0.03	3.90	0.094
0021	102.04	2.49	1.46	0.04	2.76	0.067
0022	110.88	2.69	0.78	0.02	3.54	0.086
0031	131.28	2.97	1.46	0.03	3.13	0.071
0032	107.79	2.46	1.08	0.02	2.37	0.054
0046	76.72	2.05	1.31	0.04	4.17	0.112
0055	140.38	3.68	1.43	0.04	3.60	0.094
0056	105.22	2.69	1.45	0.04	4.23	0.108
0067	113.40	2.50	1.20	0.03	4.23	0.093
0068	112.36	2.60	2.07	0.05	4.62	0.107
0103	105.36	2.16	1.05	0.02	6.08	0.125
0105	126.57	2.94	1.09	0.03	4.48	0.104
0080	94.93	2.26	1.01	0.02	3.19	0.076
0092	90.45	2.16	1.53	0.04	9.41	0.225
0093	130.42	2.68	1.70	0.03	6.68	0.137
0094	113.74	2.69	1.13	0.03	5.65	0.134
0115	86.70	---[d]	0.83	---[d]	3.66	---[d]
0116	90.65	---[d]	1.49	---[d]	4.40	---[d]
0127	103.16	2.45	1.22	0.03	4.15	0.099
0128	115.45	2.84	1.31	0.03	2.28	0.056
0129	111.14	2.89	0.95	0.02	1.63	0.042
0130	114.57	2.72	1.85	0.04	3.17	0.075
Mean	107.44	2.58	1.33	0.03	4.20	0.099
±S.D.	15.70	0.39	0.34	0.01	1.66	0.039

Table A-9 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Organ Weights of Pregnant Rabbits[a]

Exposure Level: 3 ppm

Animal Number	Liver		Spleen		Thymus	
	Absolute[b]	Relative[c]	Absolute	Relative	Absolute	Relative
81B-0023	113.36	2.43	1.30	0.03	5.41	0.116
0024	100.71	2.41	2.24	0.05	4.13	0.099
0033	92.04	2.52	1.33	0.04	1.89	0.052
0034	147.43	3.47	1.57	0.04	1.63	0.038
0036	87.10	2.26	1.88	0.05	1.60	0.042
0047	113.99	2.30	1.49	0.03	2.92	0.059
0048	101.44	2.46	1.85	0.04	4.50	0.109
0057	89.55	2.23	1.22	0.03	3.77	0.094
0058	118.35	2.64	2.13	0.05	2.48	0.055
0059	101.85	2.25	1.20	0.03	5.08	0.112
0060	179.62	3.93	3.02	0.07	4.75	0.104
0069	124.55	2.93	1.21	0.03	3.02	0.071
0071	97.13	2.29	2.27	0.05	4.60	0.109
0072	112.79	2.85	1.06	0.03	2.26	0.057
0108	86.26	2.16	0.90	0.02	3.82	0.096
0082	98.84	2.37	2.15	0.05	5.85	0.140
0083	85.25	2.29	0.82	0.02	4.37	0.117
0084	103.61	3.21	1.52	0.05	2.38	0.074
0095	118.43	2.57	1.26	0.03	7.67	0.166
0096	82.65	2.04	1.60	0.04	6.51	0.161
0117	104.86	2.62	1.46	0.04	4.49	0.112
0119	86.69	2.31	1.72	0.05	2.72	0.073
0120	100.79	2.30	2.25	0.05	5.76	0.132
0132	125.58	2.69	1.30	0.03	4.31	0.092
Mean	107.20	2.56	1.61	0.04	4.00	0.095
±S.D.	21.96	0.44	0.52	0.01	1.60	0.035

Table A-9 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Organ Weights of Pregnant Rabbits[a]

Exposure Level: 10 ppm

Animal Number	Liver		Spleen		Thymus	
	Absolute[b]	Relative[c]	Absolute	Relative	Absolute	Relative
81B-0025	144.00	2.86	1.71	0.03	6.12	0.121
0026	120.05	2.75	1.21	0.03	3.41	0.078
0038	81.12	2.07	1.31	0.03	3.38	0.086
0039	108.15	2.44	1.37	0.03	3.52	0.079
0049	87.44	2.46	2.18	0.06	4.31	0.121
0050	75.54	1.92	1.15	0.03	4.03	0.103
0061	101.46	2.33	1.06	0.02	2.71	0.062
0064	146.51	3.25	2.34	0.05	3.30	0.073
0073	113.81	2.70	13.10	0.31	4.03	0.095
0075	99.95	2.20	1.48	0.03	4.15	0.091
0076	94.02	2.19	2.37	0.06	3.12	0.073
0109	95.31	2.18	1.70	0.04	5.54	0.127
0085	93.02	1.98	1.23	0.03	5.64	0.120
0086	98.78	2.42	1.51	0.04	4.94	0.121
0087	75.07	1.88	0.91	0.02	3.05	0.076
0088	100.94	2.38	1.12	0.03	4.76	0.112
0097	105.59	2.74	1.05	0.03	4.43	0.115
0098	93.81	2.13	1.82	0.04	6.13	0.139
0121	88.32	2.24	1.21	0.03	6.47	0.164
0122	94.09	2.28	1.45	0.04	4.69	0.114
0123	86.28	1.91	1.39	0.03	5.14	0.114
0124	138.02	2.85	1.38	0.03	5.78	0.119
0133	104.83	2.72	1.52	0.04	4.46	0.116
0134	131.07	2.91	1.17	0.03	3.54	0.079
Mean	103.22	2.41	1.95	0.05	4.44	0.104
±S.D.	20.02	0.37	2.41	0.06	1.09	0.025

Table A-9 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Organ Weights of Pregnant Rabbits[a]

Exposure Level: 50 ppm

Animal Number	Liver		Spleen		Thymus	
	Absolute[b]	Relative[c]	Absolute	Relative	Absolute	Relative
81B-0027	126.13	3.31	0.73	0.02	6.95	0.183
0028	114.72	2.68	1.50	0.04	2.28	0.053
0029	81.89	2.04	0.61	0.02	7.89	0.196
0030	140.27	3.16	1.47	0.03	5.06	0.114
0041	122.64	2.69	1.75	0.04	5.58	0.122
0042	124.95	2.86	1.38	0.03	3.35	0.077
0051	136.97	2.87	1.86	0.04	3.71	0.078
0052	69.85	1.77	1.64	0.04	4.20	0.106
0053	126.86	2.64	0.91	0.02	5.82	0.121
0054	89.81	2.22	1.32	0.03	5.96	0.147
0065	128.94	2.72	2.03	0.04	5.78	0.122
0077	143.62	3.09	1.72	0.04	5.68	0.122
0078	123.56	2.57	1.59	0.03	4.32	0.090
0111	140.40	2.95	1.44	0.03	6.41	0.135
0112	116.67	2.88	1.45	0.04	4.82	0.119
0113	150.28	3.45	4.79	0.11	4.73	0.108
0090	180.95	4.33	1.17	0.03	6.33	0.151
0101	145.89	3.18	1.19	0.03	5.65	0.123
0102	108.58	2.55	1.03	0.02	7.57	0.178
0125	136.96	3.00	2.73	0.06	4.04	0.088
0135	125.47	2.98	1.40	0.03	2.91	0.069
0136	97.37	2.46	1.27	0.03	3.85	0.097
0137	104.22	2.30	1.16	0.03	5.63	0.124
0138	115.33	2.68	2.11	0.05	2.79	0.065
Mean	123.01*	2.81	1.59	0.04	5.05	0.116
±S.D.	23.88	0.51	0.82	0.02	1.49	0.037

[a]Inseminated New Zealand white rabbits were exposed to 0, 3, 10 or 50 ppm of EGME for 6 hr/day on days 6 through 18 of gestation.
[b]Grams
[c]Grams/100g body weight.
[d]Body weights not recorded at the time of cesarean section.

*Significantly different from the control value.

Table A-10

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Hematology Data for Pregnant Rabbits[a]

Exposure Level ppm	Animal Number	RBC X $10^6/mm^3$	HGB GM/DL	PCV %	MCV Cubic Microns	MCH Micro Microgm	MCHC %	PLAT X $10^3/mm^3$	WBC X $10^3/mm^3$
Control	818-0019	5.09	11.5	37.3	73.00	22.60	30.80	389.	2.6
	0020	5.30	12.0	38.9	73.00	22.60	30.80	564.	5.4
	0021	5.75	12.6	41.1	71.00	21.90	30.70	321.	7.1
	0022	4.68	10.9	34.2	73.00	23.30	31.90	372.	7.3
	0031	6.64	15.0	48.4	73.00	22.60	31.00	581.	2.0
	0032	5.38	13.3	40.0	74.00	24.70	33.30	673.	2.4
	0046	5.83	13.2	42.9	74.00	22.60	30.80	450.	6.8
	0055	5.84	12.5	41.6	71.00	21.40	30.00	550.	3.6
	0056	5.20	12.3	39.3	76.00	23.70	31.30	559.	1.6
	0067	6.46	14.8	47.1	73.00	22.90	31.40	341.	4.5
	Mean	5.62	12.8	41.1	73.10	22.83	31.20	480.	4.3
	±S.D.	0.61	1.3	4.3	1.45	0.92	0.89	121.	2.2
3	818-0023	5.14	11.7	37.1	72.00	22.80	31.50	639.	7.2
	0024	5.02	11.5	36.4	73.00	22.90	31.60	688.	8.9
	0033	5.56	13.3	40.7	73.00	23.90	32.70	439.	5.8
	0034	4.97	11.4	36.2	73.00	22.90	31.50	551.	5.0
	0036	5.69	13.2	41.3	73.00	23.20	32.00	456.	1.5
	0047	4.34	9.8	32.1	74.00	22.60	30.50	525.	7.5
	0048	5.04	11.1	35.9	71.00	22.00	30.90	295.	9.8
	0057	5.46	12.3	40.4	74.00	22.50	30.40	693.	1.9
	0058	6.47	14.0	47.1	73.00	21.60	29.70	393.	1.2
	0059	4.73	11.8	37.4	79.00	24.90	31.60	357.	1.2
	Mean	5.24	12.0	38.5	73.50	22.93	31.24	504.	5.0
	±S.D.	0.59	1.2	4.1	2.12	0.93	0.87	139.	3.3
10	818-0025	5.35	12.2	38.3	72.00	22.80	31.90	422.	6.1
	0026	5.24	11.8	37.3	71.00	22.50	31.60	185.	8.9
	0038	5.77	12.6	41.2	71.00	21.80	30.60	576.	3.8
	0039	5.90	13.8	42.8	73.00	23.40	32.20	527.	0.9
	0049	5.32	11.9	38.7	73.00	22.40	30.70	622.	6.2
	0050	5.67	11.9	39.6	70.00	21.00	30.10	454.	4.8
	0061	5.11	12.3	39.1	77.00	24.10	31.50	180.	1.7
	0064	5.16	12.2	39.6	77.00	23.60	30.80	370.	1.3
	0073	5.00	10.6	35.4	71.00	21.20	29.90	401.	3.7
	0074	5.08	11.6	36.9	73.00	22.80	31.40	398.	1.3
	Mean	5.36	12.1	38.9	72.80	22.56	31.07	414.	3.9
	±S.D.	0.31	0.8	2.1	2.44	1.01	0.77	147.	2.7
50	818-0027	5.65	12.1	40.2	71.00	21.40	30.10	792.	9.7
	0028	5.83	12.6	41.3	71.00	21.60	30.50	467.	5.2
	0029	5.63	12.9	40.2	71.00	22.90	32.10	405.	4.3
	0030	4.44	10.6	33.0	74.00	23.90	32.10	485.	6.2
	0041	5.04	11.9	37.0	73.00	23.60	32.20	447.	1.4
	0042	6.15	13.5	43.8	71.00	22.00	30.80	312.	1.2
	0051	5.26	11.6	37.6	71.00	22.10	30.90	338.	4.4
	0052	5.45	11.5	38.1	70.00	21.10	30.20	263.	2.9
	0053	4.81	11.4	35.9	75.00	23.70	31.80	497.	4.4
	0054	5.43	12.9	40.0	74.00	23.80	32.30	552.	4.6
	Mean	5.37	12.1	38.7	72.10	22.61	31.30	456.	4.4
	±S.D.	0.50	0.9	3.1	1.73	1.09	0.88	149.	2.4

[a]Inseminated New Zealand white rabbits were exposed to 0, 3, 10 or 50 ppm of EGME for 6 hr/day on days 6 through 18 of gestation. Terminal (day 29) blood samples were obtained by cardiac puncture from 10 rabbits/exposure level.

Table A-11

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Litter Summary of Observations Made at Cesarean Section in Rabbits[a]

Exposure Level: Control (0 ppm)

Animal Number	Corpora Lutea	Implantations	Pre-Implantation Loss	Resorptions	Litter Size	Sex Ratio M/F	Fetal Body Weight (g)	Fetal Crown-Rump Length (mm)
818-0019	13	11	2	1	10	5/5	36.19	92.46
0020	9	8	1	0	8	5/3	38.83	94.39
0021	10	7	3	0	7	3/4	39.74	97.14
0022	12	9	3	0	9	3/6	41.00	96.41
0031	10	9	1	1	8	4/4	31.08	89.08
0032	7	7	0	1	6	2/4	45.58	96.75
0043	Non-Pregnant							
0044	Dead on Day 28 of gestation - Non-pregnant at necropsy							
0045	Non-Pregnant							
0046	10	7	3	0	7	3/4	42.11	101.10
0055	8	5	3	0	5	2/3	49.32	106.94
0056	7	6	1	0	6	4/2	45.68	107.05
0067	8	7	1	0	7	3/4	40.66	97.53
0068	13	11	2	0	11	8/3	30.22	88.52
0103	10	9	1	0	9	5/4	35.50	93.93
0104	Non-Pregnant							
0105	8	8	0	3	5	4/1	46.56	98.64
0106	Non-Pregnant							
0079	Dead on Day 24 of gestation - Pregnant at necropsy							
0080	9	3	6	0	3	0/3	45.17	97.57
0091	Non-Pregnant							
0092	8	8	0	0	8	2/6	39.99	97.43
0093	12	11	1	0	11	8/3	43.97	103.78
0094	7	7	0	0	7	2/5	43.90	99.37
0115	13	13	0	0	13	8/5	28.55	82.37
0116	13	4	9	0	4	2/2	40.30	93.10
0127	10	9	1	0	9	4/5	35.48	90.13
0128	7	7	0	1	6	3/3	36.13	97.25
0129	7	8	0	0	8	4/4	34.65	93.16
0130	6	6	0	0	6	2/4	39.48	97.43
Mean±S.D.	9±2	8±2	16±20[b]	0.3±0.7	8±2	50/50	39.57±5.48	96.2±5.7

Table A-11 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Litter Summary of Observations Made at Cesarean Section in Rabbits[a]

Exposure Level: 3 ppm

Animal Number	Corpora Lutea	Implantations	Pre-Implantation Loss	Resorptions	Litter Size	Sex Ratio M/F	Fetal Body Weight (g)	Fetal Crown-Rump Length (mm)
818-0023	6	6	0	0	6	2/4	43.70	95.73
0024	9	4	5	0	4	3/1	43.58	100.78
0033	8	7	1	1	6	2/4	44.20	98.15
0034	11	9	2	0	9	4/5	35.99	88.99
0035	Implantation sites detected only after sodium sulfide stain							
0036	9	9	0	0	9	4/5	43.57	98.49
0047	16	14	2	1	13	3/10	36.84	88.35
0048	12	7	5	0	7	3/4	45.26	96.70
0057	8	8	0	0	8	5/3	33.44	94.85
0058	11	9	2	0	9	5/4	41.74	102.73
0059	14	12	2	0	12	4/8	33.78	94.38
0060	--[c]	2	--[c]	2	0		--	--
0069	10	10	0	3	7	4/3	37.06	94.20
0070	Implantation sites detected only after sodium sulfide stain							
0071	1[illegible]	9	3	2	7	3/4	43.37	99.81
0072	7	6	1	1	5	5/0	41.94	97.54
0107	Non-Pregnant							
0108	11	9	2	0	9	4/5	41.44	91.99
0081	Non-Pregnant							
0082	9	9	0	1	8	5/3	35.56	90.25
0083	8	7	1	1	6	3/3	33.35	90.68
0084	7	7	0	1	6	3/3	21.45	81.00
0095	9	9	0	0	9	5/4	43.19	102.14
0096	9	8	1	0	8	4/4	44.40	100.68
0117	11	9	2	0	9	3/6	33.76	89.62
0118	Delivered early on day 27 of gestation.							
0119	7	6	1	0	6	4/2	44.22	98.28
0120	15	1	14	0	1	1/0	47.40	99.80
0131	Delivered early on day 29 of gestation.							
0132	10	9	1	1	8	5/3	30.05	92.59
Mean±S.D.	10±3	8±3	17±22[b]	0.6±0.8	7±3	49/51	39.13±6.24	95.1±5.3

Table A-11 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Litter Summary of Observations Made at Cesarean Section in Rabbits[a]

Exposure Level: 10 ppm

Animal Number	Corpora Lutea	Implantations	Pre-Implantation Loss	Resorptions	Litter Size	Sex Ratio M/F	Fetal Body Weight (g)	Fetal Crown-Rump Length (mm)
818-0025	11	10	1	1	9	5/4	44.86	97.29
0026	10	10	0	0	10	5/5	37.98	87.31
0037	Non-Pregnant							
0038	10	8	2	0	8	3/5	33.95	87.33
0039	11	10	1	0	10	5/5	33.52	87.35
0040	Dead on day 13 of gestation - Pregnant at necropsy							
0049	11	7	4	2	5	2/3	42.44	92.30
0050	16	8	8	1	7	5/2	34.03	87.39
0061	9	10	0	1	9	4/5	32.30	96.31
0062	Non-Pregnant							
0063	Non-Pregnant							
0064	11	7	4	1	6	2/4	48.53	109.27
0073	10	9	1	0	9	5/4	32.37	90.16
0074	Non-Pregnant							
0075	11	11	0	2	9	4/5	35.24	90.38
0076	13	13	0	1	12	6/6	38.05	94.58
0109	11	11	0	0	11	3/8	38.75	94.05
0110	Removed from study - Broken back							
0085	11	9	2	0	9	5/4	42.54	98.42
0086	11	8	3	0	8	1/7	36.65	96.2
0087	11	10	1	2	8	5/3	37.54	95.4
0088	8	8	0	1	7	5/2	40.39	94.9
0097	8	1	7	0	1	0/1	43.80	105.1
0098	10	9	1	1	8	2/6	44.05	103.3
0121	9	8	1	3	8	3/5	38.93	90.
0122	10	5	5	1	2	1/1	41.90	95.
0123	14	14	0	2	13	10/3	36.01	91.
0124	10	10	0	0	8	3/5	40.73	94.
0133	8	4	4	4	4	1/3	32.58	91.
0134	10	10	0		6	5/1	44.25	102
Mean±S.D.	11±2	9±3	18±23[b]	1.0±1.1	8±3	48/52	38.83±4.54	94.3

Table A-11 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Litter Summary of Observations Made at Cesarean Section in Rabbits[a]

Exposure Level: 50 ppm

Animal Number	Corpora Lutea	Implantations	Pre-Implantation Loss	Resorptions	Litter Size	Sex Ratio M/F	Fetal Body Weight (g)	Fetal Crown-Rump Length (mm)
81B-0027	6	2	4	0	2	1/1	40.55	100.70
0028	13	10	3	1	9	5/4	35.59	93.20
0029	7	5	2	0	5	1/4	35.48	92.94
0030	9	7	2	0	7	1/6	42.31	98.19
0041	9	8	1	0	8	4/4	31.79	89.45
0042	8	7	1	2	5	3/2	39.70	96.26
0051	10	10	0	4	6	5/1	33.27	93.20
0052	10	8	2	0	8	3/5	39.30	97.41
0053	11	10	1	3	7	4/3	32.49	89.94
0054	7	7	0	1	6	4/2	39.87	93.90
0065	10	10	0	2	8	5/3	39.09	99.10
0066	Non-Pregnant							
0077	11	10	1	3	7	1/6	30.33	89.57
0078	10	9	1	2	7	4/3	38.66	97.64
0111	12	4	8	0	4	2/2	36.63	97.03
0112	10	9	1	1	8	5/3	31.31	88.78
0113	--[c]	5	--[c]	5	0		--	--
0114	Delivered early on day 28 of gestation.							
0089	Non-Pregnant							
0090	--[c]	7	--[c]	7	0		--	--
0099	Non-Pregnant							
0100	Delivered early on day 28 of gestation.							
0101	8	8	0	2	6	2/4	34.63	96.08
0102	10	9	1	5	4	2/2	33.63	94.40
0125	14	10	4	1	9	5/4	41.59	95.70
0126	Implantation sites detected only after sodium sulfide stain.							
0135	8	8	0	2	6	3/3	32.93	95.45
0136	8	8	0	0	8	3/5	37.19	97.71
0137	10	10	0	0	10	6/4	30.30	95.49
0138	9	10	0	5	5	3/2	32.72	96.98
Mean±S.D.	10±2	8±2	15±19[b]	1.9±2.0	6±3	50/50	35.88±3.79*	95.0±3.3

[a]Inseminated New Zealand white rabbits were exposed to 0, 3, 10 or 50 ppm of EGME for 6 hr/day on days 6 through 18 of gestation.

[b]Expressed as percent per litter, mean±S.D.

[c]Corpora lutea not recorded on totally resorbed litters.

*Significantly different from the control value.

Table A-12

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Litter Summary of External and Soft Tissue Alterations Among Litters of Rabbits[a]

Exposure Level: Control (0 ppm)

Animal Number	018-0019	0020	0021	0022	0031	0032	0046	0055	0056	0067	0068	0103	0105	0080	0092	0093	0094	0115	0116	0127	0128	0129	0130	Total Fetuses	Total Litters
EXTERNAL EXAMINATION	10	8	7	9	8	6	7	5	6	7	11	9	5	3	8	11	7	13	4	9	6	8	6	173	23
SOFT TISSUE EXAMINATION	5	4	4	5	4	3	4	3	3	4	6	5	3	3	4	6	4	7	3	5	3	4	3	95	23
TOTAL MAJOR MALFORMATIONS[b]	0	0	1	1	1	0	0	0	0	0	0	0	1	0	0	1	1	0	0	0	0	0	0	6	6
EXTERNAL ALTERATIONS																									
Arthrogryposis[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Anonychia[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Polyonychia[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Brachydactyly[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Ectrodactyly[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Syndactyly[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Microphthalmia[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Misalignment of Palatine Rugae	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Medial Rotation of Digits[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Inward Rotation of Hind Feet[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Omphalocele[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Thinning of Abdominal Wall[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hypoplastic Tail[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Kinky Tail[†]	0	0	0	0	0	0	0	0	0	0	0	0	1[c]	0	0	0	0	0	0	0	0	0	0	0	0
Narrowed Tip of Tail	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SOFT TISSUE ALTERATIONS																									
Coarctation of the Aortic Arch[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Ventricular Septal Defect[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Agenesis of Subclavian Artery[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Extra Vessel Off Aortic Arch	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Patent Ductus Arteriosis	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Hydropericardium	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Valvular Hematoma-Tricuspid	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Retroesophageal Subclavian	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	1
Edema of the Pulmonary Artery	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Diaphragmatic Hernia[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hepatic Cysts-Multifocal	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hepatic Necrosis-Focal	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Gall Bladder																									
-Aplastic[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Hypoplastic	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Bilobed	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Spleen																									
-Aplastic[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Hypoplastic[†]	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Pale	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2	2
-Accessory	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Bilobed	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Adrenal-Accessory	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	4	1
Kidney																									
- Agenesis-Unilateral[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
- Misshapen[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Dilated Renal Pelvis[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Mineral-Like Renal Deposits	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Ureter																									
-Dilated	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Convoluted	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Retrocaval	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Ovarian Agenesis[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	3	2
Hyperplastic Ovary[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Table A-12 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Litter Summary of External and Soft Tissue Alterations Among Litters of Rabbits[a]

Exposure Level: 3 ppm

Animal Number	818-0023	0024	0033	0034	0036	0047	0048	0057	0058	0059	0069	0071	0072	0108	0082	0083	0084	0093	0096	0117	0119	0120	0132	Total Fetuses	Total Litters
EXTERNAL EXAMINATION	6	4	6	9	9	13	7	8	9	12	7	7	5	9	8	6	6	9	8	9	6	1	8	172	23
SOFT TISSUE EXAMINATION	3	3	3	5	5	7	4	4	5	6	4	4	3	5	4	3	3	5	4	5	3	1	4	93	23
TOTAL MAJOR MALFORMATIONS[b]	0	1	0	0	0	1	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	4	4
EXTERNAL ALTERATIONS																									
Arthrogryposis†	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Anonychia†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Polyonychia†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Brachydactyly†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Ectrodactyly†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Syndactyly†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Microphthalmia†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Misalignment of Palatine Rugae	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Medial Rotation of Digits†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Inward Rotation of Hind Feet†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Omphalocele†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Thinning of Abdominal Wall†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hypoplastic Tail†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Kinky Tail†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Narrowed Tip of Tail	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SOFT TISSUE ALTERATIONS																									
Coarctation of the Aortic Arch†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Ventricular Septal Defect†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Agenesis of Subclavian Artery†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Extra Vessel Off Aortic Arch	1	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Patent Ductus Arteriosis	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hydropericardium	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	3
Valvular Hematoma-Tricuspid	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Retroesophageal Subclavian	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Edema of the Pulmonary Artery	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Diaphragmatic Hernia†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hepatic Cysts-Multifocal	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hepatic Necrosis-Focal	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Gall Bladder																									
-Aplastic†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1
-Hypoplastic	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Bilobed	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Spleen																									
-Aplastic†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Hypoplastic†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Pale	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0
-Accessory	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	1
-Bilobed	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Adrenal-Accessory	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Kidney																									
-Agenesis-Unilateral†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Misshapen†	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Dilated Renal Pelvis†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	1
-Mineral-Like Renal Deposits	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Ureter																									
-Dilated	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	2	2
-Convoluted	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Retrocaval	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Ovarian Agenesis†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hyperplastic Ovary†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Paraovarian Cyst	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	1
Testicular Cyst	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Table A-12 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Litter Summary of External and Soft Tissue Alterations Among Litters of Rabbits[a]

Exposure Level: 10 ppm

Animal Number	010-0075	0026	0038	0039	0049	0050	0061	0064	0073	0075	0076	0109	0085	0086	0087	0088	0097	0098	0121	0122	0123	0124	0132	0134	Total Fetuses	Total Litters
EXTERNAL EXAMINATIONS	9	10	8	10	5	7	9	6	9	9	12	11	9	8	8	7	1	8	8	2	15	8	4	6	107	24
SOFT TISSUE EXAMINATIONS	5	5	4	5	3	4	5	3	5	5	6	4	5	4	4	4	1	4	4	2	7	4	3	3	101	24
TOTAL MAJOR MALFORMATIONS[b]	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	3	3
EXTERNAL ALTERATIONS																										
Arthrogryposis[1]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Anonychia[1]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Polyonychia[1]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Brachydactyly[1]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Ectrodactyly[1]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Syndactyly[1]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Microphthalmia[1]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Misalignment of Palatine Rugae	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Medial Rotation of Digits[1]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Inverd Rotation of Hind Feet[1]	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Omphalocele[1]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Thinning of Abdominal Wall[1]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hypoplastic Tail[1]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Kinky Tail[1]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Narrowed Tip of Tail	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SOFT TISSUE ALTERATIONS																										
Coarctation of the Aortic Arch[1]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Ventricular Septal Defect[1]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Agenesis of Subclavian Artery[1]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Extra Vessel Off Aortic Arch	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	2	2
Patent Ductus Arteriosis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hydropericardium	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Valvular Hematoma-Tricuspid	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Retroesophageal Subclavian	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Edema of the Pulmonary Artery	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Diaphragmatic Hernia[1]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hepatic Cysts-Multifocal	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hepatic Necrosis-Focal	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Gall Bladder -Aplastic[1]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Hypoplastic	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Bilobed	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Spleen -Aplastic[1]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Hypoplastic[1]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Pale	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1
-Accessory	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Bilobed	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Adrenal-Accessory	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	1
Kidney -Agenesis-Unilateral[1]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Hiesshapen[1]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Dilated Renal Pelvis[1]	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
-Mineral-Like Renal Deposits	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Ureter -Dilated	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Convoluted	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Retrocaval	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Ovarian Agenesis[1]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hyperplastic Ovary[1]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Paraovarian Cyst	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Table A-12 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Litter Summary of External and Soft Tissue Alterations Among Litters of Rabbits[a]

Exposure Level: 50 ppm

Animal Number	810-0027	0028	0029	0030	0041	0042	0051	0052	0053	0054	0065	0077	0078	0111	0112	0101	0102	0125	0135	0136	0137	0138	Total Fetuses	Total Litters
EXTERNAL EXAMINATION	2	9	5	7	8	5	6	8	7	6	8	7	7	4	8	6	4	9	6	8	10	5	145	22
SOFT TISSUE EXAMINATION	2	5	3	4	4	3	3	4	4	3	4	4	4	3	4	3	3	5	3	4	5	3	80	22
TOTAL MAJOR MALFORMATIONS[b]	1	1	2	1	5	0	3	0	7	4	6	7	7	2	5	6	4	7	5	6	7	5	91	20
EXTERNAL ALTERATIONS																								
Arthrogryposis[†]	0	0	0	0	3	0	3	0	6	2	5	5	7	0	1	2	2	1	2	4	6	5	54	15
Anonychia[†]	0	0	0	0	0	0	0	0	2	0	0	3	0	0	0	5	2	1	0	0	0	1	14	6
Polyonychia[†]	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	1
Brachydactyly[†]	0	0	1	0	0	0	0	0	0	0	0	3	0	0	0	1	1	0	0	0	0	0	6	4
Ectrodactyly[†]	0	0	0	0	0	0	0	0	0	0	0	3	1	0	0	0	1	0	0	0	0	1	6	4
Syndactyly[†]	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	1
Microphthalmia[†]	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	1	3	3
Misalignment of Palatine Rugae	2	0	0	4	0	0	1	0	7	1	0	4	1	0	1	2	0	0	0	0	2	2	27	11
Medial Rotation of Digits[†]	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	1	1	0	0	0	0	0	4	3
Inward Rotation of Hind Feet[†]	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Omphalocele[†]	0	0	0	0	0	0	0	0	2	0	0	0	3	0	0	0	0	0	0	0	0	0	5	2
Thinning of Abdominal Wall[†]	0	0	0	0	0	0	0	0	3	0	0	2	0	0	0	0	0	0	0	0	0	1	6	3
Hypoplastic Tail[†]	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	2	2
Kinky Tail[†]	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	1	0	1	4	4
Narrowed Tip of Tail	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	0	1	1	0	1	6	6
SOFT TISSUE ALTERATIONS																								
Coarctation of the Aortic Arch[†]	0	0	0	0	0	0	0	0	1	0	0	4	4	0	0	0	1	0	0	0	1	2	13	6
Ventricular Septal Defect[†]	1	0	0	1	4	0	1	0	4	1	2	4	4	1	0	1	2	0	3	0	2	3	34	15
Agenesis of Subclavian Artery[†]	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	1
Extra Vessel Off Aortic Arch	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Patent Ductus Arteriosis	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1	2	0	5	4
Hydropericardium	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	1
Valvular Hematoma-Tricuspid	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	1
Retroesophageal Subclavian	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1
Edema of the Pulmonary Artery	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1
Diaphragmatic Hernia[†]	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1
Hepatic Cysts-Multifocal	0	0	0	0	0	0	0	0	2	0	0	1	0	0	0	0	0	0	0	0	0	0	1	1
Hepatic Necrosis-Focal	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1
Gall Bladder																								
-Aplastic[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	1
-Hypoplastic	0	0	0	0	0	0	0	0	0	0	1	0	1	0	1	0	1	0	0	0	0	0	4	4
-Bilobed	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Spleen																								
-Aplastic[†]	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
-Hypoplastic[†]	0	1	1	0	1	0	1	0	3	2	0	4	3	1	2	0	3	0	1	0	0	2	25	13
-Pale	1	2	2	0	2	0	0	0	0	2	1	4	2	2	3	1	1	0	3	1	1	2	30	16
-Accessory	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	3	3
-Bilobed	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	1
Adrenal-Accessory	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	2	1
Kidney																								
-Agenesis-Unilateral[†]	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	2	2
-Misshapen[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Dilated Renal Pelvis[†]	0	0	0	1	2	0	0	0	3	3	0	3	2	0	2	2	2	1	1	1	3	2	28	14
-Mineral-Like Renal Deposits	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Ureter																								
-Dilated	0	0	0	0	0	0	0	0	1	1	0	0	0	0	1	2	1	0	0	0	1	0	7	6
-Convoluted	0	0	1	0	0	0	0	0	1	2	1	0	2	0	2	0	0	0	0	0	1	2	12	8
-Retrocaval	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	2	2
Ovarian Agenesis[†]	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	1
Hyperplastic Ovary[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	1
Paraovarian Cyst	1	0	0	0	0	0	0	0	0	1	1	1	0	0	0	1	1	2	0	0	0	1	9	8
Testicular Cyst	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	2	0	0	0	5	3

[a]Inseminated New Zealand white rabbits were exposed to 0, 3, 10 or 50 ppm of EGME for 6 hr/day on days 6 through 18 of gestation.
[b]Indicates the number of fetuses in each litter which exhibited at least one major malformation. Numerous fetuses exposed to 50 ppm of EGME exhibited multiple major malformations.
[c]One control fetus exhibited hypoplastic tail and missing caudal and sacral vertebrae.
[†]Considered a major malformation.

Table A-13

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Litter Summary of Skeletal Alterations Among Litters of Rabbits[a]

Exposure Level: Control (0 ppm)

Animal Number	818-0019	0020	0021	0022	0031	0032	0046	0052	0056	0067	0068	0103	0105	0080	0092	0093	0094	0115	0116	0127	0128	0129	0130	Total Fetuses	Total Litters
SKELETAL EXAMINATION	10	8	7	9	8	6	7	5	6	7	11	9	5	5	8	11	7	13	4	9	6	8	6	173	23
SKELETAL ALTERATIONS																									
Skull																									
-Enlarged Interparietals	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Shortened Nasals, Maxillae and Mandibles[f]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Foramen-Frontal	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Crooked Hyoid	3	0	0	2	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	6	3
-Delayed Ossification																									
-Hyoid	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	1
-Frontals, Parietals, and Interparietals	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Extremities																									
-Missing Phalange(s)[f]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Missing Metacarpal(s)[f]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Missing Metatarsal(s)[f]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Delayed Ossification Tarsal(s)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Shortened Long Bones[f]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Ribs																									
-Extra																									
-Cervical[f]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Lumbar	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Shortened[f]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Fused[f]	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	2	2
-Forked[f]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	1
-Thickened	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
-Calloused[f]	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
-Irregular Pattern of Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Asymmetrical Cartilage	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Extra Site of Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Vertebrae																									
-Fused[f]	0	0	0	0	1[c]	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	2	2
-Missing																									
-Caudal[f]	0	0	0	0	0	0	0	0	0	0	0	0	1[b]	0	0	0	0	0	0	0	0	0	0	1	1
-Sacral[f]	0	0	0	0	0	0	0	0	0	0	0	0	1[b]	0	0	0	0	0	0	0	0	0	0	1	1
-Partial[f]	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
-Atlas[f]	0	0	0	0	1[c]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
-Extra Site of Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	1
-Delayed Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Misaligned[f]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Centra																									
-Misaligned	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
-Delayed Ossification	0	0	0	0	1	0	0	0	0	1	0	0	1	0	0	0	1	0	0	0	0	0	0	4	4
-Fused	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
-Extra Site of Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Fused to Vertebra	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Sternebrae																									
-Fused	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	1	0	0	3	3
-Delayed Ossification	4	7	1	6	2	2	1	1	4	2	2	7	5	2	6	1	4	10	3	6	1	4	5	62	23
-Asymmetric Cartilage	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	1
-Extra Site of Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Other																									
-Double Sternum[f]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Irregular Pattern of Ossification - Scapula	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Table A-13 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Litter Summary of Skeletal Alterations Among Litters of Rabbits[a]

Exposure Level: 3 ppm

Animal Number	BIB-0023	0024	0033	0034	0036	0047	0048	0057	0058	0059	0069	0071	0072	0108	0082	0083	0084	0095	0096	0117	0119	0120	0132	Total Fetuses	Total Litters
SKELETAL EXAMINATION	6	4	6	9	9	13	7	8	9	12	7	7	5	9	8	6	6	9	8	9	6	1	8	172	23
SKELETAL ALTERATIONS																									
Skull																									
-Enlarged Interparietals	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Shortened Nasals, Maxillae and Mandibles†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Formen-Frontal	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Crooked Hyoid	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Delayed Ossification																									
-Hyoid	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	2	2
-Frontals, Parietals, and Interparietals	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	2	2
Extremities																									
-Missing Phalange(s)†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Missing Metacarpal(s)†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Missing Metatarsal(s)†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Delayed Ossification Tarsal(s)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Shortened Long Bones†	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	1	0	0	0	0	0	0	3	3
Ribs																									
-Extra																									
-Cervical†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Lumbar	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Shortened†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Fused†	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Forked†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
-Thickened	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Calloused†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	1
-Irregular Pattern of Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Asymmetrical Cartilage	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Extra Site of Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Vertebrae																									
-Fused†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Missing																									
-Caudal†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Sacral†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Partial†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Atlas†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Extra Site of Ossification	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Delayed Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	1
-Misaligned†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Centra																									
-Misaligned	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Delayed Ossification	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Fused	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	2	2
-Extra Site of Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Fused to Vertebra	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Sternebrae																									
-Fused	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Delayed Ossification	2	1	5	3	8	7	3	6	5	9	3	2	2	2	7	3	2	3	3	6	3	1	7	93	23
-Asymmetric Cartilage	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
-Extra Site of Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Other																									
-Double Sternum†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Irregular Pattern of Ossification - Scapula	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Table A-13 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Litter Summary of Skeletal Alterations Among Litters of Rabbits[a]

Exposure Level: 10 ppm

Animal Number	81B-0025	0026	0038	0039	0049	0050	0061	0064	0073	0075	0076	0109	0085	0086	0087	0088	0097	0098	0121	0122	0123	0124	0133	0134	Total Fetuses	Total Litters
SKELETAL EXAMINATION	9	10	8	10	5	7	9	6	9	9	12	11	9	8	8	7	1	8	6	2	13	8	4	6	107	24
SKELETAL ALTERATIONS																										
Skull																										
-Enlarged Interparietals	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Shortened Nasals																										
Maxillae and Mandibles[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Foramen-Frontal	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
-Crooked Hyoid	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	2
-Delayed Ossification																										
-Hyoid	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0	2	2
-Frontals, Parietals, and Interparietals	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Extremities																										
-Missing Phalange(s)[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1
-Missing Metacarpal(s)[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Missing Metatarsal(s)[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Delayed Ossification Tarsal(s)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Shortened Long Bones[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1
Ribs																										
-Extra																										
-Cervical[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Lumbar	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Shortened[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Fused[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	1
-Forked[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Thickened	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Calloused[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Irregular Pattern of Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Asymmetrical Cartilage	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Extra Site of Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Vertebrae																										
-Fused[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Missing																										
-Caudal[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Sacral[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Partial[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Atlas[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Extra Site of Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Delayed Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Misaligned[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Centra																										
-Misaligned	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Delayed Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Fused	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Extra Site of Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Fused to Vertebra	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Sternebrae																										
-Fused	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Delayed Ossification	9	8	5	2	5	2	9	6	6	7	6	4	8	8	2	7	1	4	1	1	8	8	3	3	123	24
-Asymmetric Cartilage	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	2	2
-Extra Site of Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Other																										
-Double Sternum[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Irregular Pattern of Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
- Scapula	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Table A-13 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN RATS AND RABBITS

Individual Litter Summary of Skeletal Alterations Among Litters of Rabbits[a]

Exposure Level: 50 ppm

Animal Number	81B-0027	0028	0029	0030	0041	0042	0051	0052	0053	0054	0065	0077	0078	0111	0112	0101	0102	0125	0135	0136	0137	0138	Total Fetuses	Total Litters
SKELETAL EXAMINATION	2	9	5	7	8	5	6	8	7	6	8	7	7	4	8	6	4	9	6	8	10	5	145	22
SKELETAL ALTERATIONS																								
Skull																								
-Enlarged Interparietals	0	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0	0	0	5	1
-Shortened Nasals	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6	0	0	0	0	6	1
Maxillae and Mandibles[f]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	10	7
-Foramen-Frontal	2	0	0	0	0	1	3	0	0	1	0	1	4	1	0	1	0	2	0	1	0	3	0	14	8
-Crooked Hyoid	0	1	0	0	0	0	0	0	0	0	1	4	1	0	0	0	0	0	0	0	0	0	0	0	0
-Delayed Ossification	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	7	4
-Hyoid	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0	0	1	0	0	0	0	0	4	2
-Frontals, Parietals, and Interparietals	0	1	0	0	0	0	0	0	3	0	1	7	0	2	0	1	0	0	0	0	1	1	17	8
Extremities	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1
-Missing Phalange(s)[f]																								
-Missing Metacarpal(s)[f]	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Missing Metatarsal(s)[f]	0	0	0	0	0	0	0	0	0	0	0	4	1	0	0	0	1	0	0	0	0	0	7	4
-Delayed Ossification	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0	0	1	0	0	0	0	0	4	2
Tarsal(s)	0	0	0	0	0	0	0	0	0	0	0	6	1	0	0	1	1	0	0	0	0	0	9	4
-Shortened Long Bones[f]	0	1	0	0	0	0	0	0	3	0	1	7	0	2	0	1	0	0	0	0	1	1	17	8
Ribs	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1
-Extra																								
-Cervical[f]	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	2	2
-Lumbar	0	0	0	0	1	0	0	0	3	0	0	3	0	3	0	1	0	0	0	0	1	1	13	7
-Shortened[f]	0	0	0	0	0	0	0	0	0	1	0	0	3	0	0	0	0	0	0	0	0	0	4	2
-Fused[f]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	1
-Forked[f]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1
-Thickened	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Calloused[f]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Irregular Pattern of Ossification	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	2	2
-Asymmetrical Cartilage	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1
-Extra Site of Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	1
Vertebrae																								
-Fused[f]	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	1
-Missing																								
-Caudal[f]	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	2	2
-Sacral[f]	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
-Partial[f]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Atlas[f]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Extra Site of Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	1
-Delayed Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
-Misaligned[f]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Centra																								
-Misaligned	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	1	1
-Delayed Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	2	2
-Fused	0	0	0	0	0	0	0	0	2	0	2	1	0	0	0	0	0	0	0	0	0	0	1	1
-Extra Site of Ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-Fused to Vertebra	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	2	0	1	1	11	8
Sternebrae																	0	0	0	0	0	0	0	0
-Fused	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	1	1	1
-Delayed Ossification	0	0	0	0	1	0	0	0	1	0	0	1	0	0	1	0	0	0	0	0	0	0	2	2
-Asymmetric Cartilage	2	5	4	6	7	3	6	8	6[d]	5	8	6	7	4	8	5	4	8	5	7	9	4	11	8
-Extra Site of Ossification	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	1	0	0	0	0	127	22
Other	0	0	0	2	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	3	3
-Double Sternum[f]	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	4	3
-Irregular Pattern of Ossification - Scapula	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1

[a]Inseminated New Zealand white rabbits were exposed to 0, 5, 10 or 50 ppm of EGME for 6 hr/day on days 6 through 18 of gestation.
[b]One control fetus exhibited hypoplastic tail and missing caudal and sacral vertebrae.
[c]One control fetus exhibited fused vertebrae and missing atlas.
[d]Based on sternebral examination of six pups.
[f]Considered to be a major malformation.

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ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE†

B-17e

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November 23, 1982

†Sponsored by five U.S. ethylene glycol ethers producers under the auspices of the Chemical Manufacturers' Association under contract number GE-7.0-Ter-Ihl-Dow.

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SUMMARY

The objective of this study was to evaluate the embryotoxic and teratogenic potential of ethylene glycol monomethyl ether (EGME) in mice via inhalation. Bred CF-1 mice were exposed to 0, 10 or 50 ppm of EGME for 6 hr/day on days 6 through 15 of gestation and the fetuses examined on day 18 of gestation for any deleterious effects on embryonal or fetal development.

Among maternal mice, a slight but statistically significantly lower weight gain was observed at 50 ppm during the last 4 days of exposure. There were no other indications of a maternal effect at 10 or 50 ppm. Low incidences of major malformations were observed among control as well as exposed mice. The incidence of major malformations, considered individually or collectively within each exposure group, was not significantly different from the controls. Significant increases in the incidences of unilateral testicular hypoplasia and extra (lumbar) ribs, both considered minor alterations in mice, were observed at 50 ppm indicating a slight fetotoxic effect. There were no treatment-related effects observed among mice at 10 ppm.

INTRODUCTION

Ethylene glycol monomethyl ether (EGME, 2-methoxyethanol) is a volatile, nearly odorless liquid with the following properties:

Structural Formula:	$H_3C-O-CH_2CH_2-OH$
Molecular Weight:	76.90
Boiling Point:	124.6°C @760 mmHg
Vapor Pressure:	9.5 mmHg @25°C
Solubility:	Miscible with water
Flash Point:	107°F

EGME has been used extensively for many years as a solvent for resins, lacquers, paints, dyes, and inks, and as a detergent.

The toxicologic information concerning EGME has recently been reviewed (Rowe and Wolf, 1982). The oral toxicity of EGME is low, with an LD50 of 3.5 g/kg in rats, 0.89 g/kg in rabbits and 0.95 g/kg in guinea pigs. Moderate pain and conjunctivitis result after direct application to the eyes of rabbits, but these effects are reversible within 24 hours of application. Subchronic inhalation exposure of rats (310 ppm for 5 weeks) and dogs (750 ppm for 12 weeks) for 7 hours/day, 5 days/week resulted in hypochromasia, reduced hemoglobin concentration and decreased packed cell volume.

Miller, et al. (1981) reported the results of short term inhalation studies in which rats and mice were exposed to 0, 100, 300 or 1000 ppm for 9 days during an 11-day interval. Histopathologic changes in rats and mice exposed to 1000 ppm included moderately reduced bone marrow cellularity, hematologic abnormalities and testicular degeneration. Similar but less pronounced changes were noted in some animals in the 300 ppm group. No adverse effects were attributed to exposure to 100 ppm.

Subchronic exposure of rats and rabbits to EGME for 6 hr/day, 5 days/week for 13 weeks resulted in hematologic abnormalities, decreased testicular and thymic weights, and histopathologic changes of the testes and thymus

in rats and rabbits at 300 ppm (Miller, et al, 1982a). Similar histopathologic changes were found in the testes of three of five rabbits at 100 ppm, and in one of five rabbits at 30 ppm. In a subsequent study (Miller, et al, 1982b), no effects were found in the testes of ten rabbits exposed to 30 ppm. A fertility study (Rao, et al, 1982) was conducted concurrently with the subchronic study. Infertility was seen in male rats at 300 ppm but not at 100 or 30 ppm. No adverse reproductive effect was observed among any of the groups of exposed females. There was no evidence of a dominant lethal mutagenic effect at 30 or 100 ppm among males, however, the absence of litters at 300 ppm precluded evaluation for dominant lethality at that level.

Teratology studies of EGME in mice and rats have recently been published. Nagano, et al, (1981) reported that oral administration of EGME to pregnant ICR mice on days 7 through 14 of gestation produced fetotoxicity starting at 31.25 mg/kg/day (the lowest dose level), teratogenicity at 62.5 mg/kg/day and above, and maternal toxicity at 1000 mg/kg/day (the top dose level). Nelson, et al., (1982) reported that inhalation exposure for 7 hr/day to 50 or 100 ppm of EGME produced skeletal and cardiovascular defects in Sprague-Dawley rats.

A study was recently conducted (Hanley, et al., 1982a) in which pregnant rats and rabbits were exposed via inhalation to vapor concentrations of 0, 3, 10 and 50 ppm of EGME for 6 hr/day during the period of major organogenesis. Exposure to 50 ppm produced teratogenicity in rabbits, and slight fetotoxicity in rats. No adverse effects were observed in either species at 10 or 3 ppm.

In order to establish appropriate exposure concentrations for a definitive teratology study, a probe study was conducted to determine appropriate exposure levels of EGME in pregnant CF1 mice (Hanley, et al., 1982b). Groups of 10 bred mice were exposed to 0, 3, 10, or 50 ppm of EGME for 6 hr/day on days 6 through 15 of gestation. No indications of maternal or embryotoxicity were observed at the levels tested.

The purpose of this study was to evaluate the embryotoxic and teratogenic potential of EGME in mice via inhalation (the most probable route of human exposure) in order to establish a comparative data base with rats and rabbits. The CF-1 mouse was selected as the test species based on its extensive historical use for teratology studies within this laboratory. Pregnant mice were exposed on days 6 through 15 of gestation to EGME via inhalation and the fetuses were examined on day 18 of gestation for any deleterious effects on embryonal or fetal development. This study was sponsored by five U.S. ethylene glycol ethers producers[1], under the auspices of the Chemical Manufacturers' Association.

MATERIALS AND METHODS

Test Material: EGME for use in this study was obtained from The Dow Chemical Company, Michigan Division, Midland, Michigan and was identified as Lot No. MM810624. Analysis[2] of the sample using gas chromatography indicated 99.96% purity.

Test Animals: Stock supplies of male and female CF-1 mice (Charles River Breeding Laboratories, Inc., Portage, Michigan) were obtained. Animals were housed in wire-bottomed cages in a room designed to control temperature at approximately 22°C, relative humidity at approximately 50% and a photocycle of 12 hours light and dark. Animals were acclimated to the laboratory[3] for at least two weeks prior to breeding. Adult virgin female CF-1 mice (approximately 25-30 g at breeding) were bred to adult males (two females to one male) from the same strain. Day 0 of pregnancy was determined by the presence of a vaginal plug upon visual examination.

[1] Texaco, ICI America, PPG, Olin Chemicals and Dow Chemical, U.S.A.

[2] Analysis performed by P. Kastl, Toxicology Research Laboratory, The Dow Chemical Company, Midland, MI, 15 July 1981.

[3] Fully accredited by the American Association for Accreditation of Laboratory Animal Care (AAALAC).

All animals were uniquely identified by metal ear tags. Food (Certified Laboratory Animal Chow, Ralston Purina Company, St. Louis, Missouri) and municipal tap water were available ad libitum except during actual inhalation exposure periods. Analysis of Purina Certified Chow was performed by Ralson Purina Company to confirm that the diets provide adequate nutrition, and to quantify the levels of selected contaminants associated with the formulation process. Analysis of tap water (municipal water supply) was performed according to the Standard Operation Procedures of the Toxicology Research Laboratory.

Experimental Design: Groups of 30 and 32 bred mice were exposed by inhalation to levels of 10 and 50 ppm of EGME, respectively, for 6 hr/day on days 6 through 15 of gestation. A control group of 31 mice was exposed to filtered air in an exposure chamber in a manner similar to treated groups.

Exposure Conditions: Animals were exposed to ethylene glycol monomethyl ether (EGME) in 4.3 cubic meter stainless steel and glass chambers. Control animals were placed in an identical chamber. Temperature and humidity in the chambers were controlled by a system designed to maintain temperature and relative humidity at approximately 21°C and 50%, respectively. Temperature and relative humidity values in the chambers were recorded each exposure day.

Vapors of EGME were generated using the glass J-tube method of Miller, et al. (1980). Liquid EGME was metered at a constant rate into the glass J-tubes. Compressed air was preheated to ~80°C with a flameless heat torch (Master, Model FHT-4) and passed through the J-tube into the main chamber air supply where the vapors were further mixed by turbulence, and diluted before entering the chamber. The chamber airflow was maintained at approximately 800 liters/minute. The nominal concentration (ratio of EGME used to the chamber airflow) was calculated daily for each chamber.

The analytical concentration of EGME in each chamber was measured 2-3 times/hour using a Miran 1A infrared spectrometer with a variable path-length gas cell at a wavelength of 8.8 μm. Air standards were prepared by injecting calculated amounts of EGME into SARAN bags filled with a measured volume of filtered compressed air. These standards were passed through the IR to produce a series of responses at various concentrations, i.e., a standard curve. The concentrations of EGME in the exposure chambers were determined by interpolation from the standard curve. Standard curves were generated prior to the first exposure and at least weekly thereafter; a standard was analyzed before each exposure as a calibration check of the analytical system.

Maternal Observations: Animals were observed daily throughout the experimental period for indications of toxicity from the test material. Animals found dead were submitted for gross pathologic examination. Body weights for mice were recorded on gestation days 6, 9, 12, 16 and 18; food and water consumption were recorded at 3-day intervals starting on day 6 of gestation. Maternal liver, thymus and spleen were weighed and sections of maternal spleen, thymus, mesenteric lymph and vertebral bone marrow were preserved in 10% formalin but were not examined histologically. In addition, maternal blood was collected by cardiac puncture from at least 10 pregnant females/exposure level for hematologic examination[4] (excluding differential white cell counts on blood smears).

Fetal Observations: Test animals were sacrificed by carbon dioxide inhalation on day 18 of gestation. The uterine horns were exteriorized through a mid-line incision in the abdominal wall and the following data were recorded: 1) number and position of fetuses *in utero*, 2) number of live and dead fetuses, 3) number and position of resorption sites, 4) the sex, body weight and crown-rump length of each fetus, and 5) any gross external alterations. The uteri of apparently nonpregnant animals were stained with a 10% solution of sodium sulfide (Kopf, *et al.*, 1964) and examined for evidence of implantation sites. This procedure was

[4] Red blood cell (RBC) count, hemoglobin concentration (HGB), packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), platlet count (PLAT) and white blood cell (WBC) count. ELT-8, Ortho Instruments, Westwood, MA.

conducted solely to determine the incidence of pregnancy; implantations detected only by staining the uterus were not included in the calculation of the resorption rate. One-half of each litter, selected using a table of random numbers, was examined immediately by dissection under a low power microscope for evidence of soft tissue alterations (Staples, 1974). The heads of mouse fetuses examined by dissection were removed, placed in Bouin's fixative and examined grossly by the serial sectioning technique of Wilson (1965). All fetuses were then preserved in alcohol, eviscerated, cleared, and stained with alizarin red-S (Dawson, 1926) and examined for skeletal alterations.

Statistical Evaluation: Statistical evaluation of the frequency of alterations and of resorptions among litters and the fetal population was performed using the Wilcoxon test as modified by Haseman and Hoel (1974). Analyses of the percentage of pregnancy and other incidence data were made by the Fischer exact probability test (Siegel, 1956). The fetal sex ratio was analyzed by a binomial distribution test (Steel and Torrie, 1960). Analyses of other data were done by parametric or non-parametric analysis of variance followed by either Dunnett's test (Steel and Torrie, 1960) or Wilcoxon's test with a Bonferroni correction (Miller, 1966), as appropriate. The nominal alpha level used for statistical analysis was $\alpha = 0.05$. For food and water consumption data, statistical outliers were identified by a sequential outlier test, $\alpha = 0.02$ (Grubbs, 1969), and were deleted from the calculation of mean values.

RESULTS

Exposure Conditions: A summary of the chamber analytical and exposure concentrations, temperature and relative humidity for the exposure period is presented in Table 1. For each chamber, the daily time weighted average (TWA) analytical concentration was very close to the intended target concentration. Moreover, there was close agreement between the mean daily TWA analytical concentrations and the daily nominal concentrations, indicating that test material losses were minimized in the vapor generation and exposure systems.

Maternal Observations: No significant changes in gross appearance or demeanor were observed among mice exposed to EGME. A single death was recorded among mice exposed to 50 ppm, which resulted from trauma sustained during handling. Among mice exposed to 50 ppm, maternal weight gain on days 12 through 15 of gestation was statistically identified as being lower than the control value (Table 2) which resulted in a statistically identified lower body weight on day 16. There were no other statistically identified differences in body weight gain in any group. There were no statistical differences in food consumption (Table 3) or absolute and relative organ weights (Table 4) among EGME-exposed mice when compared to controls. Water consumption was statistically increased among mice at 10 ppm on days 15 through 17 of gestation (Table 3), but this isolated difference was not considered treatment-related. A summary of the hematologic parameters measured in pregnant mice is presented in Table 4. A statistically identified decrease in the mean hemoglobin concentration was observed among mice exposed to 10 ppm of EGME; however, there was no significant difference at 50 ppm. Hence, this apparent difference was attributed to normal variation.

Pregnancy status in mice appeared to be unaffected by exposure to up to 50 ppm of EGME. A single control litter delivered on day 16 of gestation, approximately 2 days prior to the time of scheduled cesarean section. A summary of the reproductive parameters measured at cesarean section is presented in Table 5. The mean number of fetuses per litter at 50 ppm was statistically significantly lower than the concurrent control; however, the mean litter size among historical controls was 10.5 fetuses/litter. This apparent difference was therefore not considered treatment related, but rather reflected normal variation with this species. There were no other differences from control values among the reproductive parameters measured to suggest any adverse effects from exposure.

Fetal Observations: The incidences of external, soft tissue, and skeletal alterations observed among fetal mice exposed to EGME are summarized in Table 6. The incidence of major malformations, when considered individually or collectively within each exposure group, was not statistically significantly different from the control. A total of 8 control fetuses from 8 different litters had major malformations. One control fetus

exhibited a mediocaudal malpositioning of the kidneys and the ureters were crossed and attached to the contralateral kidney. One control fetus had only 5 lumbar vertebrae, one fetus had an extra (cervical) rib and 5 individual fetuses from different litters had cleft palate. Among mice exposed to 10 ppm, 3 fetuses from 3 separate litters had major malformations; two fetuses had only 5 lumbar vertebrae and the third fetus had a cleft palate, a cervical rib and only 5 lumbar vertebrae.

At 50 ppm, 8 fetuses from a total of 5 litters had major malformations. Single instances of ablepharia, cleft palate, omphalocele and bilateral renal agenesis occurred in fetuses from separate litters at 50 ppm. One litter at 50 ppm had 4 fetuses with major malformations, 3 with cleft palate and one with only 5 lumbar vertebrae.

A number of minor alterations were observed among both control and exposed fetuses. Of these, the incidences of two were statistically identified as being increased among mice exposed to 50 ppm when compared to controls. A significant increase in the incidence of unilateral hypoplastic testicle was observed at 50 ppm. In the majority of the fetuses exhibiting this lesion (including controls), the left testicle was observed to be approximately 50% the size of the right testicle. Based on the unilateral nature of this lesion, and the incidence observed among controls, this was considered a minor effect indicative of slight fetotoxicity. Also observed among fetal mice at 50 ppm was a significant increase in the incidence of extra (lumbar) ribs. The incidences of other minor alterations which occurred among mice exposed to 10 or 50 ppm were not statistically different from the control values.

DISCUSSION

Exposure of pregnant CF-1 mice to 10 or 50 ppm of EGME for 6 hr/day on days 6 through 15 of gestation produced no evidence of a teratogenic effect. Mild fetotoxicity, evidenced by increases in the incidence of unilateral hypoplastic testicle and extra (lumbar) ribs, was observed among

fetal mice exposed to 50 ppm. Maternal effects observed at 50 ppm were minimal, consisting only of a statistically identified decrease in weight gain during the last 4 days of exposure. There were no significant treatment-related effects observed in maternal or fetal mice at 10 ppm.

The results obtained in the present study are consistent with the data reported by Nagano, et al. (1981). Nagano administered EGME orally to ICR mice at dose levels of 0, 31.25, 62.5, 125, 250, 500 and 1000 mg/kg/day on days 7 through 14 of gestation. Teratogenic effects (exencephaly, umbilical hernia, abnormal digits, and skeletal malformations) were observed at dose levels of 62.5 mg/kg/day and above. Fetotoxicity in the form of bifurcated or split cervical vertebrae and delayed ossification of the phalanges, was reported at 31.25 mg/kg/day. If one assumes an equivalent percentage of the dosage of EGME is absorbed irrespective of the route of administration, direct comparison of the results reported by Nagano, et al. (1981) and the present study is possible. Assuming a respiratory minute volume of 24 ml/min for a mouse (Guyton, 1947) and an average body weight during gestation of 35g, a 6 hour exposure to 50 ppm would correspond to an oral dose of approximately 38.4 mg/kg/day. Thus at roughly equivalent doses, fetotoxicity was observed in both studies. The differences in the specific manifestations of fetotoxicity in the two studies may reflect differences in strain or route of administration. Nonetheless, the data from these studies indicate a consistent pattern of effects within the species.

In a previous study (Hanley, et al., 1982a) in which rats and rabbits were exposed to EGME via inhalation for 6 hr/day during the critical period of gestation, severe teratogenic effects were observed among rabbits exposed to 50 ppm. Major malformations involving the cardiovascular, urogenital and/or skeletal system were observed in 63% of fetal rabbits at 50 ppm. A slight fetotoxic effect was observed among rats exposed to 50 ppm in the same study. In the present study, slight fetotoxic effects were also observed among mice exposed to 50 ppm.

Thus, rabbits are apparently more sensitive to the teratogenic effects of EGME than either rats or mice based on the comparative effects at 50 ppm in the three species. Nevertheless, 10 ppm was a no effect level in all three species (rats, rabbits, and mice) for both teratogenicity and fetotoxicity.

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TITLE OF STUDY: ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

In compliance with Good Laboratory Practice Regulations, this study was inspected by the Quality Assurance Unit and the results of these inspections reported to Management and the Study Director on the dates listed below. The report accurately reflects the data generated in accordance with the regulations and standard operating procedures of the Laboratory. All data and the reports are located at the submitting laboratory.

Study Started:	28 October 1981	Report Issued Date:	23 November 1982
Dates of Inspection:	27 October 1981	Date of Report:	27 October 1981
	9 December 1981		14 December 1981
	15 October 1982		18 October 1982

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TABLE 1

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Chamber Concentrations, Temperature and Relative Humidity

	Ethylene Glycol Monomethyl Ether, ppm		
Target Concentration	0	10	50
Number of Exposure Days	21	21	21
Analytical Concentration, ppm[a]	--	10.1±0.5	49.8±0.5
Analytical Coefficient of Variation[b]	--	5.0	1.0
Range of Analytical Concentrations[c], ppm	--	8.9-10.9	48.8-50.7
Nominal Concentration, ppm	--	10.0±0.6	46±1
Nominal/Analytical Concentration	--	0.99	0.92
Daily Temperature, °C			
Minimum $\bar{x}$ ± S.D.[d]	22±1	21±1	22±1
Maximum $\bar{x}$ ± S.D.	23±1	23±1	23±1
Daily Relative Humidity, %			
$\bar{x}$ ± S.D.[d]	49±3	49±2	51±2

[a]Data represents mean ± standard deviation of daily time weighted average (TWA).

[b]Analytical $\frac{\text{standard deviation}}{\text{mean}} \times 100$

[c]Data represents range of daily analytical TWA

[d]$\bar{x}$ ± S.D. = Mean ± standard deviation

TABLE 2

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Body Weights of Pregnant Mice[a]

Exposure Level		Ethylene Glycol Monomethyl Ether, ppm		
		0	10	50
Number of Dams		26	23	24
Maternal Body Weight (g)[b] on Gestation Days	6	34.0±2.1	34.0±2.4	34.2±2.0
	9	35.3±2.7	35.7±2.2	35.4±1.7
	12	40.4±2.3	39.9±2.3	39.9±2.7
	16	49.8±2.8	49.9±3.4	47.6±3.9*
	18	56.1±4.0	55.8±4.8	54.2±5.1
Maternal Body Weight Gain (g)[b] on Gestation Days	6-8	1.3±2.0	1.7±1.4	1.2±1.7
	9-11	5.1±1.7	4.3±1.5	4.5±1.9
	12-15	9.4±1.6	9.9±2.1	7.7±2.7*
	16-17	6.2±2.4	6.0±2.3	6.5±2.1
	6-17	22.0±3.5	21.8±4.6	20.0±4.2

[a]Bred CF-1 mice were exposed to 0, 10 or 50 ppm of EGME by inhalation for 6 hr/day on days 6 through 15 of gestation.

[b]Mean ± S.D.

*Significantly different from the control value by Dunnett's test.

See Table A-1 for individual animal data.

TABLE 3

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Food and Water Consumption of Pregnant Mice[a]

Exposure Level		Ethylene Glycol Monomethyl Ether, ppm		
		0	10	50
Number of Dams		26	23	24
Maternal Food Consumption[b] on Gestation Days	6-8	6.6±1.0	6.7±0.8	6.8±1.0
	9-11	7.2±1.0	7.1±0.7	7.2±1.0
	12-14	8.1±0.8	7.9±0.7	8.0±1.3
	15-17	10.7±9.2	8.8±1.3	8.3±1.1
Maternal Water Consumption[b] on Gestation Days	6-8	9.9±1.6	9.5±1.7	9.1±5.3
	9-11	10.5±1.3	10.6±1.8	10.3±1.8
	12-14	10.5±2.9	11.3±1.7	10.8±2.6
	15-17	10.5±1.1	12.0±2.2*	10.9±1.5

[a]Bred CF-1 mice were exposed to 0, 10 or 50 ppm of EGME by inhalation for 6 hr/day on days 6 through 15 of gestation.

[b]Grams/mouse/day, mean ± S.D.

*Significantly different from the control value by Dunnett's test.

See Tables A-2 and A-3 for individual animal data.

TABLE 4

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Organ Weights and Hematologic Parameters in Pregnant Mice[a]

Exposure Level	Ethylene Glycol Monomethyl Ether, ppm		
	0	10	50
Number of Dams	26	23	24
Maternal Organ Weight on Gestation Day 18			
Liver - absolute[b]	2.86±0.40	2.81±0.31	2.72±0.27
- relative[c]	5.10±0.58	5.04±0.38	5.05±0.45
Spleen - absolute	0.12±0.04	0.12±0.03	0.11±0.03
- relative	0.22±0.07	0.21±0.05	0.21±0.06
Thymus - absolute	0.05±0.04	0.05±0.05	0.05±0.05
- relative	0.09±0.06	0.10±0.10	0.09±0.10
Hematologic Parameters[d] Measured on Gestation Day 18			
RBC x $10^6/mm^3$	7.49±0.66	7.04±0.67	7.14±0.46
HGB (g/dl)	14.3±1.2	13.1±0.7*	13.5±0.4
PCV (%)	38.5±3.7	36.0±3.2	36.0±2.0
MCV (μ^3)	51.30±2.31	51.10±0.74	50.45±2.70
MCH (μμg)	19.07±0.85	18.73±0.85	18.90±0.88
MCHC (%)	37.14±1.93	36.61±1.38	37.52±1.74
Platelets x $10^3/mm^3$	1524±205	1416±274	1307±155
WBC x $10^3/mm^3$	3.8±2.3	3.4±3.0	2.4±1.9
N =	10	10	11

[a]Bred CF-1 mice were exposed to 0, 10 or 50 ppm of EGME by inhalation for 6 hr/day on days 6 through 15 of gestation

[b]Grams, mean ± S.D.

[c]Grams organ weight/100 grams body weight, mean ± S.D.

[d]Mean ± S.D.

*Significantly different from the control value by Dunnett's test

See Tables A-4 and A-5 for individual animal data.

TABLE 5

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Observations Made at the Time of Cesarean Section of Mice[a]

	Ethylene Glycol Monomethyl Ether, ppm		
Exposure Level	0	10	50
Number of Bred Females	31	30	32
Number of Maternal Deaths	0	0	1
Percent Pregnant[b]	87(27/31)	77(23/30)	78(25/32)
Pregnancies Detected by Stain[c]	0/4	1/7	1/7
Percent Pregnant, Total[d]	87(27/31)	80(24/30)	81(26/32)
Number of Litters	26	23	24
Implantation Sites/Dam[e]	13±2	12±2	12±2
Fetuses/Litter[e]	12.2±2.0	11.3±2.1	10.5±2.8*
Resorptions/Litter[e]	1.0±1.0	1.1±1.2	1.5±1.4
% Implantations Resorbed[f]	7(25/342)	9(25/295)	12(35/286)
% Litters with Resorptions[f]	62(16/26)	61(14/23)	75(18/24)
Litters Totally Resorbed[f]	0	0	0
Resorptions/Litters with Resorptions[f]	1.6(25/16)	1.8(25/14)	1.9(35/18)
Sex Ratio; M:F	52:48	47:53	50:50
Fetal Body Weight (g)[g]	1.24±0.11	1.27±0.07	1.27±0.10
Fetal Crown-Rump Length, mm[g]	27.7±1.4	28.1±1.2	28.1±0.9

[a]Bred CF-1 mice were exposed to 0, 10 or 50 ppm of EGME by inhalation for 6 hr/day on days 6 through 15 of gestation.

[b]Number of females with visible implantation sites at the time of cesarean section or necropsy/total number bred. One control animal which delivered a litter prior to cesarean section is included.

[c]Number of females with implantation sites detected only after staining the uterus with sodium sulfide/total number stained.

[d]Number of females pregnant at visual inspection of the uterus or after staining/total number bred.

[e]Mean ± S.D.

[f]Resorptions detected only by staining the uterus were not included in these calculations.

[g]Mean of litter means ± S.D.

*Significantly different from the control value by the modified Wilcoxon test.

See Table A-6 for individual animal data.

TABLE 6

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Incidence of Fetal Alterations Among Litters of Mice[a]

Exposure Level		Ethylene Glycol Monomethyl Ether, ppm		
		0	10	50
		Number of Fetuses (Number of Litters) Examined		
EXTERNAL EXAMINATION		317(26)	260(23)	251(24)
SOFT TISSUE EXAMINATION		165(26)	136(23)	132(24)
SKELETAL EXAMINATION		317(26)	260(23)	251(24)
BONES OF THE SKULL		152(26)	124(23)	119(23)[b]
		PERCENT AFFECTED (NUMBER AFFECTED)		
TOTAL MAJOR MALFORMATIONS[c]	F[d]	3(8)	1(3)	3(8)
	L	31(8)	13(3)	21(5)
EXTERNAL ALTERATIONS				
Ablepharia[+]	F	0	0	0.4(1)
	L	0	0	4(1)
Cleft Palate[+]	F	2(5)	0.4(1)[e]	2(1)
	L	19(5)	4(1)[e]	8(2)
Omphalocele[+]	F	0	0	0.4(1)
	L	0	0	4(1)
SOFT TISSUE ALTERATIONS				
Hepatic Hemorrhage - focal	F	0.6(1)	0	0
	L	4(1)	0	0
Hypoplastic Testicle	F	1(2)	2(3)	6(8)*
	L	8(2)	13(3)	25(6)*
Testicular Hemorrhage	F	2(4)	7(10)	7(9)
	L	12(3)	26(6)	29(7)
Epididymal Cyst(s)	F	0.5(1)	0	0
	L	4(1)	0	0
Renal Agenesis - Bilateral[+]	F	0	0	0.8(1)
	L	0	0	4(1)
Dorsomedial Renal Malpositioning with Contralaterally Attached Ureters[+]	F	0.6(1)	0	0
	L	4(1)	0	0
SKELETAL ALTERATIONS				
Skull				
-Delayed Ossification - Occipital	F	9(13)	6(7)	10(12)
	L	35(9)	26(6)	39(9)
-Foramen - Occipital	F	0	0.3(1)	0
	L	0	4(1)	0
-Extra Site of Ossification	F	1(2)	0	0
	L	3(2)	0	0

TABLE 5 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Incidence of Fetal Alterations Among Litters of Mice[a]

Exposure Level		Ethylene Glycol Monomethyl Ether, ppm		
		0	10	50
Vertebrae				
-Cervical Spur(s)	F	12(38)	9(24)	12(30)
	L	46(12)	65(15)	58(14)
-Missing (Lumbar)[†]	F	0.3(1)	1(3)[e]	0.4(1)
	L	4(1)	13(3)	4(1)
Ribs				
-Extra (Lumbar)	F	15(48)	19(49)	33(82)*
	L	54(14)	61(14)	88(21)*
-Extra (Cervical)[†]	F	0.3(1)	0.4(1)[e]	0
	L	4(1)	4(1)	0
Sternebrae				
-Delayed Ossification	F	24(76)	17(43)	31(77)
	L	69(18)	57(13)	88(21)
-Extra Site of Ossification	F	7(21)	4(9)	3(8)
	L	35(9)	26(6)	16(4)
-Foramen	F	2(6)	2(5)	4(11)
	L	15(4)	13(3)	29(7)
-Fused	F	0	0	0.4(1)
	L	0	0	4(1)
-Asymmetrical Cartilage	F	0.3(1)	0	1(3)
	L	4(1)	0	13(3)

[a]Bred CF-1 mice were exposed to 0, 10 or 50 ppm of EGME by inhalation for 6 hr/day on days 6 through 15 of gestation.

[b]Litters with 3 or fewer fetuses had all heads removed during the examination for soft tissue alterations and, therefore, no examination could be conducted on bones of the skull.

[c]Total malformations detected by external, soft tissue or skeletal examination.

[d]F = Fetuses, L = Litters

[e]One fetus at 10 ppm exhibited cleft palate, a cervical rib and was missing a lumbar vertebra.

[†]Considered a major malformation.

*Significantly different from the control value.

See Table A-7 for individual litter data.

TABLE A-1

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Individual and Mean Body Weights and Body Weight Gain of Pregnant Mice[a]

Exposure Level: Control (0 ppm)

ANIMAL NUMBER	MATERNAL BODY WEIGHT (G) DAY(S) OF GESTATION 6	9	12	16	18	MATERNAL BODY WEIGHT GAIN (G) 6-9	9-12	12-16	16-18
8101946	34.1	36.1	41.6	51.8	59.0	2.0	5.5	10.2	7.2
8101947	32.4	28.4	39.3	49.0	57.2	-4.0	10.9	9.7	8.2
8101954	34.9	35.8	40.7	49.9	56.7	0.9	4.9	9.2	6.8
8101956	38.8	40.0	45.1	54.9	60.1	1.2	5.1	9.8	5.2
8101963	32.4	35.2	39.9	51.3	56.5	2.8	4.7	11.4	5.2
8101964	35.3	35.8	42.2	47.7	60.6	0.5	6.4	5.5	12.9
8101965	31.3	33.0	37.6	44.3	48.7	1.7	4.6	6.7	4.4
8101966	32.1	33.1	38.2	48.6	54.1	1.0	5.1	10.4	5.5
8101968	33.3	34.5	37.9	46.9	51.4	1.2	3.4	9.0	4.5
8101981	33.8	34.6	39.2	49.1	55.5	0.8	4.6	9.9	6.4
8101982	31.9	34.3	39.2	48.4	55.8	2.4	4.9	9.2	7.4
8101983	31.5	33.4	37.2	46.9	53.3	1.9	3.8	9.7	6.4
8101991	32.2	35.1	39.4	48.6	55.2	2.9	4.3	9.2	6.6
8101993	34.4	36.3	40.3	51.2	57.3	1.9	4.0	10.9	6.1
8102000	35.1	36.7	40.7	50.8	57.5	1.6	4.0	10.1	6.7
8102001	36.6	38.5	44.8	54.3	61.6	1.9	6.3	9.5	7.3
8102002	34.8	36.5	40.8	52.1	57.3	1.7	4.3	11.3	5.2
8102010	36.0	37.5	41.6	46.3	43.8	1.5	4.1	4.7	-2.5
8102011	31.5	33.2	38.1	46.9	51.7	1.7	4.9	8.8	4.8
8102012	35.3	37.8	42.9	52.9	59.2	2.5	5.1	10.0	6.3
8102013	35.0	37.1	41.8	51.7	57.8	2.1	4.7	9.9	6.1
8102014	34.3	35.3	40.2	50.0	57.2	1.0	4.9	9.8	7.2
8102025	31.6	36.5	40.1	49.4	55.8	4.9	3.6	9.3	6.4
8102027	32.5	33.1	38.0	48.2	56.2	0.6	4.9	10.2	8.0
8102028	35.4	29.6	39.4	49.0	55.9	-5.8	9.8	9.6	6.9
8102029	38.3	40.5	45.3	55.9	62.7	2.2	4.8	10.6	6.8
MEAN	34.0	35.3	40.4	49.8	56.1	1.3	5.1	9.4	6.2
S.D.	2.06	2.73	2.25	2.78	4.00	2.04	1.69	1.56	2.41

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TABLE A-1 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Individual and Mean Body Weights and Body Weight Gain of Pregnant Mice[a]

Exposure Level: 10 ppm

ANIMAL NUMBER	MATERNAL BODY WEIGHT (G) DAY(S) OF GESTATION 0	9	12	16	18	MATERNAL BODY WEIGHT GAIN (G) 0-9	9-12	12-16	16-18
8101946	34.8	35.2	40.6	50.0	51.1	0.4	5.4	9.4	1.1
8101950	36.0	36.6	40.6	47.2	47.6	0.6	4.0	6.6	0.4
8101957	33.8	34.8	39.0	47.1	51.6	1.0	4.2	8.1	4.5
8101958	31.5	38.1	42.1	53.5	62.0	6.6	4.0	11.4	8.5
8101959	32.1	33.2	36.8	46.6	52.6	1.1	3.6	9.8	6.0
8101969	33.4	34.1	38.6	49.1	55.5	0.7	4.5	10.5	6.4
8101970	32.6	33.7	37.3	48.1	53.2	1.1	3.6	10.8	5.1
8101971	39.3	38.6	44.0	57.3	63.0	-0.7	5.4	13.3	5.7
8101974	36.2	38.5	38.5	54.7	61.7	2.3	0.0	16.2	7.0
8101984	36.0	36.3	38.5	44.4	49.2	0.3	2.2	5.9	4.8
8101986	36.4	38.9	44.2	54.0	61.6	0.5	5.3	9.8	7.6
8101994	33.4	34.1	40.1	50.3	57.0	0.7	6.0	10.2	6.7
8101995	30.0	31.7	37.7	49.1	55.0	1.7	6.0	11.4	5.9
8101996	35.4	37.4	41.1	51.2	58.9	2.0	3.7	10.1	7.7
8102004	34.0	36.7	38.9	46.6	49.8	2.7	2.2	7.7	3.2
8102005	33.6	36.6	40.9	51.7	57.8	3.0	4.1	10.8	6.1
8102006	36.4	38.9	43.1	52.4	59.4	2.5	4.2	9.3	7.0
8102015	30.5	32.8	36.4	44.8	51.4	2.3	3.6	8.4	6.6
8102030	32.4	34.1	38.7	47.4	53.9	1.7	4.6	8.7	6.5
8102032	31.0	32.7	37.1	46.4	54.0	1.7	4.4	9.3	7.6
8102033	33.4	35.6	41.1	51.0	60.5	2.2	5.5	9.9	9.5
8102034	32.2	34.4	39.5	49.7	53.1	2.2	5.1	10.2	3.4
8102495	35.0	36.9	43.6	54.3	64.1	1.9	6.7	10.7	9.8
MEAN	34.0	35.7	39.9	49.9	55.8	1.7	4.3	9.9	6.0
S.D.	2.39	2.18	2.33	3.41	4.84	1.41	1.45	2.11	2.32

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TABLE A-1 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Individual and Mean Body Weights and Body Weight Gain of Pregnant Mice[a]

Exposure Level: 50 ppm

ANIMAL NUMBER	MATERNAL BODY WEIGHT (G) DAYS OF GESTATION 6	9	12	16	18	MATERNAL BODY WEIGHT GAIN (G) 6-9	9-12	12-16	16-18
8101952	33.4	34.8	37.7	42.8	47.8	1.4	2.9	5.1	5.0
8101953	38.0	36.7	44.6	54.1	60.1	-1.3	7.9	9.5	6.0
8101960	32.6	35.5	39.0	44.9	50.2	2.9	3.5	5.9	5.3
8101961	34.0	36.3	40.8	52.4	59.1	2.3	4.5	11.6	6.7
8101962	35.5	37.2	42.1	51.2	59.0	1.7	4.9	9.1	7.8
8101975	33.0	34.0	38.9	48.3	55.8	1.0	4.9	9.4	7.5
8101976	31.2	32.5	35.7	44.2	48.2	1.3	3.2	8.5	4.0
8101979	32.9	33.9	37.6	45.5	49.2	1.0	3.7	7.9	3.7
8101980	31.0	32.1	35.8	43.2	48.8	1.1	3.7	7.4	5.6
8101987	34.1	35.8	39.1	47.8	54.3	1.7	3.3	8.7	6.5
8101988	33.4	34.5	38.0	46.0	53.0	1.1	3.5	8.0	7.0
8101989	34.2	34.1	35.1	38.0	40.1	-0.1	1.0	2.9	2.1
8101990	35.8	36.7	40.2	48.2	56.6	0.9	3.5	8.0	8.4
8101997	33.7	34.1	36.6	47.3	54.0	0.4	2.5	10.7	6.7
8102007	36.0	36.7	40.9	52.0	59.8	0.7	4.2	11.1	7.8
8102008	33.3	36.8	41.9	50.1	55.6	3.5	5.1	8.2	5.5
8102019	37.7	33.1	44.2	48.4	60.8	-4.6	11.1	4.2	12.4
8102020	32.1	36.7	41.0	49.8	54.5	4.6	4.3	8.8	4.7
8102022	31.3	33.5	38.1	47.8	53.9	2.2	4.6	9.7	6.1
8102498	33.6	35.1	39.9	46.5	52.2	1.5	4.8	6.6	5.7
8102498	36.3	36.7	42.2	43.1	51.4	0.4	5.5	0.9	8.3
8102499	36.2	37.6	42.8	53.5	60.9	1.4	5.2	10.7	7.4
8102500	36.0	37.9	43.1	46.9	56.6	1.9	5.2	3.8	9.7
8102501	35.5	37.8	42.9	51.5	57.8	2.3	5.1	8.6	6.3
MEAN	34.2	35.4	39.9	47.6	54.2	1.2	4.5	7.7	6.5
S.D.	1.96	1.73	2.74	3.86*	5.07	1.71	1.92	2.71*	2.09

[a]Bred CF-1 mice were exposed to 0, 10, or 50 ppm of EGME for 6 hr/day on days 6 through 15 of gestation.

*Significantly different from the control value.

TABLE A-2

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Individual and Mean Food Consumption Values of Pregnant Mice[a]

Exposure Level: Control (0 ppm)

ANIMAL NUMBER	MATERNAL FOOD CONSUMPTION (G/DAY) DAY(S) OF GESTATION 6-9	9-12	12-15	15-18
8101946	6.3	7.0	7.9	8.4
8101947	5.1	7.5	7.9	8.3
8101954	6.0	7.6	9.7	9.7
8101956	6.7	8.2	9.9	23.1
8101963	6.3	5.9	7.2	8.0
8101964	6.0	6.4	7.6	6.7
8101965	6.6	9.9	8.4	8.4
8101966	5.6	5.9	7.2	7.9
8101968	6.9	5.4	8.3	9.1
8101981	7.5	7.8	21.6#	8.6
8101982	-0.3#	7.0	7.9	8.3
8101983	6.8	6.9	8.1	8.6
8101991	5.8	7.2	7.0	7.9
8101993	5.9	7.4	7.8	8.5
8102000	6.4	7.3	7.7	8.9
8102001	7.3	8.1	8.7	31.9
8102002	6.7	6.9	8.1	9.4
8102010	6.6	7.0	8.2	9.4
8102011	8.2	8.2	8.0	31.2
8102012	7.4	8.0	8.9	8.9
8102013	7.7	9.3	9.7	31.4
8102014	6.1	6.1	7.1	8.7
8102024	6.9	7.0	8.3	N.D.
8102025	8.1	6.7	7.9	9.4
8102027	7.6	6.0	7.4	-0.2
8102028	3.7	6.8	10.9#	-10.7
8102029	6.9	7.9	8.2	8.7
MEAN	6.6	7.2	8.1	10.7
S.D.	0.96	1.03	0.79	9.22

TABLE A-2 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Individual and Mean Food Consumption Values of Pregnant Mice[a]

Exposure Level: (10 ppm)

ANIMAL NUMBER	MATERNAL FOOD CONSUMPTION (G/DAY) DAY(S) OF GESTATION 6-9	9-12	12-15	15-18
8101948	6.4	6.3	8.9	8.2
8101950	-13.1#	5.5	7.1	7.5
8101957	6.7	7.3	8.0	8.9
8101958	7.8	6.7	7.0	9.3
8101959	6.3	6.8	6.5	8.2
8101969	5.4	5.9	6.7	8.3
8101970	6.5	6.9	8.0	8.7
8101971	6.5	7.7	7.7	10.2
8101974	7.4	7.6	8.7	9.9
8101984	6.2	6.5	7.6	7.9
8101986	7.1	7.2	8.2	9.5
8101994	6.3	7.7	8.3	8.9
8101995	6.2	7.4	7.7	8.5
8101996	5.7	6.9	7.7	12.8
8102004	7.0	7.6	8.5	6.1
8102005	7.6	7.4	8.3	8.5
8102006	10.0#	15.6#	9.4	10.5
8102015	6.0	6.3	7.4	9.1
8102030	8.9	9.0	7.5	7.9
8102032	6.7	7.1	8.3	8.8
8102033	6.3	6.9	7.3	8.4
8102034	7.2	7.0	7.6	6.8
8102495	6.6	7.7	8.6	9.6
MEAN	6.7	7.1	7.9	8.8
S.D.	0.77	0.74	0.72	1.33

TABLE A-2 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Individual and Mean Food Consumption Values of Pregnant Mice[a]

Exposure Level: (50 ppm)

ANIMAL NUMBER	MATERNAL FOOD CONSUMPTION (G/DAY) DAY(S) OF GESTATION 6-9	9-12	12-15	15-18
8101952	9.0	8.1	9.6	8.1
8101953	7.8	6.5	8.2	9.2
8101960	7.2	7.5	8.4	9.1
8101961	6.4	6.4	8.1	8.4
8101962	6.8	7.2	7.2	9.0
8101975	5.9	6.4	7.2	8.1
8101976	6.8	9.5	11.6	10.5
8101979	5.7	6.4	6.8	7.4
8101980	5.5	5.9	6.5	7.8
8101987	5.9	8.0	5.2	9.8
8101988	6.2	6.5	8.0	8.2
8101989	9.3	10.5#	9.6	7.8
8101990	7.1	7.3	8.2	9.4
8101997	5.7	6.8	7.5	8.4
8101998	N.D.	N.D.	N.D.	N.D.
8101999	5.5	6.0	N.D.	N.D.
8102007	7.4	9.8	8.2	8.8
8102008	8.0	7.6	8.3	8.2
8102019	6.8	8.6	9.0	6.2
8102020	7.1	6.8	8.0	8.5
8102022	6.1	6.1	6.8	7.6
8102496	6.8	6.7	15.6#	7.4
8102498	6.6	7.5	6.9	5.5
8102499	6.4	7.4	8.0	9.1
8102500	7.6	7.6	8.5	9.0
8102501	6.9	7.1	8.2	8.1
MEAN	6.8	7.2	8.0	8.3
S.D.	0.99	1.01	1.27	1.07

[a]Bred CF-1 mice were exposed to 0, 10 or 50 ppm of EGME by inhalation for 6 hr/day on days 6 through 15 of gestation.

#Statistical outlier identified by sequential outlier test, alpha = 0.02.

N.D. = No data.

TABLE A-3

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Individual and Mean Water Consumption Values of Pregnant Mice[a]

Exposure Level: Control (0 ppm)

ANIMAL NUMBER	MATERNAL WATER CONSUMPTION (G/DAY) DAY(S) OF GESTATION 6-9	9-12	12-15	15-18
8101946	12.4	8.1	11.3	10.4
8101947	12.1	9.3	11.2	10.6
8101954	12.1	10.7	12.8	12.8
8101956	11.8	9.8	12.1	10.2
8101963	9.8	11.8	21.8#	22.6#
8101964	9.0	10.4	11.3	8.4
8101965	1.7#	N.D.	2.4	9.9
8101966	8.6	9.6	12.0	10.2
8101968	7.1	9.1	9.9	11.1
8101981	9.2	10.3	13.4	12.6
8101982	8.9	11.3	15.0	11.2
8101983	9.5	11.4	15.4	9.8
8101991	11.2	11.8	10.9	10.2
8101993	0.5#	11.2	11.4	N.D.
8102000	10.2	11.0	11.5	11.0
8102001	10.8	12.2	13.3	12.0
8102002	9.9	9.9	11.5	11.0
8102010	10.6	10.9	10.8	8.5
8102011	7.3	16.5#	5.5	10.1
8102012	8.7	11.0	8.3	11.4
8102013	10.2	11.8	5.8	17.7#
8102014	7.9	7.8	10.2	10.8
8102024	10.8	12.1	11.6	N.D.
8102025	10.4	7.6	8.0	8.7
8102027	7.3	10.7	8.9	5.5#
8102028	2.5#	11.5	9.7	9.9
8102029	11.6	11.1	8.8	9.9
MEAN	9.9	10.5	10.5	10.5
S.D.	1.58	1.32	2.88	1.14

TABLE A-3 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Individual and Mean Water Consumption Values of Pregnant Mice[a]

Exposure Level: (10 ppm)

ANIMAL NUMBER	MATERNAL WATER CONSUMPTION (G/DAY) DAY(S) OF GESTATION 6-9	9-12	12-15	15-18
8101948	13.1	8.0	13.7	10.9
8101950	21.8#	9.9	13.3	N.D.
8101957	9.5	10.6	11.5	11.5
8101958	10.7	9.6	9.9	12.1
8101959	8.6	7.6	8.6	11.8
8101969	7.1	9.5	9.3	9.8
8101970	9.8	9.8	10.6	11.1
8101971	-0.1#	8.5	10.9	11.4
8101974	10.6	12.1	13.0	13.0
8101984	9.1	15.7	13.6	13.6
8101986	9.1	10.5	10.5	11.3
8101994	10.4	12.3	11.8	N.D.
8101995	9.2	10.2	11.3	10.4
8101996	9.2	10.4	12.8	13.8
8102004	10.5	11.1	12.2	10.9
8102005	10.5	10.7	12.1	16.6
8102006	5.1	11.1	11.9	11.6
8102015	8.2	13.5	9.1	16.3
8102030	9.1	9.2	7.9	7.9
8102032	8.2	11.6	11.0	9.3
8102033	8.5	10.1	10.0	11.2
8102034	10.7	10.0	10.6	N.D.
8102495	11.6	11.7	13.3	15.1
MEAN	9.5	10.6	11.3	12.0
S.D.	1.67	1.77	1.65	2.22

#

TABLE A-3 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Individual and Mean Water Consumption Values of Pregnant Mice[a]

Exposure Level: (50 ppm)

ANIMAL NUMBER	MATERNAL WATER CONSUMPTION (G/DAY) DAY(S) OF GESTATION 6-9	9-12	12-15	15-18
8101952	16.1	8.9	13.3	11.0
8101953	13.2	6.6	11.3	11.7
8101960	10.5	12.6	15.9	11.9
8101961	12.0	9.4	12.9	13.2
8101962	10.2	11.0	12.1	12.7
8101975	11.5	10.0	10.2	12.5
8101976	1.5	N.D.	8.7	11.2
8101979	-0.3	10.1	8.4	9.3
8101980	3.1	7.8	8.2	8.7
8101987	7.3	8.4	3.7	12.7
8101988	9.6	10.2	11.8	12.2
8101989	9.7	11.5	11.7	10.8
8101990	10.7	10.5	12.1	12.2
8101997	8.8	N.D.	11.8	N.D.
8101998	N.D.	N.D.	N.D.	N.D.
8101999	9.2	11.3	N.D.	N.D.
8102007	9.2	13.8	11.4	8.9
8102008	20.1	12.3	14.1	12.5
8102019	-3.8	11.3	10.3	9.0
8102020	8.4	9.3	11.0	9.5
8102022	8.1	8.4	8.7	10.1
8102496	17.8	10.3	9.8	9.7
8102498	8.5	11.4	8.0	-25.2#
8102499	6.7	7.9	28.5#	9.9
8102500	9.6	11.8	10.1	10.0
8102501	31.1#	12.4	13.8	11.0
MEAN	9.1	10.3	10.8	10.9
S.D.	5.28	1.79	2.56	1.45

[a]Bred CF-1 mice were exposed to 0, 10 or 50 ppm of EGME by inhalation for 6 hr/day on days 6 through 15 of gestation.

#Statistical outlier identified by sequential outlier test, alpha = 0.02. Value not included in calculations.

N.D. = No data.

*Significantly different from the control value.

TABLE A-4

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Individual Organ Weights Of Pregnant Mice[a]

Exposure Level: Control (0 ppm)

Animal Number	Liver Weight		Thymus Weight		Spleen Weight	
	Absolute[b]	Relative[c]	Absolute	Relative	Absolute	Relative
818-1946	2.80	4.75	0.17	0.29	0.07	0.12
1947	2.53	4.42	0.15	0.26	0.05	0.09
1954	3.07	5.41	0.05	0.09	0.18	0.32
1956	2.97	4.94	0.03	0.05	0.12	0.20
1963	2.76	4.88	0.03	0.05	0.09	0.16
1964	2.50	4.13	0.02	0.03	0.08	0.13
1965	2.19	4.50	0.02	0.04	0.13	0.27
1966	2.53	4.68	0.04	0.07	0.11	0.20
1968	2.52	4.90	0.03	0.06	0.11	0.21
1981	2.41	4.34	0.02	0.04	0.10	0.18
1982	3.04	5.45	0.04	0.07	0.13	0.23
1983	3.60	6.75	0.04	0.08	0.14	0.26
1991	2.98	5.40	0.02	0.04	0.10	0.18
1993	2.82	4.92	0.04	0.07	0.15	0.26
2000	3.29	5.72	0.06	0.10	0.15	0.26
2001	3.20	5.19	0.04	0.06	0.13	0.21
2002	3.07	5.36	0.05	0.09	0.11	0.19
2010	1.84	4.20	0.02	0.05	0.05	0.11
2011	2.70	5.22	0.02	0.04	0.11	0.21
2012	2.88	4.86	0.04	0.07	0.14	0.24
2013	3.43	5.93	0.03	0.05	0.15	0.26
2014	3.16	5.52	0.09	0.16	0.23	0.40
2025	2.78	4.98	0.06	0.11	0.15	0.27
2027	2.98	5.30	0.04	0.07	0.12	0.21
2028	3.00	5.37	0.06	0.11	0.13	0.23
2029	3.40	5.42	0.06	0.10	0.15	0.24
Mean	2.86	5.10	0.05	0.09	0.12	0.22
±S.D.	0.40	0.58	0.04	0.06	0.04	0.07

TABLE A-4 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Individual Organ Weights Of Pregnant Mice[a]

Exposure Level: 10 ppm

Animal Number	Liver Weight		Thymus Weight		Spleen Weight	
	Absolute[b]	Relative[c]	Absolute	Relative	Absolute	Relative
318-1948	2.38	4.66	0.21	0.41	0.13	0.25
1950	2.54	5.34	0.17	0.36	0.11	0.23
1957	2.59	5.02	0.05	0.10	0.16	0.31
1958	3.30	5.32	0.05	0.08	0.10	0.16
1959	2.45	4.66	0.03	0.06	0.08	0.15
1969	2.34	5.30	0.01	0.02	0.08	0.14
1970	2.66	5.00	0.02	0.04	0.11	0.21
1971	3.24	5.14	0.02	0.03	0.09	0.14
1974	3.27	5.30	0.04	0.06	0.15	0.24
1984	2.77	5.63	0.04	0.08	0.07	0.14
1986	3.30	5.36	0.04	0.06	0.17	0.28
1994	2.85	5.00	0.03	0.05	0.13	0.23
1995	2.38	4.33	0.01	0.02	0.11	0.20
1996	3.10	5.26	0.03	0.05	0.13	0.22
2004	2.83	5.68	0.05	0.10	0.15	0.30
2005	3.07	5.31	0.07	0.12	0.12	0.21
2006	3.08	5.19	0.04	0.07	0.14	0.24
2015	2.54	4.94	0.02	0.04	0.10	0.19
2030	2.42	4.49	0.07	0.13	0.09	0.17
2032	2.83	5.24	0.06	0.11	0.13	0.24
2033	2.70	4.46	0.06	0.10	0.13	0.21
2034	2.50	4.71	0.04	0.08	0.07	0.13
2495	2.93	4.57	0.07	0.11	0.10	0.16
Mean	2.81	5.04	0.05	0.10	0.12	0.21
±S.D.	0.31	0.38	0.05	0.10	0.03	0.05

TABLE A-4 (Continued)

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Individual Organ Weights Of Pregnant Mice[a]

Exposure Level: 50 ppm

Animal Number	Liver Weight		Thymus Weight		Spleen Weight	
	Absolute[b]	Relative[c]	Absolute	Relative	Absolute	Relative
318-1952	2.62	5.48	0.19	0.40	0.11	0.23
1953	3.36	5.59	0.25	0.42	0.18	0.30
1960	2.78	5.54	0.04	0.08	0.15	0.30
1961	2.73	4.62	0.03	0.05	0.09	0.15
1962	3.14	5.32	0.05	0.08	0.17	0.29
1975	2.73	4.89	0.02	0.04	0.11	0.20
1976	2.49	5.17	0.03	0.06	0.11	0.23
1979	2.51	5.10	0.01	0.02	0.07	0.14
1980	2.26	4.63	0.02	0.04	0.09	0.18
1987	2.82	5.19	0.03	0.06	0.04	0.07
1988	2.60	4.91	0.02	0.04	0.08	0.15
1989	2.51	6.26	0.03	0.07	0.10	0.25
1990	2.81	4.96	0.04	0.07	0.10	0.18
1997	2.82	5.22	0.03	0.06	0.11	0.20
2007	2.92	4.88	0.05	0.08	0.12	0.20
2008	2.98	5.36	0.06	0.11	0.17	0.31
2019	2.90	4.77	0.03	0.05	0.09	0.15
2020	2.70	4.95	0.03	0.06	0.11	0.20
2022	2.07	3.84	0.01	0.02	0.09	0.17
2496	2.50	4.79	0.06	0.11	0.12	0.23
2498	2.55	4.96	0.05	0.10	0.09	0.18
2499	2.90	4.76	0.04	0.07	0.11	0.18
2500	2.36	5.05	0.05	0.09	0.13	0.23
2501	2.34	4.91	0.06	0.10	0.12	0.21
Mean	2.72	5.05	0.05	0.09	0.11	0.21
±S.D.	0.27	0.45	0.05	0.10	0.03	0.05

[a]Bred CF-1 mice were exposed to 0, 10 or 50 ppm of EGME for 6 hr/day on days 6 through 15 of gestation.

[b]Grams

[c]Grams/100 g body weight

TABLE A-5

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Hematology Data for Pregnant Mice[a]

Exposure level ppm	Animal Number	RBC x10 ^{6}/mm^3	HGB GM/DL	PCV %	MCV Cubic Microns	MCH Micro Microgm	MCHC %	Plat x10 ^{3}/mm^3	WBC x10 ^{3}/mm^3
Control									
0	1963	7.96	14.2	39.4	49.00	17.80	36.00	1720.	4.2
	1964	7.96	15.2	43.0	54.00	19.10	35.30	1444.	7.6
	1968	7.18	13.8	39.2	55.00	19.20	35.20	1668.	1.2
	1981	7.78	13.8	37.6	48.00	17.70	36.70	1632.	0.6
	1982	7.46	14.0	40.6	54.00	18.80	34.50	1532.	4.6
	1991	8.06	15.0	40.8	51.00	18.60	36.80	1470.	5.8
	2000	6.96	13.8	35.4	51.00	19.80	39.00	1070.	3.0
	2001	6.00	12.0	30.2	50.00	20.00	39.70	1506.	3.8
	2010	8.14	16.4	41.8	51.00	20.10	39.20	1402.	1.4
	2011	7.44	14.6	37.4	50.00	19.60	39.00	1800.	6.0
	Mean:	7.49	14.3	38.5	51.30	19.07	37.14	1524.	3.8
	±S.D.	0.66	1.2	3.7	2.31	0.85	1.93	205.	2.3
10.0	81A-1969	7.16	13.0	35.8	50.00	18.20	36.30	1606.	6.2
	1970	7.00	12.8	35.6	51.00	18.30	36.00	1050.	1.4
	1971	6.88	13.0	35.4	51.00	18.90	36.70	1358.	0.8
	1974	7.50	14.0	38.2	51.00	18.70	36.60	1524	1.0
	1984	8.24	14.6	42.6	52.00	17.70	34.30	1988.	8.6
	1986	7.84	13.8	39.0	50.00	17.60	35.40	1360.	7.8
	1994	6.72	12.6	34.8	52.00	18.80	36.20	1452.	0.8
	1995	6.72	12.8	34.6	51.00	19.00	37.00	1488.	1.2
	2005	6.22	12.4	32.0	51.00	19.90	38.80	1286.	3.2
	2006	6.14	12.4	32.0	52.00	20.20	38.80	1046.	2.6
	Mean	7.04	13.1*	36.0	51.10	18.73	36.61	1416.	3.4
	±S.D.	0.67	0.7	3.2	0.74	0.85	1.38	274.	3.0
50	81A-1976	7.56	14.2	39.2	52.00	19.00	36.70	1548	4.2
	1979	8.24	13.8	37.6	46.00	16.70	36.70	1374.	1.0
	1987	7.02	13.2	36.0	51.00	18.80	36.70	1382.	6.4
	1989	6.84	13.4	37.8	55.00	19.60	35.40	1368.	0.6
	1990	7.00	13.0	37.4	53.00	18.60	34.80	1172.	1.2
	1997	7.00	13.4	36.4	52.00	19.10	36.80	1290.	1.0
	2007	7.16	13.6	33.8	47.00	19.00	40.20	1154.	1.8
	2008	7.06	13.0	34.4	49.00	18.40	37.80	1192.	3.4
	2019	6.54	13.2	34.0	52.00	20.20	38.80	1092.	3.0
	2020	7.40	14.2	36.0	49.00	19.20	39.40	1558.	3.8
	2022	6.74	13.0	33.0	49.00	19.30	39.40	1242	0.4
	Mean	7.14	13.5	36.0	50.45	18.90	37.52	1307.	2.4
	±S.D.	0.46	0.4	2.0	2.70	0.88	1.74	155.	1.9

[a]Bred CF-1 mice were exposed to 0, 10 or 50 ppm of EGME for 6 hr/day on days 6 through 15 of gestation.

*Significantly different from the control value using Dunnett's test.

TABLE A-6

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Individual Litter Summary Of Observations Made At Cesarean Section In Mice[1]

Exposure Level: Control (0 ppm)

Animal Number	Implantations	Resorptions	Litter Size	Sex Ratio M/F	Body Weight	Crown-Rump Length (mm)
818-1945	Non-Pregnant					
1946	17	3	14	7/7	1.167	25.19
1947	18	3	15	6/9	1.169	25.71
1954	11	1	10	6/4	1.334	25.45
1955	Non-Pregnant					
1956	14	0	14	9/5	1.214	25.92
1963	15	0	15	8/7	1.197	27.53
1964	18	0	18	9/9	1.051	26.61
1965	10	1	9	4/5	1.360	29.51
1966	13	0	13	10/3	1.238	28.17
1967	Non-Pregnant					
1968	11	2	9	6/3	1.359	29.37
1981	14	0	14	7/7	1.205	27.84
1982	11	0	11	9/2	1.181	27.65
1983	11	1	10	5/5	1.469	29.66
1991	12	0	12	5/7	1.208	26.96
1992	Removed from study 11/14/81 - Airlock in water bottle					
1993	12	1	11	7/4	1.410	29.00
2000	12	0	12	3/9	1.190	25.00
2001	14	1	13	5/8	1.417	28.14
2002	14	1	13	8/5	1.258	26.54
2010	14	1	13	7/6	0.365	26.22
2011	12	2	10	4/6	1.216	28.97
2012	13	1	12	4/8	1.294	28.58
2013	11	0	11	7/4	1.333	29.00
2014	13	1	12	7/5	1.286	29.05
2024	Delivered early on day 16 of gestation					
2025	11	0	11	8/3	1.193	28.25
2026	Non-Pregnant					
2027	14	2	12	6/6	1.200	28.26
2028	12	1	11	2/9	1.085	27.39
2029	15	3	12	5/7	1.279	28.39
Mean ±S.D.	13±2	1.0±1.0	12.2±2.0	52/48	1.24±0.11	27.7±1.4

TABLE A-6

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Individual Litter Summary Of Observations Made At Cesarean Section In Mice[a]

Exposure Level: 10 ppm

Animal Number	Implantations	Resorptions	Litter Size	Sex Ratio M/F	Body Weight	Crown-Rump Length (mm)
318-1948	14	3	11	4/7	1.228	28.27
1949	Non-Pregnant					
1950	3	0	8	3/5	1.259	27.66
1957	12	1	11	4/7	1.217	26.93
1958	15	0	15	7/8	1.110	26.35
1959	12	0	12	8/4	1.319	27.63
1969	13	0	13	9/4	1.119	26.72
1970	12	0	12	3/9	1.207	27.01
1971	14	1	13	8/5	1.282	28.28
1972	Non-Pregnant					
1973	Implantations detected only after sodium sulfide stain					
1974	13	0	13	4/9	1.338	28.61
1984	7	1	6	3/3	1.338	27.37
1985	Non-Pregnant					
1986	16	4	12	5/7	1.240	28.31
1994	13	1	12	2/10	1.299	28.71
1995	13	0	13	9/4	1.296	28.59
1996	11	1	10	8/2	1.345	29.44
2003	Non-Pregnant					
2004	10	3	7	5/2	1.206	26.14
2005	14	1	13	6/7	1.256	26.31
2006	14	2	12	4/8	1.239	27.03
2015	12	2	10	4/6	1.265	28.61
2016	Non-Pregnant					
2017	Removed from study 11/18/81- out of water					
2018	Removed from study 11/18/81- airlock in water bottle					
2030	11	0	11	4/7	1.350	29.50
2031	Non-Pregnant					
2032	12	2	10	5/5	1.330	29.48
2033	14	2	12	7/5	1.384	30.16
2034	11	0	11	3/8	1.316	29.75
2495	14	1	13	8/5	1.381	29.76
Mean ±S.D.	12±2	1.1±1.2	11.3±2.1	47/53	1.27±0.07	28.1±1.2

TABLE A-6

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Individual Litter Summary of Observatons Made at Cesarean Section in Mice[a]

Exposure Level: 50 ppm

Animal Number	Implantations	Resorptions	Litter Size	Sex Ratio M/F	Body Weight(g)	C-R Length (mm)
81B-1951	Non-pregnant					
1952	12	4	8	4/4	1.173	27.83
1953	12	1	11	5/6	1.236	28.60
1960	13	5	8	5/3	1.330	27.55
1961	15	0	15	8/7	1.247	26.49
1962	11	0	11	8/3	1.411	26.56
1975	14	1	13	5/8	1.238	27.65
1976	10	3	7	0/7	1.364	28.53
1977	Non-pregnant					
1978	Non-pregnant					
1979	8	0	8	6/2	1.363	28.78
1980	11	2	9	4/5	1.358	28.38
1987	13	3	10	6/4	1.223	27.37
1988	10	0	10	4/6	1.287	28.73
1989	4	2	2	0/2	1.420	29.60
1990	12	1	11	7/4	1.280	28.24
1997	12	2	10	4/6	1.154	26.97
1998	Removed from study 11/4/81 - air lock in water bottle					
1999	Found dead following exposure - pregnant at necropsy					
2007	13	1	12	6/6	1.196	26.28
2008	11	1	10	5/5	1.237	27.01
2009	Non-pregnant					
2019	16	1	15	10/5	1.017	26.95
2020	12	1	11	4/7	1.255	28.85
2021	Non-pregnant					
2022	12	0	12	7/5	1.401	28.60
2023	Non-pregnant					
2496	11	1	10	4/6	1.318	29.13
2497	Implantations detected only after sodium sulfide staining					
2498	13	3	10	5/5	1.281	28.49
2499	15	0	15	7/8	1.149	28.21
2500	12	1	11	6/5	1.206	28.44
2501	14	2	12	5/7	1.332	29.13
Mean ±S.D.	12±2	1.5±1.4	10.5±2.8	50/50	1.27±0.10	28.1±0.9

[a]Bred CF-1 mice were exposed to 0, 10 or 50 ppm of EGME for 6 hr/day on days 6 through 15 of gestation.

TABLE A-7

ETHYLENE GLYCOL MONOBUTYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Individual Litter Summary of Fetal Alterations Among Litters of Hlcd[a]

Exposure Level: Control (0 ppm)

Animal Numbers	81-8 1946	1947	1954	1956	1963	1964	1965	1966	1968	1981	1982	1983	1991	1993	2000	2001	2002	2010	2011	2012	2013	2014	2025	2027	2028	2029	Total Fetuses	Total Litters
NUMBER OF FETUSES EXAMINED																												
EXTERNAL EXAMINATION	14	15	10	14	15	18	9	13	9	14	11	10	12	11	12	13	13	13	10	12	11	12	11	12	11	12	317	26
SOFT TISSUE EXAMINATION	7	8	5	7	8	9	5	7	5	7	6	5	6	6	6	7	7	7	5	6	6	6	6	6	6	6	165	26
SKELETAL EXAMINATION	14	15	10	14	15	18	9	13	9	14	11	10	12	11	12	13	13	13	10	12	11	12	11	12	11	12	317	26
BONES OF THE SKULL	7	7	5	7	7	9	4	6	4	7	5	5	6	5	6	6	6	6	5	6	5	6	5	6	5	6	152	26
NUMBER OF FETUSES AFFECTED																												
TOTAL MAJOR MALFORMATIONS[b]	1	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	1	1	1	0	0	0	1	1	0	8	8
External Alterations																												
Ablepharia†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Cleft palate†	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	1	1	0	5	5
Omphalocele†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Soft tissue alterations																												
Hepatic Hemorrhage - Focal	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	1
Hypoplastic Testicle	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	2	2
Testicular Hemorrhage	0	0	0	0	0	0	0	2	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	4	3
Epididymal cyst(s)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	1
Renal agenesis - bilateral†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Renal malpositioning with contralaterally attached ureters†	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	1
Skeletal alterations																												
Skull																												
Delayed ossification - occipital	0	1	1	0	0	0	0	0	1	0	1	0	0	0	0	0	1	0	0	1	1	0	3	0	3	0	13	9
Foramen - occipital	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Extra site of ossification	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	2	2
Vertebrae																												
Cervical spur(s)	8	0	1	1	0	0	0	2	7	0	0	0	0	1	1	0	2	0	0	0	2	0	0	4	3	6	38	12
Missing (lumbar)†	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Ribs																												
Extra (lumbar)	0	6	0	2	0	0	0	1	1	3	5	1	2	4	0	4	2	0	0	0	0	3	0	7	7	0	48	14
Extra (cervical)†	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Sternebrae																												
Delayed ossification	9	9	1	0	0	4	0	2	0	2	3	0	3	0	0	0	1	7	9	4	1	2	2	9	5	3	76	18
Extra site of ossification	0	0	0	5	1	0	1	0	0	2	0	1	0	2	0	7	0	0	0	0	0	1	0	1	0	0	21	9
Foramen	0	0	0	0	0	2	0	1	0	0	0	0	0	0	0	2	0	0	0	1	0	0	0	0	0	0	6	4
Fused	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Asymmetrical cartilage	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1

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TABLE A-7 (Continued)

ETHYLENE GLYCOL MONOBUTYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Individual Litter Summary of Fetal Alterations Among Litters of Mice[a]

Exposure Level: 10 ppm

Animal Numbers	B1-B 1948	1950	1957	1958	1959	1969	1970	1971	1974	1984	1986	1994	1995	1996	2004	2005	2006	2015	2030	2032	2033	2034	2495	Total Fetuses	Total Litters
NUMBER OF FETUSES EXAMINED																									
EXTERNAL EXAMINATION	11	8	11	15	12	13	12	13	13	6	12	12	13	10	7	13	12	10	11	10	12	11	13	260	23
SOFT TISSUE EXAMINATION	6	4	6	8	6	7	6	7	7	3	6	6	7	5	4	7	6	5	6	5	6	6	7	136	23
SKELETAL EXAMINATION	11	8	11	15	12	13	12	13	13	6	12	12	13	10	7	13	12	10	11	10	12	11	13	260	23
BONES OF THE SKULL	5	4	5	7	6	6	6	6	6	3	6	6	6	5	3	6	6	5	5	5	6	5	6	124	23
NUMBER OF FETUSES AFFECTED																									
TOTAL MAJOR MALFORMATIONS[b]	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	3	3
External Alterations																									
Ablepharia[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Cleft palate[†]	0	0	0	0	0	1[c]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Omphalocele[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Soft tissue alterations																									
Hepatic Hemorrhage - Focal	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hypoplastic Testicle	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0	3	3
Testicular Hemorrhage	0	0	0	0	0	3	0	1	0	0	0	2	0	0	0	0	0	2	1	0	0	0	1	10	6
Epididymal cyst(s)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Renal agenesis - bilateral[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Renal malpositioning with contralaterally attached ureters[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Skeletal alterations																									
Skull																									
Delayed ossification - occipital	1	0	0	2	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1	0	0	7	6
Foramen - occipital	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Extra site of ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Vertebrae																									
Cervical spur(s)	0	0	2	2	5	1	3	1	1	0	1	0	0	1	1	1	1	1	0	0	0	1	2	24	15
Missing (lumbar)[†]	0	0	0	0	1	1[c]	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	3	3
Ribs																									
Extra (lumbar)	0	0	0	4	1	1	1	1	0	4	2	0	0	2	2	0	11	0	2	7	0	1	10	49	14
Extra (cervical)[†]	0	0	0	0	0	1[c]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Sternebrae																									
Delayed ossification	0	1	2	13	3	1	2	0	0	0	2	4	1	0	3	7	3	0	0	1	0	0	0	43	13
Extra site of ossification	0	0	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0	0	0	3	1	0	2	9	6
Foramen	0	0	0	0	0	0	0	0	1	0	0	0	2	0	0	0	2	0	0	0	0	0	0	5	3
Fused	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Asymmetrical cartilage	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

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TABLE A-7 (Continued)

ETHYLENE GLYCOL MONOBUTYL ETHER: INHALATION TERATOLOGY STUDY IN MICE

Individual Litter Summary of Total Alterations Among Litters of Mice[a]

Exposure Level: 50 ppm

Animal Numbers	81-B 1952	1953	1960	1961	1962	1975	1976	1979	1980	1987	1988	1989	1990	1997	2007	2008	2019	2020	2022	2496	2598	2499	2500	2501	Total Fetuses	Total Litters
NUMBER OF FETUSES EXAMINED																										
EXTERNAL EXAMINATION	8	11	8	15	11	13	7	8	9	10	10	2	11	10	12	10	15	11	12	10	10	15	11	12	251	24
SOFT TISSUE EXAMINATION	4	6	4	8	6	7	4	4	5	5	5	2	6	5	6	5	8	6	6	5	5	8	6	6	132	24
SKELETAL EXAMINATION	8	11	8	15	11	13	7	8	9	10	10	2	11	10	12	10	15	11	12	10	10	15	11	12	251	24
BONES OF THE SKULL	4	5	4	7	5	6	3	4	4	5	5	0[d]	5	5	6	5	7	5	6	5	5	7	5	6	119	23
NUMBER OF FETUSES AFFECTED																										
TOTAL MAJOR MALFORMATIONS[b]	0	0	0	0	0	0	0	0	0	4	1	0	1	0	1	0	1	0	0	0	0	0	0	0	8	5
External Alterations																										
Ablepharia[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	1
Cleft palate[†]	0	0	0	0	0	0	0	0	0	3	0	0	0	0	1	0	0	0	0	0	0	0	0	0	4	2
Omphalocele[†]	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	1
Soft tissue alterations																										
Hepatic Hemorrhage - Focal	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hypoplastic Testicle	0	0	0	0	0	0	0	0	2	1	1	0	1	0	0	0	0	0	2	0	1	0	0	0	8	6
Testicular Hemorrhage	0	1	0	0	0	0	0	0	2	1	1	0	1	0	0	0	0	0	2	0	0	0	1	0	9	7
Epididymal cyst(s)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Renal agenesis - bilateral[†]	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Renal malpositioning with contralaterally attached ureters[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Skeletal alterations																										
Skull																										
Delayed ossification - occipital	0	0	0	1	0	0	0	1	0	0	0	0	0	3	2	1	1	1	0	0	0	1	1	0	12	9
Foramen - occipital	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Extra site of ossification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Vertebrae																										
Cervical spur(s)	0	3	0	1	4	0	1	1	1	3	0	0	0	0	1	1	5	1	0	2	0	5	1	0	30	14
Missing (lumbar)[†]	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Ribs																										
Extra (lumbar)	3	2	1	5	1	0	3	6	5	0	3	1	1	9	10	8	0	3	1	4	1	2	10	3	82	21
Extra (cervical)[†]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Sternebrae																										
Delayed ossification	4	2	0	2	2	3	1	2	2	8	0	1	4	6	1	0	15	3	1	3	2	5	9	1	77	21
Extra site of ossification	0	0	0	0	0	0	0	1	4	0	0	0	0	0	0	0	0	0	0	1	2	0	0	0	8	4
Foramen	0	0	1	1	0	2	0	0	0	0	0	0	1	0	0	0	2	0	0	2	0	0	0	2	11	7
Fused	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	1
Asymmetrical cartilage	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	3	3

[a]Bred CF-1 mice were exposed to 0, 10 or 50 ppm of EGME for 6 hr/day on days 6 through 15 of gestation.
[b]Total malformations detected by external, soft tissue or skeletal examination.
[c]Alterations occurred in the same fetus.
[d]Litters with three or fewer fetuses had all heads removed during examination for soft tissue alterations and therefore, no examination could be conducted on bones of the skull.
[†]Considered a major malformation.

SUMMARY

Contains NO CBI

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION TERATOLOGY STUDY IN MICE†

B-17e

By:

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Reviewed By:

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November 23, 1982

†Sponsored by five U.S. ethylene glycol ethers producers under the auspices of the Chemical Manufacturers' Association under contract number GE-7.0-Ter-Ihl-Dow.

SUMMARY

The objective of this study was to establish the maximum tolerated exposure level of ethylene glycol monomethyl ether (EGME) in pregnant rats and rabbits during the period of major organogenesis. Bred Fischer 344 rats and inseminated New Zealand white rabbits were exposed to EGME via inhalation for 6 hr/day on days 6 through 15 (rats) or 6 through 18 (rabbits) of gestation.

Among rats, maternal toxicity was observed at an exposure level of 400 ppm as evidenced by significantly reduced body weight gain and changes in spleen and thymus weights reflecting primary toxicity. Significant decreases in liver and kidney weights secondary to decreased body weight gain were also observed. Necropsy examination of these animals revealed decreased thymic size and occasional facial staining with porphyrin pigments. Rats exposed to 200 ppm of EGME exhibited similar, though less severe, indications of maternal toxicity. Embryolethality, evidenced by complete resorption of all litters, was observed in both the 200 and 400 ppm exposure groups. No evidence of maternal or embryo-toxicity was observed among rats exposed to 50 ppm of EGME.

SUMMARY

Maternal toxicity was observed among inseminated rabbits exposed to 200 or 400 ppm of EGME. Two of seven rabbits exposed to 400 ppm died during the period of exposure. Maternal body weight gain and organ weights were markedly reduced among rabbits exposed to 200 or 400 ppm of EGME. Necropsy examination revealed dose-related increases in distended gall bladder, small pale liver, decreased thymic size, pale bone marrow and decreased abdominal adipose tissue and intestinal ingesta, among rabbits exposed to 200 or 400 ppm of EGME. Complete resorption of all litters was observed among rabbits at 200 and 400 ppm. Exposure of rabbits to 50 ppm resulted in an increased incidence of resorptions.

Based on the results of this probe study, exposure levels of 200 and 400 ppm were considered maternally toxic and embryo-lethal in both rats and rabbits. An exposure level of 50 ppm was well tolerated by pregnant rats. However, exposure to 50 ppm resulted in an increased incidence of resorptions among pregnant rabbits. Therefore, exposure levels of 3, 10 and 50 ppm were selected for the definitive teratology study in both rats and rabbits.

SUMMARY

Contains NO CBI

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Date 11-9-82

ETHYLENE GLYCOL MONOMETHYL ETHER: INHALATION REPRODUCTION AND DOMINANT LETHAL STUDY IN RATS

B-17c

By:

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GE-TTG-12C

February 10, 1982

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SUMMARY

ETHYLENE GLYCOL MONOMETHYL ETHER: 13-WEEK VAPOR INHALATION STUDY WITH RATS AND RABBITS. R. R. Miller, J. A. Ayres, and J. T. Young.

ABSTRACT

Male and female Sprague-Dawley rats and New Zealand White rabbits were exposed to 0, 30, 100 or 300 ppm ethylene glycol monomethyl ether (EGME) vapors 6 hours per day, 5 days per week, for a total of 13 weeks. There were no mortalities of rats prior to scheduled sacrifice, but 2 of 5 male and 2 of 5 female rabbits in the 300 ppm group as well as 2 of 5 female rabbits in the 100 ppm group died or were sacrificed moribund during the study. The specific cause of death of most of these animals could not be determined.

Body weights as well as thymus gland and testicular weights of animals in the 300 ppm group were reduced as a result of the exposures. Hematologic analyses after 4 weeks, and again after 12 weeks, revealed abnormal depressions of cellular elements in the blood in rats and rabbits exposed to 300 ppm. Concentrations of total protein, albumin and globulins in serum of rats (but not rabbits) in the 300 ppm group were lower than for controls.

Gross pathologic observations attributed to exposure to 300 ppm EGME included decreased size of thymus gland in both sexes, small flaccid testes in males, decreased abdominal fat in some females, and decreased lymphoid tissue in some rabbits. In rabbits, a slight-to-moderate decrease in size of testes was noted in 4 of 5 animals in the 100 ppm group as well as in 2 of 5 animals exposed to 30 ppm.

Microscopic examinations of tissues revealed treatment-related degenerative changes in germinal epithelium of testes in all male rats and rabbits in the 300 ppm group, as well as in 3 of 5 male rabbits and 1 of 5 male rabbits in the 100 and 30 ppm groups, respectively.

The only effects attributed to exposure to 30 ppm EGME in this study were slight microscopic changes in testes of 1 of 5 male rabbits. A follow-up study is currently being conducted with larger group sizes to determine if these observations in testes are reproducible in male rabbits exposed to low concentrations of EGME.

SUMMARY

Groups of male and female Sprague-Dawley (CD) rats were exposed to 0, 30, 100, or 300 ppm ethylene glycol monomethyl ether (EGME, DOWANOL* EM) vapor 6 hours/day, 5 days/week for 13 weeks. The 0 and 30 ppm groups each contained 30 rats/sex and the 100 and 300 ppm groups each had 20 rats/sex. Following the exposure period, males were bred to unexposed females to evaluate reproductive capability and dominant lethality. Additional mating of 300 ppm exposed males was performed during the post-exposure period in order to evaluate the recovery of fertility prior to sacrifice at 23 weeks post-exposure. Exposed females were bred with unexposed males to assess reproductive parameters. Female rats were sacrificed 15 weeks post-exposure. At sacrifice a complete gross examination and selected tissue histopathologic evaluation was conducted.

Results of the present study indicate a potential for inhaled EGME to completely suppress fertility in male rats at the 300 ppm level. Fertility of these rats was partially reversible at 13 weeks post-exposure. Body weights of animals in the 300 ppm group were reduced as a result of the exposures. No effect on dominant lethality or fertility was observed in male rats exposed to 30 or 100 ppm EGME. Dominant lethality could not be assessed in the 300 ppm group as a result of infertility. Treatment-related pathologic alterations were observed only in male rats at the 300 ppm level and included decreased testicular size and atrophic seminiferous tubules. Female rats tolerated up to 300 ppm EGME without any adverse reproductive effects. Based on these results, it was concluded that the no-adverse effect level of EGME for fertility and reproduction was 100 ppm in rats.

SUMMARY

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Ethylene Glycol Monomethyl Ether:
Inhalation Teratology Study in Rats and Rabbits†

By:

T. R. Hanley, Jr., B. L. Yano, K. D. Nitschke and J. A. John

Reviewed by:

K. S. Rao

September 20, 1982

Toxicology Research Laboratory
Health and Environmental Sciences, U.S.A.
Dow Chemical U.S.A.
Midland, Michigan 48640

†Sponsored by the U.S. ethylene glycol ethers producers under the auspices of the Chemical Manufacturer's Association under contract number G-2.0-Ter-Ihl-Dow.

SUMMARY

The objective of this study was to determine the embryotoxic and teratogenic potential of inhaled ethylene glycol monomethyl ether (EGME) in rats and rabbits. Bred Fischer 344 rats and inseminated New Zealand white rabbits were exposed to 0, 3, 10 or 50 ppm of EGME via inhalation for 6 hours/day on days 6 through 15 (rats) or 6 through 18 (rabbits) of gestation, and the fetuses were evaluated near term.

Exposure of pregnant rabbits to 50 ppm of EGME produced conclusive evidence of teratogenicity and fetotoxicity. Significant increases in the incidences of major malformations involving the cardiovascular, urogenital and skeletal systems were observed in fetal rabbits at 50 ppm. A total of 63% of the fetuses from 91% of the litters exposed to 50 ppm exhibited at least one major malformation, with numerous fetuses exhibiting multiple alterations. By comparison, only 4% of the control fetuses from a total of 26% of the control litters exhibited major malformations. Maternal effects observed at 50 ppm were limited to a transient decrease in maternal weight gain. In addition, a significant increase in the resorption rate, and a decrease in fetal body weight were observed at 50 ppm. The resorption rate among rabbits exposed to 10 ppm was significantly higher than the concurrent control rate; however, comparison with historical data indicated this apparent increase was the result of an unusually low concurrent control value and this was not considered treatment related. No other significant differences were observed among rabbits exposed to 10 or 3 ppm.

SUMMARY

Among rats exposed to 50 ppm, a transient decrease in maternal weight gain during the initial period of exposure was observed. The incidences of major malformations among fetal rats, considered either individually or collectively at each exposure level, were not significantly increased in any exposure group when compared to controls. Isolated statistical increases in the incidences of two minor skeletal variations were observed at 50 ppm, but these increases were considered indications of only a slight fetotoxic effect. The lack of any other effects on fetal parameters among rats exposed to 50 ppm indicate these differences were of questionable toxicologic significance. There was no evidence of maternal or fetal effects among rats exposed to 3 or 10 ppm of EGME.

In conclusion, EGME was teratogenic in the rabbit by the inhalation route at 50 ppm but not at 10 or 3 ppm, and was not teratogenic in the rat at concentrations of up to 50 ppm of EGME.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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39 Old Ridgebury Road
Danbury, Connecticut 06817-0001

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CECATS DATA:
Submission # 8EHQ- 0992 -12467 SEQ. A

TYPE: INT. SUPP FLWP

SUBMITTER NAME: Union Carbide Corporation

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
0639 REFER TO CHEMICAL SCREENING
0678 CAP NOTICE

VOLUNTARY ACTIONS:
0401 NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKERS/OTHERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

SUB. DATE: 09/24/92 OTS DATE: 09/29/92 CSRAD DATE: 01/30/95

CHEMICAL NAME: Ethylene Glycol Monomethyl Ether (EGME)

CAS# 109-86-4

INFORMATION TYPE:		P F C	INFORMATION TYPE:		P F C	INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04	0216	EPI/CLIN	01 02 04	0241	IMMUNO (ANIMAL)	01 02 04
0202	ONCO (ANIMAL)	01 02 04	0217	HUMAN EXPOS (PROD CONTAM)	01 02 04	0242	IMMUNO (HUMAN)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04	0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04	0243	CHEM/PHYS PROP	01 02 04
0204	MUTA (IN VITRO)	01 02 04	0219	HUMAN EXPOS (MONITORING)	01 02 04	0244	CLASTO (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04	0220	ECO/AQUA TOX	01 02 04	0245	CLASTO (ANIMAL)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04	0221	ENV. OCCC/REL/FATE	01 02 04	0246	CLASTO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04	0222	EMER INCI OF ENV CONTAM	01 02 04	0247	DNA DAM/REPAIR	01 02 04
0208	NEURO (HUMAN)	01 02 04	0223	RESPONSE REQEST DELAY	01 02 04	0248	PROD/USE/PROC	01 02 04
0209	NEURO (ANIMAL)	01 02 04	0224	PROD/COMP/CHEM ID	01 02 04	0251	MSDS	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04	0225	REPORTING RATIONALE	01 02 04	0299	OTHER	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04	0226	CONFIDENTIAL	01 02 04			
0212	ACUTE TOX. (ANIMAL)	01 02 04	0227	ALLERG (HUMAN)	01 02 04			
0213	SUB ACUTE TOX (ANIMAL)	01 02 04	0228	ALLERG (ANIMAL)	01 02 04			
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04	0239	METAB/PHARMACO (ANIMAL)	01 02 04			
0215	CHRONIC TOX (ANIMAL)	01 02 04	0240	METAB/PHARMACO (HUMAN)	01 02 04			

TRIAGE DATA:	NON-CI	INVENTORY	ONGOING REVIEW	SPECIES	TOXICOLOGICAL CONCERN:	USE:	PRODUCTION:
	YF		YES (DROP/REFER)	MUS	LOW	Industrial solvent for resins, lacquers, paints, dyes, inks + as a detergent	
CAS SR	NO		NO (CONTINUE)	RAT RBT	MED		
	IN TERMINI		REFER		HIGH		

COMMENTS: Rats and rabbits were exposed to 0, 30, 100 or 300 ppm EGME vapors for 6 hours/day, 5 days/wk for 13 weeks. Body weights, thymus gland and testicular weights were reduced at the high dose animals. Blood analyses showed depression of cellular elements related to effect on bone marrow. Microscopic revealed degenerative changes in germinal epithelium of testes in male rats and rabbits at 300 ppm in 3/ rabbits at 100 and 1/5 rabbits at 30 ppm. No rabbit testicular effects were present the levels tested.

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CAS SR	NO		NO (CONTINUE)	RAT	MED		
	DETERMINE		REFER	RBT	HIGH		

④ Inhalation teratology - mice 10, 50 ppm GD 6-15 - slight feto toxicity at 50 ppm. no effects at 10 ppm - MOD concern

COMMENTS → ③ Inhalation Teratology - rats/rabbits - teratogenic at 50 ppm in rabbits but not rats - HIGH concern

4 Studies:
① Teratogy Probe in rats + rabbits via inhalation 6 hrs/day GD 6-15 (rats) GD 6-18 (rabbits) at 50, 200, 400 ppm - no effects at 50, dev tox (complete resorptions) at 200 + 400 ppm. - HIGH concern
② Inhalation repro + dominant lethal - rats 0, 30, 100, 300 ppm 6 hr 5d/wk for 13 weeks. Complete suppression of fertility in males at 300 ppm - partially reversible 13 wk post - exposure. NOAEL for fert + repro = 100 ppm - HIGH concern